NEPALESE NATIONAL FORMULARY

2ND EDITION

Government of Nepal

Ministry of Health and Population

Department of Drug Administration

2010

NEPALESE NATIONAL FORMULARY

Formulary Committee for 1st edition, 1997

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Preface

The concept of publishing Nepalese National Formulary (NNF) was conceived long before the adoption of National List of Essentail Drugs, Nepal (EDL). The Drug Advisory Committee recommended for the preparation of the manuscript for NNF in August 1982. A Committee comprising of Mr. A.D. Shrestha, Dr. H. Dixit, Dr. I.L. Acharya and Dr. K.K.Kafle was constituted for drafting the manuscript. Sub committees of experts for various therapeutic groups like eyes, ENT, tuberculosis, leprosy, paediatrics, obstetrics and gynaecology were also formed to get advice. The idea of NNF publication was to identify the products needed for the country according to diseases prevalence. The manuscript of NNF was completed in 1996, after which editing was done to bring NNF 1997 (First edition) through the assistance of Formulary Committee.

Nepalese National Formulary (NNF) is meant to provide information on medicines and their dosage forms available in the country. It has wide use and application in various levels of health institutions as well as for individual health care providers. There have been many changes in information about medications and in pharmacotherapy practices which necessitated the revision of NNF 1997. This edition is thoroughly revised to reflect the current practices.

I like to express my sincere thanks to chief editor Dr. Kumud Kumar Kafle, Professor and Head of Department of Clinical Pharmacology, Institute of Medicine, Tribhuvan University and Editor Mr. Bhupendra Bahadur Thapa, Chief Drug Administrator, Ministry of Health and Population for their painstaking job of editing to bring revised second edition NNF 2010. I also like to thank World Health Organization in supporting the revision and publication of NNF 2010.

I request for the comments and suggestions from the readers so that the future edition could be improved.

Radha Raman Prasad
Director
Department of Drug Administration

Introduction

Nepalese National Formulary (NNF) is meant to provide information on medicines and their dosage forms available in the country. It has wide use and application in various levels of health institutions, as well as for individual practitioners. The first edition of NNF was published in 1997. This edition is thoroughly revised to reflect the current practices. Effort has been made to include all medicines that have been registered till end of December, 2009. The following information is included in this book:

Guidance on rational prescribing

This section includes information on rational prescribing, prescription writing, adverse reaction to drugs, prescribing in elderly, terminal care, liver diseases, and renal diseases and during pregnancy and breast-feeding. Most of the information included in the tables in this section is based on the WHO Model Formulary, 2008.

Classified notes on drugs

This is the main part of the formulary. General discussion on the group of drugs is provided. Indication, adverse reactions, cautions and dose of the drug is described. The dosage forms and strength is also included. However, some of the dosage forms or some medicines may not be available in the market. In such situation, informing Department of Drug Administration (DDA) helps in developing mechanisms for making such medicines available for the patients. When a drug is included in more than one chapter, a detailed description is given in one chapter and cross-reference is made in other places. However, for the convenience of users, effort has been made to minimise the cross-references. To identify the drugs included in National List of Essential Medicines (EML), the heading is printed in ***BOLD ITALIC***, whereas other drugs are only in **BOLD**. National List of Essential Medicines is included in appendix II.

The drugs are classified according to the systems for which they are used. Furthermore, chapters on anaesthetics and poisoning are also included. In many cases, especially in case of tablet, it was difficult to provide exact information on dosage form, like, extended release or dispersible tablet or other forms. Effort is being made to computerize information on registered products, in which case, the updated information can be seen from the computer-based data at the DDA.

Formulary

Effort has been made to provide information of the dosage forms available in the market. Fixed-dose combinations of drugs that have proven benefit are included, for example, co-trimoxazole, co-careldopa etc. A list of such combination, except antiretroviral, is also included in the chapter of rational prescribing.

International Non-proprietary Names

Harmonisation of the names of the medicine has remained as a problem. The best way is to adopt the system of using International Non-proprietary Names (INN). This system is being used by many pharmacopoeias and so the generic name of the medicines is becoming uniform. In this formulary also INN has been adopted. So the reader may notice the change of many common names previously used in Nepal. In some case there is minor change of spelling. To avoid confusion, the main heading is the INN, whereas, the generic name previously used, and in many cases still common, is placed below the main heading. For example, commonly known chlorpheniramine's INN is chlorphenamine. So the heading appears as **CHLORPHENAMINE** and the commonly used generic name **Chlorpheniramine** appears just below the main heading.

Appendices

Three appendices are included. Appendix I contains detailed list of drug interactions. This section is also mainly based on the information from WHO Model Formulary, 2008. Appendix II contains National List of Essential Medicines (fourth revision, 2010). This list has been approved by Drug Advisory Committee. It has to be approved by Government of Nepal to make it official.

Information on Adverse Drug Reaction reporting is included in Appendix III. Adverse Drug Reaction reporting system has been initiated in Nepal. Nepal is the member of International Drug Monitoring Programme of WHO, which is coordinated by Uppsala Monitoring Centre. DDA is the national centre for Nepal. Appendix III includes ADR reporting form currently being used in Nepal, and the address of DDA, its branch offices as well as the hospitals functioning as regional centres. Other hospitals are encouraged to join this programme and report the adverse reaction of drugs. DDA also plans to join hands with drug manufacturers in this effort.

Comments and suggestions

For further improvement of the NNF we request to send comments and feed-back. The formulary is also available at **www.dda.gov.np.** Any comment received will be reviewed and will be included in the internet version of the Formulary. However, it can only be incorporated in next edition of the printed version.

Contents

Guidelines on Rational Prescribing

WHY DRUGS?

In the days of mixtures, the older generations of doctors were prone to make a detailed prescription with various ingredients and looked upon this task as an art. Those were the years when the available drugs were very limited and what was available was perhaps not quite as specific and quick acting nor potent as its counterpart today.

The present day doctor or health worker in Nepal is literally bombarded with literature and visitors from all sides. The various representatives come advertising their various "new and more effective products". In this connection it will perhaps be worthwhile to note the words of Lawson Wilkins who in 1962 wrote –

> *"Do not hasten to use the 400 new drugs coming on the market each year particularly if they are variant of standard drugs with which you have already had experience.*
>
> *Wait, wait, wait - and then wait.*
>
> *Let the other fellow poison his patients or learn that the drug is worthless. In the core of months or years the truth will be known and the drug may or may not be discarded. If a truly valuable 'miracle drug' appears, the whole world will probably acclaim it within months."*

Before prescribing any drug the first thought and the questions that must come into a prescriber's mind are the 'six Ws'-

1. Whether the drug should be given
2. What change is expected
3. Whether the drug chosen can do this
4. What are the side-effects of the drug
5. Whether the drug is in fact beneficial or not
6. Whether the drug combination available is rational or not

The decision as to whether a drug is necessary or not is very important in these days, when a lot of potent drugs in the market can at the same time also exert harmful effects. In the context of the developing countries, where typhoid is an important killer disease, chloramphenicol is a drug which has to be used quite often as it is a life saver. On the other hand use and abuse of it, for other less serious infections, might so sensitize the patient to the extent of inducing as aplastic anaemia from which the patient might die.

What is a drug?

A drug has been defined by a WHO scientific group as "any substance or product that is used to modify or explore physiological systems or pathological states for the benefit of the recipient".

National list of essential drugs

Essential drugs are those that satisfy the priority health care needs of the population. They should therefore be available at all times in adequate amounts and in appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. WHO has provided a model list of essential drugs, which is revised periodically. National List of Essential Drugs for Nepal was prepared in 1986 based on WHO model list of essential drugs and considering other factors such as the pattern of prevalent diseases; the treatment facilities; the training and experience of the available personnel; the genetic, demographic and environmental factors. First revision of the list was done in 1992, second revision in 1997, third revision in 2002 and fourth revision in 2010. The National List of Essential Medicines, fourth revision 2010 (draft) contains 317 drugs. The list also contains complementary drugs which are for treating rare disorders, drugs with special pharmacological properties and alternative drugs when there is no response to the main essential drug or when the latter cannot be administered for any reason.

The National Drug Policy aims at ensuring the availability of safe, effective, standard and quality drugs at affordable price, in quantity sufficient to cover the need of every corner of the country. This will be possible by implementation of the concept of essential drugs, following standard treatment schedule at various levels of health institutions, managing procurement, distribution, quality assurance of essential drugs. The essential drugs are in ***BOLD ITALICS*** in this formulary and National List of Essential Medicines 2010 (draft) is in Appendix II.

Administration of drugs

This may be by mouth in the forms of:

1. Tablet - compressed form of the drug plus a base. It may be coated.
2. Capsules - the drug is within a gelatin container which itself disintegrates once the drug reaches the stomach or intestine.
3. Linctus - the drug is contained in a liquid syrup medium
4. Mixture - the drug, either singly or with other drugs, is dissolved or diffused in water or some other solvent.
5. Emulsion - drugs in liquid state are so mixed that one is dispersed in the other in a finely divided state.

Drugs may be given by injection and this can be:

1. Intradermal / subcutaneous / intramuscular
2. Intravenous / intrathecal

Drugs can also be applied topically on the surface of wound / skin.

Drug administration: points to remember

When giving any drug whatsoever, the following points are to be considered:

1. Check the prescription to see that it is for that particular patient
2. Check the label on the bottle
3. Take out the correct amount of drug
4. Re-check the label on the bottle
5. Examine the medicine to see that it is all right
6. Make sure that the patient is in a state in which the drug is necessary for him
7. Give the drug and make a note of the time
8. Give complete information including handling or storing to the patient and confirm that the patient has understood correctly by asking to repeat the instructions.

Drug interactions

Two or more drugs given at the same time may interact with each other. The interaction may be potentiation or antagonism of one drug by another, or occasionally some other effect.

Drug interactions may be pharmacodynamic or pharmacokinetic.

Pharmacodynamic interactions occur between drugs which have similar or antagonistic pharmacological effects or adverse effects. They are usually predictable from knowledge of the pharmacology of the interacting drugs and an interaction occurring with one drug is likely to occur with a related drug.

Pharmacokinetic interactions occur when one drug increases or reduces the amount of another drug available to produce its pharmacological action. They are not easily predicted and an interaction occurring with one drug cannot be assumed to occur with a related drug unless their pharmacokinetic properties are similar.Many pharmacokinetic interactions affect only a small proportion of patients taking the combination of drugs. Many drug interactions do not have serious consequences and many which are potentially harmful occur only in a small proportion of patients. A known interaction will not necessarily occur to the same extent in all patients. Drugs with a small therapeutic ratio (such as phenytoin) and drugs which require careful dose control (such as anticoagulants, antihypertensives or antidiabetics) are most often involved. Patients at increased risk from drug interactions include the elderly and those with impaired renal or liver function.

For more detailed account *see* Appendix - I.

Drug toxicity

Regarding the whole question of drug toxicity, Goldstein recommended the following rules:

1. Don't prescribe contraindicated combinations.
2. Don't prescribe a new or little used agent in combination with other drugs.
3. Develop an order of priority of need.
4. Prescribe drugs for limited time only.
5. Be sure of kidney and liver functions.

6. Don't be misled if a multiple drug combination is tolerated by one patient.
7. Reduced effectiveness and toxicity are both common in drug interaction and may occur simultaneously.
8. Multidrug therapy may limit the beneficial effect of a single agent and lead to the progression of a disease.
9. Know which patients are seeing other physicians and what medications have been prescribed.
10. Know what over-the-counter drugs the patient is taking.
11. Record proper drug history of the patient on his case notes, particularly any history of allergic or other drug reactions.

RATIONAL PRESCRIBING

Many countries are witnessing steady increase in drug consumption and irrational use of drugs by both the prescriber and the consumer with grave possible economic and social consequences.

The five important criteria for proper drug use are:

1. Accurate diagnosis

Prescribing should be based on indication consistent with accurate diagnosis.

2. Appropriate drug

Prescribing of drug should not be made for other reasons, for instance, because of demand from the patient or to please the patient. This demands not only that appropriate drugs be prescribed but that it be taken in the right dose, at correct time intervals and for sufficient duration. The appropriate drug must be effective, be of acceptable quality and safety and be available to the patient at a price that he as part of a community can afford.

Types of irrational drug use that one comes across are:

a. *Extravagant prescribing* i.e. using sophisticated and expensive drugs, when comparable drugs that are less expensive will do. While use of expensive medication may be justified in the life threatening conditions, most illnesses respond to simple inexpensive drug and may even improve with no therapy. Some studies have found that 60% of hospitalized patient are wrongly prescribed antibiotics. Use of potent and expensive medication for these cases may deprive seriously ill patients of the needed drugs.

Prescribers are prone to have a preference for brand names but this will not only add to the cost but may add to the confusion regarding treatment.

b. *Over-prescribing and multiple-prescribing:* These are cases where drugs are prescribed where they are not indicated or are ineffective; when too many ingredients are used where one or two would have achieved the same effect; when the dose prescribed is either too large or the duration of treatment too long; or when treatment is given for several related conditions when treatment of the primary condition would have sufficed.

c. *Under-prescribing:* These are cases where the needed medication is not prescribed; when the given dose is inadequate; the interval between doses are too long; or duration of treatment is insufficient. When expensive drugs are used, this may result from inability of the patient to meet the cost of treatment.

d. *Incorrect prescribing:* This is seen when drugs selected and prescribed are of doubtful efficacy or of low efficacy for the illness concerned; or if adjustments are not made for co-existing medical, genetic and environmental and other factors.

Irrational prescribing results from many factors. Many patients request or even demand drug treatment and prescribers are compelled to comply regardless of the need and expense.

Teaching of therapeutics in medical training institutes does not give sufficient emphasis on rational prescribing practice. Prescribers are often unaware of the economic effects of their prescribing on the patients and community. There is also no continuing education of practitioners to give them the information on new drugs or recent advances in treatment. Most of the time they have to rely on the promotional literature or efforts of the pharmaceutical industry, which in itself may be biased.

3. Correct dispensing

All the resources required to bring a drug to the patient will be wasted if the dispensing process does not ensure that effective form of the drug reaches the right patient in prescribed dosage and quantity, with clear instruction on how it is to be taken. Competent and qualified pharmacists should be trained in correct dispensing and in giving clear instruction to the patient on how to use the drugs effectively. For this the pharmacists should have easy access to complete and unbiased information on the drugs used.

4. Suitable packing

The type of container used for packing may have important impact on the patient's image of the health system and his faith in medicine. This may also affect storage and deterioration. Acceptable form of bottles, plastic bags can be used and adequate labelling with full instructions should be provided.

5. Patient compliance

It is the degree to which patients will follow the medical advice and take the medicine as directed. Most countries show only 50% or less with errors in dose, dose interval or duration. Compliance is low in cases of chronic illness when patients are bored with the long treatment, in extremes of age when they are dependent on others to give them their medicines; when there are too many medicines to take or when health services are not easily accessible. Patient compliance is better if they understand the purpose of the treatment, effect of the drugs they are taking, how to follow instructions and how to recognise and report adverse reactions. For treatment to be effective, efforts should be made to improve patient compliance by providing effective labelling with instructions, education and making health services readily available.

Low cost strategies for improving adherence increase effectiveness of health interventions and reduce cost.

Drug combination - how rational are they?

Fixed-dose combination products are acceptable only when the dose of each ingredient meets the requirement of a defined population group and when the combination provides a proven advantage over single compound administered separately in therapeutic effect, safety or compliance. Fixed-dose combinations are only acceptable if the following criteria are met:

1. Clinical documentation justifies the concomitant use of more than one drug.
2. The therapeutic effect is greater than the sum of the effect of each.
3. The cost of the combination product is less than the sum of the individual products.
4. Compliance is improved.
5. Sufficient drug ratios are provided to allow dosage adjustment satisfactory for the majority of the population.

There are examples of useful drug combinations in the WHO Model List of Essential Medicines, 2009:

a. Amoxicillin + clavulanic acid (anti-infective)
b. Artemether + lumefantrine (antimalarial)
c. Benzoic acid + salicylic acid (for external use)
d. Estradiol cypionate + medroxyprogesterone acetate (injectable contraceptive)
e. Ethambutol + isoniazid (anti-tubercular)
f. Ethinylestradiol+ levonorgestrel (oral contraceptive)
g. Ethinylestradiol + norethisterone (oral contraceptive)
h. Ferrous salt + folic acid (anti-anaemic)
i. Imipenem + cilastatin (anti-infective)
j. Isoniazid + rifampicin (anti-tubercular)
k. Isoniazid + rifampicin + ethambutol (anti-tubercular)
l. Isoniazid + rifampicin + pyrazinamide (anti-tubercular)
m. Levodopa + carbidopa (Parkinson's disease)
n. Lidocaine + epinephrine (local anaesthetic)
o. Neomycin sulfate + bacitracin (for external use)
p. Sulfadoxine + pyrimethamine (antimalarial)
q. Sulfamethoxazole + trimethoprim (anti-infective)

GENERAL GUIDANCE

Medicine should be prescribed only when necessary after taking into account the risk/benefit ratio. Majority of drugs besides their therapeutic benefits have side-effects and some even toxic effects. Some of these may be dose-related and preventable, but others may appear at doses which are necessary for the

required therapeutic effect. In such conditions the prescriber will have to make a decision as to whether the benefit obtained from the use of the drug justifies the risk involved. It is particularly important during pregnancy. It is also known that many clinical symptoms are caused by self-limiting illnesses which will pass without treatment or even despite it. Use of drug such as potent antibiotics for fairly trivial condition is not justified.

Abbreviation of titles

In general, the names or titles of drugs and preparations should be written in full. Unofficial abbreviation and obsolete titles should not be used.

Non-proprietary titles

Non-proprietary or generic names should be used in prescribing as this will enable any suitable product to be dispensed, thus saving time and expense.

Proprietary names

Brand names are applied only to products marketed by owners of the trademarks. A single drug may have several brand names which cause confusion to prescribers and patients alike. It adds to the cost of treatment, as brand names are more expensive.

Dose

The dose stated is intended for general guidance and represent, unless otherwise stated, the usual range of doses suitable for adult use.

Dilutions

When it is necessary to prescribe fractional doses, liquid preparation for oral use should be diluted with suitable vehicle to make a dose volume of 5 ml or multiple of this, useless otherwise directed. Diluted preparations are less stable than the original preparation and dilution should be performed at the time of dispensing. Directions must be given on the suitable length of time the preparation can be kept to retain potency.

Strength and quantity

The strength or quantity to be contained in capsules, tablets etc. should be stated by the prescriber.

If the pharmacist receives an incomplete prescription for a systemically administered preparation the under-mentioned procedures should apply:

a. An attempt must be made to contact the prescriber and ascertain the intention.

b. If the prescriber can be contacted, details of quantity, strength and dose should be inserted by the prescriber on the incomplete prescription.

c. If the prescriber has been contacted but it is not possible to obtain a written intention regarding the incomplete prescription, the pharmacist may write on the form “prescriber contacted" and add the necessary details. This endorsement should be initialled and dated by the pharmacist.

d. Where the prescriber cannot be contacted and the pharmacist is qualified enough to make a professional judgement, a small quantity of the preparation, sufficient for 1-2 days may be dispensed and the patient asked to contact the prescriber for further action. When prepacked preparations are prescribed, the smallest pack should be dispensed. If the pharmacist has any doubt, an incomplete prescription must be referred back to the prescriber.

Advice to patients

Prescribers should advise patients if treatment is likely to affect their ability to drive motor vehicles, e.g., sedatives and antihistamines and the effect of alcohol on such drugs. When handling chemical or biological materials, particular attention must be given to the possibility of allergy, fits, explosion, radiation or poisoning. Patient must be warned to keep all medicines out of reach of children and poisons should be locked.

Labelling of containers

Name of preparations and the strength should be clearly labelled, unless the prescriber wishes otherwise. If the prescriber desires that the description of the preparation be written, e.g. "sedative tablets", it should appear on the label. This arrangement does not apply to prescription containing several ingredients.

PRESCRIPTION WRITING

Prescription is the means of direct communication between the prescriber and the dispensing pharmacist and it is essential that sound guidelines for prescription writing be followed.

Prescriptions should be written legibly in ink and should be dated. The local language is preferred. It should contain the patient’s full name and address and should be signed by the prescriber. The age of the patient must be written. This is especially important for children under 12 years of age. The name, form and strength of the drugs should be clearly stated and generic names should be used unless a specific brand name is indicated. Dose, frequency and duration of the treatment should be stated.

Old Latin phrases are a practice of the past which should be discarded as soon as possible. To lessen the chance of error in giving medicines, it is very important that the frequency and time of giving drugs should be clearly stated in easily understandable terms, which may mean writing these instructions in the language which even the patient can read and understand.

For writing doses and quantities, the following points should be noted:

a. For solids, quantities of 1 gram or more should be written as 1g etc. Quantities which are less than 1 gram or 1 mg should be written in milligrams or micrograms respectively, e.g. 500 mg or 100 micrograms and not 0.5g or 0.1 mg. When decimals are unavoidable, a zero should be written in front of the decimal points when there is no other figure e.g. 0.5 ml.

b. Micrograms and nanograms should not be abbreviated. Similarly "units" should not be abbreviated.

c. The term "millilitre" (ml) is used in medicine and pharmacy and cubic centimetre, cc or cm^3 should not be used.

For oral liquid preparations especially those for children, the dose should preferably be stated in terms of 5 ml spoonfuls.

The name of drugs and preparations should be written clearly and not abbreviated.

The route of administration and specific guidelines such as "whenever pain is severe" or "before" or "after meals" or "not to exceed twelve tablets a day" must be clearly stated. The pharmacist should be asked to label the medication.

Finally the doctor's signature must be written and the doctor's name and Nepal Medical Council registration number be printed clearly, if headed note paper is not used.

CONTROLLED DRUGS AND DRUG DEPENDENCE

Prescriptions ordering **controlled drugs** subject to prescription requirements must be signed and dated by the prescriber, and the prescriber's address specified. The prescription must always be in the prescriber's own handwriting in ink or otherwise so that it cannot be effaced. It should contain the following information:

1. The name an address of the patient
2. In the case of a preparation, the form and where appropriate, the strength of the preparation
3. The total quantity of the preparation or the number of dose units, in both words and figures
4. The dose

Dependence and misuse

The prevalence of drug dependence and misuse is a cause for concern to teachers, social workers and the police as well as to prescribers.

The most serious drugs of addiction are diamorphine (heroin), morphine, and the synthetic opiates. The likelihood, that the dose will be increased is considerable, psychic dependence is common and the withdrawal syndrome may be severe. Amphetamine misuse can also occur.

The prescriber has three main responsibilities:

1. To avoid creating dependence by introducing drugs to patients without sufficient reason. In this context, the proper use of the morphine-like drugs is well understood. The dangers of other controlled drugs are less clear because recognition of dependence is not easy and its effects and those of withdrawal are less obvious.
2. To see that the patient does not gradually increase the dose of a drug, given for good medical reasons, to the point where dependence becomes more likely. This tendency is seen especially with hypnotics and anxiolytics. A minimal amount should be prescribed in the first instance, or when seeing a new patient for the first time.
3. To avoid being used as an unwitting source or supply for addicts.

ADVERSE REACTIONS TO DRUGS (ADR)

Any drug may produce unwanted or unexpected adverse reactions. ADRs are therefore unwanted or unintended effects of a medicine including idiosyncratic effects, which occurs during its proper use. The detection and recording of these reactions is of vital importance.

'A' type reactions are dose-related, predictable and often preventable. They are usually the extension of the therapeutic effects e.g. hypoglycaemia by an antidiabetic drug. 'B' type reactions are not dose-related and occur in a few individuals and are usually the result of some peculiarity in the make-up of the individual. It may be due to allergy, idiosyncrasy or some genetically determined abnormality. They are less common, and their concurrence is difficult to predict and prevent, e.g. anaphylaxis with penicillins.

Long term effects may become manifest months or years after drug exposure so that causal relationship between the adverse effects and drug may be hard to establish. They are often irreversible by the time they are detected and are therefore very serious. Any suspicion of such an association should be reported.

Teratogenic effects are adverse effects of the drug on the foetus due to consumption by the mother during pregnancy. Prescribers should report all congenital abnormalities if they are suspected to be caused by drugs.

Factors which predispose to adverse drug reactions are overdose, error during dose adjustments or relative overdose due to age or disease. Prescribers are urged to help by reporting adverse reactions to the ADR Regional Centres or Department of Drug Administration (Appendix III). Prescribers should be particularly alert when drugs are given to the elderly.

Prevention of adverse reactions

1. Never use a drug without good indication. If the patient is pregnant, do not use a drug unless the need for it is imperative.
2. Ask the history of previous reactions, allergy or idiosyncrasy to drugs.
3. Ask if the patient is taking other drugs. Drug interactions may occur.
4. Make suitable dose adjustments for the elderly and for patients with hepatic or renal disease. Pharmacogenetic factors may also be responsible for variation in metabolism of drugs, e.g. isoniazid and tricyclic antidepressants.
5. Prescribe as few drug as possible, use drugs with which you are familiar and give clear instruction so as not to be misunderstood.
6. Use a new drug cautiously and if serious reactions are expected, warn the patient.

PRESCRIBING FOR CHILDREN

Prescribing for children is not the same as that for adults as children respond differently to drugs. This is particularly true in the neonatal period - the first month of life. During this period, their organs of excretion and metabolism and the metabolizing enzymes are not fully developed and sensitivity to drugs is therefore

increased. Calculation of dosages for children and neonates need special care and mentoring and dose adjustment will have to be made until the child weighs about 50 kg or until the child reaches puberty.

Dose calculation

Children's doses may be calculated from the adult dose using age, weight and body surface or a combination of these. Calculation by age is the easiest but the least accurate. Use of body surface is the most reliable but requires height, weight and use of a nomogram or table. Dose per square metre body surface area is calculated by dividing the adult dose by 1.76.

Body weight may be used in cases where the dose is expressed in mg/kg.

Dose = (weight in kg/ 72) X average adult dose.

Young children may require a relatively higher dose/kg body weight than adults because of higher metabolism. Other factors such as obesity may produce errors in calculation, in such cases dose should be calculated from ideal weight related to height and age.

The dose for children can be calculated from adult dose by the percentage method. In this, the dose for particular patient is calculated according to weight, or as percentage of the basic adult dose.

Approximate age	weight in kg	percentage of adult dose
Birth	2.5	10
12 months	10.0	25
3 years	15.0	33
7 years	23.0	50
12 years	40.0	75

Note: Some rough and ready rules are available to estimate length and weight.

1. Weight in kg = (Age in years + 3) X 2.5
2. Length in cm:

At birth	50 cm (±3 cm)
1 year	75 cm (±4 cm)
4 years	100 cm (±5 cm)
7 years	125 cm (±8 cm)
12 years	150 cm (±10 cm)

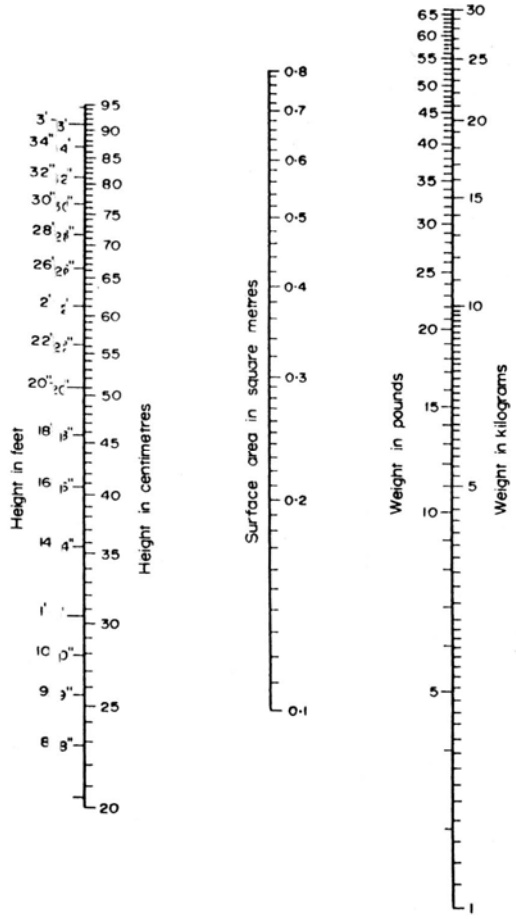
3. Surface area in square metres = (Age in years + 6) X 7/100
4. Percent of adult dose = (Weight in kg X 1.5) + 10
5. Percent of adult dose = (Age in years X 4) + 20

When any doctor/health worker is in any doubt as to the dose to be given, he should look up in the book and prescribe subsequently. It is better to be safe provider of health care than a dangerous one.

Another method of prescribing for children is by use of a nomogram as stated above.

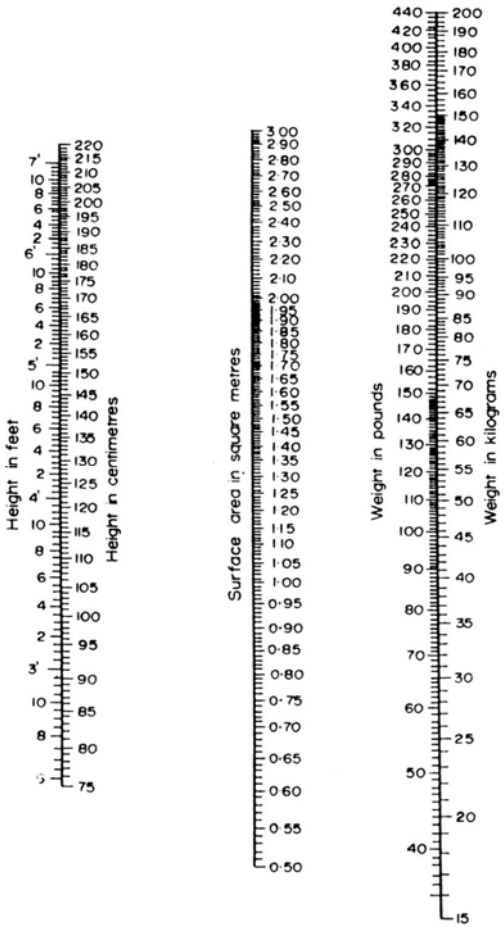
Body surface area nomogram for infants and children

To determine the surface area of the patient, draw a straight line between the point representing his height on the left vertical scale and the point representing his weigth on the right vertical scale. The point at which this line intersects the middle vertical scale represents the patient's surface area in square metres.



Body surface area nomogram for older children and adults

To determine the surface area of the patient, draw a straight line between the point representing his height on the left vertical scale to the point representing his weight on the right vertical scale. The point at which this line intersects the middle vertical scale represents the patient's surface area in square metres.



PRESCRIBING FOR THE ELDERLY

Response to drugs becomes very erratic in the elderly patient because of reduced body mass and volume of distribution of drugs. Reduced hepatic metabolising capacity and reduced renal function aggravated by prostatism, nephrosclerosis and chronic urinary-tract infection etc may result in accumulation of drug in the body. Because of this, prescribing in the elderly patients, like prescribing for children needs special care and monitoring to prevent adverse reactions.

Elderly patients also suffer from multiple diseases and symptoms, for which they are likely to receive multiple drugs and this may lead to drug interactions.

Manifestations of normal ageing, menopause, social stress or loss of a loved one may induce symptoms like sleeplessness, headache etc which may be mistaken for diseases and inappropriate prescribing with opioid analgesics, psychotropics, is common. Non-pharmacological measures may be more appropriate for such symptoms. The ageing nervous system is more sensitive to these drugs and the patient may experience severe side-effects such as drug-induced parkinsonism, postural hypotension, mental confusion. Short courses of hypnotics are occasionally useful for helping a patient through an acute illness or some crisis but effort must be made to avoid dependence. Self-medication with drugs previously prescribed is also an added complication and patients must be discouraged from these practices.

Acute illness may lead to rapid reduction in renal clearance especially if accompanied by dehydration. Hence a patient normally on maintenance drugs may suddenly develop toxicity after a bout of acute respiratory infection.

Diuretics are over-prescribed in old age and should not be used to treat simple gravitational oedema which will respond to increased movement, raising the legs and support stockings. Bleeding associated with aspirin and other NSAIDs is more common in the elderly. Many hypnotics with long half-life have serious hangover effect of drowsiness, unsteady gait, blurred speech and confusion. Those with short half-life should be used but they too can present problems.

Guidelines

1. Make sure the drug is indicated, then select from a limited range of drug and be thoroughly familiar with their effects on the elderly.
2. Dosage must be lower than the normal adult dose. It is common to start with about 50% of the adult dose.
3. Review repeat prescriptions regularly. It may be possible to stop the drug or it may be necessary to reduce the dose.
4. Simple regimens should be used. Whenever possible drugs given once or twice daily should be prescribed.
5. Write instructions fully and clearly on every prescription, so that containers can be properly labelled with clear directions.

PRESCRIBING IN TERMINAL CARE

The aim of treatment of patients with terminal illness is to keep them as comfortable, alert and free from pain as possible. They are anxious and agitated and it may be necessary to see to their emotional, financial, social and family problems and to give them the assurance they need.

The following are some guidelines to make things easier for the terminally ill.

1. Whenever possible patients should end their days in their own homes among familiar surroundings.
2. If the patient is in the hospital, it is important both doctors and nurses give time to listen to the patients. This will give support and comfort to them in their last days.

3. Number of drugs should be as few as possible as even taking of medicines may be an effort.
4. Pain: Analgesics are more effective in preventing pain than in the relief of established pain. Regular use of non-opioid analgesic will often make use of opioids unnecessary. Pain of bone secondaries may be treated with non-steroidal anti-inflammatory drugs. Codeine alone or in combination with a non-opioid in adequate dosage, may be helpful in the control of moderate pain if non-opioids alone are not sufficient. Morphine is the most useful opioid analgesic and should not be withheld if it is absolutely necessary for relief of pain. The dose should be the lowest which prevents pain; a dose of 5-20 mg every 4 hours is usually effective, but there should be no hesitation of increasing to 100 mg if necessary.
5. Miscellaneous conditions such as intractable cough dysponea, excessive respiratory secretion, restlessness and confusion will have to be treated as symptoms arise.

The important part of treating the terminally ill patient is to treat them with compassion and patience and not to leave them as objects where nothing more can be done.

PRESCRIBING IN HEPATIC IMPAIRMENT

Liver disease may alter the response to drugs. However, the hepatic reserve appears to be large and liver disease has to be severe before important changes in drug metabolism take place. The ability to eliminate a specific drug may or may not correlate with liver's synthetic capacity for substances such as albumin or clotting factors, which tends to decrease as hepatic function declines. Unlike renal disease, where estimates of renal function based on creatinine clearance correlate with parameters of drug elimination such as clearance and half-life, routine liver function tests do not reflect actual liver function but are rather markers of liver cellular damage.

The altered response to drugs in liver disease can include all or some of the following changes:

- Impaired intrinsic hepatic eliminating (metabolizing) capacity due to lack of or impaired function of hepatocytes.
- Impaired biliary elimination due to biliary obstruction or transport abnormalities (for example rifampicin is excreted in the bile unchanged and may accumulate in patients with intrahepatic or extrahepatic obstructive jaundice).
- Impaired hepatic blood flow due to surgical shunting, collateral circulation or poor perfusion with cirrhosis and portal hypertension.
- Altered volume of distribution of drugs due to increased extracellular fluid (ascites, oedema) and decreased muscle mass.
- Decreased protein binding and increased toxicity of drugs highly bound to proteins (for example phenytoin) due to impaired albumin production.
- Increased bioavailability through decreased first-pass metabolism.
- Decreased bioavailability due to malabsorption of fats in cholestatic liver disease.

In severe liver disease increased sensitivity to the effects of some drugs can further impair cerebral function and may precipitate *hepatic encephalopathy* (for example morphine).

Oedema and *ascites* in chronic liver disease may be exacerbated by drugs that cause fluid retention (for example asprin, ibuprofen, prednisolone, dexamethasone). Usually drugs are metabolized without injury to the liver. A few drugs cause dose-related hepatotoxicity. However, most hepatotoxic reactions to drugs occur only in rare persons and are unpredictable. In patients with impaired liver function the dose-related hepatotoxic reaction may occur at lower doses whereas unpredictable reactions seem to occur more frequently. Both should be avoided.

Information to help prescribing in hepatic impairment is included in the following table. The table contains only those drugs that need dose adjustment. However, absence from the table does not automatically imply safety as for many drugs data about safety are absent; it is therefore important to also refer to the individual drug entries.

Drugs to be avoided or used with caution in liver disease:

Drug	Comment
Abacavir	Avoid in moderate hepatic impairment unless essential; avoid in severe hepatic impairment
Alcuronium	Possibly slower onset, higher dose requirement and prolonged recovery time
Allopurinol	Reduce dose
Aluminium hydroxide	In patients with fluid retention, avoid antacids containing large amounts of sodium; also avoid those causing constipation (can precipitate coma)
Amidotrizoates	Use with caution in severe hepatic impairment
Amitriptyline	Sedative effects increased (avoid in severe liver disease)
Amlodipine	Half-life prolonged—may need dose reduction; consider initial dose of 2.5 mg
Amodiaquine	Avoid
Amoxicillin + clavulanic acid	Monitor liver function in liver disease. Cholestatic jaundice reported either during or shortly after treatment; more common in patients over the age of 65 years and in males; duration of treatment should not usually exceed 14 days
Artemether+ lumefantrine	Caution in severe impairment—monitor ECG and plasma potassium
Aspirin	Avoid in severe hepatic impairment—increased risk of gastro-intestinal bleeding
Azathioprine	May need dose reduction
Azithromycin	Avoid; jaundice reported
Bupivacaine	Avoid (or reduce dose) in severe liver disease
Carbamazepine	Metabolism impaired in advanced liver disease

Drug	Comment
Ceftriaxone	Reduce dose and monitor plasma concentration if both hepatic and severe renal impairment
Chlorambucil	Consider dose reduction in severe hepatic impairment—limited information available
Chloramphenicol	Avoid if possible—increased risk of bone-marrow depression; reduce dose and monitor plasma-chloramphenicol concentration
Chlorphenamine	Sedation inappropriate in severe liver disease—avoid
Chlorpromazine	Can precipitate coma; hepatotoxic
Ciclosporin	May need dose adjustment
Clindamycin	Reduce dose
Clomifene	Avoid in severe liver disease
Clomipramine	Sedative effects increased (avoid in severe liver disease)
Cloxacillin	Cholestatic jaundice may occur up to several weeks after treatment has been stopped; administration for more than 2 weeks and increasing age are risk factors
Codeine	Avoid or reduce dose—may precipitate coma
Contraceptives, oral	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Cyclophosphamide	Reduce dose
Cytarabine	Reduce dose
Dacarbazine	Dose reduction may be required in mild to moderate liver disease; avoid if severe
Daunorubicin	Reduce dose
Diazepam	Can precipitate coma
Didanosine	Insufficient information but monitor for toxicity
Doxorubicin	Reduce dose according to bilirubin concentration
Doxycycline	Avoid (or use with caution)
Efavirenz	In mild to moderate liver disease, monitor for dose-related side-effects (for example CNS effects) and monitor liver function; avoid in severe hepatic impairment
Enalapril	Closely monitor liver function in patients with hepatic impairment
Ergometrine	Avoid in severe liver disease
Erythromycin	May cause idiosyncratic hepatotoxicity
Ethinylestradiol	Avoid; *see also* Contraceptives, oral
Etoposide	Avoid in severe hepatic impairment
Fluconazole	Toxicity with related drugs
Fluorouracil	Caution advised, dose reduction may be required
Fluphenazine	Can precipitate coma; hepatotoxic

Drug	Comment
Furosemide	Hypokalaemia may precipitate coma (use potassium-sparing diuretic to prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Glibenclamide	Increased risk of hypoglycaemia in severe liver disease; avoid or use small dose; can produce jaundice
Griseofulvin	Avoid in severe liver disease
Haloperidol	Can precipitate coma
Halothane	Avoid if history of unexplained pyrexia or jaundice following previous exposure to halothane
Heparin	Reduce dose in severe liver disease
Hydralazine	Reduce dose
Hydrochlorothiazide	Avoid in severe liver disease; hypokalaemia may precipitate coma (potassium-sparing diuretic can prevent this); increased risk of hypomagnesaemia in alcoholic cirrhosis
Ibuprofen	Increased risk of gastrointestinal bleeding and can cause fluid retention; avoid in severe liver disease
Indinavir	Increased risk of nephrolithiasis; reduce dose to 600 mg every 8 hours in mild to moderate hepatic impairment; not studied in severe impairment
Iopanoic acid	Avoid in severe hepatic disease
Isoniazid	Use with caution; monitor liver function regularly and particularly frequently in the first 2 months
Levonorgestrel	Caution in active liver disease and recurrent cholestatic jaundice
Lidocaine	Avoid (or reduce dose) in severe liver disease
Lopinavir + ritonavir	Avoid oral solution because of propylene glycol content; avoid capsules in severe hepatic impairment
Magnesium hydroxide	Avoid in hepatic coma if risk of renal failure
Magnesium sulfate	Avoid in hepatic coma if risk of renal failure
Medroxyprogesterone	Avoid in active liver disease and if history of pruritus during pregnancy
Mefloquine	Avoid for prophylaxis in severe liver disease
Meglumine antimoniate	*see* Pentavalent antimony compounds
Mercaptopurine	May need dose reduction
Metformin	Withdraw if tissue hypoxia likely—manufacturers advise avoid
Methadone	Avoid or reduce dose—may precipitate coma

Drug	Comment
Methotrexate	Dose-related toxicity—avoid in nonmalignant conditions (for example, rheumatic disorders); avoid for all indications in severe hepatic impairment
Methyldopa	Manufacturer advises caution in history of liver disease; avoid in active liver disease
Metoclopramide	Reduce dose
Metronidazole	In severe liver disease, reduce total daily dose to one-third and give once daily
Morphine	Avoid or reduce dose—may precipitate coma
Nelfinavir	No information available—manufacturer advises caution
Nevirapine	Caution in moderate hepatic impairment; avoid in severe hepatic impairment
Nifedipine	Reduce dose in severe liver disease
Nitrofurantoin	Cholestatic jaundice and chronic active hepatitis reported
Norethisterone	Avoid in active liver disease and if history of pruritus or cholestasis during pregnancy
Ofloxacin	Hepatic dysfunction reported; reduce dose in severe liver disease
Paracetamol	Dose-related toxicity—avoid large doses
Pentavalent antimony compounds	Increased risk of liver damage and hepatic failure in pre-existing liver disease
Phenobarbital	May precipitate coma
Phenytoin	Reduce dose to avoid toxicity
Prednisolone	Adverse effects more common
Procainamide	Avoid or reduce dose
Procarbazine	Avoid in severe hepatic impairment
Promethazine	Avoid—may precipitate coma in severe liver disease; hepatotoxic
Propranolol	Reduce oral dose
Propylthiouracil	Reduce dose
Pyrazinamide	Monitor hepatic function—idiosyncratic hepatotoxicity more common; avoid in severe hepatic impairment
Pyrimethamine	Use with caution
Ranitidine	Increased risk of confusion; reduce dose
Rifampicin	Impaired elimination; monitor liver function; avoid or do not exceed 8 mg/kg daily
Ritonavir	*see* lopinavir + ritonavir
Saquinavir	Manufacturer advises caution in moderate hepatic impairment; avoid in severe impairment
Sodium nitroprusside	Avoid in severe liver disease
Sodium valproate	*see* valproate

Drug	Comment
Sulfadiazine	Avoid if severe
Sulfamethoxazole + trimethoprim	Manufacturer advises avoid in severe liver disease
Suxamethonium	Prolonged apnoea may occur in severe liver disease due to reduced hepatic synthesis of plasma cholinesterase
Testosterone	Preferably avoid—possibility of dose related toxicity and fluid retention
Thiopental	Reduce dose for induction in severe liver disease
Valproate	Avoid if possible—hepatotoxicity and hepatic failure may occasionally occur (usually in first 6 months)
Valproic acid	*see* valproate
Verapamil	Reduce oral dose
Vinblastine	Dose reduction may be necessary
Vincristine	Dose reduction may be necessary
Warfarin	Avoid in severe liver disease, especially if prothrombin time already prolonged
Zidovudine	Accumulation may occur

PRESCRIBING IN RENAL IMPAIRMENT

Reduced renal function may cause problems with drug therapy for the following reasons:

1. The failure to excrete a drug or its metabolites may produce toxicity.
2. The sensitivity to some drugs is increased even if the renal elimination is unimpaired.
3. The tolerance to adverse effects may be impaired.
4. The efficacy of some drugs may diminish.

The dosage of many drugs must be adjusted in patients with renal impairment to avoid adverse reactions and to ensure efficacy. The level of renal function below which the dose of a drug must be reduced depends on how toxic it is and whether it is eliminated entirely by renal excretion or is partly metabolized to inactive metabolites.

In general, all patients with renal impairment are given a *loading dose* which is the same as the usual dose for a patient with normal renal function. *Maintenance doses* are adjusted to the clinical situation. The maintenance dose of a drug can be reduced either by reducing the individual dose leaving the normal interval between doses unchanged or by increasing the interval between doses without changing the dose. The interval extension method may provide the benefits of convenience and decreased cost, while the dose reduction method provides more constant plasma concentration.

In the following table drugs are listed in alphabetical order. The table includes only drugs for which specific information is available. Many drugs

should be used with caution in renal impairment but no specific advice on dose adjustment is available; it is therefore important to also refer to the individual drug entries. The recommendations are given for various levels of renal function as estimated by the glomerular filtration rate (GFR), usually measured by the creatinine clearance (best calculated from a 24-hour urine collection). The serum-creatinine concentration is sometimes used instead as a measure of renal function but it is only a rough guide even when corrected for age, sex and weight by special nomograms.

Renal impairment is usually divided into three grades:

mild—GFR 20–50 ml/minute *or* approximate serum creatinine 150–300 micromol/litre

moderate—GFR 10–20 ml/minute *or* serum creatinine 300–700 micromol/litre

severe—GFR <10 ml/minute *or* serum creatinine >700 micromol/litre

When using the dosage guidelines the following must be considered:

- Drug prescribing should be kept to a minimum.
- Nephrotoxic drugs should, if possible, be avoided in all patients with renal disease because the nephrotoxicity is more likely to be serious.
- It is advisable to determine renal function not only before but also during the period of treatment and adjust the maintenance dose as necessary.
- Renal function (GFR, creatinine clearance) declines with age so that by the age of 80 it is half that in healthy young subjects. When prescribing for the elderly, assume at least a mild degree of renal impairment.
- Uraemic patients should be observed carefully for unexpected drug toxicity. In these patients the complexity of clinical status as well as other variables for example altered absorption, protein binding or metabolism, or liver function, and other drug therapy precludes use of fixed drug dosage and an individualized approach is required.

Drugs to be avoided or used with caution in renal impairment:

Drug	Degree of impairment	Comment
Abacavir	Severe	Avoid
Acetazolamide	Mild	Avoid; metabolic acidosis
Aciclovir	Mild	Reduce intravenous dose
		Moderate to severe Reduce dose
Alcuronium	Severe	Prolonged duration of block
Allopurinol	Moderate	100–200 mg daily; increased toxicity; rashes
		Severe 100 mg on alternate days (maximum 100 mg daily)

Drug	Degree of impairment	Comment
Aluminium hydroxide	Severe	Aluminium is absorbed and may accumulate
		NOTE. Absorption of aluminium from aluminium salts is increased by citrates which are contained in many effervescent preparations (such as effervescent analgesics)
Amidotrizoates	Mild	Reduce dose and avoid dehydration; nephrotoxic
Amiloride	Mild	Monitor plasma potassium; high risk of hyperkalaemia in renal impairment; excreted by kidney unchanged
	Moderate	Avoid
Amoxicillin	Mild to moderate	Risk of crystalluria with high doses
	Severe	Reduce dose; rashes more common and risk of crystalluria
Amoxicillin + clavulanic acid		Risk of crystalluria with high doses (particularly during parenteral therapy); reduce dose if creatinine clearance less than 30 ml/minute
Amphotericin B	Mild	Use only if no alternative; nephrotoxicity may be reduced with use of lipid formulations
Ampicillin	Severe	Reduce dose; rashes more common
Artemether + lumefantrine	Severe	Caution; monitor ECG and plasma potassium
Aspirin	Severe	Avoid; sodium and water retention; deterioration in renal function; increased risk of gastrointestinal bleeding
Atenolol	Mild to moderate	Reduce dose to max. 50 mg daily if creatinine clearance 15–35 ml/minute
	Severe	May reduce renal blood flow and adversely affect renal function; reduce dose to max. 25 mg daily if creatinine clearance less than 15 ml/minute
Azathioprine	Severe	Reduce dose
Benzathine benzylpenicillin	Severe	Neurotoxicity—high doses may cause convulsions

Drug	Degree of impairment	Comment
Benzylpenicillin	Severe	Maximum 6 g daily; neuro-toxicity—high doses may cause convulsions
Bleomycin	Moderate	Reduce dose
Carbamazepine		Manufacturer advises caution
Cefixime	Moderate	Reduce dose
Ceftazidime	Mild	Reduce dose
Ceftriaxone	Severe	Maximum 2 g daily; also monitor plasma concentration if both severe renal impairment and hepatic impairment
Chlorambucil	Moderate	Use with caution and monitor response; increased risk of myelo-suppression
Chloramphenicol	Severe	Avoid unless no alternative; dose-related depression of haematopoiesis
Chloroquine	Mild to moderate	Reduce dose in rheumatic disease
	Severe	Reduce dose for malaria prophylaxis; avoid in rheumatic disease
Chlorphenamine	Severe	Dose reduction may be required
Chlorpromazine	Severe	Start with small doses; increased cerebral sensitivity
Ciclosporin		Monitor kidney function—dose dependent increase in serum creatinine and urea during first few weeks may necessitate dose reduction (exclude rejection if kidney transplant)
Ciprofloxacin	Moderate	Use half normal dose
Cisplatin	Mild	Avoid if possible; nephrotoxic and neurotoxic
Clindamycin		Plasma half-life prolonged—may need dose reduction
Cloxacillin	Severe	Reduce dose
Codeine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Cyclophosphamide		Reduce dose
Dacarbazine	Mild to moderate	Dose reduction may be required
	Severe	Avoid
Daunorubicin	Mild to moderate	Reduce dose

Drug	Degree of impairment	Comment
Deferoxamine		Metal complexes excreted by kidneys (in severe renal impairment dialysis increases rate of elimination)
Diazepam	Severe	Start with small doses; increased cerebral sensitivity
Didanosine	Mild	Reduce dose; consult manufacturer's literature
Diethylcarbamazine	Moderate to severe	Reduce dose; plasma half life prolonged and urinary excretion considerably reduced
Digoxin	Mild	Reduce dose; toxicity increased by electrolyte disturbances
Dimercaprol		Discontinue or use with extreme caution if impairment develops during treatment
Doxycycline	Mild	Use with caution; avoid excessive doses
Efavirenz	Severe	No information available—caution advised
Eflornithine		Reduce dose
Enalapril	Mild	Use with caution and monitor response; initial dose 2.5 mg once daily if creatinine clearance less than 30 ml/minute. Hyperkalaemia and other adverse effects more common
Ephedrine	Severe	Avoid; increased CNS toxicity
Ergometrine	Severe	Manufacturer advises avoid
Erythromycin	Severe	Maximum 1.5 g daily (ototoxicity)
Ethambutol	Mild	Reduce dose; if creatinine clearance less than 30 ml/minute monitor plasma ethambutol concentration; optic nerve damage
Etoposide		Consider dose reduction
Fluconazole	Mild to moderate	Usual initial dose then halve subsequent doses
Flucytosine		Reduce dose and monitor plasma-flucytosine concentration—consult manufacturer’s literature
Fluphenazine	Severe	Start with small doses; increased cerebral sensitivity
Furosemide	Moderate	May need high doses; deafness may follow rapid i/v injection

Drug	Degree of impairment	Comment
Gentamicin	Mild	Reduce dose; monitor plasma concentrations
Glibenclamide	Severe	Avoid
Haloperidol	Severe	Start with small doses; increased cerebral sensitivity
Heparin	Severe	Risk of bleeding increased
Hydralazine	Mild	Reduce dose if creatinine clearance less than 30 ml/minute
Hydrochlorothiazide	Moderate	Avoid; ineffective
Ibuprofen	Mild	Use lowest effective dose and monitor renal function; sodium and water retention; deterioration in renal function possibly leading to renal failure
	Moderate to severe	Avoid
Imipenem + cilastatin	Mild	Reduce dose
Insulin	Severe	May need dose reduction; insulin requirements fall; compensatory response to hypoglycaemia is impaired
Iohexol	Moderate to severe	Increased risk of nephrotoxicity; avoid dehydration
Iopanoic acid	Mild to moderate	Maximum 3 g
	Severe	Avoid
Isoniazid	Severe	Maximum 200 mg daily; peripheral neuropathy
Lamivudine	Mild	Reduce dose; consult manufacturer's literature
Lidocaine	Severe	Caution
Lithium	Mild	Avoid if possible or reduce dose and monitor plasma concentration carefully
	Moderate	Avoid
Lopinavir + ritonavir		Avoid oral solution due to propylene glycol content; use capsules with caution in severe impairment
Magnesium hydroxide	Moderate	Avoid or reduce dose; increased risk of toxicity
Magnesium sulfate	Moderate	Avoid or reduce dose; increased risk of toxicity

Drug	Degree of impairment	Comment
Mannitol		Avoid unless test dose produces diuretic response
Meglumine antimoniate		*see* pentavalent antimony compounds
Meglumine iotroxate	Moderate to severe	Increased risk of nephrotoxicity; avoid dehydration
Mercaptopurine	Moderate	Reduce dose
Metformin	Mild	Avoid; increased risk of lactic acidosis
Methadone	Moderate to severe	Increased and prolonged effect; increased cerebral sensitivity
Methotrexate	Mild	Reduce dose; accumulates; nephrotoxic
	Moderate	Avoid
Methyldopa	Moderate	Start with small dose; increased sensitivity to hypotensive and sedative effect
Metoclopramide	Severe	Avoid or use small dose; increased risk of extrapyramidal reactions
Morphine	Moderate to severe	Reduce dose or avoid; increased and prolonged effect; increased cerebral sensitivity
Nelfinavir		No information available—manufacturer advises caution
Neostigmine	Moderate	May need dose reduction
Nitrofurantoin	Mild	Avoid; peripheral neuropathy; ineffective because of inadequate urine concentrations
Penicillamine	Mild	Reduce dose and monitor renal function
	Moderate to severe	Avoid
Pentamidine isetionate	Mild	Reduce dose; consult manufacturer’s literature
Pentavalent antimony compounds	Moderate	Increased adverse effects
	Severe	Avoid
Phenobarbital	Severe	Avoid large doses
Povidone–iodine	Severe	Avoid regular application to inflamed or broken mucosa
Potassium chloride	Moderate	Avoid routine use; high risk of hyperkalaemia
Procainamide	Mild	Avoid or reduce dose
Procaine	Severe	Neurotoxicity—high doses may

benzylpenicillin		cause convulsions
Drug	**Degree of impairment**	**Comment**
Procarbazine	Severe	Avoid
Proguanil	Mild	100 mg once daily
	Moderate	50 mg on alternate days
	Severe	50 mg once weekly; increased risk of haematological toxicity
Propranolol	Severe	Start with small dose; higher plasma concentrations after oral administration; may reduce renal blood flow and adversely affect renal function
Propylthiouracil	Mild to moderate	Use three-quarters normal dose
	Severe	Use half normal dose
Pyridostigmine	Moderate	Reduce dose; excreted by kidney
Pyrimethamine		Use with caution
Quinine		Reduce parenteral maintenance dose for malaria treatment
Ranitidine	Severe	Use half normal dose; occasional risk of confusion
Ritonavir		*see* lopinavir with ritonavir
Saquinavir	Severe	Dose adjustment possibly required
Sodium chloride	Severe	Avoid
Sodium bicarbonate	Severe	Avoid; specialized role in some forms of renal disease
Sodium nitroprusside	Moderate	Avoid prolonged use
Sodium valproate		*see* valproate
Spironolactone	Mild	Monitor plasma K+; high risk of hyperkalaemia in renal impairment
	Moderate	Avoid
Stavudine	Mild	20 mg twice daily (15 mg if body weight less than 60 kg)
	Moderate to severe	20 mg once daily (15 mg if body weight less than 60 kg)
Streptomycin	Mild	Reduce dose; monitor plasma concentrations
Sulfadiazine	Severe	Avoid; high risk of crystalluria
Sulfamethoxazole + trimethoprim	Mild	Use half normal dose if creatinine clearance 15–30 ml/minute; avoid if creatinine clearance less than 15 ml/minute and if plasma-sulfamethoxazole concentration cannot be monitored

Drug	**Degree of impairment**	**Comment**
Sulfasalazine	Moderate	Risk of toxicity including crystalluria—ensure high fluid intake
	Severe	Avoid
Trimethoprim	Mild	Use half normal dose after 3 days if creatinine clearance 15–30 ml/minute
	Moderate to severe	Use half normal dose if creatinine clearance less than 15 ml/minute; avoid if creatinine clearance less than 10 ml/minute (unless plasma-trimethoprim concentration monitored)
Valproate	Mild to moderate	Reduce dose
	Severe	Alter dosage according to free serum valproic acid concentration
Valproic acid		*see* valproate
Vancomycin	Mild	Reduce dose—monitor plasma-vancomycin concentration and renal function regularly
Warfarin	Severe	Avoid
Zidovudine	Severe	Reduce dose; manufacturer advises oral dose of 300–400 mg daily in divided doses or intravenous dose of 1 mg/kg 3–4 times daily

PRESCRIBING IN PREGNANCY

During pregnancy the mother and the fetus form a non-separable functional unit. Maternal well-being is an absolute prerequisite for the optimal functioning and development of both parts of this unit. Consequently, it is important to treat the mother whenever needed while protecting the unborn to the greatest possible extent.

Drugs can have harmful effects on the fetus at any time during pregnancy. It is important to remember this when prescribing for a woman of childbearing age. However, irrational fear of using drugs during pregnancy can also result in harm. This includes untreated illness, impaired maternal compliance, suboptimal treatment and treatment failures.

Such approaches may impose risk to maternal well-being, and may also affect the unborn child. It is important to know the ‘background risk’ in the context of the prevalence of drug induced adverse pregnancy outcomes. Major congenital malformations occur in 2–4% of all live births. Up to 15% of all

diagnosed pregnancies will result in fetal loss. The cause of these adverse pregnancy outcomes is understood in only a minority of the incidents.

During the *first trimester* drugs may produce congenital malformations (teratogenesis), and the greater risk is from third to the eleventh week of pregnancy. During the *second* and *third trimester* drugs may affect the growth and functional development of the fetus or have toxic effects on fetal tissues. Drugs given shortly before term or during labour may have adverse effects on labour or on the neonate after delivery. Few drugs have been shown conclusively to be teratogenic in man but no drug is safe beyond all doubt in early pregnancy. Screening procedures are available where there is a known risk of certain defects.

If possible counselling of women before a planned pregnancy should be carried out including discussion of risks associated with specific therapeutic agents, traditional medicines and abuse of substances such as nicotine and alcohol. Folic acid supplements should be given during pregnancy planning because periconceptual use of folic acid reduces neural tube defects.

Drugs should be prescribed in pregnancy only if the expected benefits to the mother are thought to be greater than the risk to the fetus. All drugs should be avoided if possible during the first trimester. Drugs which have been used extensively in pregnancy and appear to be usually safe should be prescribed in preference to new or untried drugs and the smallest effective dose should be used. Well known single component drugs should usually be preferred to multi-component drugs.

The following list includes drugs which may have harmful effects in pregnancy and indicates the trimester of risk. It is based on human data but information on *animal* studies has been included for some drugs when its omission might be misleading.

Drugs to be avoided or used with caution in pregnancy:

(Absence of a drug from the list does not imply safety.)

Drug	Comment
Abacavir	Toxicity in *animal* studies; it may be desirable to initiate antiretroviral therapy after the first trimester, although for pregnant women, who are severely ill, the benefit of early therapy outweighs the potential risk to the fetus
Acetazolamide	Not used to treat hypertension in pregnancy First trimester: Avoid (toxicity in animal studies)
Aciclovir	Not known to be harmful; limited absorption from topical preparations
Albendazole	Contraindicated in cestode infections; First trimester: avoid in nematode infections

Drug	Comment
Alcohol	First, second trimesters: Regular daily drinking is teratogenic (fetal alcohol syndrome) and may cause growth retardation; occasional single drinks are probably safe Third trimester: Withdrawal may occur in babies of alcoholic mothers
Alcuronium	Does not cross placenta in significant amounts; use only if potential benefit outweighs risk
Allopurinol	Toxicity not reported; use only if no safer alternative and disease carries risk for mother or child
Amitriptyline	Manufacturer advises avoid unless essential, particularly during first and third trimesters
Amlodipine	No information of use in humans; risk to fetus should be balanced against risk of uncontrolled maternal hypertension
Amodiaquine	Use only if no safer alternative
Amoxicillin	Not known to be harmful
Amoxicillin + clavulanic acid	Not known to be harmful
Amphotericin B	Not known to be harmful but use only if potential benefit outweighs risk
Ampicillin	Not known to be harmful
Artemether	First trimester: Avoid
Artemether + lumefantrine	First trimester: Avoid
Artesunate	First trimester: Avoid
Asparaginase	Avoid
Aspirin	Third trimester: Impaired platelet function and risk of haemorrhage; delayed onset and increased duration of labour with increased blood loss; avoid analgesic doses if possible in last few weeks (low doses probably not harmful); with high doses, closure of fetal ductus arteriosus *in utero* and possibly persistent pulmonary hypertension of newborn; kernicterus in jaundiced neonates
Atenolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension
Atropine	Not known to be harmful
Azathioprine	Transplant patients should not discontinue azathioprine on becoming pregnant; use in pregnancy should be carefully supervised; there is no evidence that azathioprine is teratogenic—reports of premature birth and low birthweight; spontaneous abortion reported following maternal or paternal exposure

Drug	Comment
Azithromycin	Limited information available—use only if adequate alternatives not available
Beclometasone	Benefit of treatment, for example in asthma, outweighs risk
Benzathine benzylpenicillin	Not known to be harmful
Benznidazole	First trimester: avoid
Benzylpenicillin	Not known to be harmful
Betamethasone	Benefit of treatment, for example in asthma, outweighs risk
Bleomycin	Avoid (teratogenic and carcinogenic in *animal* studies)
Bupivacaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block; lower doses of bupivicaine for intrathecal use during late pregnancy
Calcium folinate	Manufacturer advises use only if potential benefit outweighs risk
Carbamazepine	First trimester: Risk of teratogenesis including increased risk of neural tube defects (counselling and screening and adequate folate supplements advised, for example 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used Third trimester: May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding
Cefixime	Not known to be harmful
Ceftazidime	Not known to be harmful
Ceftriaxone	Not known to be harmful
Chlorambucil	Avoid; use effective contraception during administration to men or women
Chloramphenicol	Third trimester: Neonatal 'grey' syndrome
Chlormethine	Avoid
Chloroquine	First, third trimesters: Benefit of prophylaxis and treatment in malaria outweighs risk
Chlorphenamine	No evidence of teratogenicity
Chlorpromazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Ciclosporin	There is less experience of ciclosporin in pregnancy but it does not appear to be any more harmful than azathioprine; use in pregnancy should be supervised in specialist units
Ciprofloxacin	All trimesters: Avoid—arthropathy in *animal* studies; safer alternatives available
Cisplatin	Avoid (teratogenic and toxic in *animal* studies)
Clindamycin	Not known to be harmful

Drug	Comment
Clomifene	Possible effects on fetal development
Clomipramine	Manufacturer advises avoid unless essential, particularly during first and third trimester
Cloxacillin	Not known to be harmful
Codeine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Contraceptives, oral	Epidemiological evidence suggests no harmful effects on fetus
Cyclophosphamide	Avoid (use effective contraception during and for at least 3 months after administration to men or women)
Cytarabine	Avoid (teratogenic in *animal* studies)
Dacarbazine	Avoid (carcinogenic and teratogenic in *animal* studies); ensure effective contraception during and for at least 6 months after administration to men or women
Dactinomycin	Avoid (teratogenic in *animal* studies)
Dapsone	Third trimester: Neonatal haemolysis and methaemoglobinaemia; folic acid 5 mg daily should be given to mother
Daunorubicin	Avoid (teratogenic and carcinogenic in *animal* studies)
Deferoxamine	Teratogenic in *animal* studies; manufacturer advises use only if potential benefit outweighs risk
Dexamethasone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Diazepam	Avoid regular use (risk of neonatal withdrawal symptoms); use only if clear indication such as seizure control (high doses during late pregnancy or labour may cause neonatal hypothermia, hypotonia and respiratory depression)
Didanosine	Manufacturer advises use only if potential benefit outweighs risk
Diethylcarbamazine	Avoid: delay treatment until after delivery
Digoxin	May need dosage adjustment
Diloxanide	Defer treatment until after first trimester
Doxorubicin	Avoid (teratogenic and toxic in *animal* studies); with liposomal product use effective contraception during and for at least 6 months after administration to men or women

Drug	Comment
Doxycycline	First trimester: Effects on skeletal development in *animal* studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Efavirenz	Avoid (potential teratogenic effects)
Eflornithine	All trimesters: Avoid
Emtricitabine	Use only if essential – no information available
Enalapril	All trimesters: Avoid; may adversely affect fetal and neonatal blood pressure control and renal function; also possible skull defects and oligohydramnios; toxicity in *animal* studies
Ephedrine	Increased fetal heart rate reported with parenteral ephedrine
Ergocalciferol	High doses teratogenic in *animals* but therapeutic doses unlikely to be harmful effects on foetus
Erythromycin	Not known to be harmful
Ethambutol	Not known to be harmful
Ethinylestradiol	Epidemiological evidence suggests no harmful effects on fetus
Ethosuximide	First trimester: May possibly be teratogenic; risk of teratogenicity greater if more than one antiepileptic used
Etoposide	Avoid (teratogenic in *animal* studies)
Fluconazole	Avoid (multiple congenital abnormalities reported with long-term high doses)
Flucytosine	Teratogenic in *animal* studies; manufacturer advises use only if potential benefit outweighs risk
Fluorouracil	Avoid (teratogenic)
Fluphenazine	Third trimester: Extrapyramidal effects in neonate occasionally reported
Furosemide	Not used to treat hypertension in pregnancy
Gentamicin	Second, third trimesters: Auditory or vestibular nerve damage, risk probably very small with gentamicin, but avoid unless essential (if given, serum-gentamicin concentration monitoring essential)
Glibenclamide	Third trimester: Neonatal hypoglycaemia; insulin is normally substituted in all diabetics; if oral drugs are used therapy should be stopped at least 2 days before delivery

Drug	Comment
Griseofulvin	Avoid (fetotoxicity and teratogenicity in *animals*); effective contraception required during and for at least 1 month after administration (important: effectiveness of oral contraceptives reduced); also men should avoid fathering a child during and for at least 6 months after administration
Haloperidol	Third trimester: Extrapyramidal effects in neonate occasionally reported
Halothane	Third trimester: Depresses neonatal respiration
Heparin	All trimesters: Maternal osteoporosis has been reported after prolonged use; multidose vials may contain benzyl alcohol—some manufacturers advise avoid
Hydralazine	Avoid during first and second trimesters; no reports of serious harm following use in third trimester
Hydrochlorothiazide	Not used to treat hypertension in pregnancy Third trimester: May cause neonatal thrombocytopenia
Hydrocortisone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention
Ibuprofen	Avoid unless potential benefit outweighs risk Third trimester: With regular use closure of fetal ductus arteriosus *in utero* and possibly persistent pulmonary hypertension of the newborn. Delayed onset and increased duration of labour
Idoxuridine	Teratogenic in *animal* studies
Imipenem+cilastatin	Use only if potential benefit outweighs risk (toxicity in *animal* studies)
Indinavir	Avoid if possible in first trimester; theoretical risk of hyperbilirubinaemia and renal stones in neonate if used at term
Insulin	All trimesters: Insulin requirements should be assessed frequently by an experienced diabetes clinician
Iodine	Second, third trimesters: Neonatal goitre and hypothyroidism
Ipratropium	Not known to be harmful
Isoniazid	Not known to be harmful
Ivermectin	Delay treatment until after delivery
Ketamine	Third trimester: Depresses neonatal respiration

Drug	Comment
Lamivudine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters
Levamisole	Third trimester: Avoid
Levodopa + carbidopa	Toxicity in *animal* studies
Levonorgestrel	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus
Levothyroxine	Monitor maternal serum-thyrotrophin concentration—levothyroxine may cross the placenta and excessive dosage can be detrimental to fetus
Lidocaine	Third trimester: With large doses, neonatal respiratory depression, hypotonia, and bradycardia after paracervical or epidural block
Lithium	First trimester: Avoid if possible (risk of teratogenicity including cardiac abnormalities) Second and third trimesters: Dose requirements increased (but on delivery return to normal abruptly); close monitoring of serum-lithium concentration advised (risk of toxicity in neonate)
Lopinavir + ritonavir	Avoid if possible in first trimester; avoid oral solution due to high propylene glycol content
Magnesium sulfate	Third trimester: not known to be harmful for short-term intravenous administration in eclampsia but excessive doses may cause neonatal respiratory depression
Mebendazole	Toxicity in *animal* studies. Contraindicated in cestode infections First trimester: Avoid in nematode infections
Medroxyprogesterone	Avoid (genital malformations and cardiac defects reported in male and female fetuses); inadvertent use of depotmedroxyprogesterone acetate contraceptive injection in pregnancy unlikely to harm fetus
Mefloquine	Use only if other antimalarials inappropriate
Melarsoprol	All trimesters: Avoid
Mercaptopurine	Avoid (teratogenic)
Metformin	All trimesters: Avoid; insulin is normally substituted in all diabetics
Methadone	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Methotrexate	Avoid (teratogenic; fertility may be reduced during therapy but this may be reversible); use effective contraception during and for at least 6 months after administration to men or women

Drug	Comment
Methyldopa	Not known to be harmful
Metoclopramide	Not known to be harmful
Metronidazole	Avoid high-dose regimens
Mifepristone	If treatment fails, pregnancy must be terminated by another method
Misoprostol	Potent uterine stimulant, may be teratogenic—if medical abortion fails, pregnancy must be terminated by another method
Morphine	Third trimester: Depresses neonatal respiration; withdrawal effects in neonates of dependent mothers; gastric stasis and risk of inhalation pneumonia in mother during labour
Naloxone	Use only if potential benefit outweighs risk
Nelfinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters
Neostigmine	Third trimester: Neonatal myasthenia with large doses
Nevirapine	Avoid if possible in first trimester; benefit of treatment considered to outweigh risk in second and third trimesters
Niclosamide	*T. solium* infections in pregnancy should be treated immediately
Nifedipine	Some dihydropyridines are teratogenic in *animals*, but risk to fetus should be balanced against risk of uncontrolled maternal hypertension; may inhibit labour (used for premature labour)
Nifurtimox	First trimester: Avoid
Nitrofurantoin	Third trimester: May produce neonatal haemolysis if used at term
Nitrous oxide	Third trimester: Depresses neonatal respiration
Norethisterone	In oral contraceptives, epidemiological evidence suggests no harmful effects on fetus In higher doses masculinization of female fetuses and other defects reported
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Ofloxacin	All trimesters: Avoid—arthropathy in *animal* studies; safer alternatives available
Oxamniquine	If immediate treatment not required schistosomiasis treatment should be delayed until after delivery
Paracetamol	Not known to be harmful
Penicillamine	All trimesters: Fetal abnormalities reported rarely; avoid if possible

Drug	Comment
Pentamidine isetionate	Potentially fatal visceral leishmaniasis must be treated without delay. Should not be withheld in trypanosomiasis even if evidence of meningoencephalitic involvement. Potentially fatal *P. carinii* (*P. jiroveci*) pneumonia must be treated without delay
Pentavalent antimony compounds	Potentially fatal visceral leishmaniasis must be treated without delay
Phenobarbital	First, third trimesters: Congenital malformations; risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding
Phenoxymethylpenicillin	Not known to be harmful
Phenytoin	First, third trimesters: Congenital malformations (screening advised); adequate folate supplements should be given to mother (for example folic acid 5 mg daily); risk of teratogenicity greater if more than one antiepileptic used. May possibly cause vitamin K deficiency and risk of neonatal bleeding; if vitamin K not given at birth, neonate should be monitored closely for signs of bleeding. Caution in interpreting plasma concentrations—bound may be reduced but free (or effective) unchanged
Phytomenadione	Use only if potential benefit outweighs risk—no specific inform available
Podophyllum resin	All trimesters: Avoid—neonatal death and teratogenesis have been reported
Potassium iodide	Second, third trimesters: Neonatal goitre and hypothyroidism
Povidone–iodine	Second, third trimesters: Sufficient iodine may be absorbed to affect the fetal thyroid
Praziquantel	*T. solium* infections in pregnancy should be treated immediately Benefit of treatment in schistosomiasis outweighs risk If immediate treatment not considered essential for fluke infections, treatment should be delayed until after delivery
Prednisolone	Benefit of treatment, for example in asthma, outweighs risk; risk of intrauterine growth retardation on prolonged or repeated systemic treatment; corticosteroid cover required by mother during labour; monitor closely if fluid retention

Drug	Comment
Primaquine	Third trimester: Neonatal haemolysis and methaemoglobinaemia. Delay treatment until after delivery
Procarbazine	Avoid (teratogenic in *animal* studies and isolated reports in humans)
Proguanil	Benefit of prophylaxis and of treatment outweighs risk. Adequate folate supplements should be given to mother
Promethazine	No evidence of teratogenicity
Propranolol	May cause intrauterine growth restriction, neonatal hypoglycaemia, and bradycardia; risk greater in severe hypertension
Propylthiouracil	Second, third trimesters: Neonatal goitre and hypothyroidism
Pyrazinamide	Use only if potential benefit outweighs risk
Pyridostigmine	Third trimester: Neonatal myasthenia with large doses
Pyrimethamine	First trimester: Theoretical teratogenic risk (folate antagonist); adequate folate supplements should be given to the mother. First trimester: avoid in Pneumocystosis and toxoplasmosis
Quinidine	Not known to be harmful at therapeutic doses
Quinine	First trimester: High doses are teratogenic; but in malaria benefit of treatment outweighs risk
Ranitidine	Not known to be harmful
Retinol	First trimester: Excessive doses may be teratogenic
Rifampicin	First trimester: Very high doses teratogenic in *animal* studies Third trimester: Risk of neonatal bleeding may be increased
Ritonavir	*see* lopinavir with ritonavir
Salbutamol	Appropriate to use for asthma; high doses should be given by inhalation only—parenteral use can affect the myometrium and possibly cause cardiac problems
Saquinavir	Avoid if possible in first trimester; potential benefit of treatment considered to outweigh risk in second and third trimesters
Silver sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sodium nitroprusside	Potential for accumulation of cyanide in fetus—avoid prolonged use
Sodium valproate	*see* valproate
Spironolactone	Toxicity in *animal* studies

Drug	Comment
Stavudine	Avoid if possible in first trimester; increased risk of lactic acidosis and hepatic steatosis
Streptokinase	All trimesters: Possibility of premature separation of placenta in first 18 weeks; theoretical possibility of fetal haemorrhage throughout pregnancy; risk of maternal haemorrhage on postpartum use
Streptomycin	Second, third trimesters: Auditory or vestibular nerve damage; avoid unless essential (if given, serum-streptomycin concentration monitoring essential)
Sulfadiazine	Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded In toxoplasmosis, avoid in first trimester, but may be given in second and third trimester if danger of congenital transmission
Sulfadoxine + pyrimethamine	In malaria, benefit of prophylaxis and treatment outweigh risk. First trimester: Possible teratogenic risk (pyrimethamine a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sulfamethoxazole + trimethoprim	First trimester: Teratogenic risk (trimethoprim a folate antagonist) Third trimester: Neonatal haemolysis and methaemoglobinaemia; fear of increased risk of kernicterus in neonates appears to be unfounded
Sulfasalazine	Third trimester: Theoretical risk of neonatal haemolysis; adequate folate supplements should be given to mother
Suxamethonium	Mildly prolonged maternal paralysis may occur
Tamoxifen	Avoid—possible effects on fetal development; effective contraception must be used during treatment and for 2 months after stopping
Testosterone	All trimesters: Masculinization of female fetus
Tetracycline	First trimester: Effects on skeletal development in *animal* studies Second, third trimesters: Dental discoloration; maternal hepatotoxicity with large doses
Thiopental	Third trimester: Depresses neonatal respiration; dose should not exceed 250 mg
Trimethoprim	First trimester: Teratogenic risk (folate antagonist)
Vaccine, BCG	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus

Drug	Comment
Vaccine, influenza	Not known to be harmful
Vaccine, Measles	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus; avoid MMR
Vaccine, MMR	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, poliomyelitis, live	First trimester: Theoretical risk of congenital malformations, but need for vaccination may outweigh possible risk to fetus
Vaccine, rubella	Avoid; pregnancy should be avoided for 1 month after immunization
Vaccine, yellow fever	First trimester: Theoretical risk of congenital malformations, however need for vaccination may outweigh possible risk to fetus especially after the 6th month of pregnancy; pregnant women should be advised *not* to travel to areas where there is a risk of exposure to yellow fever
Valproate	First, third trimesters: Increased risk of congenital malformations and developmental delay (counselling and screening advised—folic acid supplement may reduce risk of neural tube defects); risk of teratogenicity greater if more than one antiepileptic used; neonatal bleeding (related to hypofibrinaemia) and neonatal hepatotoxicity also reported
Vancomycin	Use only if potential benefit outweighs risk—plasma-vancomycin concentration monitoring essential to reduce risk of fetal toxicity
Vecuronium	Use only if potential benefit outweighs risk—no information available
Verapamil	May reduce uterine blood flow with fetal hypoxia; may inhibit labour
Vinblastine	Avoid (limited experience suggests fetal harm; teratogenic in *animal* studies)
Vincristine	Avoid (teratogenicity and fetal loss in *animal* studies)
Warfarin	All trimesters: Congenital malformations; fetal and neonatal haemorrhage
Zidovudine	Avoid if possible in first trimester; benefit of treatment considered to outweightrisk in second and third trimesters

PRESCRIBING DURING BREAST-FEEDING

Administration of some drugs (for example, ergotamine) to nursing mothers may harm the infant, whereas administration of others (for example, digoxin) has little effect. Some drugs inhibit lactation (for example, estrogens).

Toxicity to the infant can occur if the drug enters the milk in pharmacologically significant quantities. The concentration in milk of some drugs (for example, iodides) may exceed the concentration in the maternal plasma so that therapeutic doses in the mother may cause toxicity to the infant. Some drugs inhibit the infant's sucking reflex (for example, phenobarbital). Drugs in breast milk may, at least theoretically, cause hypersensitivity in the infant even when the concentration is too low for a pharmacological effect.

The following table lists drugs:

- which should be used with caution or which are contraindicated in breast-feeding for the reasons given above;
- which, on present evidence, may be given to the mother during breast-feeding, because they appear in milk in amounts which are too small to be harmful to the infant;
- which are not known to be harmful to the infant although they are present in milk in significant amounts.

For many drugs insufficient evidence is available to provide guidance and it is advisable to administer only drugs essential to a mother during breast-feeding. Because of the inadequacy of information on drugs in breast milk the following table should be used only as a guide; absence from the table does not imply safety.

Infants should be exclusively breastfed for the first 6 months of life; thereafter they should receive appropriate complementary food and continue to be breastfed up to 2 years of age or beyond.

Advice in the table may differ from other sources, including manufacturer's product literature.

Drugs present in breast –milk:

Drug	Comment
Abacavir	Antiretroviral drugs may be present in breast milk, and may reduce viral load in breast milk and reduce the risk of transmission through breast-feeding. However, the concentration of antiretroviral drugs in breast milk may not be adequate to prevent viral replication and there is therefore possibility of promoting the development of drug-resistant virus which could be transmitted to the infant. Avoid breast-feeding if possible. Otherwise, exclusive breast-feeding is recommended during the first months of life, then should be discontinued as soon as feasible.
Acetazolamide	Amount too small to be harmful
Aciclovir	Significant amount in milk after systemic administration, but considered safe to use
Alcohol	Large amounts may affect infant and reduce milk consumption
Alcuronium	No information available
Allopurinol	Present in milk—not known to be harmful

Drug	Comment
Amiloride	Manufacturer advises avoid—no information available
Amitriptyline	Presence in milk possible; monitor infant
Amlodipine	Presence in milk possible; monitor infant
Amodiaquine	No information available
Amoxicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Amoxicillin + clavulanic acid	Trace amounts in milk
Amphotericin B	No information available
Ampicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Artemether + lumefantrine	Discontinue breast-feeding during and for 1 week after stopping treatment; present in milk in *animal* studies
Asparaginase	Breast-feeding contraindicated
Aspirin	Short course safe in usual dosage; monitor infant; regular use of high doses could impair platelet function and produce hypoprothrombinaemia in infant if neonatal vitamin K stores low; possible risk of Reye syndrome
Atenolol	Significant amounts in milk; safe in usual dosage; monitor infant
Atropine	Small amount present in milk; monitor infant
Azathioprine	Breast-feeding contraindicated
Azithromycin	Present in milk; limited information available—use only if no suitable alternative
Beclometasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses—the amount of *inhaled* drug in breast milk is probably too small to be harmful
Benzathine benzylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Benzylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Betamethasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses

Drug	Comment
Bleomycin	Breast-feeding contraindicated
Bupivacaine	Amount too small to be harmful
Carbamazepine	Continue breast-feeding; adverse effects possible (severe skin reaction reported in 1 infant), monitor infant for drowsiness
Cefixime	Probably present in milk but safe in usual dosage; monitor infant
Ceftazidime	Excreted in low concentrations; safe in usual dosage; monitor infant
Ceftriaxone	Excreted in low concentrations; safe in usual dosage; monitor infant
Chlorambucil	Breast-feeding contraindicated
Chloramphenicol	Continue breastfeeding; use alternative drug if possible; may cause bone-marrow toxicity in infant; concentration in milk usually insufficient to cause 'grey syndrome'
Chlormethine	Breast-feeding contraindicated
Chloroquine	For malaria prophylaxis, amount probably too small to be harmful; inadequate for reliable protection against malaria; avoid breast-feeding when used for rheumatic disease
Chlorphenamine	Safe in usual dosage; monitor infant for drowsiness
Chlorpromazine	Continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Ciclosporin	Present in milk—manufacturer advises avoid
Ciprofloxacin	Continue breast-feeding; use alternative drug if possible; high concentrations in breast milk
Cisplatin	Breast-feeding contraindicated
Clindamycin	Amount probably too small to be harmful but bloody diarrhoea reported in 1 infant
Clofazimine	Limited information available—can cause reversible skin discoloration in nursing infant
Clomifene	May inhibit lactation
Clomipramine	Small amount present in milk; continue breastfeeding; adverse effects possible; monitor infant for drowsiness
Cloxacillin	Trace amounts in milk; safe in usual dosage; monitor infant
Codeine	Amount too small to be harmful

Drug	Comment
Contraceptives, oral	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start 6 weeks after birth or later)
Cyclophosphamide	Breast-feeding contraindicated during and for 36 hours after stopping treatment
Cytarabine	Breast-feeding contraindicated
Dacarbazine	Breast-feeding contraindicated
Dactinomycin	Breast-feeding contraindicated
Dapsone	Although significant amount in milk risk to infant very small; continue breast-feeding; monitor infant for jaundice
Daunorubicin	Breast-feeding contraindicated
Deferoxamine	Manufacturer advises use only if potential benefit outweighs risk—no information available
Dexamethasone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Diazepam	Continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Didanosine	*see* abacavir
Digoxin	Amount too small to be harmful
Diloxanide	Manufacturer advises avoid
Dimercaprol	Avoid
Dopamine	No information available
Doxorubicin	Breast-feeding contraindicated
Doxycycline	Continue breastfeeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Efavirenz	*see* abacavir
Eflornithine	Avoid
Enalapril	Amount probably too small to be harmful
Ephedrine	Irritability and disturbed sleep reported
Ergocalciferol	Caution with high doses; may cause hypercalcaemia in infant
Erythromycin	Only small amounts in milk—not known to be harmful
Ethambutol	Amount too small to be harmful

Drug	Comment
Ethinylestradiol	Use alternative method of contraception; may inhibit lactation; *see also* contraceptives, oral
Ethosuximide	Significant amount in milk; continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Etoposide	Breast-feeding contraindicated
Fluconazole	Present in milk; safe in usual dosage; monitor infant
Flucytosine	Manufacturer advises avoid
Fluorouracil	Discontinue breast-feeding
Fluphenazine	Amount excreted in milk probably too small to be harmful; continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Furosemide	Amount too small to be harmful
Gentamicin	Amount probably too small to be harmful; monitor infant for thrush and diarrhoea
Glibenclamide	Theoretical possibility of hypoglycaemia in infant
Griseofulvin	Avoid—no information available
Haloperidol	Amount present in milk probably too small to be harmful; continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Halothane	Present in milk
Hydralazine	Present in milk but not known to be harmful; monitor infant
Hydrochlorothiazide	Continue breast-feeding; may inhibit lactation
Hydrocortisone	Systemic effects in infant unlikely with maternal dose of *less than equivalent* of prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Ibuprofen	Amount too small to be harmful; short courses safe in usual doses
Imipenem + cilastatin	Present in milk—manufacturer advises avoid
Indinavir	*see* abacavir
Insulin	Amount too small to be harmful
Iodine	Stop breast-feeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk
Isoniazid	Monitor infant for possible toxicity; theoretical risk of convulsions and neuropathy; prophylactic pyridoxine advisable in mother and infant

Drug	Comment
Ivermectin	Avoid treating mother until infant is 1 week old
Lamivudine	Present in milk; *see* abacavir
Levamisole	Breast-feeding contraindicated
Levodopa + carbidopa	Present in milk—levodopa may inhibit lactation
Levonorgestrel	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start 6 weeks after birth or later)
Levothyroxine	Amount too small to affect tests for neonatal hypothyroidism
Lidocaine	Amount too small to be harmful
Lithium	Present in milk and risk of toxicity in infant; continue breast-feeding; monitor infant carefully, particularly if risk of dehydration
Lopinavir + ritonavir	*see* abacavir
Lumefantrine	*see* artemether + lumefantrine
Mebendazole	Amount too small to be harmful
Medroxyprogesterone	Present in milk—no adverse effects reported (preferably start injectable contraceptive 6 weeks after birth or later)
Mefloquine	Present in milk but risk to infant minimal
Mercaptopurine	Breast-feeding contraindicated
Metformin	Present in milk but safe in usual doses; monitor infant
Methadone	Withdrawal symptoms in infant; dose should be as low as possible and infant monitored to avoid sedation
Methotrexate	Breast-feeding contraindicated
Methyldopa	Amount too small to be harmful
Methylthioninium chloride	No information available—avoid
Metoclopramide	Present in milk; adverse effects possible; monitor infant for adverse effects
Metronidazole	Significant amount in milk; continue breast-feeding; avoid large doses; use alternative drug if possible
Mifepristone	Avoid breast-feeding for 14 days after administration
Misoprostol	No information available—manufacturer advises avoid
Morphine	Short courses safe in usual doses; monitor infant

Drug	Comment
Naloxone	No information available
Nelfinavir	*see* abacavir
Neostigmine	Amount probably too small to be harmful; monitor infant
Nevirapine	Present in milk; *see* abacavir
Nifedipine	Small amount in milk; continue breast-feeding; monitor infant
Nitrofurantoin	Only small amounts in milk but could be enough to produce haemolysis in G6PD deficient infants
Norethisterone	Combined oral contraceptives may inhibit lactation—use alternative method of contraception until weaning or for 6 months after birth; progestogen-only contraceptives do not affect lactation (preferably start injectable contraceptive 6 weeks after birth or later)
Nystatin	No information available, but absorption from gastrointestinal tract negligible
Ofloxacin	Continue breast-feeding; use alternative drug if possible
Oxamniquine	No information available, but considered preferable to avoid
Paracetamol	Small amount present in milk: short courses safe in usual dosage; monitor infant
Penicillamine	No information available—manufacturer advises avoid unless potential benefit outweighs risk
Pentamidine isetionate	Manufacturer advises avoid unless essential
Pentavalent antimony compounds	Avoid
Phenobarbital	Continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Phenoxymethylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Phenytoin	Small amount present in milk; continue breast-feeding; adverse effects possible; monitor infant for drowsiness
Potassium iodide	Stop breast-feeding; danger of neonatal hypothyroidism or goitre; appears to be concentrated in milk
Povidone–iodine	Avoid; iodine absorbed from vaginal preparations is concentrated in milk

Drug	Comment
Praziquantel	Avoid breast-feeding during and for 72 hours after treatment; considered safe to continue breast-feeding in treatment of schistosomiasis
Prednisolone	Systemic effects in infant unlikely with maternal dose of *less than* prednisolone 40 mg daily; monitor infant's adrenal function with higher doses
Primaquine	No information available; risk of haemolysis in G6PD-deficient infants
Procainamide	Present in milk; continue breastfeeding; monitor infant
Procaine benzylpenicillin	Trace amounts in milk; safe in usual dosage; monitor infant
Procarbazine	Breast-feeding contraindicated
Proguanil	Amount probably too small to be harmful when used for malaria prophylaxis; inadequate for reliable protection against malaria in breastfed infant
Promethazine	Safe in usual dosage; monitor infant for drowsiness
Propranolol	Present in milk; safe in usual dosage; monitor infant
Propylthiouracil	Monitor infant's thyroid status but amounts in milk probably too small to affect infant; high doses might affect neonatal thyroid function
Pyrantel	No information available
Pyrazinamide	Amount too small to be harmful
Pyridostigmine	Amount probably too small to be harmful
Pyrimethamine	Significant amount—avoid administration of other folate antagonists to infant; avoid breast-feeding during toxoplasmosis treatment
Quinidine	Significant amount but not known to be harmful
Quinine	Present in milk—continue breast-feeding and monitor infant; risk of haemolysis in G6PD-deficient infants
Ranitidine	Significant amount present in milk, but not known to be harmful
Retinol	Theoretical risk of toxicity in infants of mothers taking large doses
Rifampicin	Amount too small to be harmful
Ritonavir	*see* lopinavir with ritonavir
Salbutamol	Safe in usual dosage; monitor infant

Drug	Comment
Saquinavir	*see* abacavir
Senna	Continue breast-feeding; monitor infant for diarrhoea
Silver sulfadiazine	Continue breast-feeding; monitor infant for jaundice—small risk of kernicterus in jaundiced infants particularly with long acting sulphonamides, and of haemolysis in G6PD-deficient infants
Sodium nitropruside	No information available
Sodium valproate	*see* valproate
Spectinomycin	No information available
Spironolactone	Amount probably too small to be harmful
Stavudine	*see* abacavir
Streptomycin	Present in milk; continue breast-feeding—monitor infant for thrush and diarrhoea
Sulfadiazine	Monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants; caution in ill or premature infants
Sulfadoxine + pyrimethamine	Monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfadoxine); caution in ill or premature infants
Sulfamethoxazole + trimethoprim	Monitor infant for jaundice—small risk of kernicterus in jaundiced infants and of haemolysis in G6PD-deficient infants (due to sulfamethoxazole); caution in ill or premature infants
Sulfasalazine	Use with caution; monitor infant for jaundice—small amounts in milk (1 report of bloody diarrhoea and rashes); theoretical risk of neonatal haemolysis especially in G6PD-deficient infants; caution in ill or premature infants
Suxamethonium	No information available
Tamoxifen	Suppresses lactation; avoid unless potential benefit outweighs risk
Testosterone	Avoid; may cause masculinization in the female infant or precocious development in the male infant; high doses suppress lactation
Tetracaine	No information available

Drug	Comment
Tetracycline	Continue breast-feeding; use alternative drug if possible (absorption and therefore discoloration of teeth in infant probably usually prevented by chelation with calcium in milk)
Thiamine	Severely thiamine-deficient mothers should avoid breast-feeding as toxic methyl-glyoxal excreted in milk
Thiopental	Present in milk—not known to be harmful
Trimethoprim	Present in milk; safe in usual dosage;
Valproate	Amount too small to be harmful
Vaccine, Influenza	Not known to be harmful
Vancomycin	Present in milk—significant absorption following oral administration unlikely
Vecuronium	No information available
Verapamil	Amount too small to be harmful
Vinblastine	Breast-feeding contraindicated
Vincristine	Breast-feeding contraindicated
Warfarin	Risk of haemorrhage; increased by vitamin K deficiency; warfarin appears safe
Zidovudine	*see* abacavir

Chapter - One

Drugs Acting on the Gastro-intestinal System

1.1 Antacids and Simeticone

Antacids are those agents which react chemically to neutralise or buffer existing quantities of stomach acid. They have no direct effect on acid output but will increase pH value from stomach contents, thus providing relief in ulcer dyspepsia and non-erosive gastro-oesophageal reflux.

ALUMINIUM HYDROXIDE

It reacts with hydrochloric acid to form aluminium chloride and water. About 17-30% of aluminium chloride formed is absorbed and is rapidly excreted by kidneys in patients with normal renal function.

Indications: adjunct to healthy life style, with other drugs for the relief of symptoms in ulcer dyspepsia. Antacids are also used for the relief of non-erosive gastro-oesophageal reflux.

Adverse effects and cautions: most frequent adverse effect of aluminium antacids is constipation. Haemorrhoids and fissures, or faecal impaction may occur.

In patients with severe renal function impairment, aluminium may accumulate.

Drug interactions: antacids can interfere with the absorption of other drugs. The absorption of digoxin, azithromycin, ciprofloxacin, norfloxacin, ofloxacin, rifampicin, tetracyclines, iron salts and isoniazid especially can be reduced, resulting in sub-clinical response. It is thus advisable to administer drugs at least one hour before antacids to avoid such problem.

Dose: 1-2 tablets chewed 4 times daily and at bed time or as required or 5-10 ml 4 times daily between meals and at bed time or as required; CHILD 6-12 years, up to 5 ml 3 times daily.

Preparation available

Aluminium Hydroxide and Magnesium Hydroxide Oral Suspension: Preparations containing dried aluminium hydroxide gel 250 mg and magnesium hydroxide 250 mg are usually available. Most of the preparations contain simeticone and some also contain algenic acid.

Aluminium Hydroxide and Magnesium Hydroxide Tablets: Tablets containing dried aluminium hydroxide gel 250 mg and magnesium hydroxide 250 mg are usually available. Some formulations contain simeticone.

Aluminium Hydroxide and Magnesium Trisilicate Tablets: Tablets containing dried aluminium hydroxide gel 250 mg and magnesium hydroxide 500 mg are usually available. Some formulations contain simeticone.

CALCIUM CARBONATE

It reacts with hydrochloric acid to form calcium chloride, carbon dioxide and water. A limited amount of calcium is absorbed and hypercalcaemia may occur. In some patients, metabolic alkalosis and the milk-alkali syndrome may occur.

Indications: *see* under aluminium hydroxide.

Adverse effects and cautions: the major limiting factor to the chronic use of calcium carbonate is gastric hypersecretion and acid rebound which has occurred even following a single dose.

Drug interactions: *see* under aluminium hydroxide.

MAGALDRATE

It is a chemical combination of aluminium and magnesium hydroxide and sulphate. Magaldrate does not simply simulate physical mixtures of magnesium and aluminium hydroxides. It has minimal sodium content.

Dose: 0.8-1.6 g daily

Indications, adverse effects, cautions and drug interactions: see under aluminium hydroxide.

Preparation available

Magaldrate Oral Suspension: Each 10 ml containing 400 mg or 800 mg of magaldrate is usually available. Most of the preparations contain simeticone and some also contain algenic acid.

Magaldrate Tablets: Each tablet containing 400 mg and 800 mg of magaldrate is usually available. Some prapartions contain simeticone.

MAGNESIUM HYDROXIDE AND MAGNESIUM TRISILICATE

Magnesium hydroxide and magnesium trisilicate rapidly react with hydrochloric acid to form magnesium chloride and water. About 15-30% of the magnesium chloride is absorbed and is rapidly excreted by the kidneys in patients with normal renal function.

Indications: *see* under aluminium hydroxide.

Adverse effects and cautions: magnesium containing antacids commonly cause a laxative effect.

In patients with severe renal impairment, hypermagnesaemia characterised by hypotension, nausea, vomiting, ECG changes and mental depression has occurred after magnesium containing antacids.

Drug interactions: *see* under aluminium hydroxide.

Dose: 250-500 mg 3-4 times a day.

Preparation available: *see* under aluminium hydroxide.

SIMETICONE

Activated Dimethicone, Activated Polydimethylsiloxane, Simethicone

Its use is based on its antifoam properties. It allows gas bubbles in the gastro-intestinal tract to coalesce and be expelled.

Indications: symptomatic treatment of flatulence, evidence of benefit in infantile colic is uncertain.

Adverse effects and cautions: no adverse effects have been reported.

Preparation available: *see* under aluminium hydroxide and magaldrate.

SODIUM BICARBONATE

It is a rapid acting antacid, but absorbed bicarbonate may cause alkalosis in excessive doses. Antacids other than sodium bicarbonate neutralize gastric secretions but generally do not cause metabolic alkalosis. It should not be prescribed alone for the relief of dyspepsia.

Dose: 600-1800 mg in divided doses.

Preparation available

Sodium Bicarbonate Tablets: Each tablet containing 300 mg of sodium bicarbonate is usually available.

1.2 Anti - spasmodics

Anti-spasmodics are drugs which act as a smooth muscle relaxant.

ATROPINE AND ***HYOSCINE***

Atropine is principal alkaloid of belladonna. The belladonna extract contains atropine and hyoscine (scopolamine). Atropine and hyoscine are naturally occurring antimuscarinic drugs. Atropine is more potent than hyoscine in its antimuscarinic action on the heart, bronchial tree and intestinal smooth muscle and less potent than scopolamine in its antimuscarinic action on iris, ciliary body, salivary, bronchial and sweat glands. In contrast to hyoscine, atropine stimulates the CNS in usual doses.

Following oral administration, onset of action of belladonna occurs in 1-2 hours and action lasts for 4 hours. Following intramuscular administration peak plasma concentration of atropine is reached within 30 minutes and lasts for 2-3 hours.

Indications: symptomatic relief of gastro-intestinal disorders characterized by smooth muscle spasm. Hyoscine is also effective in genito-urinary disorders characterised by smooth muscle spasm. Atropine sulphate is also used to reverse muscarinic effects associated with toxic exposure to anticholinesterase compounds (organophosphorus poisoning), mydriasis, cycloplegia and pre-medication.

Adverse effects and cautions: dry mouth, blurred vision, cycloplegia, dilatation of pupils, photophobia (especially with scopolamine), urinary hesitancy and retention, tachycardia and constipation.

Anti-spasmodics are contraindicated in angle closure glaucoma and in patients with known hypersentivity to the drugs. These drugs are also contraindicated in prostatic hypertrophy, in tachycardia secondary to cardiac insufficiency or thyrotoxicosis. The use of drugs during pregnancy should be made only when the potential benefits justify the possible risk to the foetus.

ATROPINE SULFATE

Dose: Premedication, by intravenous injection, 200-600 micrograms immediately before induction of anesthesia and in incremental doses of 100 micrograms for the treatment of bradycardia.

By intramuscular injection, 300-600 micrograms 30-60 minutes before induction; CHILD 20 micrograms/kg.

For control of muscarinic side effects of neostigmine, in reversal of competitive neuromuscular block, by intravenous injection, 0.6-1.2 mg.

Bradycardia, particularly complicated by hypotension after myocardial infarction, intravenous injection of 300 micrograms, increasing to 1 mg if necessary.

Antidote to organophosphorous poisoning, by intramuscular or intravenous injection, 1 to 2 mg, repeated in 20-30 minutes as soon as cyanosis has cleared.

Preparation available

Atropine Injection*:* Atropine injection is a sterile solution of atropine sulfate in water for injection. Injection containing 1 mg atropine sulfate/ml is usually available.

HYOSCINE BUTYLBROMIDE

Dose: By mouth, 20 mg 4 times daily; CHILD 6-12 years, 10 mg 3 times daily.

By intramuscular or intravenous injection (acute spasm) 20 mg repeated after 30 minute if necessary.

Preparation available

Hyoscine Butylbromide Injection: Injection containing 20 mg/ml of hyoscine butylbromide is usually available. Hyoscine butylbromide injection should be protected from light.

Hyoscine Butylbromide Tablets: Each tablet containing 10 mg and 20 mg of hyoscine butylbromide is usually available.

CLIDINIUM

It is a synthetic quaternary ammonium antimuscarinic drug. Onset of action is one hour and effect lasts up to 3 hours.

Indications: *see* under dicyclomine.

Dose: 2.5 mg 3-4 times a day before meals and at bed time; this may be increased to 5 mg four times a day if necessary.

Adverse effects and cautions: see under atropine and hyoscine

Preparation available

Clidinium Bromide Tablets: Each tablet containing 2.5 mg of clidinium bromide is usually available.

DICYCLOVERINE HYDROCHLORIDE

Dicyclomine Hydrochloride

It is a synthetic tertiary amine. It has elimination half-life of 9-10 hours.

Indications: symptomatic relief of gastro-intestinal disorders characterised by smooth muscle spasm.

Adverse effects and cautions: see under atropine and hyoscine.

Dose: 10-20 mg 3 times daily, CHILD 6-24 months 5-10 mg up to 3-4 times daily, 15 minutes before feeds, 2-12 years 10 mg 3 times daily.

Preparation available

Dicycloverine Oral Solution: Each 5ml of oral solution containing 10 mg of dicycloverine hydrochloride is usually available.

Dicycloverine Drop: Each ml containing 10 mg of dicycloverine hydrochloride is usually available.

Dicycloverine Injection: Injection containing 10 mg/ml dicycloverine hydrochloride is usually available.

Dicycloverine Tablets: Each tablet containing 10 mg and 20 mg of dicycloverine hydrochloride is usually available.

FLAVOXATE HYDROCHLORIDE

It is an anti-muscarinic drug with some non-specific direct relaxant effect on smooth muscle. It decreases spasm of the gastro-intestinal tract, biliary tract, ureter and uterus in therapeutic doses.

Indications: urinary frequency and incontinence, urgency, dysuria, bladder spasms due to catheterisation.

Adverse effects and cautions: see atropine and hyoscine; also fatigue and vertigo.

Dose: 200 mg 3 times daily; CHILD under 12 years not recommended.

Preparation available

Flavoxate Tablets: Each tablet containing 200 mg of flavoxate hydrochloride is usually available.

ISOPROPAMIDE

It is also a synthetic quaternary ammonium antimuscarinic drug. Following oral administration the duration of action is 10-12 hours.

Indications: *see* under clidinium.

Adverse effects and cautions: *see* under atropine and hyoscine.

Dose: 5-10 mg every 12 hours.

Preparation available

Isopropamide Iodide Tablets: Each tablet containing the equivalent of 5 mg of isopropamide is usually available.

MEBEVERINE HYDROCHLORIDE

Indications: irritable bowel syndrome.

Adverse effects and cautions: rash, urticaria, angiooedema.

The drug is contra-indicated in paralytic ileus.

The drug should be used with caution in pregnancy.

Dose: ADULT and CHILD over 10 years 135 mg 3 times daily preferably 20 minutes before meals; CHILD under 10 years not recommended.

Preparation available

Mebeverine Hydrochloride Tablets: Each tablet containing 135 mg of mebeverine hydrochloride is usually avaliable.

Mebeverine Suspension: Suspension of mebeverine embonate containing equivalent to 50 mg/5 ml of mebeverine hydrochloride is usually available.

OXYPHENONIUM BROMIDE

It is also synthetic quaternary ammonium antimuscarinic drug. It has elimination half life of 3.2 hours.

Indications: see under clidinium.

Adverse effects and cautions: see under atropine and hyoscine.

Dose: 5-10 mg 4 times daily.

Preparation available

Oxyphenonium Tablets: Each tablet containing 5 mg and 10 mg of oxyphenonium is usually available.

PROPANTHELINE

It is also synthetic quaternary ammonium antimuscarinic drug. The duration of action is 6 hours.

Indications: see under clidinium.

Adverse effects and cautions: see under atropine and hyoscine.

Drug interactions: absorption of levodopa may decrease if concurrently administered.

Dose: 15 mg 3 times daily at least 1 hour before meals and 30 mg at night, maximum 120 mg daily.

Preparation available

Propantheline Tablets: Each tablet containing 15 mg of propantheline bromide is usually available. They are coated.

1.3 Ulcer healing drugs

Peptic ulcer involves the stomach, duodenum and lower oesophagus. General and inexpensive measures like healthy life style, stopping smoking and taking antacids should be promoted. The possibility of malignant disease should be considered in all patients over the age of 40 years who are suspected of having an ulcer.

Gastric and duodenal ulcers are healed by 4-8 weeks treatment with H_2 - receptor antagonists but there is a high rate of relapse (greater than 70% over 2 years) requiring maintenance therapy. Relapses can be prevented very successfully by eradicating *Helicobacter pylori* which is causally associated with most peptic ulers (except those related to NSAID use).

BISMUTH CHELATE

Tripotassium dicitratobismuthate is a bismuth chelate which promotes healing of gastric and duodenal ulcers. It adheres to ulcerated gastric and duodenal mucosa, forming a physical barrier. It is effective against *Helicobacter pylori.*

Indications: benign gastric and duodenal ulcers.

Adverse effects and cautions: constipation, darkening of tongue and black faeces.

Drug interactions: coating of ulcer bases by bismuth is most effective at low pH and its effect may decrease if given with drugs which suppress acid secretion.

Dose: Adult 240 mg twice daily or 120 mg 4 times daily 30 minutes before meals, taken for 28 days, followed by further 28 days if necessary; maintenance not indicated but course may be repeated after interval of 1 month, CHILD not recomended.

Milk should not be drunk during treatment. Antacid should not be taken half an hour before or after a dose.

Preparation available

Tripotassium Dicitratobismuthate Tablets: Each tablet containing 120 mg of tripotassium dicitratobismuthate is usually available.

CIMETIDINE, FAMOTIDINE AND *RANITIDINE*

Ranitidine, famotidine and cimetidine are H_2 - receptor antagonists. The drugs competitively inhibit the action of histamine on the H_2- receptors of parietal cells, reducing gastric acid output and concentration under basal and nocturnal conditions and also when stimulated by food, insulin, histamine and caffeine.

Indications: benign duodenal ulcer, gastric ulcer, reflux oesophagitis and Zollinger- Ellison syndrome.

Adverse effects and cautions: headache, dizziness, myalgia, nausea, skin rash and diarrhoea or constipation. Cimetidine binds to androgen receptor and this contributes to the sexual dysfunctions such as loss of libido, impotence and gynaecomastia.

H_2 - receptor antagonist should be used with caution in patients with impaired renal function.

Safety of famotidine in children younger than 12 years of age has not been established. The use of drug during pregnancy should be made only when clearly needed.

CIMETIDINE

Dose: By mouth, benign gastric or duodenal ulcer, 400 mg twice daily or 800 mg at night for at least 4 weeks, maintenance, 400 mg at night; CHILD 25-30 mg/kg daily in divided doses, INFANT 20 mg/kg daily in divided doses.

By intramuscular injection, 200 mg every 4-6 hours; by slow intravenous injection, 200 mg given over at least 2 minutes.

By intravenous infusion, 400 mg in 100 ml of normal saline infused over ½ -1 hour or by continuous infusion at an average rate of 50-100 mg/hour over 24 hours.

Preparation available

Cimetidine Injection: Injection containing 100 mg of cimetidine per ml is usually available.

Cimetidine Tablets: Each tablet containing 200 mg and 400 mg of cimetidine in uaually available.

FAMOTIDINE

Dose: Benign gastric and duodenal ulceration treatment, 40 mg at night for 4-8 weeks; maintenance, 20 mg at night.

Reflux oesophagitis, 20-40 mg twice daily for 6-12 weeks.

Zollinger - Ellison syndrome, 20 mg every 6 hours (higher dose in those who have previously been receiving another H_2 antagonist)

Preparation available

Famotidine Tablets: Each tablet containing 20 mg and 40 mg of famotidine is usually available.

Famotidine Injection: Injection containing 10 mg per ml of famotidine is usually available.

RANITIDINE

Dose: By mouth, benign gastric or duodenal ulcer, 150 mg twice daily or 300 mg at night for 4-8 weeks, up to 6 weeks in chronic episodic dyspepsia, and up to 8 weeks in NSAID-associated ulceration. Maintenance 150 mg at night.

Reflux oesophagitis, 150 mg twice daily or 300 mg at night for up to 8 weeks, or if necessary 12 weeks.

Gastric acid reduction (prophylaxis of acid aspiration) in obstetrics, by mouth 150 mg at onset of labour, then every 6 hours; surgical procedures, by intramuscular or slow intravenous injection, 50 mg 45-60 minutes before induction of anaesthesia or by mouth, 150 mg 2 hours before induction of anaesthesia.

By intramuscular injection, 50 mg every 6-8 hours. By intravenous

infusion, 25 mg/hour for 2 hours; may be repeated every 6-8 hours.

Preparation available

Ranitidine Injection: Injection containing 25 mg per ml of ranitidine (as hydrochloride) is usually available.

Ranitidine Tablets: Each tablet containing 150 mg and 300 mg of ranilidine (as hydrochloride) is usually available.

ESOMEPRAZOLE, LANSOPRAZOLE, *OMEPRAZOLE*, PANTOPRAZOLE AND RABIPRAZOLE

They are specific inhibitors of "proton pump" (hydrogen-potassium adenosine triphosphate) of the apical membrane of the parietal cell, thereby inhibition of gastric acid.

Indications: benign gastric and duodenal ulcer, NSAID-associated duodenal or gastric ulcer, duodenal or benign gastric ulcer associated with *Helicobacter pylori*, reflux oesophagitis, Zollinger-Ellison syndrome.

Adverse effects and cautions: nausea, vomiting, diarrhoea, abdominal colic, skin rash, headache and dizziness.

Proton pump inhibitors should be used with caution in pregnancy and in breast-feeding, patients with liver disease.

Proton pump inhibitors may mask the symptoms of gastric cancer; particular care is required in those presenting with 'alarm features', in such cases gastric malignancy should be ruled out before treatment.

Drug interactions: Omeprazole inhibits hepatic metabolism of certain drugs. Clearance of diazepam is reduced by about 50 percent.

ESOMEPRAZOLE

Dose: By mouth, duodenal ulcer associated with *Helicobacter pylori*, 20 mg twice daily.

NSAID-associated gastric ulcer, ADULT over 18 years, 20 mg once daily for 4–8 weeks; prophylaxis in patients with an increased risk of gastro-duodenal complications who require continued NSAID treatment, 20 mg daily.

Gastro-oesophageal reflux disease, ADULT and CHILD over 12 years, 40 mg once daily for 4 weeks, continued for further 4 weeks if not fully healed or symptoms persist; maintenance 20 mg daily; symptomatic treatment in the absence of oesophagitis, 20 mg daily for up to 4 weeks, then in ADULTS over 18 years 20 mg daily when required. CHILD not recommended.

The tablets should not be chewed or crushed, but should be swallowed whole *or* dispersed in water.

By intravenous injection over at least 3 minutes *or* by intravenous infusion, gastro-oesophageal reflux disease, ADULT over 18 years, 40 mg once daily; symptomatic reflux disease without oesophagitis, 20 mg daily; continue until oral administration possible. CHILD not recommended.

Preparation available

Esomeprozole Tablets: Each tablet containing 20 mg and 40 mg of esomeprazole (as magnesium trihydrate) is usually available.

Esomeprazole Injection: Each vial containing 40 mg of esomeprazole (as sodium salt) powder for reconstitution is usually available.

OMEPRAZOLE

Dose: Benign gastric and duodenal ulcer (including those complicating NSAID therapy) 20 mg daily for 4 weeks in duodenal ulceration or 8 weeks in gastric ulceration; in severe cases increased to 40 mg daily, long term use not recommended.

Zollinger- Ellison syndome, intially 60 mg once daily, usual range 20-120 mg daily (above 80 mg in 2 divided doses).

Reflux oesophagitis, 20 mg daily for 4 weeks, followed by a further 4-8 weeks if not fully healed; 40 mg daily has been given for 8 weeks in reflux oesophagitis refractory to other treatment, may be continued at 20 mg daily.

Preparation available

Omeprazole Capsules: Omeprazole capsules contain enteric coated granules. Each capsule containing 10 mg and 20 mg of omeprazole is usually available.

LANSOPRAZOLE

Dose: Duodenal ulcer, 30 mg daily in the morning for 4 weeks, maintenance 15 mg daily, benign gastric ulcer, 30 mg daily in the norming for 8 weeks, NSAID-associated duodenal or gastric ulcer, 15-30 mg once daily for 4 weeks, continued for further 4 weeks if not fully healed.

Reflux oesophagitis, 30 mg daily in the morning for 4 weeks, continued for further 4 weeks if not fully healed.

Zollinger-Ellison syndrome, initially 60 mg once daily adjusted according to response; daily dose of 120 mg or more given in two divided doses.

Preparation available

Lansoprazole Capsules: Lansoprazole capsules contain interic coated granules. Eah capsule containing 15 mg and 30 mg of lansoprazole is available.

PANTOPRAZOLE

Dose: Duodenal ulcer, 40 mg daily in the morning for 2 weeks, continued for further 2 weeks if not fully healed. Benign gastric ulcer, 40 mg daily in the morning for 4 weeks continued for further 4 weeks if not fully healed.

Reflux oesophagitis, 20-40 mg daily in the morning for 4 weeks, continued for further 4 weeks if not fully healed, maintenance 20 mg daily, increased to 40 mg daily if symptom returns.

Zollinger-Ellison syndrome, initially 80 mg once daily adjusted according to response.

By intravenous injection over at least 2 minutes or by intravenous infusion, duodenal ulcer, gastric ulcer and gastro-oesophegeal reflux, 40 mg daily until oral administation can be resumed.

Preparation available

Pantoprazole Tablets: Each tablet containing 20 mg and 40 mg of pantoprazole is available.

Pantoprazole Injection: Injection containing 40 mg pantoprazole is available.

RABEPRAZOLE SODIUM

Indications: *see* under omeprazole.

Adverse effects and cautions: see under omeprazole; also cough, rhinitis, chest pain, anorexia, weight gain.

Dose: Benign gastric ulcer, 20 mg daily in the morning for 6 weeks, continued for further 6 weeks if not fully heeled.

Duodenal ulcer, 20 mg daily in the morning for 4 weeks, continued for further 4 weeks if not fully heeled.

Gastro-oesophagal reflux, 20 mg once daily for 4-8 weeks; maintenance 10-20 mg daily.

Duodenal and benign gastric ulcer associated with *Halicobacter pylori*, 20 mg twice daily with other drugs.

CHILD not recommended.

Preparation available

Rabeprazole Tablets: Each tablet containing 10 mg and 20 mg of rabeprazole sodium is usually available.

SUCRALFATE

It is a complex of aluminium hydroxide and sulphated sucrose which adheres to ulcerated gastric and duodenal mucosa, but not to healthy mucosa. The dense, sticky layer that forms in an ulcer crater is thought to provide a physical barrier separating acid and pepsin from the ulcer base, which then has an opportunity to heal. The use of antacids within 30 minutes of a dose of sucralfate should be avoided.

Indications: benign gastric and duodenal ulceration, chronic gastritis.

Adverse effects and cautions: constipation, diarrhoea, dry mouth, nausea, dizziness and backache.

Safety and efficacy of sucralfate in children have not been established. The drug should be used during pregnancy only when clearly needed.

Drug interactions: Concomitant use with cimetidine, phenytoin, tetracyclines and fluoroquinolones results in a reduction in bioavailability of these drugs.

Sucralfate should be taken at least 2 hours after administration of other drugs.

Dose: 2 g twice daily (on rising and at bedtime) or 1 g 4 times daily, 1 hour before meals and at bedtime, taken up to 4-6 weeks or in resistant cases 12 weeks; maximum 8 g daily.

Prophylaxis of stress ulceration (suspension) 1g 6 times daily (maximum 8 g daily).

Preparation available

Sucralfate Tablets: Each tablet containing 1g of sucralfate is usually available.

1.4 Anti – emetics

CYCLIZINE

It is anti-histamine which acts by depressing labyrinth excitability and conduction in vestibular cerebellar pathway.

Indications: nausea, vomiting, motion sickness, vertigo.

Adverse effects and cautions: drowsiness, dizziness, dry mouth, constipation, blurred vision and difficult urination.

Problems in humans have not been documented during its use in pregnancy.

Drowsiness may affect performance of skilled tasks (e.g. driving). Effects of alcohol are enhanced.

Dose: By mouth, cyclizine hydrochloride 50 mg up to 3 times daily CHILD, 6-12 years 25 mg, up to 3 times daily.

Preparation available

Cyclizine Tablets: Tablets containing 50 mg of cyclizine hydrochloride is usually available.

DIMENHYDRINATE

The pharmacological effect of dimenhydrinate is believed to result principally from its diphenhydramine moiety. Its exact mechanism of action is unknown.

Indications: vertigo, motion sickness. It is less effective than promethazine, cyclizine, hyoscine and meclizine.

Adverse effects and cautions: drowsiness, blurred vision, dryness of mouth, dizziness and palpitation.

Use of drug in pregnancy requires that the potential benefit be weighed against the possible risk.

Dose: 50-100 mg 3-4 times daily. CHILD 1-6 years 12.5-25 mg, 7-12 years 25-50 mg, up to 3 times daily. Motion sickness, first dose 30 minutes before journey.

Preparation available

Dimenhydrinate Tablets: Each tablet containing 50 mg of dimenhydrinate

is usually available.

DOMPERIDONE

It blocks dopamine (D_2) receptors in the CTZ. It also increases the tone in the lower oesophageal sphincter, enchances contractions of the gastric antrum and relexes the pyloric sphincter. It crosses the blood-brain barrier poorly, so less risk of adverse effects in the central nervous system. Dystonic rections with domperidone are much fewer than with metoclopramide.

Indications: nausea, vomiting, dyspepsia, gastro-oesophegeal reflux.

Adverse effects and cautions: gynaecomastia, galactorrhoea, rashes and dystonic reactions.

The drug should be used in pregnancy only when clearly needed. The drug should be used with caution in nursing women.

Dose: acute nausea and vomiting 10-20 mg every 6-8 hours, CHILD, 250-500 micrograms/kg every 6-8 hours.

Functional dyspepsia, 10-20 mg 3 times daily before food and 10-20 mg at night; maximum period of treatment 12 weeks; CHILD not recommended.

Preparation available

Domperidone Tablets: Each tablet containing 10 mg of domperidone in usually available.

Domperidone Oral Suspension: Each ml containing 1 mg of domperidone is usually available.

MECLOZINE HYDROCHLORIDE

Indications, adverse effects and cautions: *see* under cyclizine.

Dose: 25-50 mg daily, in single or divided doses.

Preparation available

Meclozine Tablets: Each tablet containing 12.5 mg of meclozine hydrochloride is usually available.

METOCLOPRAMIDE

The antiemetic activity is mediated via direct effect on medullary chemoreceptor trigger zone (CTZ) by blocking dopamine receptors in the CTZ. Metoclopramide also accelerates gastric emptying and intestinal transit from the duodenum to the ileocaecal valve by increasing the amplitude and duration of oesophageal, gastric contractions and by relaxing the pyloric sphincter and the duodenal bulb. The lower oesphageal sphincter pressure is increased.

Indications: nausea and vomiting, particularly in gastrointestinal disorders and during treatment with cytotoxic drugs or radiotherapy. The drug is also used for the management of gastric stasis and gastroesophageal reflux.

Adverse effects and cautions: restlessness, drowsiness and fatigue are most frequent adverse effects and occur in about 10% of patients. Extrapyramidal reactions may occur in all age groups and at any dose but

occur most frequently in children and young adults following i.v. administration of high doses of the drug. Gynaecomastia, galactorrhoea and menstrual disorders may occur (due to stimulation of prolactin secretion).

Metoclopramide is contraindicated in patients with history of seizure disorders (frequency and severity of seizures may be increased). The drug is also contraindicated in patients receiving drugs that are likely to cause extrapyramidal reactions (frequency and severity of seizure may be increased). The drug should be used during pregnancy only when clearly needed. The drug should be used with caution in nursing women.

Dose: By mouth or intramuscular injection or by intravenous injection over 1-2 minutes, 10 mg (5 mg in young adult 15-19 years under 60 kg) 3 times daily; CHILD up to 1 year (up to 10 kg) 1 mg twice daily, 1-3 years (10-14 kg) 1 mg 2-3 times daily, 3-5 years (15-19 kg) 2 mg 2-3 times daily, 5-9 years (20-29 kg) 2.5 mg 3 times daily, 9-14 years (30 kg and over) 5 mg 3 times daily.

Preparation available

Metoclopramide Injection: Injection containing the equivalent of 5 mg per ml of anhydrous metoclopramide hydrochloride is usually available. Metoclopamide should be protected from light.

Metoclopramide Oral Solution: Each 5ml of oral solution containing 5 mg of anhydrous metoclopramide hydrochloride is usually available. Metoclopramide oral solution should be protected from light.

Metoclopramide Tablets: Each tablet containing the equivalent of 10 mg of anhydrous metoclopramide hydrochloride is usually available. Metoclopramide tablets should be protected from light.

ONDANSETRON

It is a serotonin (5-HT_3) receptor antagonist. 5-HT_3 receptors are present in several critical sites involved in emesis, including vagal afferents, solitary tract nucleus (STN) and CTZ.

Indications: prevention and treatment of nausea and vomiting associated with chemotherapy or radiotherapy, prevention and treatment of post-operative nausea and vomiting.

Adverse effects and cautions: headache, constipation, hiccups, flushing, involuntary movements, chest pain, transient visual disturbances, dizziness, arrhythmias, hypotension.

The drug should be used with caution in pregnancy, breast-feeding, moderate or severe liver impairment.

Drug interactions: concomitant administration with rifampicin or carbamazepine or phenytion will acclerate metabolism of the drug and reduce the effect.

Dose: Prevention of nausea and vomiting associated with chemotherapy or radiotherapy, by mouth 8 mg 1-2 hours before treatment; by intramuscular or slow intravenous injection, 8 mg immediately before treatment then by mouth, 8 mg every 12 hours for up to 5 days; CHILD, by slow intravenous

injection or intravenous infusion over 15 minutes, 5 mg/m^2 immediately before chemotherapy then, 4 mg by mouth every 12 hours for up to 5 days.

Prevention of post-operative nausea and vomiting, by mouth, 16 mg 1 hour before anaesthesia or 8 mg 1 hour before anaesthesia followed by 8 mg at intervals of 8 hours for 2 further doses; by intramuscular or slow intravenous injection, 4 mg at induction of anaesthesia; CHILD over 2 years, by slow intravenous injection, 100 micrograms/kg (maximum 4 mg) before, during or after induction of anaesthesia.

Treatment of post-operative nausea and vomiting, by intramuscular or slow intravenous injection, 4 mg; CHILD over 2 years, by slow intravenous injection, 100 micrograms/kg (maximum 4 mg).

Preparation available

Ondansetron Injection: Injection containing 4 mg per ml of ondansetron (as hydrochloride) in 2-ml and 4-ml vial is usually available.

Ondansetron Tablets: Each tablet containing 4 mg and 8 mg of ondansetron (as hydrochloride) is usually available.

PROCHLORPERAZINE

It is a phenothiazine which acts as central dopamine antagonist by blocking the chemoreceptor trigger zone (CTZ).

Indications: nausea, vomiting, vertigo, labyrinthine disorders.

Adverse effects and cautions: dry mouth and drowsiness. Side effects are rare with anti-emetic doses but extrapyramidal symptoms may occur with high doses.

Safe use of drug during pregnancy has not been established. Safety and efficacy in children under 2 years have not been established.

Dose: By mouth, nausea and vomiting, Prochlorperazine maleate or mesylate, acute attack, 20 mg initially then 10 mg after 2 hours; prevention 5-10 mg 2-3 times daily; CHILD (over 10 kg only) 250 micrograms/kg 2-3 times daily.

Labyrinthine disorders, 5 mg 3 times daily, gradually increased if necessary to 30 mg daily in divided doses, and then reduced after several weeks to 5-10 mg daily.

By deep intramuscular injection, nausea and vomiting 12.5 mg when required followed if necessary after 6 hours by an oral dose as above.

Preparation available

Prochlorperazine Injection: Injection containing 12.5 mg per ml of prochlorperazine mesylate in water for injection free from dissolved air is usually available. Prochlorperazine injection should be proctected from light.

Prochlorperazine Tablets: Each tablet containing 5 mg and 25 mg of prochlorperazine maleate is usually available. Prochlorperazine tablets should be protected from light.

PROMETHAZINE

The antiemetic activity is not precisely known but may be mediated via central anticholinergic actions.

Indications: nausea, vomiting, vertigo, motion sickness, labyrinthine disorders.

Adverse effects and cautions: drowsiness, dryness of mouth, blurring of vision, confusion, disorientation and fatigue. Leucopaenia, agran-ulocytosis and thrombocytopenic purpurea has been reported rarely. Promethazine is contraindicated in patients who have received larger doses of CNS depressants and/or who are comatosed. Respiratory depression, sleep apnoea, sudden infant deaths have occurred in infants and young children.

Safe use of promethazine during pregnancy (except during labour) has not been established. Promethazine should be used during pregnancy only when the potential benefits justify the possible risk to the foetus. The drug is known to be distributed in milk. The drug should be used with caution in nursing women. The drug is not recommended in children under 2 years.

Drug interactions: Promethazine may potentiate the sedative action of opiates, other CNS depressants, antihistamines and alcohol.

PROMETHAZINE HYDROCHLORIDE

Dose: Motion sickness prevention, 25 mg at bed time on night before travelling, repeat following morning if necessary; CHILD 2-5 years, 5 mg at night and following morning; 5-10 years, 10 mg at night and following morning.

By deep intramuscular injection 25-50 mg; CHILD 5-10 years 6.25-125 mg.

Preparation available

Promethazine Injection: Injection containing 25 mg per ml of promethazine hydrochloride is usually available. Promethazine injection should be protected from light.

Promethazine Oral Solution: Each 5ml of oral solution containing 5 mg of promethazine hydrochloride is usually available. Promethazine oral solution should be protected from light and stored at a temperacture not exceeding 25°.

Promethazine Hydrochloride Tablets: Each tablet containing 10 mg and 25 mg of promethazine hydrochloride is usually available. Promethazine hydrochloride tablets are coated.

PROMETHAZINE THEOCLATE

It acts longer than promethazine hydrochloride.

Indications: *see* under promethazine hydrochloride.

Dose: 25-75 mg, maxium 100 mg daily; CHILD 5-10 years, 12.5-37.5 mg daily.

Motion sickness prevention, 25 mg at bed time on night before travelling or 25 mg 1-2 hours before travelling; CHILD 5-10 years half adult dose.

For severe vomiting in pregnancy, 25 mg at bed time, maximum of 100 mg daily.

Preparation available

Promethazine Theoclate Tablets: Each tablet containing 25 mg of promethazine theoclate is usually available. Promethazine theoclate tablets should be protected from light.

TRIFLUOPERAZINE

Indications: *see* under prochlorperazine.

Adverse effects and cautions: see under prochlorperazine.

Dose: Antiemetic, 2-4 mg daily in divided doses, maximum 6 mg daily; CHILD 3-5 years, up to 1 mg daily, 6-12 years up to 4 mg daily.

Preparation available

Trifluoperazine Tablets: Each tablet containing 1 mg and 5 mg of trifluoperazine (as hydrochloride) is usually available.

1.5 Antidiarrhoeal drugs

DIPHENOXYLATE AND ATROPINE

Diphenoxylate is an opiate derivative resembling pethidine. It probably acts both locally and centrally to reduce intestinal motility. Atropine is added in the preparation below the therapeutic level in an attempt to prevent abuse by deliberate over dose.

Indications: symptomatic treatment of acute diarrhoea and chronic mild ulcerative colitis.

Adverse effects and cautions : dryness of skin and mucous membranes, thirst, tachycardia, urinary retention (all due to atropine), abdominal discomfort or distension, paralytic ileus, sedation, dizziness, respiratory depression, and coma.

Diphenoxylate preparations are contraindicated in children younger than 4 years and should be used with particular caution in younger children. The drug should not be administered to pregnant women unless the potential benefits to the patient outweigh the possible risk to the foetus. The drug is also distributed into milk and the effects of drugs may occur in breast-fed infants.

Dose: Initial dose for adults is 4 tablets, followed by 2 tablets every 6 hours until diarrhoea is controlled; CHILD 4-8 years, 1 tablet 3 times daily, 9-12 years 1 tablet 4 times daily.

Preparation available

Diphenoxylate Hydrochloride and Atropine Sulfate Tablets: Each tablet containing 2.5 mg of diphenoxylate hydrochloride and 25 micrograms of atropine sulphate is usually available.

LOPERAMIDE

It slows intestinal motility by effect on receptors along the small intestinal wall.

Indications: control and symptomatic relief of acute non-specific diarrhoea and chronic diarrhoea.

Adverse effects and cautions: abdominal pain, distension or discomfort, constipation, dizziness, dry mouth, nausea and vomiting. Children may be more sensitive to adverse CNS effects of drug than adults. Loperamide should not be used in the treatment of diarrhoea resulting from some infections.

The drug is contraindicated in patients with a known hypersensitivity to the drug.

Safe use of drug during pregnancy has not been established. Safety and efficacy of drug in children younger than 4 years of age have not also been established.

Dose: Acute diarrhoea, 4 mg initially followed by 2 mg after each loose stool for up to 5 days; usual dose 6-8 mg daily; maximum 16 mg daily; chronic diarrhoea in adults initially 4-8 mg daily in divided doses; subsequently adjusted accordance to response and given in 2 divided doses for maintenance.

Preparation available

Loperamide Capsules: Each capsule containing 2 mg of loperamide hydrochloride is usually available.

ORAL REHYDRATION SALTS (ORS)

Oral rehydration salts (ORS) are specifically intended for the replacement of water and salts lost in acute diarrhoea. These losses may be prevented by the use of ORS. Dehydration must be corrected as rapidly as possible, particularly in infants and young children.

The volume of fluid required and the rate at which it should be given depend upon:

- The weight (age) of the child
- Initial degree of dehydration
- Rate of fluid loss as long as the diarrhoea persists.

Adverse effects and cautions: vomiting (too rapid administration), hypernatraemia and hyperkalaemia (overdose in renal impairment or administration of too concentrated solution).

The cleanest possible water should be used to prepare ORS solution. If there is doubt with purity, use boiled and cool water. Solution should be prepared daily. If an infant vomits after taking ORS, give it more slowly after 10 minutes, in small sips at short intervals.

Antibacterials should not be given in acute diarrhoea except in cholera and shigellosis.

Dose: According to fluid loss, usually, 200 - 400 ml solution after every loose motion; INFANT 1-1.5 times usual feed volume; CHILD 200 ml after every loose motion.

Preparation available

Oral Rehydration Salt: Oral rehydration salts are oral powders containing anhydrous glucose, sodium chloride, potassium chloride and sodium citrate. After being dissoloved in the requisite volume of water, they are intended for the prevention and treatment of dehydration due to diarrhoea, including maintenance therapy. Oral rehydration salts may contain suitable flavouring agents.

The composition of one of the formulations in use is described below in term of the amount in grams to be dissolove in sufficient water to produce 1000 ml. It is that recommended by the diarrhoeal disease control programme of the World Health Organization (WHO) and the United Nations Children Fund (UNICEF)

Sodium Chloride	2.6 g
Potassium chloride	1.5g
Tri-Sodium citrate	2.9 g
Anhydrous Glucose	13.5 g

Oral rehydration salts should be protected from moisture. They are kept in sachets, preferably made of aluminium foil, containing quantity to prepare one litre of solution. Any portion of the solution prepared that remains unused 24 hours after preparation should be discarded.

ZINC SULFATE

Indication: adjunct to ORS in acute diarrhoea.

Dose: INFANT under 6 months 10 mg (elemental zinc) daily for 10-14 days; CHILD 6 months-5 years 20 mg (elemental zinc) daily for 10-14 days.

Adverse effects and cautions: abdominal pain, dyspepsia, nausea, vomiting, diarrhoea, headache, gastritis.

Zinc may accumulate in acute renal failure.

Drug interactions: The absorption of ciprofloxacin, levofloxacin, ofloxacin, ferrous salts and calcium salts can be reduced.

Preparation available

Zinc Sulfate Dispersible Tablets: Dispersible tablets of zinc sulfate containing equivalent of 10 mg and 20 mg of elemental zinc are available.

1.6 Cathartic drugs

Cathartics, laxative and purgative are terms describing drugs that promote defaecation. A balanced diet including adequate fluid intake and fibre is of value in preventing constipation.

Bulk-forming cathartics, stool softeners are preferred to other laxatives in patients with conditions in which straining at defaecation should be avoided (e.g. angina, myocardial infarction, vascular disease, diseases of anus or rectum, hernias, recent rectal surgery).

BISACODYL

It is a stimulant cathartic and produces evacuation in 10 - 12 hours after oral administration of therapeutic dose. If rectally administered evacuation will be produced within 20 minutes to one hour.

Indications: constipation, bowel evacuation before radiological procedures and surgery.

Adverse effects and cautions: see under senna.

Dose: By mouth for constipation, 5-10 mg at night; occasionally necessary to increase to 15-20 mg; CHILD, more than 6 years, 5 mg.

By rectum in suppositories for constipation, 10 mg in the morning, CHILD under 10 years, 5 mg.

Before radiological procedures and surgery, 10 mg by mouth at bed time before procedure and if necessary, a 10 mg suppository 1 hour before procedure; CHILD 4-10 years, 5 mg by mouth, night before procedure and 5 mg suppository following morning.

Preparation available

Bisacodyl Suppository: Suppository containing 5 mg and 10 mg of bisacodyl are usually available.

Bisacodyl Tablets: Bisacodyl tablets are made gastric resistant by enteric coating or by other means. Each tablet containing 5 mg of bisacodyl is usually available.

BRAN

It is a bulk-forming cathartic and is most useful in simple constipation in the elderly, constipation following surgery or during pregnancy, and fissure, haemorrhoids and ulcerative colitis.

Indications: constipation.

Adverse effects and cautions: abdominal distension, painfullness and urgent calls to stool.

It should not be used in patients with neurological disorder of the bowel as it may lead to obstruction of the colon.

DOCUSATE SODIUM

Dioctyl Sodium Sulphosuccinate

It is a stool softener and produces softening of the faeces generally within 1-2 days.

Indications: constipation, adjunct in abdominal radiological procedures.

Adverse effects and cautions: rashes and transitory gastro-intestinal cramping pain.

Dose: By mouth, chronic constipation, up to 500 mg daily in divided doses; initial dose should be large and gradually reduced; CHILD over 6 months 12.5-25 mg 3 times daily.

With barium meal, 400 mg.

Preparation available

Docusate Tablets: Each tablet containing 100 mg of docusate sodium is usually available.

Docusate Sodium Syrup: Each 5ml containing 50 mg of docusate sodium is usually available.

Docusate Sodium Drops: Each ml containing 25 mg of docusate sodium is usually available.

ISPAGHULA HUSK

Isapgol husk

It is a bulk-forming cathartic and is also useful in patients who cannot tolerate bran.

Indications: constipation.

Adverse effects and cautions: abdominal distension and flatulence. Adequate fluid intake to be maintained to avoid intestinal obstruction.

Dose: 0.5-2g.

Preparation available

Ispaghula Husk: Powder without excipient or containing about 50 % of excipient is usually available.

LACTULOSE

It is an osmotic cathartic and produces evacuation 24-48 hours after administration of the drug. Besides, the drug is also used in hepatic encephalopathy, as drug also causes a decrease in blood ammonia concentration.

Indications: constipation and hepatic encephalopathy.

Adverse effects and cautions: nausea, vomiting and gaseous distention.

The drug should be used with caution in patients with diabetes mellitus because lactulose solution may contain free lactose and galactose. It should be administered during pregnancy only when the potential benefits justify the possible risks to the foetus.

Dose: Expressed in terms of the elixir containing 3.35g/5ml. Constipation, initially 15 ml twice daily, gradually reduced according to patient's needs, child under 1 year 2.5 ml, 1-5 years 5 ml, 6-12 years 10 ml twice daily, gradually reduced. Hepatic encephalopathy, 30-50 ml 3 times daily, subsequently adjusted to produce 2-3 soft stools daily.

Preparation available

Lactulose Solution: Each 5ml of solution containing 3.35 g of lactulose with other ketoses is usually available.

LIQUID PARAFFIN

It acts by lubricating the faeces and produces evacuation after 6-8 hours when administered orally.

Indications: constipation.

Adverse effects and cautions: lipoid pneumonia due to aspiration of liquid paraffin. Chronic use of the drug may impair the absorption of fat soluble vitamins like A, D and K. Systemic absorption of liquid paraffin has caused foreign body granulomatous reactions particularly in mesenteric lymph nodes, liver, and spleen.

Dose: 10-30 ml at night when required.

Preparation available

Liquid Paraffin Emulsion: Emulsion containing 25%v/v of liquid paraffin is usually available.

MAGNESIUM HYDROXIDE ORAL SUSPENSION

Milk of Magnesia

It is an osmotic cathartic and has action similar to magnesium sulfate. It also acts in 2-4 hours.

Indications: constipation.

Adverse effects and cautions: see under senna.

Dose: 15-30 ml, when required.

Preparation available

Magnesium Hydroxide Oral Suspension: Suspension containing about 8% hydrated magnesium oxide usually available.

MAGNESIUM SULFATE

It is a saline cathartic and produces evacuation within 2-4 hours.

Indications, adverse effects and cautions: see under senna.

Dose: Laxative, 5-10 g, dissolved in 240 ml of water.

SENNA

It is a stimulant cathartic and produces evacuation within 8-12 hours and so should be given at bed time. Normally partially purified glycosides, called sennosides, are used in pharmaceutical dosage form.

Indications: constipation, bowel evacuation before abdominal radiological procedures, endoscopy and surgery.

Adverse effects and cautions: mild griping may occur.

The drug should be avoided except when straining. It will exacerbate a condition (such as angina) or increase the risk of rectal bleeding as in haemorrhoids. The drug should be preferably avoided in children and pregnancy.

The drug should not be used if patient has acute abdominal pain, nausea, vomiting or dehydration. Patient should consult qualified medical practitioner if sudden changes in bowel habits persists for longer than 2 weeks or if use of cathartic for one week has no effect.

Dose: Equivalent to 23 mg of sennoside at bed time.

Preparation available

Sennosides Tablets: Each tablet containing total sennosides equivalent to 11.5 mg of sennoside B is usually available.

1.7 Anti-inflammatory drugs

Ulcerative colitis and Crohn disease are chronic inflammatory diseases of the intestinal tract. Effective management requires drug therapy, attention to nutrition, and in severe or chronic active disease, surgery. Acute attacks of mild to moderate severity affecting the rectum (proctitis) or the rectosigmoid (distal colitis) require local treatment with a corticosteroid (such as **hydrocortisone**) or an aminosalicylate (such as **sulfasalazine**). More extensive disease or disease not responsive to local treatment requires oral therapy; an oral aminosalicylate alone can sometimes be used in mild disease affecting the colon but addition of an oral corticosteroid for 4–8 weeks is usually necessary. Because of the risk of intestinal perforation, rectal administration of hydrocortisone must be used with extreme caution in patients with severe ulcerative disease and should not be given to such patients without conducting a thorough proctological examination. Severe extensive or fulminant disease needs hospital admission and intravenous corticosteroid administration; other therapy may include intravenous fluid and electrolyte replacement, blood transfusion, and possibly parenteral nutrition and antibacterials.

Metronidazole may be beneficial in the treatment of active Crohn disease particularly with perianal involvement, possibly through its antibacterial activity. Other antibacterials should be given if specifically indicated (for example, sepsis associated with fistulas and perianal disease) and for managing bacterial overgrowth in the small bowel.

Immunosuppressant drugs can be useful in patients with chronically active disease, particularly in patients unresponsive to corticosteroids or those with corticosteroid-dependent disease. **Methotrexate** is sometimes used to treat Crohn disease unresponsive to immunosuppressants.

HYDROCORTISONE

Indications: ulcerative colitis, proctitis, proctosigmoiditis.

Adverse effecs and cautions: local pain or burning sensation; rectal bleeding (reported with use of enema); exacerbation of untreated infections; suppositories may stain fabrics; systemic adverse effects.

Proctological examination required before treatment; systemic absorption may occur; prolonged use should be avoided.

Use of enemas in bowel obstruction, bowel perforation, or extensive fistulas and untreated infections should be avoided.

Dose: Ulcerative colitis, proctitis, by rectum (suppositories), ADULT 25 mg twice daily for 2 weeks; may be increased to 25 mg 3 times daily or 50 mg twice daily in severe cases; in factitial proctitis treatment may be required for 6–8 weeks

Ulcerative colitis, ulcerative proctitis, ulcerative proctosigmoiditis, by rectum (retention enema), ADULT 100 mg at night for 21 days or until clinical and proctological remission; if no clinical and proctological improvement after 21 days, discontinue; treatment for 2–3 months may be required for proctological remission; when used for more than 21 days, discontinue gradually using 100 mg every other night for 2–3 weeks

Preparation available

Hydrocortisone Acetate Suppository: Suppository containg 25 mg of hydrocoritisone acetate is usually available.

SULFASALAZINE

Indications: ulcerative colitis; Crohn's disease; severe rheumatoid arthritis.

Adverse effects and cautions: nausea, vomiting, epigastric discomfort, headache, rashes; occasionally fever, minor hematological abnormalities such as Heinz-body anaemia, reversible neutropenia, tolate deficiency; urine may be coloured orange.

It should be given with caution to the patient with history of allergy; hepatic and renal disease; G6PD deficiency; slow acetylator status. There is the risk of haematological and hepatic toxicity. Differential white cell, red sell and platelet counts initially and at monthly intervals for first three months, liver function tests at monthly intervals for first three months should be carried out.

Dose : Ulcerative colitis, by mouth, ADULT 1-2 g four times daily in acute attack until remission, reducing a maintenance dose of 500 mg 4 times daily; CHILD over 2 years, 40-60 mg/kg daily in acute attack, reducing to maintenance dose of 20-30 mg/kg daily.

Active Crohn disease, by mouth, ADULT 1-2 g 4 times daily in acute attack until remission occurs; CHILD over 2 years, 40-60 mg/kg daily in acute attack.

Ulcerative colitis, Crohn colitis, by rectum (suppositories, used alone or in conjunction with oral therapy) ADULT, 0.5-1 g morning and night after bowel movement. As an enema, ADULT 3 g at night, retained for at least 1 hour; CHILD not a suitable formulation.

Preparation available

Sulfasalazine Tablets*:* Each tablet containing 500 mg of sulphasalazine is usually available.

Sulfasalazine Suppositories: Each suppository containing 500 mg of sulphasalazine is usually available.

1.8 Anti - haemorrhoidal drugs

These are usually a combination of a local anaesthetic e.g. **lidocaine**, anti-inflammatory e.g. **hydrocortisone** and astringent such as **zinc oxide**, **hamamelis** and **bismuth subgallate**. Adjustment of the diet to avoid hard stools, the use of bulk-forming materials such as **bran** and high residue diet are helpful.

Indications: haemorrhoids (piles) and anal fissure.

Adverse effects and cautions: local irritation and extensive rashes may occur.

Local anaesthetics may cause sensitisation of the anal skin when used for more than 2 weeks. Corticosteroids are suitable for occasional short term use, but prolonged use can cause atrophy of the anal skin.

Antihaemorrhoidal preparations may be safely used during pregnancy and lactation.

1.9 Drugs affecting biliary composition and flow

The use of laparoscopic cholecystectomy and of endoscopic biliary techniques has limited the place of the bile acid ursodeoxycholic acid in gallstone disease. Patients should be given dietary advice (including avoidance of excessive cholesterol and calories) and they require radiological monitoring. Long-term prophylaxis may be needed after complete dissolution of the gallstones has been confirmed because they may recur in up to 25% of patients within one year of stopping treatment.

URSODEOXYCHOLIC ACID

Indications: dissolution of gall stones, primary biliary cirrhosis.

Adverse effects and cautions: nausea, vomiting, diarrhoea, gallstone calcification, pruritus.

The drug should be avoided in pregnancy, radio-opaque stones, non-functioning gall bladder.

Dose: Dissolution of gall stones, 8–12 mg/kg daily as a single dose at bedtime or in two divided doses, for up to 2 years; treatment is continued for 3–4 months after stones dissolve.

Primary biliary cirrhosis, 10-15 mg/kg daily in 2-4 divided doses.

Preparation available

Ursodeoxycholic acid Tablets: Each tablet containing 150 mg of ursodeoxycholic acid is usually available.

Ursodeoxycholic acid Capsulas: Each capsule containing 250 mg of ursodeoxycholic acid is usually available.

Chapter - Two

Drugs Acting on the Cardiovascular System

2.1 Anti-anginal drugs

2.1.1 Nitrates

GLYCERYL TRINITRATE* AND *ISOSORBIDE DINITRATE

Their action not specifically known but thought to cause a reduction of myocardial oxygen demand. The predominant action is venous dilatation. This causes venous pooling and reduces the volume of blood returning to the heart i.e. reduces pre-load. This in turn reduces pressure in the ventricle and thus lessens oxygen requirement. Nitrates do not increase total coronary blood flow in patients with angina but they appear to redistribute blood to ischaemic regions. The onset of action of nitroglycerin and isosorbide dinitrate is 1-3 minutes and 2-5 minutes respectively after sublingual administration. The onset of action of nitroglycerin ointment is within 30 minutes. Isosorbide dinitrate produces its effect 15-40 minutes after oral administration. The duration of action of sublingual nitroglycerin and isosorbide dinitrate is 30-60 minutes and 1-2 hour respectively. The duration of action of oral isosorbide dinitrate and glyceryl trinitrate ointment is 4-6 hour and 4-8 hour respectively.

Indications: acute attacks of angina pectoris, prophylaxis of angina pectoris, left ventricular failure.

Adverse effects and cautions: throbbing headache (most frequent in early therapy), dizziness, flushing, tachycardia, syncope and cardiovascular collapse.

Drug interactions: concomitant use of ACE inhibitors, Angiotensin–II antagonists, beta-blockers, calcium channel blockers and alcohol may cause hypotension.

GLYCERYL TRINIRATE

Nitroglycerin

Dose: Sublingually, 0.3 -1 mg, repeated as required.

Prophylaxis, 2.6-12.8 mg as controlled release tablets, 3 times daily or 10 mg 2-3 times daily.

Preparation available

Glyceryl Trinitrate Tablets: Each tablet containing 0.5 mg of glyceryl trinitrate is usually available.

Glyceryl Trinitrate Controlled Release Tablets: Each tablet containing 2.6 mg and 6.4 mg of glyceryl trinitrate are usually available.

ISOSORBIDE DINITRATE

Dose: Sublingually, 5-10 mg

By mouth, daily in divided doses, angina 30-120 mg, left ventricular failure 40-160 mg, up to 240 mg if required.

Preparation available

Isosorbide Dinitrate Tablets: Each tablet containing 5 mg and 10 mg of isosorbide dinitrate are usually available.

ISOSORBIDE MONONITRATE

The hepatic first pass metabolism is much less than for the dinitrate so systemic bioavailability is more reliable after oral administration.

Indications: prophylaxis of angina pectoris, adjunct in congestive heart failure.

Adverse effects and cautions: *see* under glyceryl trinitrate.

Dose: Initially 20 mg 2-3 times daily or 10 mg twice daily in those who have not previously received nitrates; up to 120 mg daily in divided doses.

Preparation available

Isosorbide Mononitrate Tablets: Each tablet containing 10 mg, 20 mg and 40 mg of isosorbide mononitrate are usually available.

Isosorbide Mononitrate Sustained Release Tablets: Each tablet containing 50 mg of isosorbide mononitrate is usually available.

2.1.2 Beta-blockers

These drugs block the agonistic effect of the sympathetic neuro- transmitters by competing for receptor binding sites. When they predominantly block the beta-1 receptor in cardiac tissue, they are said to be cardio-selective. When they block both beta-1 and beta-2 receptors they are said to be nonselective.

ATENOLOL

It is a selective beta-blocker which selectively inhibits cardiac and lipolytic beta-receptors at low doses. The drug competitively blocks beta-1 and beta-2 adrenergic receptors at high doses (more than 100 mg daily).

Indications: hypertension (efficacy similar to other beta-blockers), chronic stable angina, supra-ventricular arrhythmias, secondary prevention after acute myocardial infarction**.**

Adverse effects and cautions: see under propranolol.

Drug interactions: see under propranolol.

Dose: By mouth, hypertension, 25-50 mg daily (higher doses rarely necessary), angina, 100 mg daily in 1 or 2 doses, arrhythmias, 50-100 mg daily.

By intravenous injection, arrhythmias, 2.5 mg at a rate of 1 mg/minute, repeated at 5 minute intervals to a maximum of 10 mg.

Early intervention within 12 hours of infarction, 5 mg by slow intravenous injection, then by mouth 50 mg after 15 minutes, 50 mg after 12 hours, then 100 mg daily.

By intravenous infusion, arrhythmias, 150 micrograms/kg over 20 minutes, repeated every 12 hours if required.

Preparation available

Atenolol Tablets: Each tablet containing 50 mg and 100 mg of atenolol is usually available.

Atenolol Injection: Injection containing 500 micrograms/ml of atenolol in 10-ml vial is usually available.

BISOPROLOL

It is a cardioselective beta-blocker.

Indications: hypertension, angina, adjunct in heart failure.

Adverse effects and cautions: *see* under propranolol.

Dose: hypertension and angina, usually 10 mg once daily (5 mg may be adequate in some patients); maximum 20 mg daily.

Adjunct in stable moderate to severe heart failure, initially 1.25 mg once daily (in the morning) for 1 week then, if well tolerated, increased to 2.5 mg once daily for1 week, then 3.75 mg once daily for 1 week, then 5 mg once daily for 4 weeks, then 7.5 mg once daily for 4 weeks, then 10 mg once daily, maximum 10 mg daily.

Preparation available

Bisoprolol Tablets: Each tablet containing 2.5 mg, 5 mg and 10 mg of bisoprolol fumarate is usually available.

CARVEDILOL

It is a beta-blocker with additional an arteriolar vasodilating action and longer duration of action.

Indications: hypertension, angina, adjunct to diuretics, digoxin or ACE inhibitors in symptomatic chronic heart failure.

Adverse effects and cautions: postural hypotension, headache, dizziness, bradycardia and impotence.

Cautions: see under propranolol.

Dose: Hypertension, initially 12.5 mg once daily, increased after 2 days to usual dose of 25 mg once daily, if necessary may be further increased at intervals of at least 2 weeks to maximum 50 mg daily in single or divided doses.

Angina, initially 12.5 mg twice daily, increased after 2 days to 25 mg twice daily.

Adjunct in heart failure, initially 3.125 mg twice daily (with food), dose increased at intervals of at least 2 weeks to 6.25 mg twice daily, then to 12.5 mg twice daily, then to 25 mg twice daily.

Preparation available

Carvedilol Tablets: Each tablet containing 3.125 mg, 6.25 mg, 12.5 mg and 25 mg of carvedilol is usually available.

METOPROLOL

It is a selective beta-blocker which selectively inhibits cardiac and lipolytic beta-1 receptors at low doses. The drug competitively blocks beta-1 and beta-2 adrenergic receptors at high doses.

Indications: *see* under atenolol.

Adverse effects and cautions: see under propranolol.

Drug interactions: see under propranolol.

Dose: By mouth, hypertension, initially 100 mg daily, increased if necessary to 200 mg daily in 1-2 doses (higher doses rarely necessary). Angina, 50-100 mg 2-3 times daily. Arrhythmias, usually 50 mg 2-3 times daily up to 300 mg daily in divided dose if necessary. Migraine prophylaxis, 100-200 mg daily in divided doses. Thyrotoxicosis (adjunct), 50 mg 4 times daily.

By intravenous injection, arrhythmias up to 5 mg at rate 1-2 mg/minute, repeated after 5 minutes if necessary, total dose 10-15 mg. In surgery, 2-4 mg by slow intravenous injection at induction or to control arrhythmias developing during anaesthesia; 2 mg doses may be repeated to a maximum of l0 mg.

Early intervention within 12 hours of infarction, 5 mg by intravenous injection every 2 minutes to a maximum 15 mg, followed after 15 minutes by 50 mg by mouth every 6 hours for 48 hours; maintenance 200 mg in divided doses.

Preparation available

Metoprolol Tartrate Injection: Injection containing 1 mg of metoprolol tartrate per ml is usually available.

Metoprolol Tartrate Tablets: Each tablet containing 50 mg and 100 mg of metoprolol tartrate is usually available.

PROPRANOLOL

It is a non-selective beta-adrenergic blocking agent. The drug reduces the oxygen requirement of the heart because of beta adrenergic blockade.

The drug is also effective in hypertension. Precise mechanism of action is not known but possibilities include reduced cardiac output and inhibition of renin release by the kidneys. The effectiveness of drug in cardiac arrhythmia is because of decrease in conduction velocity through sinoatrial and atrioventricular nodes and decrease in myocardial automaticity via beta-adrenergic blockade.

Indications: chronic stable angina, supraventricular arrhythmias, secondary prevention after acute myocardial infarction, thyrotoxicosis, migraine prophylaxis.

Adverse effects and cautions: bradycardia and heart block, tiredness, fatigue, weakness, bronchospasm especially in asthmatics, congestive cardiac failure, hallucinations, nightmares and sexual dysfunction.

Propranolol should be used with caution in patients with inadequate cardiac function and bronchospastic disease. Abrupt withdrawal of drug may exacerbate angina symptoms or precipitate myocardial infarction in patients with coronary artery disease.

Safe use of propranolol during pregnancy has not been established. The drug gets distributed into milk; the drug should be used with caution in nursing women. Safety and efficacy of propranolol in children have not been established.

Drug interactions: When propranolol is administered with diuretics, ACE inhibitors, Angiotensin-II receptor antagonists, calcium channel blockers, the hypotensive effect of propranolol may be increased. Propranolol may enhance the bradycardia produced by cardiac glycosides.

Dose: By mouth, hypertension, initially 80 mg twice daily, increased at weekly intervals as required; maintenance 160-320 mg daily. Portal hypertension, initially 40 mg twice daily increased to 80 mg twice daily according to heart-rate; maximum 160 mg twice daily.

Phaeochromocytoma (only with an alpha blocker), 60 mg daily for 3 days before surgery.

Angina, initially 40 mg 2-3 times daily; maintenance 120-240 mg daily. Arrhythmias, hypertrophic obstructive cardiomyopathy, anxiety, tachycardia and thyrotoxicosis (adjunct), 10-40 mg 3-4 times daily.

Anxiety with symptoms such as palpitations, sweating, tremor, 40 mg twice daily, increased to 3 times daily if necessary.

Prophylaxis after infarction, 40 mg 4 times daily for 2-3 days, then 80 mg twice daily, beginning 5-21 days after infarction. Migraine prophylaxis and essential tremor, initially 40 mg 2-3 times daily; maintenance 80-160 mg daily.

By intravenous injection, arrhythmias and thyrotoxic crisis, 1 mg over 1 minute; if necessary repeat at 2 minute intravals; maximum 10 mg (5 mg in anaesthesia).

Preparation available

Propranolol Injection: Injection containing 1 mg per ml of propranolol hydrochloride is usually available.

Propranolol Tablets: Each tablet containing 10 mg, 40 mg and 80 mg of propranolol hydrochloride is usually available.

2.1.3 Calcium Antagonists

The exact mechanism by which these calcium antagonists inhibit calcium ion influx across the slow calcium channels in not known. By inhibiting calcium influx these drugs inhibit the contractile processes of cardiac and vascular smooth muscle, thereby coronary or systemic vascular tone may be diminished.

AMLODIPINE

It resembles nifedipine in its effects and does not reduce myocardial contractility. It does not produce clinical deterioration in heart failure. It has longer duration of action and can be given once daily.

Indications: prophylaxis of angina, hypertension.

Adverse effects and cautions: flushing, headache, ankle oedema, abdominal pain, palpitation, hypotension, impotence and gynaecomastia.

It should be used with caution in patients with hepatic impairment and pregnancy.

The drug is contraindicated in patients with unstable angina, cardiogenic shock, significant aortic stenosis and breast-feeding.

Drug interactions: *see* under verapamil.

Dose: hypertension or angina, initially 5 mg once daily; maximum 10 mg once daily.

Preparation available

Amlodipine Tablets: Each tablet containing 5 mg amlodipine (as besilate) is usually available.

DILTIAZEM

It is a calcium antagonist, similar to verapamil to cause sinoatrial and AV nodal depression. It has less negative inotropic effect than varapamil.

Indications, adverse effects and cautions: see under verapamil.

Dose: angina, 60 mg 3 times daily (ELDERLY initially twice daily); increased if necessary to 360 mg daily.

Preparation available

Diltiazem Tablets: Each tablet containing 30 mg and 60 mg of diltiazem hydrochloride is usually available.

FELODIPINE

It resembles amlodipine in its effects.

Indications: *see* under amlodipine.

Adverse effects and cautions: see under amlodipine.

Drug interactions: see under verapamil.

Dose: Hypertension initially 5 mg (ELDERLY 2.5 mg) daily in the morning; usual maintenance dose 5-10 mg once daily.

Angina, initially 5 mg daily in the morning, increased if necessary to 10 mg once daily.

NIFEDIPINE

It is a calcium antagonist and in contrast to verapamil, nifedipine has little or no effect on SA and AV nodal conduction. It has no anti-arrhythmic action.

Indications: prophylaxis of angina, hypertension.

Adverse effects and cautions: dizziness, giddiness, flushing, lightheadedness, peripheral oedema and palpitation.

Nifedipine should be used with caution in patients with congestive heart failure or aortic stenosis, especially in those receiving concomitant beta-blocking agents, because nifedipine may precipitate or worsen heart failure.

When nifedipine therapy is initiated in patients with angina, they should be warned that the drug may cause increased angina.

Nifedipine should be used during pregnancy only when the potential benefits justify the possible risks to the foetus.

Drug interactions: *see* under verapamil.

Dose: Raynaud's phenomenon, initially 5 mg 3 times daily with or after food; usual maintenance 5-20 mg 3 times daily.

Hypertension and angina prophylaxis, 20 mg twice daily with or after food. Usual maintenance 10-40 mg twice daily.

Preparation available

Nifedipine Capsules: Each capsule containing 5 mg and 10 mg of nifedipine is usually available.

NIMODIPINE

It is a calcium channel blocker and is related to nifedipine, but its effect is preferentially seen on cerebral arteries.

Indications: prevention and treatment of ischaemic neurological deficits following aneurysmal subarachnoid haemorrhage.

Adverse effects and cautions: hypotension, flushing, headache, sweating and feeling of warmth, gastro-intestinal disorders.

The drug is contra-indicated within one month of myocardial infarction and unstable angina.

The drug should be used with caution in cerebral oedema, hypotension, pregnancy, hepatic or renal impairment, concomitant administration of other calcium channel blockers or beta-blockers.

Dose: Prevention, by mouth, 60 mg every 4 hours, starting within 4 days of aneurysmal subarachnoid haemorrhage and continued for 21 days.

Treatment, by intravenous infusion via central catheter, initially 500 micrograms/hour, increased after 2 hours to 1 mg/hour if no severe fall in blood pressure; continue for at least 5 days (maximum 14 days); if surgical intervention during treatment, continue for at least 5 days after surgery; maximum total duration of use 21 days.

Preparation available

Nimodipine Tablets: Each tablet containing 30 mg nimodipine is usually available.

Nimodipine Injection: Each vial containing 200 micrograms/ml of nimodipine is usually available.

VERAPAMIL HYDROCHLORIDE

It has substantial inhibitory effects on the cardiac conduction system. Verapamil reduces after load and myocardial contractility.

Indications: supraventricular arrhythmias, angina pectoris, hypertension.

Adverse effects and cautions: constipation, nausea, abdominal discomfort, headache, dizziness, gingival hyperplasia, bradycardia and heartblock.

Verapamil should be used with caution in patients with moderately severe to severe ventricular dysfunction or heart failure since the drug may precipitate or worsen heart failure.

The drug is contraindicated in patients with severe hypotension, cardiogenic shock, second or third degree AV block. The drug should be used during pregnancy only when clearly needed.

Drug interactions: Incidence of congestive heart failure, arrhythmia and severe hypotension may be increased when verapamil is administered concurrently with a beta-adrenergic blocking agent.

Oral verapamil may increase serum digoxin concentration by 50-70% during the first week of verapamil therapy, dosage of digoxin should generally be reduced and the patient monitored closely for clinical response and digitalis toxicity.

Verpamil may potentiate the hypotensive actions of ACE inhibitors, Angiotensin-II receptor antagonists, beta-blockers and diuretics.

Dose: By mouth, supraventricular arrhythmias 40-120 mg 3 times daily; angina, 80-120 mg 3 times daily; hypertension, 240-480 mg daily in 2-3 divided doses.

By slow intravenous injection over 2 minutes (3 minutes in elderly), 5-10 mg (preferably with ECG monitoring); in paroxysmal tachyarrhythmias a further 5 mg after 5-10 minutes if required.

Preparations available

Verapamil Injection: Injection containing 2.5 mg/ml of verapamil hydrochloride is usually available. Verapamil injection should be protected from light.

Verapamil Tablets: Each tablet containing 40 mg, 80 mg and 240 mg of verapamil hydrochloride is usually available. They are coated.

2.2 Antiarrhythmic agents

Myocardial cells having this property of automacity are located in SA node, in certain areas of atria, in the lower part of AV node (at the junction of Bundle of His) and throughout Purkinje's network. The time from the beginning of action potential upstroke to the end of repolarisation i.e. from the begining of QRS to just after T-wave is called effective refractory period. Effective absolute refractory period is from the beginning of depolarisation to the beginning of upstroke of T wave.

Re-entry and antomacity are believed to be the major arrhythmogenic mechanisms. Majority of available antiarrhythmic drugs are believed to modify these mechanisms and are classified as follows:

Type I: They impair the entry of Na+ into the cells, slow the rate of depolarisation and as a result reduce the excitability of atrial and ventricular muscle. The rate of depolarisation in ectopic pacemakers is slowed more than that of SA node allowing SA node to retain domination of cardiac rhythm. Thus these drugs directly interfere with depolarisation of cardiac membrane i.e. exert membrane stabilising effect. They also have local anaesthetic properties.

Most of the drugs in this type increase effective refractory period abolishing impulse entry. All drugs except lignocaine which does not affect atrial cells may be used to treat arrhythmias arising in the atria and ventricles, e.g. quinidine, procainamide, disopyramide, lignocaine.

Type II: Beta BIockers: These drugs have antisympathetic activity. Sympathetic activity is believed to cause ectopic pacemaker activity and propagate reentrant rhythms particularly when myocardium has been sensitized by ischaemia e.g. after myocardial infarction; e.g. propranolol, metoprolol, atenolol, esmolol.

Type III: They prolong effective refractory period without altering the resting membrane potential or rate of depolarisation. The interval or time required for re-excitation is prolonged and hence arrhythmias are suppressed e.g. amiodarone.

Type IV: They block slow inward flux of calcium i.e. interfere with calcium conductance in SA and AV node. Depolarisation is also delayed increasing functional refractory period in AV node making it unresponsive to reentrant rhythms. Pacemaker activity of SA node is also suppressed, e.g. verapamil.

Many of the drugs classified as above may have more than one type of antiarrhythmic effect e.g. beta blockers, may have Type I effect.

ADENOSINE

It has very short duration of action.

Indications: paroxysmal supraventricular tachycardia (including Wolff-Parkinson-White syndrome)

Adverse effects and cautions: chest pain, transient facial flush, bronchospasm, nausea and severe bradycardia.

The drug should be used with caution in patients with arterial fibrillation or flutter and heart transplant.

The drug is contraindicated in patients with pre-existing second or third degree AV block, asthma and sick sinus syndrome.

Dose: Rapid intravenous injection into central or large peripheral vein, 3 mg over 2 seconds with cardiac monitoring; if necessary followed by 6 mg after 1-2 minutes, and then by 12 mg after a further 1-2 minutes.

AMIODARONE

It has a very long half-life and only needs to be given once daily. It is used in the treatment of arrhythmias particularly when other drugs are ineffective or contraindicated.

Indications: paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation or flutter, and ventricular fibrillation

Adverse effects and cautions: nausea, vomiting, raised serum transaminases, bradycardia and pulmonary toxicity

Liver function test and thyroid function tests should be done before

treatment and then every 6 months. Serum potassium measurement and chest X-ray should be done before treatment.

The drug is contraindicated in sinus bradycardia, SA heart block and iodine sensitivity.

Safe use of drug in second and third trimester of pregnancy or breast–feeding has not been established.

Dose: 200 mg 3 times daily for 1 week reduced to 200 mg twice daily; ventricular fibrillation, by intravenous infusion over at least 3 minutes 300 mg.

ATENOLOL: *see* under section 2.1.2, beta blockers.

DISOPYRAMIDE

Indications: atrial and ventricular arrhythmias including those resistant to lignocaine.

Adverse effects and cautions: hypotension, AV block, dry mouth, blurred vision.

The drug should be used with caution and in reduced dose in patients with renal or hepatic insufficiency.

The drug is contraindicated in patients with preexisting second or third degree AV block and cardiogenic shock. Safe use of drug in third trimester of pregnancy has not been established.

Dose: By mouth 300-800 mg daily in divided doses.

By slow intravenous injection, 2 mg/kg over at least 5 minutes to a maximum of 150 mg, with ECG monitoring.

Preparation available

Disopyramide Capsules: Each capsule containing the equivalent of 100 mg and 150 mg of disopyramide is usually available.

Disopyramide Injection: Injection containing 10 mg disopyramide (as phosphate) in 5-ml ampoule is usually available.

ISOPRENALINE

It is an almost pure beta stimulator and has positive inotropic action on the heart i.e. increases cardiac output, it also causes peripheral vasodilation.

Indications: bradycardia in patients with heart block, control attacks of Stokes Adams Syndrome.

Adverse effects and cautions: tachycardia, hypotension, arrhythmias, tremor and sweating.

The drug is contraindicated in patients with preexisting cardiac arrhythmias (especially tachycardia) other than those arrhythmias which may respond to drug.

Dose: By mouth, initially 30 mg every 6 hours, range 90-840 mg daily (but oral route rarely used). By intravenous infusion, 0.5-10 micrograms/minute.

Preparation available

Isoprenaline Injection: Injection containing 0.2 mg per ml of isoprenaline hydrochloride is usually available. Isoprenaline injection should be protected from light and stored at a temperature not exceeding 25°.

Isoprenaline Tablets: Each tablet containing 20 mg of isoprenaline sulfate is usually available.

LIDOCAINE HYDROCHLORIDE
Lignocaine Hydrochloride

Indications: ventricular arrhythmias, especially after myocardial infarction.

Adverse effects and cautions: bradycardia, hypotension, asystole, paresthesia, twitching and dizziness.

Lignocaine should be used with caution to patients with liver disease and congestive heart failure.

The drug is contraindicated in all grades of AV block, SA disorders and severe myocardial depression.

Safe use of drug during pregnancy has not been established.

Dose: By intravenous injection, in patients without gross circulatory impairment, 100 mg as a bolus over a few minutes, followed by infusion of 4mg/minute for 30 minutes, 2 mg/minute for 2 hours, then 1 mg/minute.

Preparation available

Lidocaine Injection: Injection containing 1% and 2% of lidocaine hydrochloride is usually available.

PROCAINAMIDE HYDROCHLORIDE

Indications: ventricular arrhythmias especially after myocardial infarction, arterial tachycardia.

Adverse effects and cautions: nausea, rashes, diarrhoea, lupus erythematosus syndrome, reduced cardiac output and heart failure.

The drug is contraindicated in patients with second or third degree heart block, heart failure and hypotension.

The drug should be used with caution in patients with renal and hepatic disease. Safe use of drug during pregnancy has not been established.

Drug interactions: When procainamide is administered with beta blockers, other antiarrhythmics, there is increased myocardial depression.

Dose: By mouth, ventricular arrhythmias, up to 50 mg/kg daily in divided doses every 3-6 hours, preferably controlled by monitoring plasma-procainamide concentration (therapeutic concentration usually within range 3-10 micrograms/ml); atrial arrhythmias, higher doses may be required.

By slow intravenous injection, rate not exceeding 50 mg/minute, 100 mg with ECG monitoring repeated at 5 minute intervals until arrhythmia controlled; maximum 1g.

By intravenous infusion 500-600 mg over 25-30 minutes with ECG monitoring, followed by maintenance at rate of 2-6 mg/minute, then if necessary oral antiarrhythmic treatment as above, starting 3-4 hours after infusion.

Preparation available

Procainamide Injection: Injection containing procainamide hydrochloride 100 mg per ml is usually available.

Procainamide Tablets: Each tablet containing 250 mg of procainamide hydrochloride is usually available.

QUINIDINE

Indications: Suppression of supraventricular tachycardia, ventricular arrhythmias.

Adverse effects and cautions: hypotension, nausea, vomiting, cinchonism, thrombocytopenia and haemolytic anaemia.

Quinidine should be used with extreme caution in patients with first or second degree heart block, uncompensated heart failure and myocarditis.

The drug is contraindicated in patients with complete AV block. Safety and efficacy of drug in children have not been established. The drug should be used during pregnancy when clearly needed.

Dose: By mouth 200 - 400 mg 3-4 times daily.

Preparation available

Quinidine Tablets: Each tablet containing 100 mg and 200 mg of quinidine, as sulfate is usually available.

PROPRANOLOL: *see* under section 2.1.2, beta blockers.

VERAPAMIL: *see* under section 2.1.3, calcium antagonists.

2.3 Antihypertensive drugs

No consistent or important differences have been found between the major classes of antihypetensives in term of antihypertensive effects, side effects or change to quality of life.

ATENOLOL: *see* under section 2.1.2, beta-blockers

CAPTOPRIL

It is an angiotensin converting enzyme (ACE) inhibitor. The drug appears to reduce blood pressure in hypertensive patients and produce beneficial haemodynamic effects in patients with congestive heart failure mainly by suppressing the renin- angiotensin - aldosterone system. Captopril prevents the conversion of angiotensin I to angiotensin II (a potent vasoconstrictor) by competing with the physiologic substrate (angiotensin I) for the active site of ACE, the affinity of the drug for ACE is far greater than that of angiotensin I.

Indications: mild to moderate essential hypertension, adjunctive treatment in congestive heart failure, severe hypertension resistant to other treatment, following myocardial infarction, diabetic nephropathy in insulin dependent diabetes.

Adverse effects and cautions: rash, profound hypotension (usually with first dose, especially in patients taking high dose of diuretics, on low sodium diet, dehydrated, on dialysis), taste impairment, leucopenia, proteinuria, persistent dry cough. Captopril may cause neutropenia and must be used under close supervision. Drug should be used with caution in patients with renal impairment.

The drug should be used in pregnancy only when the potential benefits justify the possible risk to the foetus. The safety and efficacy of drug in children have not been established. Captopril should be used with caution in nursing mothers.

Drug interactions: Captopril decreases aldosterone secretion. It is unwise to combine drug with potassium supplements or potassium sparing diuretics. Hyperkalaemia may result especially if there is any pre-existing renal impairment.

When captopril is administered with alcohol, alpha blockers, general anesthetic agents, angiotensin II receptor antagonists, beta blockers, calcium channel blockers, the hypotensive effect is increased.

Dose: Hypertension, used alone, initially 12.5 mg twice daily; if used in addition to diuretic, in elderly, initially 6.25 mg twice daily (first dose at bedtime); usual maintenance dose 25 mg twice daily; maximum 50 mg twice daily (rarely 3 times daily in severe hypertension).

Heart failure (adjunct), initially 6.25-12.5 mg under close medical supervision, usual maintenance dose 25 mg 2-3 times daily.

Diabetic nephropathy, 75-100 mg daily in divided doses, in severe renal impairment, initially 12.5 mg twice daily.

Prophylaxis after infarction in clinically stable patients with asymptomatic or symptomatic left ventricular dysfunction, initially 6.25 mg, starting as early as 3 days after infarction, dose increased over several weeks to 150 mg daily in divided doses.

Preparation available

Captopril Tablets: Each tablet containing 25 mg and 50 mg of captopril is usually available.

ENALAPRIL

It is an angiotensin converting enzyme inhibitor. The activity of enalapril is due to active metabolite, enalaprilat. Its duration of action is approximately 24 hours, captopril acts for 6-12 hours.

Indications: hypertension, heart failure.

Adverse effects and cautions: persistent dry cough, headache, loss of taste, diarrhoea, hypotension (usually with initial dose), skin rash and angioedema of the extremities, myocardial infarction, angina, impotence.

The drug should be used with caution in patients with impaired liver function. The safe use of drug in pregnancy has not been established.

Drug interactions: *see* under captopril.

Dose: Hypertension used alone, initially 5 mg daily; if used in addition to diuretic, in elderly patients or in renal impairment, initially 2.5 mg daily; usual maintenance dose 20 mg daily maximum 40 mg daily.

Heart failure (adjunct), asymptomatic left ventricular dysfunction, initially 2.5 mg daily under close medical supervision; increased over 2-4 weeks to usual maintenance 20 mg daily.

Preparation available

Enalapril Maleate Tablets: Each tablet containing 2.5 mg, 5 mg, 10 mg and 20 mg of enalapril maleate is usually available.

FUROSEMIDE

It is a loop-diuretic. It inhibits the reabsorption of electrolytes in the ascending limb of the loop of Henle. The drug also decreases reabsorption of sodium and chloride and increases potassium excretion in the distal renal tubule. It acts within 1 hour of oral administration and diuresis is complete within 6 hours.

Indications: hypertension resistant to thiazide, oedema, oligourea due to renal failure.

Adverse effects and cautions: hypokalemia, hyponatraemia, tinnitus, reversible or permanent hearing impairment or reversible deafness, rashes, loss of appetite, vomiting, diarrhoea, constipation, hyperuricaemia and gout.

Furosemide should be used with caution in patients with hepatic cirrhosis.

The drug is contraindicated in patients with renal failure with anuria. Furosemide should be used during pregnancy only when the potential benefits justify the possible risks to the foetus.

Drug interactions: Patients receiving cardiac glycoside, furosemide predisposes the patient to digitalis toxicity principally due to hypokalemia. The hypotensive effects enhanced when given concomitantly with ACE inhibitors, alcohol, alpha blockers, general anaesthetic agents, angiotensin-II receptor antagonists, beta blockers and calcium channel blockers. Concomitant administration of furosemide and aminoglycosides may result in increased incidence of ototoxicity.

Dose: By mouth, oedema, initially 40 mg in the morning, maintenance 20 - 40 mg daily, increased in resistant oedema to 80 mg daily; CHILD 1-3 mg/kg daily. Oliguria, initially 250 mg daily if necessary larger closes, increasing in steps of 250 mg, may be given every 4-6 hours to maximum of a single dose of 2 g (rarely used).

By intramuscular injection or slow intravenous injection (rate not exceeding 4 mg/minutes, initially 20-50 mg; CHILD 0.5-1.5 mg/kg to a maximum daily dose of 20 mg. By intravenous infusion (by syringe pump if necessary) in oliguria, initially 250 mg over 1 hour (rate not exceeding 4 mg/minute), if satisfactory urine output not obtained in the subsequent hour further 500 mg over 2 hours, then if no satisfactory response within subsequent hour, further 1 g over 4 hours, if no response obtained dialysis probably required; effective dose (up to 1 g) can be repeated every 24 hours.

Preparation available

Furosemide Injection: An injection containing 10 mg/ml of furosemide is usually available. Furosemide injection should be protected from light.

Furosemide Tablets: Each tablet containing 40 mg of furosemide is usually available.

HYDRALAZINE HYDROCHLORIDE

Causes direct relaxation of arteriolar vascular smooth muscle with a consequent decrease in peripheral vascular resistance and a fall in blood pressure. Heart rate, stroke volume and cardiac output is increased through reflex sympathetic stimulation.

Indications: moderate to severe hypertension

Adverse effects and cautions: tachycardia, palpitation, hypotension, nausea, vomiting, systemic lupus erythematosus like syndrome, weight gain and headache. Patients who are slow acetylator of hydralazine may have high risk of SLE. Complete blood count, LE cell preparation, antinuclear antibody should be performed before and periodically during prolonged hydralazine therapy.

Safe use of drug during pregnancy has not been established in first and second trimester.

Drug interactions: When used with diuretics or other anti-hypertensives, the hypotensive effect increased.

Dose: By mouth, 25 mg twice daily, increased to a maximum of 50 mg twice daily.

By slow intravenous injection, 5-10 mg over 20 minutes, may be repeated after 20-30 minutes. By intravenous infusion, initially 200-300 micrograms/minute, maintenance usually 50-150 micrograms/minute.

Preparation available

Hydralazine Injection: Each sealed container containing 20 mg of hydralazine hydrochloride in usually available. It is prepared by dissolving hydralazine hydrochloride for injection in the requisite amount of water for injection immediatly before use. For intravenous infusion hydralazine hydrochloride for injection should be dissloved in, and then diluted with an appropriate volume of a suitable diluents. Hydralazine injection deteriorates on storage and should be used immediately after preparation. The sealed container should be protected from light and stored at a temperature not exceeding 25°. Solution containing glucose should not be used in the preparation of the intravenous infusion.

Hydralazine Tablets: Each tablet containing 25 mg of hydralazine hydrochloride is usually available. Hydralazine tablets should be protected from light and stored at a temperature not exceeding 25°.

HYDROCHLOROTHIAZIDE

It is a thiazide diuretic which enhances excretion of sodium, chloride and water by interfering with the transport of sodium ions across the renal tubular epithelium. The primary site of action is at the beginning of distal convoluted tubule. It acts within 1-2 hours of oral administration and effect lasts for about 12-24 hours. In addition to increasing sodium and chloride excretion, thiazides affect excretion of other electrolytes. Potassium excretion is substantially increased because of the increased amount of sodium reaching the distal tubular site of the sodium potassium exchange.

Thiazides have hypotensive activity in hypertensive patients, and they augment the action of other hypotensive agents. The precise mechanism of hypotensive action has not been determined, but it has been postulated that part of this effect is caused by direct arteriolar dilation.

Indications: hypertension, oedema.

Adverse effects and cautions: hypokalaemia, hyperuricemia, skin rash, thrombocytopenia, hyperglycemia, postural hypotension, impotence.

Thiazides should be used with cautions in patient with severe renal disease because the drugs decrease glomerular filtration rate (GFR) and may precipitate azotemia.

The routine use of thiazides is contraindicated in pregnant women, severe hepatic impairment.

Drug interaction: patients receiving cardiac glycoside, hypokalaemia produced by the thiazides predispose the patients to digitalis toxicity.

The hypotensive effect of most other hypotensive agents like ACE inhibitors, alpha blockers, angiotensin-II receptor antagonists, beta blockers and calcium channel blockers is enhanced by the thiazide diuretics.

Dose: Oedema, initially 25-50 mg daily, maintenance 25-50 mg on alternate days. Hypertension, 12.5 mg daily, can be increased to 25-50 mg daily if necessary.

Preparation available

Hydrochlorothiazide Tablets: Each tablet containing 25 mg and 50 mg of hydrochlorothiazide is usually available.

INDAPAMIDE

It is a diuretic. Its antihypertensive effect is thought to be the result of reduction in peripheral vascular resistance.

Indications: hypertension, congestive heart failure

Adverse effects and cautions: skin rash, hypokalaemia, anorexia, diarrhoea, orthostatic hypotension.

The drug should be used with caution in pregnancy and breast-feeding.

Efficacy and safety of the drug has not been established in children.

The drug is contra-indicated in severe hepatic impairment.

Dose: Orally, 2.5 mg once a day, adjusted according to response after 1-4 weeks up to 5 mg once a day.

Preparation available

Indapamide Tablets: Each tablet containing 2.5 mg of indapamide is usually available.

LISINOPRIL

It is an ACE inhibitor.

Indications: essential and renovascular hypertension, adjunctive treatment in congestive heart failure, following myocardial infarction in haemodynamically stable patients, diabetic nephropathy in normotensive

insulin-dependent and hypertensive non-insulin dependent diabetes mellitus.

Adverse effects and cautions: profound hypotension, rash, tachycardia, myocardial infarction, sweating, impotence.

cautions: *see* under captopril.

Dose: Hypertension, initially 10 mg daily, if used in addition to diuretic or renal impairment, initially 2.5-5 mg daily; usual maintenance dose 20 mg once daily; maximum 80 mg daily.

Heart failure (adjunct), initially 2.5 mg daily; usual maintenance dose 5-20 mg daily.

Diabetic nephropathy, initially 2.5 mg daily adjusted to achieve a sitting diastolic blood pressure below 75 mm Hg in normotensive insulin dependent diabetes and below 90 mm Hg in hypertensive non-insulin dependent diabetes; usual dose range 10-20 mg daily.

Prophylaxis after myocardial infarction, systolic blood pressure over 120 mm Hg, 5 mg within 24 hours, followed by further 5 mg 24 hours later, then 10 mg after a further 24 hours, and continuing with 10 mg once daily for 6 weeks; systolic blood pressure 100-120 mm Hg, initially 2.5 mg, increasing to maintenance dose of 5 mg once daily.

Preparation available

Lisinopril Tablets: Each tablet containing 2.5 mg, 5 mg, 10 mg and 20 mg of lisinoprol (as dehydrate) is usually available.

LOSARTAN

It is angiotensin–II receptor antagonists. Unlike ACE inhibitors, it does not inhibit the breakdown of bradykinin and other kinins, thus unlikely to cause the persistent dry cough.

Indications: hypertension, congestive heart failure, diabetic nephropathy in type 2 diabetes mellitus.

Adverse effects and cautions: hypotension, dizziness, diarrhoea, pruritus, rash, taste disturbance, thrombocytopenia.

The drug should be avoided in pregnancy and breast-feeding.

The drug should be used with caution in renal artery stenosis, moderate to severe renal impairment or liver impairment, aortic or mitral valve stenosis.

Dose: Usually, 50 mg once daily (intravascular volume depletion initially 25 mg once daily); if necessay increased after several weeks to 100 mg once daily.

Preparation available

Losartan Tablets: Each tablet containing 25 mg and 50 mg of losartan is usually available.

METHYLDOPA

Methyldopa is decarboxylated to form alphamethylnorepinephrine in the CNS, where it lowers arterial pressure by stimulation of central alpha receptor. At central level alpha-2-receptor stimulation occurs in medulla and as a result,

decrease in sympathetic outflow occurs.

Indications: hypertension in pregnancy.

Adverse effects and cautions: oedema, vomiting, dry mouth, sedation, dizziness, sexual dysfunction, lupus erythematosus like syndrome.

The drug should be used with caution in patients with history of liver disease or renal impairment.

The drug is contraindicated in patients with active liver disease and depression. The drug can be used during pregnancy.

Dose: By mouth, 250 mg 2-3 times daily, gradually increased at intervals of 2 or more days; maximum daily dose 3 g.

Preparation available

Methyldopa Tablets: Each tablet containing the equivalent of 250 mg of anhydrous methyldopa is usually available. They are coated. Methyldopa tablets should be protected from light.

METOPROLOL: *see* under section 2.1.2, beta-blockers

MINOXIDIL

It reduces peripheral vascular resistance and blood pressure as a result of a direct vasodilating effect on vascular smooth muscle, mainly on arterioles.

Indications: severe hypertension.

Adverse effects and cautions: oedema, weight gain, tachycardia and hypertrichosis (elongation, thickening and increased pigmentation of fine body hair).

Minoxidil should be used with caution in patients with recent myocardial infarction.

The drug is contraindicated in patients with pheochromocytoma, since drug's hypotension effect may stimulate secretion of catecholamine from the tumour.

Minoxidil should be used during pregnancy only when the potential benefits justify the possible risk to the foetus. Minoxidil is distributed into milk; the drug should be used with caution in nursing women.

Drug interactions: When minoxidil is used with diuretics or other hypotensive drugs, the hypotensive effect of minoxidil is increased.

Dose: Intially 5 mg (elderly 2.5 mg) daily, in 1-2 doses, increased by 5-10 mg every 3 or more days; maximum usually 50 mg daily.

Preparation available

Minoxidil Tablets: Each tablet containing 5 mg and 10 mg of minoxidil is usually available.

NIFEDIPINE: *see* under section 2.1.3, calcium antagonists.

PRAZOSIN

Prazosin and terazosin are selective α_1-blocking drugs. Terazosin is more effective than finasteride in benign prostatic hyperplasia.

Indications: hypertension.

Adverse effects and cautions: postural hypotension, dizziness, headache, palpitation, drowsiness, priapism.

The drug is contraindicated in congestive heart failure.

The drug should be used with caution in pregnancy, renal or hepatic impairment. The first dose of the drug may cause collapse due to hypotension.

Dose: 500 micrograms 2-3 times daily for 3-7 days, the initial dose on retiring to bed at night; increased to 1 mg 2-3 times daily for further 3-7 days.

Preparation available

Prazosin Tablets: Each tablet containing 1 mg, 2.5 mg and 5 mg of prazosin is usually available.

PROPRANOLOL**:** *see* under section 2.1.2, beta-blockers.

RAMIPRIL

It is ACE inhibitors. It is metabolised to an active metabolite ramiprilat.

Indications: hypertension, congestive heart failure, prophylaxis after myocardial infarction, prophylaxis of cardiovascular events or stroke.

Adverse effects and cautions: see under enalapril.

Dose: Hypertension, initially 1.25 mg once daily, increased at intervals of 1-2 weeks; usual range 2.5-5 mg once daily; maximum 10 mg once daily.

Heart failure (adjunct), initially 1.25 mg once daily under close medical supervision, increased if necessary at intervals of 1-2 weeks; maximum 10 mg daily.

Prophylaxis after myocardial infarction, initially 2.5 mg twice daily, increased after 2 days to 5 mg twice daily; maintenance 2.5-5 mg twice daily.

Prophylaxis of cardiovascular evets or stroke, initially 2.5 mg once daily, increased after 1 week to 5 mg once daily, then increased after a further 3 weeks to 10 mg once daily.

Preparation available

Ramipril Tablets/Capsules: Each tablet/capsule containing 1.25 mg, 2.5 mg, 5 mg and 10 mg of ramipril is usually available.

RESERPINE

It depletes noradrenaline from its storage sites in the adrenergic nerves. Sympathetic activity is reduced, peripheral resistance is lowered and blood pressure falls.

Indications: hypertension.

Adverse effects and cautions: drowsiness, nasal congestion, depression, bradycardia.

Reserpine is contraindicated in patients with mental depression, active peptic ulcer.

Safe use of drug in pregnancy has not been established.

Dose: Hypertension, initial 100-500 micrograms daily for 2 weeks, subsequently reduced to the lowest dose necessary to maintain the response, dose of up to 250 micrograms and dose normally should not exceed 500 micrograms.

Preparation available

Reserpine Tablets: Each tablet containing 250 micrograms of reserpine is usually available.

SILDENAFIL

It is a phosphodiesterase type-5 inhibitor.

Indications: pulmonary arterial hypertension, erectile dysfunction.

Adverse effects and cautions: headache, flushing, visual disturbances, vomiting, dizziness, raised intra-ocular pressure, rash, priapism.

The drug is contraindicated in patients receiving nitrates, in patients in whom sexual activity inadvisable, hypotension, myocardial infarction, unstable angina.

The drug should be used with caution in cardiovascular disease, anatomical deformation of the penis, hepatic impairment, renal impairment, active peptic ulceration, patients receiving other drugs.

Dose: Pulmonary arterial hypertension, 20 mg 3 times daily; CHILDREN aged from neonates up to 18 years of age, 250 to 500 micrograms/kg given orally every 4 to 8 hours, adjusted according to response up to a maximum of 2 mg/kg every 4 hours.

Erectile dysfunction, ADULT over 18 years initially 50 mg approximately 1 hour before sexual activity, subsequent doses adjusted according to response to 25-100 mg as single dose as needed; maximum single dose 100 mg.

Sildenafil should not be taken more than once in 24 hours.

Preparation available

Sildenafil Tablets: Each tablet containing 25 mg, 50 mg and 100 mg of sildenafil (as citrate) is usually available.

SODIUM NITROPRUSSIDE

It is given by intravenous infusion to control severe hypertensive crisis.

Indications: hypertensive crisis; controlled hypotension in anaesthesia; acute or chronic heart failure.

Adverse effects and cautions: associated with over rapid reduction in blood pressure, headache, dizziness, nausea, retching, abdominal pain, perspiration, palpitations, apprehension, retrostemal discomfort; occasionally reduced platelet count, acute transient phlebitis.

It should be used with caution in patient with hypothyroidism, severe renal impairment, ischaemic heart disease, impaired cerebral circulation, blood pressure and plasma cyamide concentration should be monitored.

Dose: Hypertensive crisis, intravenous infusion, 0.5-1.5 micrograms/kg/minute initially then adjusted; usual range 0.5-6 micrograms/kg/minute.

Heart failure 10-15 micrograms/minute, increased every 5-10 minutes as necessary, usual range 10-200 micrograms/minutes.

Preparation available

Sodium Nitroprusside Intravenous Solution: Solution containing 10 mg of sodium nitroprusside per ml is usually available.

TAMSULOSIN

It is also a selective alpha-blocker.

Indications: benign prostatic hyperplasia.

Adverse effects and cautions: see under prazosin; also contra-indicated in severe liver impairment.

Dose: 400 micrograms daily as a single dose.

Preparation available

Tamsulosin Capsules: Each capsule containing 400 micrograms of tamsulosin hydrochloride is usually available.

TERAZOSIN

It is also a selective alpha-blocker.

Indications: hypertension, benign prostatic hyperplasia (BPH).

Adverse effects and cautions: *see* under prazosin, also thrombocytopenia, decreased libido, weight gain, dyspnoea.

Dose: Hypertension, 1 mg at bed time; dose doubled after 7 days if necessary; usual maintenance dose 2-10 mg once daily.

BPH, 1 mg at bed time; if necessay dose may be doubled at intervals of 1-2 weeks according to response.

Preparation available

Terazosin Tablets: Each tablet containing 1 mg, 2 mg and 5 mg of terazosin is usually available.

VALSARTAN

It is angiotensin-II receptor antagonist. It is as effective as captopril in patients with myocardial infarction complicated by left ventricular systolic dysfunction.

Indications: hypertension, myocardial infarction with left ventricular failure or left ventricular systolic dysfunction.

Adverse effects and cautions: *see* under losartan.

Dose: Hypertension, usually 80 mg once daily (initially 40 mg once daily in intravascular volume depletion); if necessary increased after at least 4 weeks to 160 mg daily.

Myocardial infarction, initially 20 mg twice daily increased over several weeks to 160 mg twice daily if tolerated.

Preparation available

Valsartan Capsules: Each capsule containing 40 mg, 80 mg and 160 mg of valsartan is usually available.

2.4 Cardiac glycosides

They act by inhibiting the activity of the Na+/K+/ATP-ase pump which increases the calcium ions available for contraction. The positive ionotropic response produced, improves cardiac output and reduces the residual volume.

Cardiac glycosides prolong effective refractory period of AV node and reduce the number of impulses reaching the ventricle and thus allows them to fill well before contraction.

DIGOXIN

It is the cardiac glycoside of choice for routine use.

Indications: heart failure, supra ventricular arrhythmias (particularly atrial fibrillation)

Adverse effects and cautions: loss of appetite, nausea, vomiting and yellow vision. Commonest toxic effect in the heart is irritability as indicated by ventricular extrasystole, heart block, bigeminy (coupling). Toxicity manifests when plasma level is more than normal of 2 nanogram. Hypokalaemia predisposes to it.

The drug should be used with caution in patients with hypothyroidism, acute myocardial infarction, since the likelihood of cardiac glycoside induced arrhythmias is increased in these patients.

The drug is contraindicated in patients with second degree AV block, ventricular tachycardia or fibrillation.

Safe use of drug during pregnancy has not been established.

Drug interactions: When digoxin is administered with beta blockers and verapamil, there is increased risk of AV block and bradycardia.

Dose: By mouth, rapid digitalization, 1-1.5 mg in divided doses over 24 hours; less urgent digitalisation, 0.25-0.5 mg daily (higher dose divided).

Maintenance, 62.5-500 micrograms daily (higher dose divided) according to renal function and, in atrial fibrillation, on heart rate response, usual range, 125-250 micrograms daily (elderly 125 micrograms)

By intravenous infusion, 0.75-1 mg, (suggested volume 50 ml) over two or more hours (too rapid a rate of administration is associated with nausea and

risk of arrhythmias); this is followed by normal maintenance therapy by mouth.

Preparation available

Digoxin Injection: A sterile solution of digoxin in water for injection and ethanol or other suitable solvents. Each ml containing 250 micrograms of digoxin is usually available. Digoxin injection should be protected from light.

Digoxin Tablets: Each tablet containing 62.5 micrograms, 125 micrograms and 250 micrograms of digoxin is usually available.

Paediatric Digoxin Oral Solution: Solution containing 50 micrograms of digoxin per ml in a suitable flavoured vehicle is usually available. It should be protected from light and stored at a temperature not exceeding 25°.

2.5 Diuretics

They can be classified in the following four groups:

a. Thiazides and related diuretics e.g., hydrochorothiazide, bendrofluazide, chlortalidone.
b. Loop diuretics e.g. frusemide, bumetanide.
c. Potassium-sparing diuretics e.g. spironolactone, amiloride, triamterene.
d. Osmotic diuretics: mannitol

AMILORIDE HYDROCHLORIDE

It is a potassium-sparing diuretic, which acts about 2 hours after oral administration, reaching a peak in 6-10 hours and persisting for about 24 hours.

Indications: oedema, potassium conservation with thiazide and loop diuretic.

Adverse effects and cautions: hyperkalaemia, hyponatraemia, postural hypotension, diarrhea, loss of appetite, dizziness.

Amiloride should be used with caution in patients with diabetes mellitus, mild renal impairment.

The drug is contraindicated in patients with hyperkalaemia and moderate renal impairment.

Dose: Used alone, initially 10 mg daily or 5 mg twice daily, maximum 20 mg daily.

With other diuretics, congestive heart failure and hypertension, initially 5-10 mg daily; cirrhosis with ascites, initially 5 mg daily.

Preparation available

Amiloride Tablets: Each tablet containing 5 mg of amiloride hydrochloride is usually available.

BENDROFLUAZIDE

It is a thiazide diuretic with duration of diuretic action more than 18 hours.

Indications: hypertension, oedema.

Adverse effects and cautions: *see* under hydrochlorothiazide.

Dose: oedema, initially 5-10 mg in the morning, daily or on alternate days; maintenance 5-10 mg 1-3 times weekly

Hypertension**,** 2.5 mg in the morning; higher doses rarely necessary.

Preparation available

Bendrofluazide Tablets: Each tablet containing 2.5 mg of bendrofluazide is usually available.

BUMETANIDE

It is a loop diuretic which acts directly on the ascending limb of loop of Henle to inhibit sodium and chloride reabsorption. Bumetanide also appears to inhibit electrolyte reabsorption in the proximal renal tubule. It acts within 1 hour of oral administration and diuresis is complete in 6 hours. The drug decreases uric acid excretion and increases serum uric acid concentration.

Indications: oedema, oliguria due to renal failure.

Adverse effects and cautions: see under furosemide.

Bumetamide should be used with caution in patients with hepatic cirrhosis and ascites since sudden alterations in fluid and electrolyte balance may precipitate hepatic encephalopathy.

The drug is contraindicated in patients with renal failure with anuria.

Bumetanide should be used during pregnancy only when the potential benefits justify the possible risk to foetus.

Drug interactions: *see* under furosemide.

Dose: By mouth, 1 mg in the morning, repeated after 6-8 hours if necessary; severe cases, increased up to 5 mg or more daily; elderly, 0.5 mg daily may be sufficient.

Preparation available

Bumetanide Tablets: Each tablet containing 1 mg of bumetanide is usually available

CHLORTALIDONE

Chlorthalidone

It is pharmacologically similar to thiazide diuretics. Its diuretic action lasts for 24-72 hours.

Indications: hypertension, oedema, mild to moderate chronic heart failure.

Adverse effects and cautions: see under hydrochlorothiazide.

Dose: Oedema, up to 50 mg daily.

Hypertension, 25 mg increased to 50 mg if necessary, in the morning.

Heart failure, 25-50 mg in the morning, increased if necessary to 100-200 mg daily.

Preparation available

Chlortalidone Tablets: Each tablet containing 50 mg of chlortalidone is usually available.

FUROSEMIDE: *see* under section 2.3, antihypertensive drugs.

HYDROCHLOROTHIAZIDE: *see* under section 2.3, antihypertensive drugs.

MANNITOL

The drug acts mainly by elevating the osmotic pressure of the glomerular filtrate to such extent that tubular reabsorption of water and solutes is affected. Mannitol is effective only when renal blood flow and glomerular filtration exist. The osmotic effect of mannitol causes water to be drawn from cells to extracellular fluid.

Indications: cerebral oedema, reduction of intraocular pressure.

Adverse effects and cautions: acidosis, thirst, urinary retention, chills, fever, angina-like chest pain. Extravasation of mannitol should be avoided, local oedema and skin necrosis may occur.

Mannitol is contraindicated in patients with severe pulmonary congestion, congestive heart failure, active intracranial bleeding. Mannitol should be used during pregnancy only when clearly needed.

Dose: By intravenous infusion, diuresis, 50-200 g, over 24 hours, preceded by a test dose of 200 mg/kg by slow intravenous injection. Cerebral oedema, l g/kg as a 20% solution given by rapid intravenous infusion.

Preparation available

Mannitol Intravenous Infusion: Intravenous infusion containing 10% and 20% w/v of mannitol is usually available. Mannitol intravenous infusion should be stored at a temperature of 20-30°. Exposure to lower temperature may cause the deposition of crystal, which should be dissolved by warming before use.

POLYTHIAZIDE

It is a thiazide diuretic with duration of diuretic action of 24-48 hours.

Indications: hypertension, oedema.

Adverse effects and cautions: see under hydrochlorothiazide.

Dose: usually 1-4 mg daily; in hypertension 500 micrograms daily may be adequate.

Preparation available

Polythiazide Tablets: Each tablet containing 1 mg of polythiazide is usually available. Polythiazide tablets should be protected from light.

SPIRONOLACTONE

It is a potassium sparing diuretic which competitively inhibits aldosterone on the distal tubule, thereby producing increased excretion of sodium chloride and water and decreased excretion of potassium. It takes 2-3 days to achieve maximum diuretic effect.

Indications: oedema and ascites in cirrhosis of liver, nephrotic syndrome, congestive heart failure, primary hyperaldosteronism.

Adverse effects and cautions: hyperkalaemia, loss of appetite, nausea, vomiting, gynaecomastia, menstrual irregularities, impotence.

Spironolactone should be used with caution in patients with impaired renal function or hepatic disease.

The drug is contraindicated in patients with hyponatraemia, hyperkalaemia. Safe use of spironolactone during pregnancy has not been established.

Dose: 100-200 mg daily; increased to 400 mg if required; CHILD initially 3 mg/kg daily in divided doses.

Preparation available

Spironolactone Tablets: Each tablet containing 25 mg and 100 mg of spironolactone is usually available. Spironolactone tablets should be protected from light.

TORASEMIDE

It is a loop diuretic. It has properties similar to those of furosemide and bumetanide.

Indications: oedema, hypertension.

Adverse effects and cautions: see under bumetanide.

Dose: Oedema, 5 mg once daily, preferably in the morning, increased if required to 20 mg once daily; maximum 40 mg daily.

Hypertension, 2.5 mg daily, increased if necessary to 5 mg once daily.

Preparation available

Torasemide Tablets: Each tablet containing 2.5 mg, 5 mg and 10 mg of torasemide is usually available.

TRIAMTERENE

It is a potassium-sparing diuretic which does not inhibit aldosterone. The drug acts directly on the distal renal tubule to inhibit sodium-potassium ion exchange.

Indications: oedema, potassium conservation with thiazides and loop diuretics.

Adverse effects and cautions: nausea, vomiting, diarrhoea, muscle cramps, dizziness and hyperkalaemia.

Potassium supplementation in any form as high potassium diet, potassium salt should not be given.

Dose: Initially 150-250 mg daily, reducing to alternate days after 1 week, taken in divided doses after breakfast and lunch, lower initial dose when given with other diuretics.

Preparation available

Triamterene Tablets: Each tablet containing 50 mg of triamterene is usually available.

2.6 Drugs used in cardio-vascular shock

DOPAMINE HYDROCHLORIDE

This is a cardiac stimulant. It exerts an inotropic effect on the myocardium resulting in an increased cardiac output. Dopamine increases systolic and pulse pressure with no or little increase in diastolic pressure. It is therefore used in cardiogenic shock.

The dose of dopamine is critical. Dopamine has been reported to dilate renal and mesenteric vasculature leading to increased glomerular filtration rate, renal blood flow and sodium excretion in low to moderate doses and is presumed to be the result of an action on dopaminergic receptors. In high doses, alpha-adrenergic effects become more prominent and may result in increased peripheral resistance and renal vasoconstriction.

Indications: cardiogeic shock in myocardial infarction or cardiac surgery.

Adverse effects and cautions: ectopic beats, nausea, vomiting, tachycardia, anginal pain, palpitation, dyspnoea, headache, hypotension, hypertension and peripheral vasoconstriction.

The drug should not be used in patients with uncorrected tachyarrhythmias or in cases of pheochromocytoma.

Dopamine is a potent drug and must be diluted before administration to the patient. Fluids to which it can be added are: sodium chloride injection, 5% dextrose injection, sodium chloride and 5% dextrose injection, ringer lactate solution and 1/6 molar sodium lactate solution.

Dopamine should not be added to any alkaline solution as it will be inactivated.

There has been insufficient experience to establish safety and efficacy of dopamine in children. The effect of dopamine on the human fetus is not known. The drug should be used in pregnant women when the possible benefits justify the possible risk to the foetus.

Dose: By intravenous infusion, 2-5 micrograms/kg/minute initially.

Preparation available

Dopamine Injection: Concentrate solution containing 40 mg/ml of dopamine hydrochloride in 5 ml and 10 ml vial is usually available. It is prepared immediately before use in accordance with the manufacruter's instruction. It should be protected from light.

DOBUTAMINE

This is a cardiac stimulant. It also increases cardiac contractility with little effects on rate.

Indications: inotropic support in infarction, cardiac surgery, septic shock and cardiogenic shock.

Adverse effects and cautions: tachycardia, increase in systolic blood pressure, phlebitis.

The drug should be used with caution in severe hypotension, complicating cardiogenic shock.

Dose: By intravenous infusion, 2.5 – 10 micrograms/kg/minute, adjusted according to response.

Preparation available

Dobutamine Injection: Concentrate solution containing 12.5 mg/ml of dobutamine (as hydrochloride) in 20 ml vial is usually available.

EPHEDRINE HYDROCHLORIDE

It raises blood pressure transiently by acting on alpha-adrenergic receptors to constrict peripheral blood vessels.

The danger of vasoconstrictors (ephedrine, noradrenaline, phenylephrine) is that they raise blood pressure at the expense of perfusion of vital organs such as the kidney.

Indications: reversal of hypotension from spinal or epidural anaesthesia.

Adverse effects and cautions: nausea, vomiting, anginal pain, hypertension, hypotension, tachycardia (sometimes bradycadia), urine retention.

The drug should be used with caution in ischemic heart disease, hypertension and diabetes.

The drug is contraindicated in breast-feeding mothers.

Dose: Slow intravenous injection, 3-6 mg repeated every 3-4 minutes.

Preparation available

Ephedrine Injection: Injection containing 3 mg/ml of ephedrine hydrochloride in 10 ml ampoule is usually available.

EPINEPHRINE

Adrenaline

Powerful sympathomimetic drug and relaxes bronchial smooth muscle by beta 2-adrenergic receptors. It is the drug of choice for anaphylactic shock and severe allergic responses. It has been used as a potent bronchodilator but as it is very short acting, repeated administration is necessary and this leads to tolerance of the drug.

Indications: cardiac arrest, adjunct with local anaesthetics.

Adverse effects and cautions: tachycardia, tremor, chest pain, irregular heart beats, headache, nausea, vomiting, nervousness, restlessness and weakness.

Adrenaline is contraindicated in patients with shock (other than anaphylactic shock). Adrenaline should not be used during labour as it may delay the second stage.

Drug interactions: It should be avoided in patients who are on tricyclic antidepressants as it may cause cardiac arrhythmias, hypertension or tachycardia.

Dose: Acute anaphylaxis, by intramuscular injection, 0.5-1 ml, to be repeated every 10 minutes according to blood pressure and pulse, until improvement occurs. CHILD, 2-5 years 0.2-0.4 ml, 6-12 years, 0.5 ml. Dosage to be repeated as in adult.

Cardiac arrest, adrenaline 1 in 10,000 is recommended in a dose of 10 ml by central venous injection.

Preparation available

Adrenaline Injection: Adrenaline injection is a sterile, isotonic solution containing 0.18 % w/v of adrenaline acid tartarate in water for injection. Adrenaline injection should be protected from light. Adrenaline injection contains the equivalent of adrenaline 1 in 1000 (mg in 1ml).

2.7 Anticoagulants and antagonists

ACENOCOUMAROL

It is an oral anticoagulant. It has more rapid effect on prothrombin time. It acts for 2 days.

Indications: *see* under warfarin.

Adverse effects and cautions: *see* under warfarin.

Dose: 4-12 mg on first day, 4-8 mg on second day, maintenance dose usually 1-8 mg daily.

Preparation available

Acenocoumarol Tablets: Each tablet containing 1 mg, 2 mg, 3 mg and 4 mg of Acenocoumarol is usually available.

***HEPARIN* AND LOW MOLECULAR WEIGHT HEPARINS**

Heparin is an anticoagulant drug which acts by catalyzing the inhibition of coagulation factors including thrombin, IXa and Xa by antithrombin. The dose of drug should be guided by the measurement of APTT (activated partial thromboplastin time).

Indications: deep-vein thrombosis, myocardial infarction, prophylaxis in general and orthopedic surgery.

Adverse effects and cautions: haemorrhage, thrombocytopenia, hypersensitivity reaction and osteoporosis (after prolonged use).

Heparin is contraindicated in presence of active bleeding from any site, haemophilia, purpura and thrombocytopenia.

Dose: Prophylaxis of deep-vein thrombosis and pulmonary embolism, by subcutaneous injection, 5 000 units 2 hours before surgery, then every 8-12 hours for 7 days or until patient is ambulent; during pregnancy 5 000 – 10 000 units every 12 hours.

Treatment of deep-vein thrombosis and pulmonary embolism, by intravenous injection, loading dose of 5 000 units (75 units/kg) followed by continuous infusion of 18 units/kg/hour or by subcutaneous injection of 15,000 units every 12 hours (laboratory monitoring essential - preferably on a daily basis).

Preparation available

Heparin Injection: Heparin injection is a sterile solution of heparin sodium in water for injection; the pH of the solution may be adjusted by the addition of a suitable alkali. Injection of heparin sodium containing 1000 and 5000 units in 1 ml is usually available. Heparin injection should be stored at a temperature not

exceeding 25° and should preferably be kept in a container sealed by fusion of the glass.

LOW MOLECULAR WEIGHT HEPARINS

Enoxaparin, bemiparin and **dalteparin** are low molecular weight heparins. They are as effective and as safe as heparin in the prevention of venous thrombo-embolism. They have long duration of action. The standard prophylactic regimen does not require monitoring.

Indications: prophylaxis of deep-vein thrombosis in medical and surgical patients, treatment of deep-vein thrombosis and pulmonary embolism.

Adverse effects and cautions: see under heparin.

Dose: Dalteparin, prophylaxis of deep-vein thrombosis in surgical patients, by subcutaneous injection, moderate risk, 2500 units 1-2 hours before surgery, then 2500 units every 24 hours for 5-7 days or longer; high risk 2500 units1-2 hours before surgery, than 2500 units 8-12 hours later (or 5000 units on the evening before surgery, then 5000 units on the following evening), then 5000 units every 24 hours for 5-7 days or longer.

Prophylaxis of deep vein thrombosis in medical patients, by subcutaneous injection, 5000 units every 24 hours.

Treatment of deep vein thrombosis and pulmonary embolism, by subcutaneous injection, as a single daily dose. Adult and body-weight under 46 kg, 7 500 units daily; 46-56 kg 10 000 units daily; 57-68 kg, 12500 units daily.

Enoxaparin, prophylaxis of deep-vein thrombosis especially in surgical patients, by subcutaneous injection, moderate risk, 20 mg (2000 units) about 2 hours before surgery then 20 mg (2000 units) every 24 hours for 7-10 days; high risk (e.g. orthopaedic surgery), 40 mg (4000 units) 12 hours before surgery, then 4000 units every 24 hours for 7-10 days.

Prophylaxis of deep-vein thrombosis in medical patients by subcutaneous injection, 4000 units every 24 hours for at least 6 days until patient ambulent (maximum 14 days).

PHYTOMENADIONE

Vitamin K_1

It has the same activity as naturally occuring vitamin K_1 which is required for the synthesis of blood coagulation factors II, VII, IX and X.

Indications: antagonists to warfarin, prophylaxis against haemorrhagic disease of newborn.

Adverse effects and cautions: hypersensitivity characterised by flushing of the face, bronchospasm, dyspnoea, hypotension.

The drug is contraindicated in persons who are hypersensitive to the drug.

Dose: Warfarin-induced hypoprothrombinaemia, 5-10 mg by slow intravenous injection.

Prophylaxis, haemorrhagic disease of newborn, by intramuscular injection, 0.5-1 mg as single dose.

Preparation available

Phytomenadione Injection: Injection containing 2 mg and 10 mg per ml of phytomenadione is usually available. Phytomenadione injection deteriorates on exposure to light and should be stored in the dark. It should not be allowed to freeze. The injection should not be used if separation has occurred or if oil droplets have appeared.

Phytomenadione Tablets: Each tablet containing 10 mg of phytomenadione is usually available. Phytomenadione tablets should be chewed before swallowing or allowed to dissolve in the mouth.

PROTAMINE SULFATE

It is a strongly basic substance which acts as a heparin antagonist *in vitro* and *in vivo* by complexing with strongly acidic heparin to form a stable salt. It only partially reverses the effects of low molecular weight heparins

Indications: heparin overdose.

Adverse effects and cautions: hypotension, bradycardia, flushing, urticaria and angioedema.

Dose: By slow intravenous injection, 1 mg neutralises 100 units heparin when given within 15 minutes; if longer time, less protamine required as heparin rapidly excreted, maximum 50 mg.

Preparation available

Protamine Sulfate Injection: Injection containing 10 mg of protamine sulfate per ml in 5-ml ampoule is usually available.

WARFARIN

It is most widely used oral anticoagulant. It inhibits the synthesis of vitamin K-dependent clotting factors such as VII, IX & X and also factor II. There is a latent period of 48-72 hours before full anticoagulant effects occur.

Indications: prophylaxis of embolism in rheumatic heart disease and atrial fibrillation, prophylaxis and treatment of venous thrombosis and pulmonary embolism, prophylaxis with prosthetic heart valve.

Adverse effects and cautions: haemorrhage, nausea, vomiting and abdominal cramps.

The drug should be used with caution in any condition where risk of haemorrhage is present. The baseline prothrombin time should be determined wherever possible.

The drug is contraindicated in patients with ulcerations of gastro-intestinal tract, severe hypertension, bacterial endocarditis and in pregnancy.

Dose: Initial dose, 10 mg for 2 days, subsequent doses, 3-9 mg daily, in accordance with the prothrombin activity of blood.

Preparation available

Warfarin Tablets: Each tablet containing 5 mg of warfarin sodium is usually available. Warfarin tablets should be protected from light.

2.8 Anti-platelet drugs

ASPIRIN

Acetylsalicylic Acid

It affects platelet function by inhibiting the enzyme prostaglandin cyclooxygenase in platelets, thereby preventing the formation of the aggregating agent thromboxane A_2. This action is irreversible; the effects persist for the life of the platelets exposed. Lower doses are used as a platelet aggregating inhibitor. Higher doses do not improve efficacy but definitely increase toxicity, especially bleeding.

Indications: prophylaxis of cerebrovascular disease or myocardial infarction

Adverse effects and cautions: adverse effects in most cases are dose related and are relatively rare when low doses are used. Gastric erosions with gastro-intestinal bleeding and hypersensitivity reactions with skin rashes. Asthma may be provoked in some individuals.

The drug is contraindicated in children under 16 years and in breast-feeding mothers, active peptic ulcer, haemophilic and other bleeding disorders

Dose: Prophylaxis of cerebrovascular disease or myocardial infarction, 75-300 mg daily. A single dose of 150-300 mg is given as soon as possible after an ischemic event, preferably dispersed in water or chewed.

Preparation available

Aspirin Tablets: Each tablet containing 50 mg, 75 mg and 300 mg of aspirin is usually available.

CLOPIDOGREL

It is an antiplatelet drug.

Indications: prevention of ischemic events with symptomatic ischemic disease, acute coronary syndrome without ST segment elevation (given with aspirin).

Adverse effects and cautions: diarrhea, dyspepsia, abdominal pain, bleeding disorders (including gastro-intestinal and intracranial).

The drug should be used with caution in pregnancy, liver impairment, renal impairment; risk of increased bleeding form trauma, surgery or other pathological conditions.

Dose: 75 mg once daily.

Acute coronary syndrome, initially 300 mg then 75 mg daily (with aspirin).

Preparation available

Clopidogrel Tablets: Each tablet containing 75 mg of clopidogrel (as hydrogen sulfate) is usually available.

DIPYRIDAMOLE

It inhibits phosphodiesterase, raising the intracellular cyclic AMP concentration. This prevents platelet aggregation and favours local vasodilatation.

Indications: thromboembolism (prophylaxis)

Adverse effects and cautions: gastrointestinal irritation, throbbing headache, vasodilation and hypotensive effects such as dizziness, flushing or even syncope.

Dose: By mouth, 300-600 mg daily in 3-4 divided doses before food.

Preparation available

Dipyridamole Tablets: Each tablet containing 25 mg and 100 mg of dipyridamole is usually available.

2.9 Thrombolytic agents

STREPTOKINASE

It is a protein produced by beta-hemolytic streptococci. It promotes plasmin formation; plasmin is an enzyme that degrades fibrin clots as well as fibrinogen and other plasma proteins including the procoagulant factors V and VIII. Conversion of plasminogen to plasmin occurs within the thrombus or embolus as well as on its surface and in circulating blood. Therapy with thrombolytic drugs tends to dissolve both pathological thrombi and also fibrin deposited at the site of vascular injury.

The effects of streptokinase on coagulation usually disappear within a few hours but may persist for up to 12 hours after discontinuation of intravenous infusion.

Indications: pulmonary embolism, deep venous thrombosis, acute myocardial infarction, central retinal venous or arterial thrombosis.

Adverse effects and cautions: nausea, vomiting, bleeding, hypotension.

The drug is contraindicated in recent haemorrhage, trauma or surgery, severe hypertension and active internal bleeding.

Safety and efficacy of streptokinase in children have not been established. Safe use of drug during pregnancy has not been established.

Streptokinase is strongly antigenic, repeated administration elicits antibodies which diminish the effect and may cause allergic reactions.

Drug interactions: concomitant use of streptokinase and oral anticoagulants or heparin may increase the risk of haemorrhage. Concomitant use of Streptokinase and drugs that affect platelet function such as aspirin, indomethacin, dipyridamole etc. should be avoided to avoid possible increased risk of haemorrhage.

Dose: By intravenous infusion, in deep vein thrombosis, pulmonary embolism, retinal thrombosis, 250,000 units over 30 minutes, then 100,000 units every hour for up to 12-72 hours according to condition.

Myocardial infarction, 1,500,000 units over 60 minutes.

Preparation available

Streptokinase Injection: Sealed container of streptokinase for injection containing 250 000 units and 750 000 units of streptokinase is usually available. It is prepared by dissolving streptokinase for injection in the requisite amount of water for injection immediately before use.

The sealed container should be protected from light and stored at a temperature of 2-8°, under these conditions the content is expected to retain their potency for 2 years.

UROKINASE

It is isolated from urine. Unlike streptokinase, it acts directly on the endogenous fibrinolytic system to convert plasminogen into the proteolytic enzyme plasmin, which in turn acts in the way described under streptokinase. The fibrinolytic effect of urokinase usually disappears within a few hours but increased thrombin time, decreased plasma levels of fibrinogen and plasminogen, and increased levels of the degradation products of fibrinogen and fibrin may persist for up to 12-24 hours following discontinuance of the intravenous infusion.

Urokinase also induces an anticoagulant effect because of resulting high levels of the degradation products of fibrinogen and fibrin.

Indications: *see* under streptokinase.

Adverse effects and cautions: *see* under streptokinse. The drug should be used during pregnancy only when clearly needed. In contrast to streptokinase, urokinase is non-antigenic; however, mild allergic reactions including bronchospasm and rash have been reported.

Drug interactions: *see* under streptokinase.

Preparation available

Urokinase Injection: Injection containing 25,000 units, 50,000 units, 100,000 units and 500,000 units per vial is usually available.

2.10 Lipid-regulating drugs (drugs used in hyperlipidaemia)

Lipid regulating drug therapy must be combined with advice on diet and lifestyle measures to reduce cardiovascular disease risk including, if appropriate, reduction of blood pressure and use of aspirin.

Treament with statins reduces myocardial infarction, coronary deaths, the risk of stroke, and overall mortality rate. They are the drugs of choice in patients with a high risk of cardiovascular disease.

***ATORVASTATIN* AND SIMVASTATIN**

These are statins which competitively inhibit 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase, an enzyme involved in cholesterol synthesis, especially in the liver. They are more effective than cholestyramine, gemfibrozil, nicotinic acid in lowering LDL-cholesterol but less effective than gemfibrozil in reducing triglycerides.

ATORVASTATIN

Indications: primary hypercholesterolaemia, homozygous or heterozygous familial hypercholesterolaemia or mixed hyperlipidaemia in patients who have not responded adequately to diet and other appropriate measures.

Adverse effects and cautions: reversible myositis, headache, angina, chest pain, arthralgia, anorexia, weight gain.

The drug should be used with caution in patients with liver disease or with a high alcohol intake. Liver function tests should be carried out before and within 1-3 months of starting treatment and thereafter at intervals of 6 months for 1 year, unless indicated sooner by signs or symptoms suggestive of hepatotoxicity.

The drug is contraindicated in active liver disease, pregnancy and breast-feeding.

Drug interactions: concominent use of atorvastatin and clarithromycin increases plasma concentration of atorvastatin.

Dose: Primary hyperlipidaemia and combined hyperlipidaemia, usually 10 mg once daily; if necessary may be increased at intervals of at least 4 weeks to maximum 80 mg once daily; CHILD 10-13 years usually 10 mg once daily.

Familial hypercholesterolaemia, initially 10 mg daily, increased at intervals of at least 4 weeks to 40 mg once daily; if necessary, further increased to maximum 80 mg once daily. CHILD 10-13 years up to 20 mg once daily.

Preparation available

Atorvastatin tablets: Each tablet containing 10 mg of atorvastatin (as calcium trihydrate) is usually available.

SIMVASTATIN

Indications: *see* under atorvastatin

Adverse effects and cautions: *see* under atorvastatin, and also dizziness, jaundice, pancreatitis.

Cautions: *see* under atorvastatin. The drug should also be used with caution in impaired renal function.

Drug interactions: concomitant use of simvastatin with clarithromycin, erythromycin, diltiazem increases risk of myopathy.

Dose: Primary hypercholesterolaemia, combined hyperlipidaemia, 10-20 mg daily at night, adjusted at intervals of at least 4 weeks.

Homozygous familiar hypercholesterolaemia, 40 mg daily at night or 80 mg daily in 3 divided doses (with largest dose at night).

Preparation available

Simvastatin Tablets: Each tablet containing 10 mg, 20 mg and 40 mg of simvastatin is usually available.

CHOLESTYRAMINE RESIN

It binds bile acids in the gut and thus interrupts the enterohepatic circulation. It increases hepatic conversion of cholesterol into bile acids and promotes receptor mediated uptake of LDL cholesterol from plasma. The drug lowers LDL cholesterol but can aggravate triglycerides.

Indications: adjunct to dietary therapy to decrease elevated serum cholesterol and LDL concentrations.

Adverse effects and cautions: constipation, abdominal pain and distention, anorexia, biliary colic, and skin rash.

There are no adequate data to show full safety of drug in pregnancy.

Drug interactions: long term high-dose cholestyramine therapy may impair the absorption of fat-soluble vitamins from gastro-intestinal tract. Absorption of thyroid hormones, warfarin have been reduced.

Dose: Lipid reduction, (after initial introduction over 3-4 week) 12-24 g daily in water in single or up to 4 divided doses, up to 36 g daily if necessary; pruritus, 4-8 g daily in water.

Preparation available

Cholestyramine Powder: Each sachet containing 4 g of cholestyramine is usually available.

CLOFIBRATE

It decreases serum very low-density lipoprotein (VLDL) and low density lipoprotein (LDL) concentrations in healthy individuals and abnormal lipoproteins in patients with type III hyperlipoproteinemia. Serum triglycerides concentrations are usually reduced more than cholesterol concentrations. The exact mechanism by which clofibrate lowers serum concentrations of triglycerides and cholesterol is unknown.

Indications: adjunct to dietary therapy to decrease elevated serum triglyceride and cholesterol concentrations.

Adverse effects and cautions: nausea, abdominal discomfort, vomiting, flu-like syndrome characterised by myalgia or myositis, headache, dizziness, breast tenderness in men, impotence and cholesterol cholelithiasis with long term use.

Clofibrate is contraindicated in patients with severe renal or hepatic impairment.

Safe use of clofibrate during pregnancy has not been established. Safety and efficacy of drug in children younger than 14 years of age have not been established.

Drug interactions: clofibrate may potentiate the anticoagulant effects of warfarin or dicumarol.

Clofibrate has been reported to increase diuretic effect of furosemide and hypoglycaemic effect of sulphonylureas. Concomitant administration of cholestyramine with clofibrate decreases the rate of absorption of clofibrate.

Dose: Over 65 kg 2g daily, 50-65 kg, 1.5g daily, in 2 or 3 divided doses.

Preparation available

Clofibrate Capsules: Each capsule containing 500 mg clofibrate is usually available.

FENOFIBRATE

It decreases serum triglycerides and increases HDL levels.

A statin is preferred to fibrates in patients with raised triglycerides or low HDL-cholesterol.

Indications: severe hypertriglyceridemia.

Adverse effects and cautions: gastro-intestinal disturbances, rash, urticaria, fatigue, headache, impotence.

The drug is contra-indicated in pregnancy, breast-feeing, severe hepatic impairment.

The drug should be used with caution in renal impairment. Liver function tests recommended every 3 months for first year.

Dose: Initially 200 mg daily in divided doses.

Preparation available

Fenofibrate Capsules: Each capsule containing 200 mg of fenofibrate is usually available.

GEMFIBROZIL

It decreases serum triglycerides in healthy individuals and in patients with hypertriglyceridemia. It has variable effects on LDL-cholesterol. The exact mechanism of action of gemfibrozil has not been established.

Indications: adjunct to dietary therapy in hyperlipidaemias of types IIa, IIb, III, IV and V.

Adverse effects and cautions: abdominal and epigastic pain, diarrhoea, nausea, anorexia, headache, sexual dysfunction, myopathy, myositis, urticaria and pruritus.

Gemfibrozil is contraindicated in patients who have a history of hypersensitivity to the drug, in patients with preexisting gallbladder disease, hepatic dysfunction.

There are no adequate data to show full safety of drug in pregnancy. Safety and efficacy of drug in children younger than 18 years of age have not been established.

Drug interactions: gemfibrozil may potentiate the anticoagulant effects of oral anticogulants.

Dose: 1.2 g daily usually in 2 divided doses; range 0.9-1.2 g daily.

Preparation available

Gemfibrozil Capsules: Each capsule containing 300 mg of gemfibrozil is usually available.

NICOTINIC ACID

Niacin

It decreases both cholesterol and triglyceride concentrations and increases HDL concentration. The exact mechanism by which nicotinic acid decreases serum cholesterol and triglyceride concentrations is unknown.

Indications: adjunct to statin in dyslipidaemia or used alone if statin not toletated.

Adverse effects and cautions: diarrhoea, nausea, vomiting, flushing, palpitations, dizziness, pruritus and rash.

The drug is contraindicated in patients with arterial haemorrhage, active peptic ulcer, breast feeding.

The drug should not be used in pregnant women unless the possible benefits outweigh the potential risk.

Dose: Initially 100-200 mg 3 times daily, gradually increased over 2-4 weeks to l-2 g 3 times daily.

Preparation available

Nicotinic Acid Tablets: Each tablet containing 50 mg and 250 mg of nicotinic acid is usually available.

2.11 Antifibrinolytic drug

ETAMSYLATE

Ethamsylate

It is a haemostatic agent. It reduces capillary bleeding.

Indications: blood loss in menorrhagia.

Adverse effects and cautions: headache, rashes.

Dose: 500 mg 4 times daily during menstruation.

Preparation available

Etamsylate Tablets: Each tablet containing 500 mg of etamsylate is usually available.

TRANEXAMIC ACID

It inhibits fibrinolysis.

Indications: menorrhagia, epistaxis, thrombolytic overdose.

Adverse effects and cautions: nausea, vomiting, diarrhoea, disturbances in colour vision.

The drug should be used with caution in renal impairment and pregnancy.

The drug is contraindicated in severe renal impairment and thromboembolic disease.

Dose: Menorrhagia (initiated when menstruation started) 1 g 3 times daily for up to 4 days, maximum 4 g daily

Local fibrinolysis, 15-25 mg/kg 2-3 times daily.

Preparation available

Tranexamic Acid Tablets: Each tablet containing 500 mg of tranexamic acid is usually available.

Chapter - Three

Drugs Acting on the Respiratory System

3.1 Anti-asthmatic drugs

Mild to moderate attack of asthma can be treated with oral aerosol administration of beta 2-adrenoceptor or corticosteroid.

The oral route is used when administration by inhalation is not possible. Solutions for nebulisation are used for acute severe asthma.

AMINOPHYLLINE

Aminophylline is a theophylline compound with ethylene-diamine and acts by competitive inhibition of adenosine receptor, adenosine causes bronchoconstriction.

Indications: acute severe asthma, reversible airways obstruction.

Adverse effects and cautions: tachycardia, nausea, vomiting, cardiac arrhythmias, fall in blood pressure and sometimes even convulsions.

Rapid injection may result in sudden death from dysrythmias. Theophylline has a low therapeutic index; therefore, cautious dosage determination is essential. Individuals metabolise drug at different rates, appropriate dosage must be determined for each patient by carefully monitoring patient response and tolerance, pulmonary function and serum theophylline concentrations.

Dose: By mouth, 100 mg, 3-4 times daily after meal.

Acute severe asthma, by slow intravenous injection (over 20 minutes), 250 -500 mg (5 mg/kg) when necessary; maintenance, if required, in patient not previously treated with theophylline, 500 micrograms/kg/hour by slow intravenous infusion. CHILD by slow intravenous injection (over 20 minutes), 5 mg/kg; maintenance, if required, in the patients not previously treated with theophylline, 6 months to 9 years 1 mg/kg/hour, 10 -16 years 0.8 mg/kg/hour by slow intravenous infusion.

Preparation available

Aminophylline Injection: Aminophylline injection is a sterile solution of aminophylline or aminophylline hydrate in water for injection free from carbon dioxide. Injection containing 250 mg of aminophylline in 10 ml is usually available.

Aminophylline Tablets: Each tablet containing 100 mg of aminophylline is usually available. Aminophylline tablets should be kept in an air tight container protected from light.

BAMBUTEROL

It is pro-drug of terbutaline.

Indications: *see* under terbutaline.

Adverse effects and cautions: *see* under terbutaline.

Dose: Initially, 10 mg once daily at bed time, increased if necessary after 1-2 weeks to 20 mg once daily; CHILD not recommended.

Preparation available

Bambuterol Tablets: Each tablet containing bambuterol hydrochloride 10 mg and 20 mg is usually available.

EPHEDRINE HYDROCHLORIDE

This stimulates alpha and beta receptors and also stimulates release of nor-adrenaline from sympathetic nerve endings. It is given orally and has a longer duration of effect.

Indications: reversible airways obstruction.

Adverse effect and cautions: arrhythmias, insomnia, tremor, tachycardia.

The drug should be used with caution in patients with hypertension, severe renal impairment and prostate hypertrophy.

Dose: 15-60 mg 3 times daily; CHILD 3 times daily, up to 1 year 7.5 mg, 1-5 years 15 mg, 6-12 years 30 mg.

Preparation available

Ephedrine Hydrochloride Tablets: Each tablet containing 30 mg of ephedrine hydrochloride is usually available.

IPRATROPIUM BROMIDE

It is an antimuscarinic bronchodilator which can provide short-term relief in chronic asthma. The short acting beta-2 agonists act more quickly and are preferred. Its maximal effect after aerosol inhalation is seen 30-60 minutes after use; its duration of action is 3-6 hours.

Adverse effects and cautions: dry mouth, headache, constipation, tachycardia.

The drug should be used with caution in patients with acute angle-closure glaucoma and prostatic hyperplasia.

Dose: By aerosol inhalation, 20-40 micrograms, 3-4 times daily; CHILD up to 6 years 20 micrograms 3 times daily, 6-12 years, 20-40 micrograms 3 times daily.

By inhalation of powder 40 micrograms 3-4 times daily; CHILD under 12 years, not recommended.

Preparation available

Ipratropium Aerosol Inhalation: Pressurised inhalation containing 20 micrograms of ipatropium bromide per metered inhalation is usually available.

SALBUTAMOL

This is short-acting selective beta -2 agonist and has minimal action on the heart. It is used for the relief of airways obstruction. Its action starts in 15 minutes after oral ingestion and 5 minutes of inhalation and can last for 3-5 hours after inhalation and 4-6 hours after oral administration. Mild to moderate symptoms of asthma respond rapidly to inhalation of selective short-acting beta-2 agonist.

Indications: reversible airways obstruction.

Adverse effects and cautions: muscle cramps, dizziness, headache, tremor and palpitation.

Drug should be used with caution in hyperthyroidism, hypertension and diabetes mellitus.

Drug interactions: concomitant use of high dose of salbutamol and corticosteroids or diuretics increases the risk of hypokalaemia.

Dose: By mouth, 4 mg (elderly and sensitive patient initially 2 mg) 3-4 times daily; maximum single dose 8 mg (but unlikely to provide much extra benefit or to be tolerated), CHILD under 2 years 100 micrograms/kg 4 times daily; 2-6 years 1-2 mg 3-4 times daily; 6-12 years 2 mg.

By subcutaneous or intramuscular injection, 500 micrograms, repeated every 4 hours if necessary.

By slow intravenous injection, 250 micrograms repeated if necessary. By intravenous infusion, initially 5 micrograms/minute, adjusted according to response and heart-rate usually in range 3-20 micrograms/minute or more if necessary.

By aerosol inhalation, 100-200 microgams (1-2 puffs); for persistent symptoms up to 3-4 times daily; CHILD 100 micrograms (1 puff) increased to 200 micrograms (2 puffs) if necessary. Prophylaxis in exercise induced bronchospasm, 200 micrograms (2 puffs); CHILD 100 micrograms (1 puff).

By inhalation of a powder, 200-400 micrograms; for persistent symptoms up to 3-4 times daily; CHILD 200 micrograms. Prophylaxis in exercise-induced bronchospasm (powder), 400 micrograms; CHILD 200 micrograms.

By inhalation of nebulised solution, adult and CHILD over 18 months, chronic bronchospasm unresponsive to conventional therapy and severe acute asthma, 2.5 mg, repeated up to 4 times daily, increased to 5 mg if necessary, CHILD *2.5* mg increased to 5 mg if required.

Preparation available

Salbutamol Aerosol Inhalation: Pressurised inhalation containing 100 micrograms of salbutamol per metered inhalation is usually available.

Salbutamol Dry Powder: Each blister containing 200 micrograms of salbutamol in powder form is usually available.

Salbutamol Injection: Injection containing 50 micrograms and 500 micrograms of salbutamol (as sulfate) per ml is usually available.

Salbutamol Oral Solution: Each 5ml of oral solution containing the equivalent of 2 mg of salbutamol (as sulfate), is usually available.

Salbutamol Tablets: Each tablet containing the equivalent of 2 mg, 4 mg and 8 mg of salbutamol (as sulfate), is usually available.

SALMETEROL

It is a long acting selective beta-2 agonist, which is administered by inhalation. Its duration of action is 12 hours. It has slower onset of action, it should not be used for the relief of an acute attack. It provides symptomatic relief and improves lung function and quality of life in patients with COPD.

Indications: reversible airways obstruction (including nocturnal asthma and prevention of exercise-induced bronchospasm) in patients requiring long-term regular bronchodilator therapy, chronic obstructive pulmonary disease.

Adverse effects and cautions: see under salbutamol. It can produce paradoxical bronchospasm.

Dose: By inhalation, asthma, 50 micrograms twice daily, up to 100 micrograms twice daily in more severe cases; CHILD over 4 years, 50 micrograms twice daily.

Chronic obstructive pulmonary disease, 50 micrograms twice daily.

Preparation available

Salmeterol Aerosol Inhalation: Pressurised inhalation containing 25 micrograms of salmeterol (as xinafoate) per metered inhalation is usually available.

SODIUM CROMOGLICATE

This is one of the drugs used in the prophylaxis of asthma. It is not a bronchodilator and cannot be used in the treatment of an acute attack. As it is not properly absorbed from the gastrointestinal tract it is given by inhalation. About 5 -10 % of the dose reaches the lungs. It acts by inhibiting mediator release from bronchial mast cells. The exact mechanism is not known.

Indications: prophylaxis of asthma, allergic rhinitis, allergic conjunctivitis.

Adverse effects and cautions: inhalation sometimes causes coughing or transient symptoms of asthma.

Dose: Inhalation of powder, adults and children, 20 mg 4 times daily, increased in severe cases to 8 times daily.

Preparation available

Sodium Cromoglicate Insufflation: Each insufflation containing 20 mg of sodium cromoglicate in hard gelatin capsule is usually available. The capsules are intended for use in an inhaler and not to be swallowed. Sodium cromoglicate insufflation should be protected from moisture and stored at a temperature not exceeding 30°.

TERBUTALINE SULFATE

Similar in action to salbutamol as it is also a selective beta 2-agonist. Its action starts in 30 minutes after oral ingestion and 5-30 minutes of inhalation and action lasts for 4-8 hours after oral and 3-5 hours after inhalation.

Indications: *see* under salbutamol.

Adverse effects and cautions: *see* under salbutamol.

Dose: By mouth, 2.5-5 mg 2-3 times daily; CHILD 75 micrograms/kg 3 times daily.

By subcutaneous, intramuscular or slow intravenous injection 250-500 micrograms up to 4 times daily; CHILD 2-15 years 10 micrograms/kg to a maximum of 300 micrograms.

By continuous intravenous infusion as a solution containing 3-5 micrograms/ml, 1.5-5 micrograms/minute for 8-10 hours, reduce dose for children.

By aerosol inhalation, adults and children 250-500 micrograms (1-2 puffs), for persistent symptoms up to 3-4 times daily.

Preparation available

Terbutaline Aerosel Inhalation: Pressurised inhalation containing 250 micrograms of terbutaline sulfate per metered dose is usually available.

Terbutaline Injection: Injection containing 500 micrograms per ml of terbutaline sulfate is usually available.

Terbutaline Tablets: Each tablet containing 2.5 mg and 5 mg of terbutaline sulfate is usually available.

THEOPHYLLINE

It relaxes bronchial smooth muscle by competitive inhibition of adenosine, adenosine causes bronchoconstriction. It also acts by inhibiting phosphodiesterases thereby increasing cyclic AMP and GMP. It stimulates the CNS. It increases cardiac output by its effect on the myocardium.

Indications: *see* under aminophylline.

Adverse effects and cautions: see under aminophylline.

Dose: 125 mg 3-4 times daily after food, increased to 250 mg if required; CHILD 7-12 years 62.5-125 mg 3-4 times daily.

Preparation available

Theophylline Tablets: Each tablet containing 250 mg of theophylline is usually available.

3.1.1 Corticosteroids

Their mode of action seems to be manifold. They:

- decrease vascular permeability.
- modulation of cytokine and chemokine production.

Corticosteroids can be given orally, or by aerosol inhalation or parenterally.

They should not be used for long period as they can bring about adverse reaction. They do not directly relax airway smooth muscle and thus have little effects on acute brochoconstriction. Alleviation of symptoms usually occurs 3-7 days after inhalation. Beclomethasone, budesonide and fluticasone are equally effective. Inhaled corticosteroids are recommended for prophylactic treatment of asthma when patients are using a beta-2 agonist more than 3 times a week or if symptoms disturb sleep more than once a week or if the patient has suffered exacerbations in the last 2 years requiring a systemic corticosteroid or a nebulised bronchodilator.

An acute attack of asthma should be treated with a short course of an oral corticosteroid starting with a high dose.

BECLOMETHASONE DIPROPIONATE

It is a synthetic corticosteroid which has been shown to relieve symptoms of bronchial asthma in most adults and children. Although some improvement may occur when therapy is initiated, optimum symptomatic relief may require 1-4 weeks of continuous oral inhalation therapy even in patients who have not previously received systemic corticosteroid therapy.

Indications: *see* under budesonide.

Adverse effects and cautions: *see* under budesonide.

Drug interactions: see under budesonide.

Dose: by aerosol inhalation, 200 µg twice daily; CHILD, 50-100 micrograms 2-4 times daily.

BUDESONIDE

Indications: prophylaxis of asthma

Adverse effects and cautions: inhaled corticosteroids have considerably fewer systemic effects than oral corticosteroids. Oropharyngeal candidiasis, cough, adrenal suppression (usually with higher doses of inhaled drug and in children), growth retardation (usually with oral drug and in children), glaucoma (prolonged high dose of inhaled drug), cataract (inhaled drug).

An inhaled corticosteroid should be used cautiously in active or quiescent tuberculosis.

Drug interactions: concomitant use of corticosteroids (generally other than topical and inhaled) antagonise hypotensive effect of ACE inhibitors, alpha-blockers, angiotensin-II receptor antagonists and calcium channel blockers.

Dose: By inhalation of powder, when starting treatment, during period of severe asthma and while reducing or discontinuing oral corticosteroid, 0.2-1.6 mg daily in 2 divided dose; in less severe cases 200-400 micrograms once daily (each evening); CHILD under 12 years 200-800 micrograms daily in 2 divided doses.

By inhalation of nebulised suspension, when starting treatment, during periods of severe asthma and while reducing or discontinuing oral corticosteroid, 1-2 mg twice daily; CHILD 3 months – 12 years, 0.5-1 mg twice daily. Maintenance, usually half above doses.

HYDROCORTISONE: *see* under section 8.1, adrenal hormones and synthetic substitutes.

3.2 Antitussives (Cough suppressants)

These are used to treat troublesome, nonproductive dry cough. These act by suppressing a cough which may be irritative, unproductive and troublesome to the patient. Sputum retention may occur as a result of cough suppression and this can be harmful in patients with chronic bronchitis and bronchiectasis. It should however be noted that children under one year should not be given cough remedies which contain codeine or similar opioid antitussives.

CODEINE PHOSPHATE

It suppresses the cough reflex by a direct central action, probably in the medulla or pons. It also exerts a drying effect on respiratory tract mucosa and to increase viscosity of bronchial secretions.

Indication: nonproductive cough.

Adverse effects and cautions: nausea, constipation, respiratory depression in sensitive patients or in large doses. Prolonged use may produce physical dependence.

The drug should be used with caution in patients with asthma, severe prostatic hypertrophy and hepatic disease.

Dose: Mild to moderate pain, 30-60 mg every 4 hours when necessary, to a maximum of 240 mg daily. CHILD 1-12 years, 3 mg/kg daily in divided doses.

Dry or painful cough, 15-30 mg 3-4 times daily. CHILD 5-12 years, 7.5-15 mg 3-4 times daily.

Preparation available

Paediatric Codeine Linctus: The solution should not contain more than 3 mg/5 ml of codeine phosphate.

Codeine Phosphate Tablets: Each tablet containing 15 mg of codeine phosphate is usually available. Codeine phosphate tablet should be protected from light.

DEXTROMETHORPHAN

The antitussive activity of the drug is about equal to that of codeine. It acts centrally elevating threshold for coughing. Its activity persists for 5-6 hours. The drug produces no analgesia or addiction or CNS depression

Indications: nonproductive cough.

Adverse effects and cautions: nausea and dizziness.

Dose: 10-20 mg every four hours or 30 mg every 6-8 hours; CHILD, 6-12 years 5-10 mg every 4-8 hours to a maximum of 60 mg in 24 hours, and 2-6 years 2.5-5 mg every 4 hours, to a maximum of 30 mg in 24 hours.

Preparation available

Dextromethorphan Hydrobromide Syrup: Each 5ml containing 10 mg and 30 mg of dextromethorphan hydrobromide is usually available.

NOSCAPINE

It is as effective as codeine. The drug is non-addicting.

Indications: nonproductive cough.

Adverse effects and cautions: drowsiness and nausea.

Safe use of drug during pregnancy has not been established.

Dose: up to 50 mg in divided doses.

Preparation available

Noscapine Linctus: 5 ml of linctus containing 15 mg of noscapine is usually available. Noscapine linctus should be stored at a temperature not exceeding 25°.

PHOLCODINE

It is as effective as codeine and acts by same mechanism. It does not cause drying of sputum, bronchoconstriction, constipation and is devoid of abuse potential.

Indications: nonproductive cough.

Dose: 5-10 ml 3-4 times daily; CHILD 1-2 years 2.5-5 ml, 2-5 years 5 ml, 5-12 years 5-10 ml.

Preparation available

Pholcodine Liquid: Each 5 ml containing 1.5 mg of pholcodine is usually available.

3.3 Mucolytic agents

These drugs are often used to facilitate expectoration by reducing sputum viscosity and elasticity in chronic asthma and bronchitis. Few patients, however, have been shown to derive much benefit from them. Mucolytic therapy should be stopped if the is no benefit after a 4-week trial.

BROMHEXINE

It has been found to improve ventilatory capacity and reduce the frequency of exacerbation in chronic bronchitis. However, it is not known which patients are most likely to benefit.

Indications: reduction of sputum viscosity in COPD.

Adverse effects and cautions: gastrointestinal irritation.

Dose: By mouth, 8 to 16 mg three times daily; CHILD under 5 years 4 mg twice daily, 5-12 years 4 mg four times daily.

Preparation available

Bromhexine Tablets: Each tablet containing 8 mg of bromhexine hydrochloride is usually available.

Bromhexine Syrup: Each 5ml containing 4 mg of bromhexine hydrochloride is usually available.

CARBOCISTEINE

Indications: reduction of sputum viscosity in COPD.

Adverse effects and cautions: skin rashes, occasional gastro- intestinal irritation;

Dose: 750 mg 3 times daily initially; then 1.5 g daily in divided doses; CHILD 2-5 years 62.5-125 mg 4 times daily, 6-12 years 250 mg 3 times daily.

Preparation available

Carbocisteine Capsules: Each capsule containing 375 mg of carbocisteine is usually available.

Carbocisteine Syrup: Each 5ml containing 250 mg of carbocisteine is usually available.

3.4 Systemic nasal decongestants

Sympathomimetic amines such as phenylephrine, pseudoephedrine act on alpha-adrenergic receptors in the mucosa of the respiratory tract to produce vasoconstriction which temporarily reduces the swelling associated with inflammation of the mucous membranes lining the nasal passages. These preparations may not be as effective as topical nasal decongestants but unlike the preparation for local application, they do not give rise to rebound nasal congestion.

PHENYLEPHRINE

The therapeutic effectiveness of oral phenylephrine as a nasal decongestant has been questioned, especially at the usual oral dose.

Indications: nasal congestion associated with acute or chronic rhinitis, common cold, sinusitis.

Adverse effects and cautions: increased heart rate, palpitation, tremors, ventricular premature contractions and hypertension.

The drug should be used with caution in patients with diabetes, hypertension, ischaemic heart disease, hepatic impairment, renal impairment.

The safety of the drug in pregnancy and lactation has not been established.

Dose: By mouth, 5 mg 3-4 times a day.

Preparation available

Phenylephrine Tablets: Each tablet containing 5 mg of phenylephrine hydrochloride is usually available.

PSEUDOEPHEDRINE

Indications: nasal congestion associated with acute or chronic rhinitis, common cold, sinusitis. In patients with otic inflammation or infection, the drug may be useful in opening obstructed Eustachian tube.

The drug may be used as an adjunct to analgesics, antihistamines, antitussives when indicated.

Adverse effects and cautions: nervousness, restlessness, dizziness, insomnia, headache and drowsiness. Larger doses may cause lightheadedness, nausea and /or vomiting.

The drug should be used with caution in patients with prostatic hypertrophy, ischaemic heart disease, glaucoma and diabetes mellitus.

Dose: 60 mg 3-4 times daily; CHILD 1 mg/kg 4 times daily.

Preparation available

Pseudoephedrine Syrup: Each 5 ml containing 30 mg pseudoephedrine hydrochloride is usually available.

Pseudoephedrine Tablets: Each tablet containing 60 mg of pseudoephedrine hydrochloride is usually available.

Chapter - Four

Drugs Acting on the Central Nervous System

4.1 Opioid analgesics

They are usually used to relieve moderate to severe pain particularly of visceral origin.

BUPRENORPHINE

It is 25-50 times more potent than morphine. It is given by sublingual, intramuscular or intravenous injection. Tablet of buprenorphine is available for sublingual administration. The onset of analgesia occurs in about 15 minutes following intramuscular injection and more rapid than this with intravenous administration. Peak analgesia occurs within one hour following intramuscular and somewhat quicker with intravenous administration. Analgesia may be maintained up to 6 hours or more.

Indications: moderate to severe pain, peri-operative analgesia, adjunct in the treatment of opioid dependence.

Unlike pentazocine, the drug may be administered to patients with angina and acute myocardial infarction.

Adverse effects and cautions: *see* under morphine. It has less dependence or abuse liability than other potent opioid analgesics.

Drug interactions: *see* under morphine

Dose: By intramuscular or slow intravenous injection, 300-600 micrograms every 6-8 hours, child over 6 months 3-6 micrograms/kg every 6-8 hours (maximum 9 micrograms/kg). By sublingual administration, initially 200-400 micrograms every 8 hours; CHILD over 6 years (16-25 kg), 100 micrograms every 6-8 hours, 25-37.5 kg 100-200 micrograms every 6-8 hours, 37.5-50 kg 200-300 micrograms every 6-8 hours.

Preparation available

Buprenorphine Injection: An injection containing 0.3 mg/ml of buprenorphine, as hydrochloride, is usually available.

Buprenorphine Sublingual Tablets: Each tablet containing 200 micrograms of buprenorphine (as hydrochloride) is usually available.

BUTORPHANOL

It is a competitive mu (μ)-receptor antagonist but exert its analgesic effect by acting as agonist at kappa (κ) receptors. Its duration of action is similar to

morphine and 2-3 mg of the drug produces analgesia and respiratory depression equal to 10mg morphine.

It increases pulmonary arterial pressure and work of the heart.

Indications: to relieve acute pain.

Adverse effects and cautions: drowsiness, sweating, weakness, nausea, physical dependence.

Dose: By intramuscular injection, 1-4 mg every 3-4 hours; by intravenous injections, 0.5-2 mg every 3-4 hours.

Preparation available

Butorphanol Injection: Injection containing 1 mg and 2 mg of butorphanol tartrate per ml in a vial is usually available.

CODEINE PHOSPHATE

It is usually given orally. Its effect comes in 15-30 minutes and analgesia is maintained for 4-6 hours. Codeine has good antitussive activity.

Indications: relief of mild to moderate pain.

Adverse effects and cautions: tolerance and dependence, sedation, dizziness, nausea and constipation.

The drug should be avoided in children less than 1 year. The drug should be used with caution in patients with asthma, prostatic hypertrophy, hepatic disease, moderate and severe renal impairment, third trimester of pregnancy.

Dose: 30-60 mg every 4 hours when necessary, to a maximum of 240 mg daily; CHILD 1-12 years, 3 mg/kg daily in divided doses.

Preparation available: *see* under section 3.2, antitussives.

METHADONE HYDROCHORIDE

It is an opioid agonist, less sedating than morphine. It has extended duration of action in suppressing withdrawal symptoms in physically dependent individuals.

Indications: adjunct in treatment of opioid dependence, cough in terminal disease.

Adverse effects and cautions: *see* under morphine.

Drug interactions: Rifampicin and phenytoin accelerate the metabolism of methadone and can precipitate withdrawal symptoms.

Dose: Adjunct in treatment of opioid dependence, initially 10–40 mg daily, increased by up to 10 mg daily (maximum weekly increase 30 mg) until no signs of withdrawal or intoxication; usual dose range 60–120 mg daily; CHILD not recommended.

Preparation available

Methadone Oral Concentrate: Concentrated solution containing methadone hydrochloride 10 mg/ml is usually available. The preparation is diluted to required strength before dispensing.

MORPHINE

It is usually given by subcutaneous or intramuscular injection and its effect comes in fifteen minutes. Peak analgesia occurs within 50-90 minutes following subcutaneous injection, 30-60 minutes after intramuscular injection and 20 minutes after intravenous injection. Analgesia may be maintained up to 7 hours. Maximal respiratory depression occurs within 7 minutes, 30 minutes and 90 minutes following intravenous, intramuscular and subcutaneous injections respectively.

Indications: relieve acute or chronic pain. The drug is also used parenterally for preoperative sedation, as a supplement to anaesthesia and for analgesia during labour. Morphine is used in patients with acute pulmonary oedema. Morphine is used in relieving pain of myocardial infarction, palliative care.

Adverse effects and cautions: respiratory depression, postural hypotension, nausea and vomiting, constipation, urticaria and itch, tolerance and addiction.

It should be used with caution in those with asthma, hypotension, decreased respiratory reserve, third trimester of pregnancy, moderate and severe renal impairment.

The drug should be avoided in patients with raised intracranial pressure or head injury since, in addition to interfering with respiration, affects pupillary responses, vital for neurological assessment.

Drug interactions: morphine potentiates the hypotensive and sedative effects of other drugs such as phenothiazines and antidepressants.

Dose: Acute pain, by subcutaneous or intramuscular injection, 10 mg every 4 hours; CHILD up to 1 month 150 micrograms/kg, 1-12 months 200 micrograms/kg, 1-5 years 2.5-5 mg, 6-12 years 5-10 mg. By slow intravenous injection ¼-½ corresponding intramuscular dose.

Myocardial infarction, by slow intravenous injection (2 mg/minute), 10 mg followed by further 5-10 mg if necessary.

Preparation available

Morphine Sulfate Injection: Injection containing 10 mg per ml of morphine sulphate is usually available. It should be protected from light.

Morphine Sulfate Tablets: Each tablet containing 10 mg, 20 mg, and 30 mg of morphine sulphate is usually available. 30 mg and 60 mg tablets are available is sustained release form.

NALTREXONE

It is an opioid antagonist. It is much more effective than naloxone by the oral route. It also has longer duration of action.

Indications: treatment of compulsive users of opioids, alcoholism.

Adverse effects and cautions: nausea, vomiting, anxiety, abdominal pain, headache, sleeping difficulty, loss of appetite, diarrhoea, constipation, delayed ejaculation, joint and muscle pain.

The drug is contra-indicated in patients currently dependent on opioids, acute hepatitis or liver failure.

The drug should be used with caution in hepatic or renal impairment, pregnancy and breast-feeding.

Liver function tests should be done before and during treatment.

Dose: 25 mg initially then 50 mg daily; the total weekly dose may be divided and given on 3 days of the week for improved compliance; CHILD not recommended.

Preparation available

Naltrexone Tablets: Each tablet containing 50 mg of naltrexone hydrochloride is usually available.

PENTAZOCINE

It has analgesic and has both agonist and antagonistic effects. It precipitates withdrawal symptoms, including pain in patients dependent on other opioids. It is given by oral, subcutaneous and intramuscular injection. The onset of analgesia occurs within 15-30 minutes following oral, 15-20 minutes following subcutaneous or intramuscular injections. Peak analgesia occurs within 1-3 hours following oral, 1 hour following subcutaneous or intramuscular injection.

Analgesia may be maintained up to 3 hours or longer following oral and about 2 hours following subcutaneous or intramuscular injections. Following intravenous administration, the onset of analgesia occurs within 2-3 minutes, peak analgesia within 15 minutes and the duration of analgesia is about 1 hour.

Indications: moderate to severe pain. It is not recommended in patients with myocardial infarction as it increases work load on the heart.

Adverse effects and cautions: similar to morphine. Euphoria, sedation and nausea occur most frequently but vomiting occurs less frequently than with morphine.

Contraindications and cautions: *see* under morphine.

Drug interactions: pentazocine potentiates the hypotensive and sedative effects of other drug such as phenothiazines, hypnosedatives and anxiolytics.

Dose: By mouth, pentazocine hydrochloride 50 mg every 3-4 hours preferably after food (range 25-100 mg); CHILD 6-12 years 25 mg. By subcutaneous, intramuscular or intravenous injection, moderate pain, pentazocine 30 mg, severe pain 45-60 mg every 3-4 hours. CHILD over 1 year, by subcutaneous or intramuscular injection, up to 1 mg/kg, by intravenous injection up to 500 micrograms/kg.

Preparation available

Pentazocine Injection: Injection containing the equivalent of 30 mg/ml of pentazocine, as lactate, is usually available. Pentazocine injection should be proctected from light.

Pentazocine Tablets: Each tablet containing 25 mg of pentazocine hydrochloride is usually available.

PETHIDINE

It is usually given by subcutaneous or intramuscular injection. It is also given by slow intravenous or by slow continuous intravenous infusion. Pethidine

appears to have a more rapid onset (within 10 minutes) and shorter duration of action than morphine. Peak analgesia occurs about 40-60 minutes after subcutaneous administration and 30-50 minutes after intramuscular injection. Analgesia may be maintained for 2-4 hours following subcutaneous or intramuscular administration.

Indications: moderate to severe pain and obstetric analgesia.

Adverse effects and caution: similar to morphine but it may cause more severe nausea and hypotension than morphine. It produces less constipation and urinary retention. It produces same degree of respiratory depression, euphoria and sedation as morphine in equianalgesic doses.

Cautions: *see* under morphine. It may increase ventricular rate through a vagolytic action, the drug should be used with caution in patients with atrial flutter and other supra ventricular tachycardias.

Dose: By mouth, 50-150 mg every 4 hours; CHILD 0.5-2 mg/kg.

By subcutaneous or intramuscular injection, 25-100 mg, repeated after 4 hours; CHILD by intramuscular injection, 0.5-2 mg/kg.

By slow intravenous injection 25-50 mg repeated after 4 hours.

Obstetric analgesia, by subcutaneous or intramuscular injection, 50-100 mg, repeated 1-3 hours later if necessary; maximum 400 mg in 24 hours.

Preparation available

Pethidine Injection: Injection containing 50 mg per ml of pethidine hydrochloride is usually available.

Pethidine Tablets: Each tablet containing 50 mg of pethidine hydrochloride is usually available.

TRAMADOL HYDROCHLORIDE

It produces analgesia by opioid effect and by inhibition of norephinephrine and serotonin. It is less effective than morphine or pethidine in severe pain. Analgesia begins within an hour of oral dosing and peak analgesia occurs within 2-3 hours. The duration of analgesia is about 6 hours.

Indications: moderate to severe pain, obstetric analgesia.

Adverse effects and cautions: nausea, vomiting, dry mouth, sedation, headache.

Contraindications and cautions: *see* under morphine.

Dose: By mouth, 50-100 mg not more often than every 4 hours, total of more than 400 mg not usually required.

By intramuscular or intravenous injection (over 2-3 minutes) or by intravenous infusion, 50-100 mg every 4-6 hours.

Preparation available

Tramadol Tablets: Each tablet containing 50 mg of tramdol hydrochloride is usually available.

Tramadol Injection: Each vial containing 50 mg of tramadol hydrochloride per ml is usually available.

4.2 Antiepileptics

CARBAMAZEPINE

Its antiepileptic activity is similar to phenytoin.

Indications: all forms of epilepsy except absence seizure (petitmal), trigeminal neuralgia.

Adverse effects and cautions: gastrointestinal disturbances, dizziness, drowsiness, blurred vision, leucopenia and aplastic anaemia, mild transient generalized erythematous rash.

The drug should be used with caution in patients with hepatic impairment and renal impairment.

Carbamazepine should not be administered to patients with a history of previous bone-marrow depression, AV conduction abnormalities. Safe use of drug during pregnancy has not been established.

Drug interactions: carbamazepine induces hepatic enzymes. Regular dosage promotes its own metabolism and that of other drugs metabolized in the liver, including phenobarbital, ethosuximide, phenytoin, oral contraceptives and oral anticoagulants.

Dose: Epilepsy, initially 100-200 mg 1-2 times daily, increased slowly to usual dose of 0.8-1.2 g daily in divided doses; in some cases 1.6 g daily may be needed; CHILD, daily in divided doses, up to 1 year, 100-200 mg, 1-5 years 200- 400 mg, 5-10 years 400-600 mg, 10-15 years 0.6-l g.

Trigeminal neuralgia, initially 100 mg 1-2 times daily, increased gradually according to response; usual dose 200 mg 3-4 times daily up to 1.6 g daily in some patients.

Preparation available

Carbamazepine Tablet: Each tablet containing 100 mg, 200 mg and 400 mg of carbamazepine is usually available.

Carbamazepine Oral Solution: Each 5ml of oral solution containing 100 mg of carbamazepine is usually available.

CLOBAZAM

It is a benzodiazepine.

Indications: adjunct in epilepsy, anxiety.

Adverse effects and cautions: see under diazepam.

Dose: Epilepsy, 20-30 mg daily; maximum 60 mg daily; CHILD over 3 years, not more than half adult dose.

Anxiety, 20-30 mg daily in divided doses or as a single dose at bed time, increased in severe anxiety (in hospitalised patients) to a maximum of 60 mg daily in divided doses, ELDERLY 10-20 mg daily.

Preparation available

Clobazam Tablets: Each tablet containing 10 mg of clobazam is usually available.

CLONAZEPAM

It is a benzodiazepine.

Indications: all types of epilepsy, status epileptics.

Adverse effects and cautions: dizziness, drowsiness, muscle hypotonia, restlessness, salivary or bronchial hypertension in infants and small children, sexual dysfunction, dependence and withdrawal.

The drug should be used with caution in pregnancy and breast-feeding mothers. The drug is contraindicated in respiratory depression, acute pulmonary insufficiency.

Dose: 1 mg (elderly 500 micrograms) initially at night for 4 nights, increased according to response over 2-4 weeks to usual maintenance dose of 4-8 mg daily to 3-4 divided doses; CHILD up to 1 year, initially 250 µg increased as above to usual maintenance dose of 0.5-1 mg, 1-5 years, initially 250 micrograms increased as above to 1-3 mg, 5-12 years, initially 500 micrograms increased as above to 3-6 mg.

Preparation available

Clonazepam Tablets: Each tablet containing 500 micrograms of clonazepam is usually available.

DIAZEPAM

The drug does not abolish the abnormal discharge of the epileptic focus, but it suppresses the spread of seizure activity.

Indications: status epilepticus, convulsions due to poisoning.

Adverse effects and cautions: apnoea and hypotension (rapid parenteral administration), thrombophlebitis, sedation, drowsiness, ataxia, headache, muscle weakness.

Facilities for mechanical ventilation should always be at hand and the patient should remain under close observation for at least one hour. The danger of apnoea and hypotension are reduced if injections are administered slowly.

Drug interactions: patients concurrently receiving central depressant drugs including antidepressants, hypnotics and anaesthetics are at increased risk of developing sedative effects.

Dose : By intravenous injection, 10-20 mg at a rate of 0.5 ml (2.5 mg) per 30 seconds, repeated if necessary after 30-60 minutes; may be followed by intravenous infusion to maximum 3 mg/kg over 24 hours; CHILD 200-300 micrograms/kg.

Preparation available

Diazepan Injection: Injection containing 5 mg/ml of diazepam is usually available. Dizapam injection should be protected from light.

ETHOSUXIMIDE

It acts by inhibiting T current.

Indications: absence (petitmal) seizures.

Adverse effects and cautions: gastro-intestinal disturbances, drowsiness, dizziness, ataxia, headache and mild euphoria. Rarely psychotic states,

rashes, leucopenia and agranulocytosis. The drug should be used with caution in patients with hepatic or renal disease. Safe use of drug during first trimester of pregnancy or lactation has not been established.

Dose: Adult and CHILD over 6 years, initially, 500 mg daily increased by 250 mg at intervals of 4-7 days to usual dose of 1-1.5 g daily; occasionally up to 2 g daily may be needed; CHILD up to 6 years 250 mg daily, increased gradually to usual dose of 20 mg/kg daily.

Preparation available

Ethosuximide Capsules: Each capsule containing 250 mg of ethosuximide is usually available.

Ethosuximide Oral Solution: Each 5ml containing 250 mg of ethosuximide is usually available. Ethosuximide oral solution should be stored at a temperature not exceeding 25°.

GABAPENTIN

The anticonvulsant mechanism of action of the drug is unknown.

Indications: adjunctive treatment of partial seizures, with and without secondary generalisation.

Adverse effects and cautions: ataxia, dizziness, fatigue, drowsiness, weight gain, diplopia.

The drug should not be withdrawn suddenly (may cause anxiety, insomnia, sweating, pain – taper off over at least 1 week).

The drug should be used with caution in pregnancy, breast-feeding, renal impairment.

Dose: Epilepsy, 300 mg on day 1, then 300 mg twice daily on day 2, then 300 mg 3 times daily on day 3, then increased according to response in steps of 300 mg daily (in 3 divided doses) to a maximum 2.4 g daily; CHILD 6-12 years 10 mg/kg on day 1, then 20 mg/kg on day 2, then 25-35 mg/kg daily, maintenance 900 mg daily.

Preparation available

Gabapentin Capsules: Each capsule containing 300 mg of gabapentin is usually available.

LAMOTRIGINE

It is an antiepileptic drug. It is useful for monotherapy or as an adjunct to treatment with other antiepileptic drugs.

Indications: partial, secondarily generalised tonic-clonic seizures, Lennox-Gastaut syndrome.

Adverse effects and cautions: dizziness, ataxia, blurred or double vision, nausea, vomiting, rash, Stevens-Johnson syndrome.

The drug should be used with caution in pregnancy, breast-feeding, renal or hepatic impairment.

Dose: Monotherapy, initially 25 mg daily for 14 days, increased to 50 mg daily for further 14 days, then increased by maximum of 50-100 mg daily every 7-14 days; usual maintenance as monotherapy, 100- 200 mg daily in 1-2 divided doses.

Adjunctive therapy with valproate, initially 25 mg every other day for 14 days then 25 mg daily for further 14 days, thereafter increased by maximum of 25-50 mg daily every 7-14 days; usual maintenance 100-200 mg daily in 1-2 divided doses.

Preparation available

Lamotrigine Tablets: Each tablet containing 25 mg, 50 mg and 100 mg of lamotrigine is usually available.

OXCARBAZEPINE

It is a prodrug and gets converted to its main active metabolite. It is less potent enzyme inducer than is carbamazepine.

Indications: monotherapy or adjunct therapy for partial seizures.

Adverse effects and cautions: abdominal pain, nausea, vomiting, headache, drowsiness, ataxia, depression, tremor, diarrhoea, constipation, rash, nystagmus, Stevens-Johnson syndrome.

The drug should be used with caution in pregnancy, breast-feeding, hepatic or renal impairment, hypersensitivity to carbamazepine.

Dose: Initially 300 mg twice daily increased according to response in steps of up to 600 mg daily at weekly intervals; usual dose range 0.6-2.4 g daily in divided doses; CHILD over 6 years, 8-10 mg/kg daily in 2 divided doses increased according to response in steps of up to 10 mg /kg daily at weekly intervals.

Preparation available

Oxcarbazepine Tablets: Each tablet containing 150 mg and 300 mg of oxcarbazepine is usually available.

PARALDEHYDE

It shows anticonvulsant activity in subhypnotic doses.

Indications: status epilepticus

Adverse effects and cautions: rashes

The drug is contraindicated in patients with gastric disorders.

Drug interactions: concomitant administration with other CNS depressants such as alcohol will have increased sedative effects.

PHENOBARBITAL

It shows marked anticonvulsant activity and acts by potentiation of synaptic inhibition through action on GABA receptors.

Indications: all forms of epilepsy except absence seizures, status epilepticus.

Adverse effects and cautions: sedation, drowsiness, vertigo, ataxia, skin rashes, behavioural changes, irritability and impaired learning (in children) and dependence.

Discontinuation of treatment occasionally induces status epilepticus which is often refractory to other drugs.

Drug interactions: It induces hepatic microsomal enzyme systems leading to its own increased metabolism and that of other drugs such as carbamazepine, warfarin, oral contraceptives and corticosteroids thereby their decreased plasma concentration.

Dose: By mouth, 60-180 mg at night; CHILD 5-8 mg/kg daily.

Status epilepticus, by intravenous injection (dilute injection 1 in 10 with water for injection) 10 mg/kg, not more than 100 mg/minute.

Preparation available

Phenobarbital Sodium Tablets: Each tablet containing 30 mg and 60 mg of phenobarbital sodium is usually available.

Phenobarbital Injection: Injection containing 200 mg of phenobarbital sodium per ml is usually available.

PHENYTOIN

It acts by limiting the repetitive firing of action potentials evoked by a sustained depolarisation.

Indications: all forms of epilepsy except absence seizures, trigeminal neuralgia.

Adverse effects and cautions: gingival hyperplasia, acne, hirsutism and skin rash. These adverse effects may occur at therapeutic level. Nystagmus, ataxia, diplopia, sedation, nausea and vomiting occur at high plasma level.

Safe use of phenytoin during pregnancy has not been established.

Drug interactions: Phenytoin metabolism may be impaired by drugs that inhibit liver enzymes. The following agents cause phenytoin to accumulate and may precipitate toxicity e.g. isoniazid, chloramphenicol, sulphonamides. Phenytoin metabolism can be induced by the following agents resulting low plasma level of phenytoin e.g. carbamazepine, alcohol and steroids. Phenytoin can induce its own metabolism and that of other drugs e.g. oral contraceptives.

Dose: By mouth, initially 3-4 mg/kg daily or 150-300 mg daily (as a single dose or two divided doses) increased gradually as necessary (plasma monitoring); usual dose 200-500 mg daily; CHILD 4-8 mg/kg daily (1 or 2 doses).

By slow intravenous injection (with blood pressure and ECG monitoring) status epilepticus, 15 mg/kg at a rate not exceeding 50 mg per minute, as a loading dose. Maintenance doses of about 100 mg should be given thereafter at intervals of every 6-8 hours, monitored by measurement of plasma concentration; rate and dose reduced according to weight. CHILD 15 mg/kg as a loading dose. Not recommended by intramuscular injection.

Preparation available

Phenytoin Capsules: Each capsule containing 100 mg of phenytoin sodium is usually available.

Phenytoin Oral Suspension: Each 5 ml of oral suspension containing 100 mg phenytoin is usually available.

Phenytoin Tablets: Each tablet containing 100 mg of phenytoin sodium is usually available. They are coated.

VALPROIC ACID

The action is similar to phenytoin.

Indications: All types of epilepsy.

Adverse effects and cautions: nausea and gastric irritation, weight gain, increased appetite, thrombocytopenia, transient hair loss, oedema, drug induced hepatitis, sedation and drowsiness.

Hepatic function should be performed before treatment and at frequent interval of 2 months for the first six months. Safe use of drug during pregnancy has not been established.

Drug interactions: valproic acid inhibits enzyme system in liver with increased plasma concentration of ethosuximide, lamotrigine.

Dose : By mouth-initially, 600 mg daily in divided doses, preferably after food, increasing by 200 mg/day at 3 days intervals to a maximum of 2.5 g daily in divided doses, usual maintenance 1-2 g daily (20-30 mg/kg daily); CHILD up to 20 kg (about 4 years), initially 20 mg/kg daily in divided doses, may be increased provided plasma concentration monitored; over 20 kg, initially 400 mg daily in divided doses increased gradually to 20-30 mg/kg daily; maximum 35 mg/kg daily.

By intravenous injection (over 3-5 minutes) or by intravenous infusion, continuation of valproate treatment when oral therapy not possible, same as current dose by oral route. Initiation of valproate therapy when oral valproate not possible by intravenous injection (over 3-5 minutes), 400-800 mg (up to 10 mg/kg) followed by intravenous infusion up to maximum 2.5 g daily; CHILD, usually 20-30 mg/kg daily.

Preparation available

Sodium Valproate Tablets: Each tablet containing 200 mg of sodium valproate is usually available.

4.3 Antiparkinsonism Drugs

AMANTADINE

Indications: Parkinson's disease (but drug induced not extrapyrimidal symptoms, post-herpetic neuralgia.

Adverse effects and cautions: anorexia, nausea, nervousness, inability to concentrate, insomnia, dizziness, convulsions, hallucinations or feelings of detachment, blurred vision, gastro-intestinal disturbances, livedo reticularis and peripheral oedema; rarely leucopenia, rashes.

The drug should be taken with caution in hepatic or renal impairment, congestive heart disease, confused or hallucinatory states.

Abrupt withdrawal in Parkinson's disease should be avoided.

Performance of skilled tasks, like driving, may be affected.

The drug is contraindicated in pregnancy, breast-feeding, epilepsy, severe renal impairment.

Dose: Parkinsonism, 100 mg daily increased after one week to 100 mg twice daily, usually in conjunction with other treatment.

Post-herpetic neuralgia 100 mg twice daily for 14 days, continued for further 14 days if necessary.

Preparation available

Amantadine Capsules: Each capsule containing 100 mg of amantadine hydrochloride in usually available.

BENZTROPINE

It is a synthetic anticholinergic drug.

Indications: *see* under trihexyphenidyl.

Adverse effects and cautions: see under trihexyphenidyl.

Dose: By mouth, 0.5 mg daily usually at bedtime, gradually increased; maximum 6 mg daily; usual maintenance dose 1-4 mg daily in single or divided doses.

Preparation available

Benztropine Tablets: Each tablet containing 2 mg of benztropine mesilate is usually available.

BROMOCRIPTINE

It is a direct dopamine receptor agonist which has a similar range of actions as levodopa.

Indications: Parkinsonism (but not drug induced), prolactinoma, prevention or suppression of lactation.

Adverse effects and cautions: headache, constipation, dizziness, nausea, confusion, leg cramps and loss of appetite.

Use of drug in breast-feeding mother prevents lactation in mothers. Patient should be alerted when driving or doing jobs requiring alertness because of possible drowsiness or dizziness.

Preparation available

Bromocriptine Tablets: Each tablet containing 1.25 mg and 2.5 mg of bromocriptine (as mesilate) is usually available.

CARBIDOPA AND LEVODOPA

Co-careldopa

Levodopa is immediate precursor of dopamine; levodopa is decarboxylated in the brain to replenish striatal dopamine.

Dopamine itself can not be given as it is not absorbed orally and does not cross the blood-brain barrier. Levodopa improves bradykinesia and rigidity more than tremor.

Carbidopa is a decarboxylase inhibitor which inhibits decarboxylation of levodopa to dopamine. Carbidopa is available in combination with levodopa and concurrent administration inhibits the peripheral decarboxylation of levodopa, thus more levodopa is available for transport to the brain. Carbidopa generally

decreases levodopa dose requirements by 70-80%, reduces the incidence of levodopa-induced nausea and vomiting and may provide a smoother response to levodopa. The total dose of carbidopa should be at least 70 mg.

Indications: Parkinsonism (but not drug induced)

Adverse effects and cautions: anorexia, nausea, postural hypotension, tachycardia, arrhythmias, abnormal involuntary movements, psychiatric effects such as psychosis, depression or hypomania.

The drug is contraindicated in closed-angle glaucoma. The drug should be used with caution in patients with a history of myocardial infarction. It should be used with caution to patient with a history of a active peptic ulcer because there is a possibility of upper gastrointestinal haemorrhage. Periodic evaluation of hepatic, cardiovascular, and renal function is advisable. Safe use of levodopa during pregnancy and in breast-feeding has not been established.

Drug interactions: pyridoxine promotes metabolism of levodopa by decarboxylase causing reversal ofantiparkinsonism effect of levodopa.

Phenothiazines (chlorpromazine, fluphenazine, prochlor-perazine, trifluoperazine) and butyrophenones (haloperidol, droperidol) antagonise the therapeutic effects of levodopa.

Anticholinergics are frequently co-prescribed since they act synergistically to reduce the tremor of parkinsonism. They may, however, slow gastric emptying and reduce absorption of levodopa.

Concominant use of levodopa with ACE inhibitors and angiotensin-II antagonists will enhance hypotesive effects of these drugs.

Dose: Expressed as levodopa, initially 100 mg 3 times, increased by 50-100 mg daily or alternate days according to response.

Preparation available

Co-careldopa Tablets: Each tablet containing 25 mg of carbidopa and 250 mg of levodopa and also 25 mg of carbidopa and 100 mg of levodopa is usually available.

ORPHENADRINE HYDROCHLORIDE

It is also synthetic anticholinergic drug.

Indications: *see* under trihexyphenidyl.

Adverse effects and cautions: see under trihexyphenidyl, may cause insomnia.

Dose: 150 mg daily in divided doses, gradually increased; maximum 400 mg daily.

Preparation available

Orphenadrine Hydrochloride Tablets: Each tablet containing 50 mg of orphenadrine hydrochloride is usually available.

TRIHEXYPHENIDYL HYDROCHLORIDE

Benzhexol hydrochloride

It is a synthetic anticholinergic drug. It is mainly effective in reducing

tremor and rigidity but without significant action on bradykinesia.

Indications: Parkinsonism, drug induced extrapyramidal symptoms (but not tardive dyskinesia).

Adverse effects and cautions: dry mouth, constipation, dizziness, blurred vision, gastro- intestinal disturbances and less commonly tachycardia.

Trihexyphenidyl should be used with caution in patients with conditions in which anticholinergic effects are undesirable.

Dose: 1 mg daily gradually increased; usual maintenance dose 5-15 mg daily in 3-4 divided doses, CHILD not recommended.

Preparation available

Trihexyphenidyl Tablets: Each tablet containing 2 mg of trihexypehnidyl hydrochloride is usually available.

4.4 Anxiolytics

4.4.1 Benzodiazepines

These are the most important anxiolytics and the group includes: the drugs like diazepam, chlordiazepoxide, oxazepam, alprazolam and lorazepam. Although there is a tendency to prescribe these drugs to almost anyone with stress-related symptoms, unhappiness or minor physical disease, their use in many situations is unjustified. They are not appropriate for treating depression or chronic psychosis.

Anxiolytic treatment should be limited to the lowest possible dose for the shortest possible time since dependence develops with continuous use, the drug should be withdrawn slowly. Antipsychotics, in low doses, are also sometimes used in severe anxiety for their sedative action but long-term use should be avoided in view of a possible risk of tardive dyskinesia .

Benzodiazepines currently available range from short acting drugs such as oxazepam and lorazepam. The others are longer acting agents.

Indications: short-term use in anxiety (diazepam, lorazepam, alprazolam, chlordiazepoxide), insomnia associated with anxiety (diazepam, lorazepam, oxazepam), adjunctive treatment of acute alcohol withdrawal (diazepam, chlordiazepoxide), skeletal muscle spasm (diazepam, chlormezanone)

Adverse effects and cautions: drowsiness, dizziness, ataxia, confusion, physical dependence (more with short-acting agents), changes in libido.

Benzodiazepines should be used with caution in pegnancy and breast-feeding and patients with hepatic or renal disease. Patients should be warned that benzodiazepines may impair mental alertness. Benzodiazepines should not be used in patients with respiratory depression, severe hepatic impairment.

Drug interactions: concomitant use with ACE inhibitors, alpha-blockers and angiotensin-II receptor antagonists will produce enhanced hypotensive effects. There is increased sedative effect of opioid analgesics and general anaesthesia.

ALPRAZOLAM

Dose: 0.25 to 0.5 mg three times daily by mouth, increased where necessary up to a total daily dose of 3 mg. In elderly or debilitated patients an initial dose of 0.25 mg twice or thrice daily has been suggested. CHILD not recommended.

Preparation available

Alprazolam Tablets: Each tablet containing 0.25 mg, 0.5 mg and 1 mg of alprazolam is usually available.

CHLORDIAZEPOXIDE

Dose: Anxiety, 10 mg 3 times daily increased if necessary to 60-100 mg daily in divided doses, elderly (or debilitated) half adult dose. CHILD not recommended.

Preparation available

Chlordiazepoxide Tablets: Each tablet containing 10 mg of chlordiazepoxide is usually available. Tablets should be stored at a temperature not exceeding 25°.

DIAZEPAM

Dose: By mouth, anxiety, 2 mg 3 times daily, increased if necessary to 15-30 mg daily in divided doses; elderly (or debilitated) half adult dose.

Insomnia associated with anxiety, 5-15 mg at bed time.

Child night terrors and somnambulism, 1-5 mg at bed time.

By intramuscular injection or slow intraveneous injection (into a large vein, at a rate of not more than 5 mg/minute), for severe acute anxiety, control of acute panic attack, and acute alcohol withdrawl, 10 mg repeated after not less than 4 hours if necessary.

Intravenous infusion: maximum of 3 mg/kg over 24 hours, CHILD 0.2-0.3 mg/kg

Note: Only use intramuscular route when oral and intravenous routes not possible.

Preparation available

Diazepam Injection: Injection containing 5 mg/ml of diazepam is usually available. Diazepam injection should be protected from light.

Diazepam Oral Solution: Each 5ml of oral solution containing 2 mg of diazepam is usually available. Diazepam oral solution should be protected from light and stored at a temperature not exceeding 25°.

Diazepam Tablets: Each tablet containing 2 mg, 5 mg and 10 mg of diazepam are usually available. Diazepam tablets should be protected from light.

LORAZEPAM

Dose: By mouth, anxiety, 1-4 mg daily in divided doses; elderly (debilitated) half adult dose; insomnia associated with anxiety 1-2 mg at bed time.

By intramuscular or slow intravenous injection (into a large vein) acute panic attacks 25-30 micrograms/kg repeated every 6 hours if necessary; CHILD not recommended.

Note: Only use intramuscular route when oral and intravenous routes not possible.

Preparation available

Lorazepam Injection: Injection containing 2 mg per ml of lorazepam is usually available. Lorazepam injection should be protected from light and stored at a temperature of 2-8°.

Lorazepam Tablets: Each tablet containing 1 mg and 2 mg of lorazepam is usually available. Lorazepam tablets should be protected from light and stored at a temperature not exceeding 25°.

NITRAZEPAM

It is a long acting benzodiazepine.

Indications: insomnia.

Adverse effects and cautions: drowsiness and lightheadedness the next day, ataxia, amnesia, dependence.

The drug is contraindicated in respiratory depression, acute pulmonary insufficiency, severe hepatic impairment, chronic psychosis.

The drug should be used with caution in hepatic or renal impairment, pregnancy, breast-feeding, respiratory disease.

Dose: 5-10 mg at bedtime; ELDERLY 2.5-5 mg; CHILD not recommended.

Preparation available

Nitrazepam Tablets: Each tablet containing 5 mg and 10 mg of nitrazepam is usually available.

OXAZEPAM

Dose: anxiety- 15-30 mg (elderly or debilitated 10-20 mg) 3-4 times daily; CHILD not recommended.

Insomnia associated with anxiety 15-25 mg (maximum 50 mg) at bedtime; CHILD not recommended.

Preparation available

Oxazepam Tablets: Each tablet containing 15 mg and 30 mg of oxazepam is usually available. Oxazepam tablets should be protected from light and stored at a temperature not exccding 25°.

ZOLPIDEM

It is a non-benzodiazepine hypnotic.

It has short duration of action.

Indications: insomnia.

Adverse effects and cautions: nausea, vomiting, headache, dizziness, diarrhoea, ataxia, memory disturbances, changes in libido.

The drug is contraindicated in severe hepatic impairment, pregnancy, breast-feeding, acute or severe respiratory depression.

The drug should be used with caution in depression, hepatic impairment, elderly, renal impairment.

Dose: 10 mg at bed time; ELDERLY 5 mg; CHILD not recommended.

Preparation available

Zolpidem Tablets: Each tablet containing 5 mg and 10 mg of zolpidem tartrate is usually available.

4.4.2 Beta-blockers

Propranolol and metoprolol (lipophilic beta-blockers that enter the CNS) can reduce the autonomic symptoms (nervousness and muscle tremor) but do not affect psychological symptoms (worry, tension and fear).

Indications: treatment of somatic symptoms

Adverse effects and cautions: see under 2.1.2, beta-blockers

Dose: Propranolol, 40 mg once daily, increased to 40 mg 3 times daily if necessary.

4.5 Antipsychotics

They are also known as neuroleptics and can be classified into typical and atypical antipsychotics.

4.5.1 Typical antipsychotics

This group includes drugs like chlorpromazine, thioridazine, fluphenazine, prochlorperazine, trifluoperazine and haloperidol. This group of drugs have a range of other pharmacological properties other than antipsychotic effect which is of importance in causing adverse effects.They act by blocking D_2 receptors, which may give rise to extrapyramidal effects and hyperprolactinaemia. The drug should be gradually withdrawn after long term use.

Indications: schizophrenia and related psychoses, mania, short term adjunctive treatment of severe anxiety (all phenothiazines), intractable hiccup**.**

Adverse effects and cautions: extrapyramidal symptoms (marked with fluphenazine, prochlorperazine, trifluoperazine, haloperidol), anti-cholinergic effects (marked with thioridazine), sedation (marked with chlorpromazine), postural hypotension (marked with chlorpromazine and thioridazine), hypothermia, galactorrhoea, impotence and cholestatic jaundice, dizziness, headache, excitement and insomnia.

Phenothiazines should be used with caution in patients with hepatic and renal impairment, epilepsy, prostatic hypertrophy.

Safe use during pregnancy has not been established.

CHLORPROMAZINE HYDROCHLORIDE

Dose: By mouth, schizophrenia and other psychoses, mania, short term adjunctive treatment of severe anxiety, psychomotor agitation, excitement, and violent or dangerously impulsive behaviour, initially 25 mg 3 times daily (or 75 mg at night) adjusted according to response, to usual maintenance dose of 75-300 mg daily (but up to 1 g daily may be required in psyshoses); child 1-5 years 0.5 mg/kg every 4-6 hours (maximum 40 mg daily); 6-12 years third to half adult dose (maximum 75 mg daily); ederly, (or debilitated) third to half adult dose.

Intractable hiccup, 25-50 mg 3-4 times daily.

By deep intramuscular injection, (for relief of acute symptoms), 25-50 mg every 6-8 hours; child as dose by mouth.

Preparation available

Chlorpromazine Injection: An injection containing 25 mg/ml of chlorpromazine hydrochloride is usually available.

Chlorpromazine Oral Solution: Each 5 ml containing 5 mg of chlorpromazine hydrochloride is usually available.

Chlorpromazine Tablets: Each tablet containing 10 mg, 25 mg, 50 mg, 100 mg, and 200 mg of chlorpromazine hydrochloride is usually available.

FLUPHENAZINE

Dose: Schizophrenia and other psychoses, mania, initially 2-10 mg daily in 2-3 divided doses adjusted according to response to 20 mg daily, doses above 20 mg daily (10 mg in elderly) only with special caution.

Short-term adjunctive management of severe anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behaviour, initially 1 mg twice daily, increased as necessary to 2 mg twice daily. CHILD not recommended.

Maintenance in schizophrenia and other psychoses, by deep intramuscular injection, into the gluteal muscle, test dose 12.5 mg (6.25 mg in elderly) then after 4-7 days 12.5–100 mg repeated at intervals of 14-35 days, adjusted according to response; CHILD not recommended.

Preparation available

Fluphenazine Hydrochloride Tablets: Each tablet containing 1 mg of fluphenazine hydrochloride is usually available.

Fluphenazine Decanoate Depot Injection: Injection containing 25 mg per ml in sesame oil is usually available. Fluphenazine decanoate injection should be protected from light. The injection is for intramuscular injection only.

HALOPERIDOL

Dose: By mouth, schizophrenia and other psychoses, mania, short term adjunctive management of psychomotor agitation, excitement and violent or

dangerously impulsive behaviour, initially 1.5-3 mg, 2-3 times daily or 3- 5 mg, 2-3 times daily in severely affected or resistant patients; in resistant schizophrenia up to 30 mg daily may be needed; adjusted according to response to lowest effective maintenance dose (as low as 5- 10 mg daily). ELDERLY (or debilitated) initially half adult dose, CHILD initially 25-50 micrograms/kg daily to a maximum of 10 mg.

Short-term adjunctive management of severe anxiety, adults 500 micrograms twice daily. Intractable hiccup, 1.5 mg 3 times daily adjusted according to response; CHILD not recommended.

By intramuscular or intravenous injection, 2-10 mg subseqent doses being given every 4-8 hours according to response to a maximum 18 mg daily; severely disturbed patients may require initial dose of up to 18 mg; CHILD not recommended.

Preparation available

Haloperidol Injection: Injection containing 5 mg per ml of haloperidol is usually available. Haloperidol injection should be protected from light.

Haloperidol Oral Solution: Oral solution containing 2 mg per ml of haloperidol is usually available. Haloperidol oral solution should be protected from light and stored at a temperature of 15-25°.

Haloperidol Tablets: Each tablet containing 1.5 mg, 5 mg, 10 mg and 20 mg of haloperidol is usually available.

PIMOZIDE

Dose: Schizophrenia, initially 2 mg daily, adjusted according to response in increments of 2-4 mg at intervals of not less than 1 week; ELDERLY half usual dose; CHILD not recommended.

Monosymptomatic hypochondriacal psychosis, paranoid psychoses, initially 4 mg daily, adjusted according to response in increments of 2-4 mg at intervals of not less than 1 week; maximum 16 mg daily.

ELDERLY half usual starting dose; CHILD not recommended.

Preparation available

Pimozide Tablets: Each tablet containing 2 mg and 4 mg of pimozide is usually available.

PROCHLORPERAZINE: *see* under section 1.4, antiemetics.

THIORIDAZINE

Dose: Schizophrenia and other psyshoses, mania, 150-600 mg daily (initially in divided doses); maximum 800 mg daily (Hospital patient only) for up to 4 weeks.

Short term adjunctive management of psychomotor agitation, excitement, violent or dangerously impulsive behaviour, 75-200 mg daily.

Short term adjunctive management of severe anxiety, agitation, and

restlessness in the elderly, 30-100 mg daily; child (severe mental or behavioural problems only) under 5 years 1 mg/kg daily, 5-12 years 75-150 mg daily (in severe cases, up to 300 mg daily).

Preparation available

Thioridazine Tablets: Each tablet containing 10 mg, 25 mg, 50 mg and 100 mg of thioridazine hydrochloride is usually available. They are coated.

TRIFLUOPERAZINE

Dose : Schizophrenia and other psychoses, initially 5 mg twice daily, increased by 5 mg after 1 week, then at intervals of 3 days, according to response; child up to 12 years, initially up to 5 mg daily in divided doses, adjusted according to response, age and body weight.

Preparation available

Tritluoperazine Tablets: Each tablet containing 5 mg and 10 mg of trifluoperazine hydrochloride is usually available. They are coated.

4.5.2 Atypical neuroleptics

This group includes clozapine, olanzapine and risperidone. These drugs produce extrapyramidal symptoms less frequently than typical neuroleptics. Clozapine and olanzapine cause little or no elevation of prolactin concentration. Changing to an atypical neuoleptics in not necessary if a typical neuroleptic has controlled symptoms adequately and the individual does not suffer unacceptable adverse effects.

CLOZAPINE

Indications: schizophrenia (including psychosis in Parkinson's disease) in patients unresponsive to, or intolerant of, typical neruoleptics.

Adverse efecs and cautions: weight gain, hyperglycaemia and diabetes, constipation, dizziness, extrapyramidal symptoms, nausea, vomiting, tachycardia, hypertension, dry mouth, anorexia, neutropenia and agranulocytosis.

The drug is contraindicated in myocarditis, cardiomyopathy, severe renal impairment, bone-marrow disorders and breast-feeding.

The drug should be used with caution in pregnancy and patients with hepatic impairment, prostate hypertrophy.

Dose: schizophrenia, ADULT over 16 years, 12.5 mg once or twice (elderly 12.5 mg once) on first day then 25-50 mg (elderly 25-37.5 mg) on second day then increased gradually (if well tolerated) in steps of 25-50 mg daily (elderly maximum 25 mg daily) over 14-21 days up to 300 mg daily in divided doses.

Preparation available

Clozapine Tablets: Each tablet containing 25 mg and 100 mg of clozapine is usually available.

OLANZAPINE

Indications: schizophrenia, mania.

Adverse effects and cautions: weight gain, hyperglycaemia and diabetes, extrapyramidal symptoms, antimuscarinic effects, drowsiness, bradycardia, hypotension, increased appetite.

The drug is contraindicated in angle-closure glaucoma, acute myocardial infarction, severe hypotension or bradycardia and breast-feeding.

The drug should be used with caution in diabetes, prostatic hypertrophy, hepatic impairment, renal impairment and pregnancy.

Dose: Schizophrenia, combination therapy for mania, preventing recurrence in bipolar disorder, ADULT over 18 years, 10 mg daily adjusted to usual range of 5-20 mg daily, maximum 20 mg daily.

Preparation available

Olanzepine Tablets: Each tablet containing 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg and 20 mg of olanzepine is usually available.

RISPERIDONE

Indications: acute and chronic psychosis, mania.

Adverse effects and cautions: weight gain, hyperprolactinaemia (galactorrhoea, menstrual disturbances, gynaecomastia), priapism, cerebrovascular accident, tachycardia, neutropenia, thrombocytopenia.

The drug is contraindicated in breast-feeding.

The drug should be used with caution in pregnancy, hepatic impairment, and renal impairment.

Dose: Psychosis, 2 mg in 1-2 divided doses on first day then 4 mg in 1-2 divided doses on second day; usual dose range 4-6 mg daily; ELDERLY (or in hepatic or renal impairment) initially 500 micrograms twice daily increased in steps of 500 micrograms twice daily to 1-2 mg twice daily; CHILD under 15 years not recommended.

Preparation available

Risperidone Tablets: Each tablet containing 1 mg 2 mg, 3 mg and 4 mg of risperidone is usually available.

4.6 Antidepressants

Amitriptyline, doxepin, clomipramine, imipramine, nortriptyline, trimipramine, amoxapine and trazodone are tricyclic and related antidepressants. Fluoxetine, paroxetine and sertraline are selective serotonin re-uptake inhibitors (SSRIs). These two groups are most widely used. Choice of antidepressant should be based on the individual patient's requirements including the presence of concomitant disease, existing therapy, suicide risk and previous response to atidepressant therapy.

Tricyclic antidepressants may be suitable for many depressed patients. Although SSRIs appear to be better tolerated than older drugs, the difference is too

small to justify always choosing SSRIs as first line treatment.

SSRIs have fewer antimuscarinic side-effects than the tricyclics and they are also less cardiotoxic in overdose. SSRIs are also preferred to tricyclics for depression in patients with diabetes.

The response to antidepressant therapy is usually delayed with a lag period of up to two weeks and at least six weeks before maximum improvement occurs. It is important to use doses that are sufficiently high for effective treatment, but not so high to cause toxic effects. The use of more than one antidepressant at a time is not recommended since this does not enhance effectiveness and it may result in enhanced adverse effects or interactions.

4.6.1 Tricyclic and related drugs

The drugs can be divided into those with more or less sedative effect. Those with sedative effect include amitryptyline, doxepin, trazodone, and trimipramine. Those with less sedative effect incude imipramine, amoxapine and nortryptyline.

AMITRIPTYLINE HYDROCHLORIDE

Indications: depressive illness, nocturnal enuresis.

Adverse effects and cautions: sedation, dry mouth, blurred vision, constipation, difficulty with micturition, postural hypotension, tachycardia, arrhythmias, sweating, tremor, leucopenia, agranulocytosis, thrombocytopenia, behavioural disturbances (particularly children), jaundice, anorexia, nausea, diarrhoea and vomiting.

The drug is contraindicated in the acute recovery phase following myocardial infarction, arrhythmia (particularly heart block), manic phase and severe liver disease. The drug should be used with caution in patients for whom excessive anticholinergic activity could be harmful, such as those with benign prostatic hypertropahy or history of urinary retention or angle-closure glaucoma. Safe use of drug in third trimester of pregnancy has not been established. Safe use of drug in children below 16 years of age has not been established.

The drug is dangerous in overdose.

Drug interactions: tricyclic antidepressants may be additive with or may potentiate the action of central nervous system depressants such as alcohol, sedatives or hypnotics.

Dose: By mouth, depression, initially 75 mg (elderly and adolescents 30-75 mg) daily in divided doses or as a single dose at bed time increased gradually as necessary to maximum 150-200 mg; CHILD under 16 years not recommemded.

Nocturnal enuresis, CHILD 7-10 years 10 -20 mg, 11-16 years 25-50 mg at night; maximum period of treatment (including gradual withdrawal) 3 months.

Preparation available

Amitriptyline Tablets: Each tablet containing 10 mg, 25 mg and 75 mg of amitriptyline hydrochloride is usually available. Amitriptyline tablets are coated.

AMOXAPINE

Indications, adverse effects, cautions, drug interactions: see under amitriptyline

Dose: Initially 100-150 mg daily in divided doses or as a single dose at bed time increased as necessary to maximum 300 mg daily.

ELDERLY initially 25mg twice daily increased as necessary after 5-7 days to maximum 50 mg 3 times daily. CHILD under 16 years not recommended.

Preparation available

Amoxapine Tablets: Each tablet containing 50 mg and 100 mg of amoxapine is usually available. Amoxapine tablets should be stored in an air tight container.

CLOMIPRAMINE

Indications: depressive illness, phobic and obsessional states.

Adverse effects and cautions: see under amitriptyline.

Dose: Depressive illness, initially 10 mg daily, increased gradually as necessary to 30-50 mg daily in divided doses or single dose at bed time; maximum 250 mg daily; ELDERLY initially 10 mg daily increased carefully over approximately 10 days to 30-75 mg daily; CHILD not recommended.

Phobic and obsessional states, initially 25 mg daily (ELDERLY 10 mg daily) increased over 2 weeks to 100-150 mg daily; maximum 250 mg daily; CHILD not recommended.

Preparation available

Clomipramine Tablets: Each tablet containing 10 mg, 25 mg and 50 mg of clomipramine is usually available.

DOXEPIN

Indications: depressive illness, particularly where sedation is required.

Adverse effects, cautions and drug interactions: see under amitriptyline

Dose: Initially 75 mg (elderly 10-50 mg) daily in 3 divided doses or as a single dose at bedtime, increased to maximum 300 mg daily in three divided doses; CHILD not recommended.

Preparation available

Doxepin Capsules: Each capsule containing the equivalent of 10 mg, 25 mg and 75 mg of doxepin is usually available.

IMIPRAMINE

Indications: depressive illness, nocturnal enuresis.

Adverse effects and cautions: see under amitriptyline but it is less sedating.

Drug interactions: see under amitriptyline.

Dose: Depression, initially up to 75 mg daily in divided doses increased gradually to 150-200 mg (up to 300 mg in hospital patient); up to 150 mg may be given as a single dose at bedtime. ELDERLY initial 10 mg daily, increased gradually to 30-50 mg daily; CHILD not recommended.

Noctural enuresis, CHILD 7 years 25 mg, 8-11 years 25-50 mg, over 11 years 50-75 mg at bed time; maximum period of treatment (including gradually withdrawal) 3 months.

Preparation available

Imipramine Tablets: Each tablet containing 25 mg and 75 mg of Imipramine hydrochloride is usually available. They are coated.

MAPROTILINE

Indications: depressive illness, particularly where sedation is required.

Adverse effects, cautions and drug interactions: see under amitriptyline.

Dose: Initially 25-75 mg (eldery 30 mg) daily in 3 divided doses or as a single dose at bedtime, increased gradually as necessary to maximum 150 mg daily; CHILD not recommended.

Preparation available

Maprotiline Hydrochloride Tablets: Each tablet containing 75 mg of maprotiline hydrochloride is usually available.

MIANSERIN

Indications: depressive illnesss, particularly where sedation is required.

Adverse effects and cautions: see under amitriptyline but other adverse effects include leucopenia, agranulocytosis and aplastic anaemia, arthralgia, arthritis and influenza-like syndrome. Anticholinergic and cardiovascular adverse effects are milder and less common.

A full blood count is recommended every 4 weeks during the first 3 months of treatment. Clinical monitoring should be continued and treatment stopped and a full blood count obtained if fever, sore throat, stomatitis or other signs of infection develop.

Dose: Intially 30-40 mg (elderly 30 mg) daily in divided doses or as a single dose at bedtime, increased gradually as necessary; usual dose range 30-90 mg; CHILD not recommended.

Preparation available

Mianserin Tablets: Each tablet containing 10 mg, 20 mg and 30 mg of Mianserin hydrochloride is usually available. Mianserin tablets should be protected from light.

MIRTAZAPINE

It is a presynaptic α2-antagonist. It increases central noradrenergic and serotonergic neurotransmission.

Indications: major depression.

Adverse effects and cautions: sedation, increased appetite and weight gain, oedema, postural hypotension, convulsions, tremor, abnormal dreams, rash, reversible agranulocytosis, severe hyponatraemia.

The drug should be used with caution in pregnancy, breast-feeding, hepatic or renal impairment, epilepsy, hypotension, history of urinary retention, diabetes mellitus, angle-closure glaucoma.

Dose: Initially 15 mg daily at bedtime increased within 2-4 weeks according to response; maximum 45 mg daily as a single dose at bedtime or in 2 divided doses; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Mirtazapine Tablets: Each tablet containing 15 mg, 30 mg and 45 mg of mirtazapine is usually available.

NORTRIPTYLINE

Indications: depressive illness, nocturnal enuresis.

Adverse effects and cautions: *see* under amitriptyline but less sedating.

Drug Interactions: see under amitriptyline

Dose: Initially 30-50 mg (ELDERLY 30 mg) daily in single or divided doses, increased gradually as necessary to maximum 100 mg daily.

Nocturnal enuresis, CHILD 7 years 10 mg, 8-11 years 10-20 mg, over 11 years 25-35 mg at night, maximum period of treatment (including withdrawal) 3 months.

Preparation available

Nortriptyline Tablets: Each tablet containing the equivalent of 25 mg of nortriptyline is usually available. They are coated.

TRAZODONE HYDROCHLORIDE

Indications: depressive illness particularly where sedation is required, anxiety.

Adverse effects and cautions: *see* under amitriptyline but fewer anticholinergic and cardiovascular effects, rarely priapism

Drug interactions: *see* under amitriptyline.

Dose: Depression, initially 150 mg (elderly 100 mg) daily in divided doses after food or as a single dose at bedtime, may be increased to 300 mg daily; hospital patient up to maximum 600 mg daily in divided doses: CHILD not recommended.

Anxiety, 75 mg daily, increasing if necessary to 300 mg daily; CHILD not recommended.

Preparation available

Trazodone Tablets: Each tablet containing 25 mg, 50 mg and 100 mg of trazodone hydrochloride is usually available.

TRIMIPRAMINE

Indications: depressive illness, particularly where sedation is required.

Adverse effects, cautions and drug interactions: see under amitriptyline

Dose: Initially, 50-75 mg daily in divided doses or as a single dose at bedtime, increased as necessary to maximum of 300 mg daily.

ELDERLY 10-25 mg, 3 times daily initially, half adult maintenance dose may be sufficient; CHILD not recommended.

Preparation available

Trimipramine Tablets: Each tablet containing 10 mg, 25 mg and 75 mg of trimipramine (as maleate) is usually available. They are coated.

4.6.2 Selective Serotonin Re-uptake Inhibitors (SSRIs)

These drugs selectively inhibit the re-uptake of serotonin (5-HT).

ESCITALOPRAM

Indications: depressive illness, generalised anxiety disorder, panic disorder.

Adverse effects and cautions: see under fluoxetine; also postural hypotension, taste disturbance, fatigue.

Dose: Depressive illness and generalised anxiety disorder, 10 mg once daily increased if necessary to maximum 20 mg daily; ELDERLY initially half adult dose, lower maintenance dose may be sufficient; CHILD and ADOLESCENT under 18 years not recommended.

Panic disorder, initially 5 mg daily increased to 10 mg daily after 27 days, maximum 20 mg daily; ELDERLY initially half adult dose, lower maintenance dose may be sufficient; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Escitalopram Tablets: Each tablet containing 5 mg, 10 mg and 20 mg of escitalopram (as oxalate) is usually available.

FLUOXETINE

It is effective for treating depressive illness in children and adolescent also. However, it is associated with a small risk of self-harm and suicidal thoughts. The dose of the drug should be tapered over few weeks to avoid withdrawal features including anxiety, dizziness, sweating, sleep disturbances.

Indications: major depression, bulimia nervosa.

Adverse effects and cautions: gastro-intestinal disturbances, anorexia with weight loss, postural hypotension, taste disturbances, sexual dysfunction, ataxia, urinary retention and frequency.

The drug is contraindicated in manic phase. The drug should be used with caution in epilepsy, cardiac disease, diabetes, angle-closure glaucoma, pregnancy, breast-feeding, children and adolescents.

Dose: Major depression, 20 mg once daily increased after 3 weeks if necessary.

Bulimia nervosa, 60 mg once daily; maximum 80 mg once daily; CHILD and ADOLESCENT unde 18 years not recommended.

Preparation available

Fluoxetine Capsules: Each capsule containing 10 mg, 20 mg, 40 mg and 60 mg of fluoxetine (as hydrochloride) is usually available.

FLUVOXAMINE

It is also a SSRI.

Indications: depressive illness, obsessive-compulsive disorder.

Adverse effects and cautions: see under fluoxetine; also palpitation, tachycardia.

Dose: Depression, initially 50-100 mg daily in the evening, increased gradually if necessary to maximum 300 mg daily (over 150 mg in divided doses); usual maintenance dose 100 mg daily; CHILD and ADOLESCENT under 18 years not recommended.

Obsessive-compulsive disorder, initially 50 mg in the evening increased gradually if necessary after some weeks to maximum 300 mg daily (over 150 mg in divided doses); usual maintenance dose 100-300 mg daily; CHILD over 8 years initially 25 mg daily increased if necessary in steps of 25 mg every 4-7 days to maximum 200 mg daily (over 50 mg in divided doses).

Preparation available

Fluvoxamine Tablets: Each tablet containing 50 mg and 100 mg of fluvoxamine is usually available.

PAROXETINE

Indications: major depressive disorder, generalised anxiety disorder, obsessive-compulsive disorder, panic disorder, socialphobia, generalsed anxiety disorder. Post-traumatic stress disrder.

Adverse effects and cautions: asthenia (unusual tiredness or weakness), extrapyramidal reactions, withdrawal features, constipation, diarrhoea, drowsiness, dryness of mouth, palpitation, myalgia, sexual dysfunction, weight loss or gain.

The drug is contraindicated in patients with history of mania.

The drug should be used with caution in patients with neurological impairment, seizures, severe hepatic impairment, severe renal impairment, children and adolescents.

Dose: Major depression, social anxiety disorder, post-traumatic disorder, generalised anxiety disorder, usually 20 mg each morning (maximum 50 mg, ELDERLY 40 mg); CHILD and ADOLESCENT under 18 years not recommended.

Panic disorder, initially 10 mg each morning, increased gradually in steps of 10 mg to usual dose of 40 mg daily (maximum 60 mg daily, ELDERLY 40 mg daily); CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Paroxetine Tablets: Each tablet containing 10 mg, 20 mg, 30 mg and 40 mg of paroxetine (as hydrochloride) is usually available.

SERTRALINE

Indications: major depressive disorder, panic disorder, obscessive-compulsive disorder, post-traumatic stress disorder in adults.

Adverse effects and cautions: sexual dysfunction (decreased sexual desire or ability, delayed ejaculation is most common), anorexia, breast tenderness or enlargement, extrapyramidal effects, palpitation, skin rash, drowsiness, dryness of mouth, weight loss, headache.

The drug is contraindicated in patients with history of mania.

The drug should be used with caution in patients with hepatic or renal impairment, seizure disorders, neurological impairment, children and adolescents.

Dose: Major depression initially 50 mg daily, increased if necessary by increments of 50 mg over several weeks to maximum 200 mg daily, usual maintenance dose 50 mg daily, CHILD and ADOLESCENT under 18 years not recommended.

Post-traumatic stress disorder, initially 25 mg daily, increased after 1 week to 50 mg daily, dose increased in steps of 50 mg over several weeks to maximum 200 mg daily ; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Sertraline Tablets: Each tablet containing 25 mg, 50 mg and 100 mg of sertraline (as hydrochloride) is usually available.

4.7 Anti-manic agent

Drugs are used both to control acute attacks and also to prevent their recurrence. Benzodiazepines may be helpful in initial stages of treatment until lithium achieves its full effets. Valproic acid is used in the treatment of manic episodes associated with bipolar disorder. Carbamazepine may be used for the prophylaxis of bipolar disorder.

LITHIUM CARBONATE

The mechanism of action of lithium in not clear.

Indications: prophylaxis and treatment of mania, prophylaxis of bipolar disorder, prophylaxis of unipolar depression.

Adverse effects and cautions: nausea and vomiting, drowsiness, confusion, headache, fits, ataxia, oedema, weight gain, fine tremor, polydipsia.

Monitoring of serum lithium concentrations every three months. Lithium should be used with caution in elderly patients since they appear to be more susceptible to adverse effects of the drug. Lithium should generally not be used in patients with renal or cardiovascular disease or severe dehydration since the risk of toxicity is increased in these patients. Lithium should be used during pregnancy only in life- threatening situations or severe disease.

Drug interactions: indomethacin, ibuprofen, mefenamic acid, naproxen, diclofenac, ACE inhibitors, angiotensin-II receptor antagnists have been reported to increase serum lithium concentrations by reducing excretion of lithium.

Dose: Up to 1.5 g daily in single or divided doses subsequent doses in accordance with the plasma concentration of lithium.

Preparation available

Lithum Carbonate Tablets: Each tablet containing 150 mg and 300 mg of lithium carbonate is usually available.

4.8 Antipyretic analgesics

ASPIRIN

Acetylsalicylic acid

It possesses analgesic, anti-inflammatory and anti-pyretic activity.

Indications: mild to moderate pain, fever, antiplatelet.

Adverse effects and cautions: dyspepsia, epigastric distress, gastrointestinal bleeding, mucosal lesions (erosive gastritis, gastric ulcer), tinnitus and hearing loss is caused by high dose aspirin, prolongation of bleeding time, hypersensitivity reactions with skin rashes and asthma.

The drug should be used with caution in patients with active gastrointestinal lesions (erosive gastritis, peptic ulcer), impaired renal function, impaired hepatic function, asthma, third trimester of pregnancy.

The drug is contraindicated in patient with bleeding disorders such as haemophilia, previous or active peptic ulcer, children and adolescents under 16 years, breast-feeding.

Drug interactions: aspirin enhances the risk of bleeding when used with warfarin and other anticoagulants.

Dose: Mild to moderate pain and pyrexia, 300-900 mg every 4-6 hours when necessary; maximum 4 g daily; CHILD and ADOLESCENT not recommended.

Preparation available

Aspirin Tablets: Each tablet containing 50 mg, 75 mg and 300 mg of aspirin is usually available.

Dispersible Aspirin Tablets: Each tablet containing 350 mg of aspirin is usually available. Dispersible tablets should be kept in a well closed container and stored at a temperature not exceeding 25°. Dispersible tablets should be dispersed in water immediately before use.

PARACETAMOL

Acetaminophen

It lowers body temperature in patients with fever but rarely lowers normal body temperature, in equal doses, the degree of analgesia and antipyresis produced by paracetamol is similar to that produced by aspirin. It has poor anti-inflammatory activity.

Indications: mild to moderate pain, fever.

Adverse effects and cautions: pruritic maculopapular rash and urticaria, neutropenia and thrombocytopenia; rarely agranulocytosis. Liver damage on overdose.

Paracetamol should be used with caution in patients with renal impairment.

Dose: By mouth, 0.5-1 g every 4-6 hours to a maximum of 4 g daily; child 3 months-1 year 60-120 mg, 1-5 years 120-250 mg, 6-12 years 250-500 mg; these doses may be repeated every 4-6 hours,, when necessary (maximum of 4 doses in 24 hours).

By intravenous infusion over 15 minutes, ADULT and CHILD over 50 kg, 1 g every 4-6 hours, maximum 4 g daily.

Preparation available

Paediatric Paracetamol Oral Solution: Paediatric paracetamol oral solution containing 150 mg per ml of paracetamol in a suitable flavoured vehicle is available. Paediatric paracetamol oral solution should be protected from light.

Paracetamol Oral Suspension: Oral suspension containing 125 mg of paracetamol per 5 ml is usually available. Paracetamol oral suspension should be proctected from light.

Paracetamol Tablets: Each tablet containing 500 mg of paracetamol is usually available. Pracetamol tablets should be protected from light.

Paracetamol Injection: Injection containing 150 mg/ml of paracetamol is usually available.

4.9 Antimigraine drugs

Most migraine headaches respond to analgesics such as aspirin or paracetamol, but as peristalsis is often reduced during migraine attacks the medication may not be sufficiently well absorbed to be effective; dispersible or effervescent preparations should therefore preferably used. NSAIDs like ibuprofen, naproxen and diclofenac are also used.

Concomitant anti-emetic treatment may be required. If treatment with analgesic is inadequate, an attack may be treated with sumatriptan.

ERGOTAMINE TARTRATE

Indications: acute attacks of migraine and migraine variants unresponsive to analgesics.

Adverse effects and cautions: nausea, vomiting, abdominal pain and occasionally increased headache; repeated high dosage may cause ergotism with gangrene and confusion; pleural and peritoneal fibrosis may occur with excessive use.

Ergotamine is contraindicated in peripheral vascular disease, coronary heart disease, obliterative vascular disease and Raynand's syndrome, hepatic or renal impairment, sepsis, severe or inadequately controlled hypertension, hyperthyroidism, pregnancy and breast feeding, porphyria.

Dose: 2 mg at onset repeated after 30-60 minutes if necessary; maximum 8 mg in 24 hours; child not recommended.

Preparation available

Ergotamine Tablet: Each tablet containing 2 mg of ergotamine tartrate is usually available.

SUMATRIPTAN

It should not be prescribed for a patient who has not previously been diagnosed as a migraine or a to a migraine patient with atypical symptoms; until it has been determined that the patient's headache is not occurring secondary to potentially serious neurological condition (cerebrovascular accident or subarachnoid haemorrhage).

It acts by agonist action on the 5-HT (serotonin) IB/ID receptors.

Indications: treatment of acute migraine attacks, cluster headache.

Adverse effects and cautions: chest pain, and tightness (coronary vasoconstriction), drowsiness, hypotension, braycardia or tachycardia, nausea, vomiting, dizziness.

The drug is contraindicated in ischemic heart disease, previous myocardial infarction, coronary vasospasm, uncontrolled or severe hypotension.

The drug should be used with caution in pregnancy, breast-feeding, hepatic impairment.

Dose: By mouth, 50 mg (some patient may require 100 mg) as soon as possible after onset (patient not responding should not take second dose for the same attack); dose may be repeated after not less than 2 hours if migraine recurs. CHILD and ADOLESCENT under 18 years not recommended.

By subcutaneous injection, 6 mg as soon as possible after onset (patients not responding should no take second dose for same attack); dose may be repeated once after not less than 1 hour if migraine recurs; maximum12 mg in 24 hours; CHILD and ADOLESCENT under 18 years not recommended.

The drug should be given intravenously; it may cause coronary vasospasm and angina.

Preparation available

Sumetriptan Tablets: Each tablet containing 50 mg and 100 mg of sumatriptan (as succinate) is usually available.

Sumetriptan Injection: Injection containing 10 mg/ml of sumatriptan (as succinate) is usually available.

4.10 Drug used in substance dependence

4.10.1 Drug used in alcohol dependence

The alcohol withdrawal syndrome, in most cases symptoms do not require treatment and disappear within a few days, but more severe cases may require managed withdrawal from alcohol to avoid complications.

Benzodiazepines are usually the drugs of first choice because of their sedative, anxiolytic and anticonvulsant properties. If given promptly, benzodiazepines can prevent progression to seizures and delirium tremens. Longer-acting drugs such as chlordiazepoxide or diazepam may be more effective against withdrawal seizures and provide smoother withdrawal, while shorter-acting ones such as lorazepam or oxazepam have a smaller risk of producing oversedation and may be more suitable for use in the elderly and, since they do not rely on hepatic enzymes for their metabolism, for patients with liver disease.

Because of the risk of dependence benzodiazepines should only be given in short courses.

Once the initial acute withdrawal of alcohol is achieved, treatment may be required to maintain long-term abstinence. Pharmacotherapy should only be used as an adjunct to psychotherapy and supportive care.

DISULFIRAM

Disulfiram is used as an adjunct to the treatment of alcohol dependence. It gives rise to extremely unpleasant systemic reactions after the ingestion of even small amounts of alcohol because it leads to accumulation of acetaldehyde in the body. Reactions include flushing of the face, throbbing headache, palpitations, tachycardia, nausea, vomiting and with large doses of alcohol, arrhythmias, hypotension and collapse. Even small amounts of alcohol included in many oral medications may be sufficient to precipitate a reaction.

Indications: adjunct in the treatment of chronic alcohol dependence (under special supervision).

Adverse effects and cautions: initially drowsiness and fatigue; nausea, vomiting, halitosis, reduced libido; rarely psychotic reactions, allergic dermatitis, peripheral neuritis, hepatic cell damage.

Alcohol must not be consumed for at least 24 hours before initiating treatment.

Dose: 800 mg as single dose on first day, reducing over 5 days to 100-200 mg daily; should not be continued for longer than 6 months without reviews.

CHILD not recommended.

CHLORDIAZEPOXIDE

It is used to decrease withdrawal symptoms but also has a dependence potential.

Indications: withdrawal symptoms.

Adverse effects and cautions: *see* under section 4.4.1, benzodiazepines.

Dose: 10-50 mg 4 times daily, gradually reducing over 7-14 days.

4.10.2 Drug used in smoking cessation

BUPROPION HYDROCHLORIDE

Amfebutamone hydrochloride

Its mechanism of action in smoking cessation is not clear.

Indications: adjunct to smoking cessation in combination with motivational support.

Adverse effects and cautions: insomnia, dry mouth, gastro-intestinal disturbances, tremor, headache, dizziness, depression, rash, pruritus, sweating.

The drug is contra-indicated in patients with a history of seizures, eating disorders, CNS tumour, pregnancy, breast-feeding.

The drug should be used with caution in hepatic or renal impairment, elderly, predisposition to seizures.

Dose: Start 1-2 weeks before target stop date, initially 150 mg daily for 6 days then 150 mg twice daily (maximum single dose 150 mg, maximum daily dose 300 mg; minimum 8 hours between doses); maximum period of treatment 7-9 weeks; discontinue if abstinence not achieved at 7 weeks; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Bupropion Tablets: Each sustained-release tablet containing 150 mg of bupropion hydrochloride is usually available.

Chapter - Five

Drugs used in Musculoskeletal and Joint Diseases

5.1. Non-steroidal anti-inflammatory drugs (NSAIDs)

Salicylates and other agents share the capacity to suppress the signs and symptoms of inflammation. NSAIDs have analgesic and anti-inflammatory effect.

Paracetamol and NSAIDs have similar analgesic activity, but paracetamol is preferred particularly in elderly. Differences in anti-inflammatory activity between NSAIDs are small, but there is considerable variation in individual patient response. About 60 % of patients will respond to any NSAID. Among the rest, those who do not respond to one may respond to another.

The main differences between NSAIDs are in the incidence and type of adverse effects. Selective inhibitors of cyclo-oxygenase-2 are associated with a lower risk of serious gastro-intestinal side effects than non-selective NSAIDs. There are concerns about cardiovascular safety of selective inhibitors.

ACECLOFENAC

Its actions and adverse effects are similar to naproxen.

Indications: rheumatoid arthritis, osteoarthritis and ankylosing spondylitis.

Adverse effects and cautious: see under naproxen.

Dose: 100 mg twice daily; CHILD not recommended.

Preparation available

Aceclofenac Tablets: Each tablet containing 100 mg of aceclofenac is usually available.

ASPIRIN

Aspirin shows anti-inflammatory properties in high doses. There is little anti-inflammatory effect with less than 3 g daily dose.

Indications: rheumatic fever, rheumatoid arthritis and other inflammatory joint and other musculo-skeletal disorders, antiplatelet.

Adverse effects and cautions: Gastrointestinal discomfort, ulceration, bleeding, vertigo, hypersensitivity reactions (bronchospasm, rashes, angioedema), and increased uric acid level.

Contraindication, cautions, dose and preparation available: *see* under section 4.8, antipyretic analgesics.

Drug interactions: *see* under section 4.8, analgesic antipyretic.

Dose: 0.3-1 g every 4 hours after food; maximum 8 g in acute conditions.

DICLOFENAC

It has anti-inflammatory, analgesic and antipyretic properties. It achieves high synovial concentration. It is rapidly absorbed following oral administration.

Indications: rheumatic disease, osteoarthritis and other musculo-skeletal disorders, acute gout, post-operative pain.

Adverse effects and cautions: Gastro-intestinal distress, occasionally gastro-intestinal bleeding and gastric ulceration. Adverse effects are seen in approximately 20 % of patients.

The drug is contraindicated in pregnancy.

The drug should be used with caution in breast-feeding, renal or cardiac or hepatic impairment.

Dose: By mouth, 75-150 mg daily in 2-3 divided doses, preferably after food.

By deep intramuscular injection into the gluteal muscle, acute exacerbations and post operative, 75 mg once daily (twice daily in severe cases) for maximum of 2 days. Ureteric colic, 75 mg then a further 75 mg after 30 minutes if necessary.

By intravenous infusion, 75 mg repeated after 4-6 hours for maximum 2 days.

Maximum total dose by any route 150 mg.

CHILD, 1 year or over, juvenile arthritis by mouth 1-3 mg/kg daily in divided doses.

Preparation available

Diclofenac Sodium Tablets: Each tablet containing 50 mg and 100 mg of diclofenac sodium are usually available. They are usually enteric coated.

Diclofenac Injection: Injection containing 25 mg/ml diclofenac sodium is usually available.

FLURBIPROFEN

It is readily absorbed following oral administration and achieves high synovial concentration. The efficacy of drug is comparable to that of aspirin.

Indications: rheumatic disease, other musculo-skeletal disorders, mild to moderate pain including dysmenorrhoea, post-operative pain.

Adverse effects and cautions: similar to ibuprofen but more gastro-intestinal adverse effects than ibuprofen.

Contra-indications and cautions: see under diclofenac.

Drug interactions: *see* under aspirin.

Dose: By mouth, 150 mg -200 mg daily in divided doses, increasesd in acute conditions to 300 mg daily. Dysmenorrhoea, initially 100 mg; then 50-100 mg every 4-6 hours; maximum 300 mg daily.

Preparation available

Flurbiprofen Tablets: Each tablet containing 50 mg, 100 mg and 200 mg of flurbiprofen is usually available. Flurbiprofen tablets are coated.

IBUPROFEN

It has anti-inflammatory, analgesic and antipyretic properties. The drug is often prescribed in lower doses, at which it is analgesic but inferior as an anti-inflammatory agent. It has fewer adverse effects than other NSAIDs but its anti-inflammatory activity is weaker.

Indications: rheumatic disease, musculo-skeletal disorders, post-operative pain, dysmenorrhoea.

Adverse effects and cautions: Gastrointestinal irritation, bleeding, rash, pruritis, tinnitus, dizziness, headache, fluid retention, vertigo.

Contra-indications and cautions: see under diclofenac.

Drug interactions: see under aspirin.

Dose: Initially 1.2-1.8 g daily in 3-4 divided doses preferably after food, increased if necessary to maximum of 2.4 g daily; maintenance dose of 0.6-1.2 g daily may be adequate, CHILD, 20-30 mg/kg daily in divided doses (juvenile arthritis, up to 40 mg/kg daily), not recommended for children under 5 kg.

Preparation available

Ibuprofen Tablets: Each tablet containing 200 mg, 400 mg and 600 mg of ibuprofen is usually available. Ibuprofen tablets are coated.

INDOMETHACIN

It is well absorbed after oral administration. It has an action equal to or superior to that ofnaproxen but with a high incidence of adverse effects.

Indications: acute gouty arthritis, rheumatic disease, dysmenorrhoea, musculo-skeletal disorders, closure of ductus arteriosus.

Adverse effects and cautions: abdominal pain, diarrhoea, gastrointestinal haemorrhage, severe headache, dizziness, confusion, depression, psychosis, thrombocytopenia, aplastic anaemia, hypertension and hyperkalaemia.

The drug is contraindicated in pregnancy and should be used with caution in breast-feeding, epilepsy and Parkinsonism; CHILD not recommended.

Drug interactions: see under aspirin.

Dose: Rheumatic disease, 50-200 mg daily in divided doses, with food; CHILD not recommended.

Acute gout, 150-200 mg daily in divided doses.

Dysmenorrhoea, up to 75 mg daily.

Preparation available

Indomethacin capsules: Each capsule containing 25 mg of indomethacin is usually available.

KETOPROFEN

It is rapidly absorbed from gastrointestinal tract. Its anti-inflammatory properties are similar to ibuprofen but has more adverse effects.

Indications, adverse effects and cautions: see under ibuprofen.

Contraindication and cautions: see under diclofenac.

Dose: By mouth, rheumatic disease 100-200 mg daily in 2-4 divided doses with food. Pain and dysmenorrhoea, 50 mg up to 3 times daily; CHILD not recommended.

Preparation available

Ketoprofen Capsules: Each capsules containing 50 mg of ketoprofen is usually available.

MEFENAMIC ACID

Its anti-inflammatory properties are weaker than aspirin.

Indications: osteoarthritis, rheumatoid arthritis, dysmenorrhoea, post-operative pain.

Adverse effects and cautions: diarrhoea, rashes, thrombocytopenia, haemolytie anaemia and drowsiness.

Contraindications, cautions and drug interactions: see under aspirin.

Dose: 500 mg 3 times daily preferably after food; CHILD over 6 months, 25 mg/kg daily in divided doses for not longer than 7 days except in juvenile arthritis.

Preparation available

Mefenamic Acid Tablets: Each tablet containing 250 mg and 500 mg of mefenamic acid is usually available.

METHOTREXATE

It is a disease-modifying anti-rheumatic drug.

Indications: moderate to severe rheumatoid arthritis.

Adverse effects and cautions: myelosuppression, mucositis, loss of appetite, intestinal ulceration and bleeding, diarrhoea, pulmonary oedema, impotence, loss of libido.

The drug is contraindicated in pregnancy, breast-feeding, active infection, renal or hepatic impairment.

The drug should be used with caution in blood disorders (blood count, liver and renal function tests should be performed before starting treatment and repeated weekly), peptic ulceration, pleural effusion.

Dose: By mouth, 7.5 mg once weekly (as a single dose or divided into 3 doses of 2.5 mg given at intervals of 12 hours), maximum total weekly dose 20 mg.

Preparation available

Methotrexate Tablets: Each tablet containing 2.5 mg of methotrexate is usually available.

NAPROXEN

Its actions are similar to ibuprofen. It produces more adverse effects than ibuprofen.

Indications: *see* under diclofenac.

Adverse effects and cautions: *see* under diclofenac but it is better tolerated.

Dose: 0.5-1 g daily in 2 divided doses; CHILD (over 5 years) juvenile arthritis, 10 mg/kg daily in 2 divided doses.

Acute musculoskeletal disorders and dysmenorrhoea, 500 mg initially, then 250 mg every 6-8 hours as required; CHILD under 16 years not recommended.

Acute gout, 750 mg initially, then 250 mg every 8 hours until attack has passed; CHILD under 16 years not recommended.

Preparation available

Naproxen Tablets: Each tablet containing 250 mg of naproxen is usually available.

PARACETAMOL*: *see under section 4.8, antipyretic analgesics.

NIMESULIDE

It is a NSAID. It exhibits relative selectivity for cyclooxygenase-2 inhibition.

Indications: *see* ibuprofen.

Adverse effects and cautions: *see* under ibuprofen.

Dose: 200-300 mg daily in divided doses.

Preparation available

Nimesulide Tablets: Each tablet containing 100 mg of nimesulide is usually available.

PIROXICAM

It has long half-life permitting once daily dosing. It is readily absorbed in the stomach. It has more gastro-intestinal adverse effects than ibuprofen.

Indications: rheumatic disease, musculo-skeletal disorders, acute gout.

Adverse effects and cautions: gastrointestinal dyscomfort, dizziness, tinnitus, headache and rash.

Gastrointestinal symptoms are encountered in 20 % of patients.

Contra-indications and cautions: see under diclofenac.

Dose: Rheumatic disease, initially 20 mg daily, maintenance 10-30 mg daily, in single or divided doses.

CHILD (over 6 years), juvenile arthritis, less than 15 kg, 5 mg daily; 16-25 kg, 10 mg; 26-45 kg, 15 mg; over 46 kg, 20 mg

Acute musculoskeletal disorders, 40 mg daily in single or divided doses for 2 days, then 20 mg daily for 7-14 days; CHILD not recommended.

Acute gout, 40 mg initially, then 40 mg daily in single or divided doses for 4-6 days; CHILD not recommended.

By deep intramuscular injection into gluteal muscle, for initial treatment of acute conditions, as dose by mouth.

Preparation available

Piroxicam Capsules: Each capsule containing 10 mg and 20 mg of piroxicam are usually available.

Piroxicam Dispersible Tablets: Each tablet containing 20 mg of piroxicam is usually available.

Piroxicam Injection: Each ml containing 20 mg of piroxicam is usually available.

5.2 Drugs for treatment of gout

Acute attacks of gout are usually treated with high doses of NSAIDs such as indomethacin, naproxen, diclofenac, piroxicam. Ibuprofen has weaker anti-inflammatory properties than other NSAIDs and is therefore less suitable for the treatment of gout. Aspirin is not suitable in the acute attack because it increases plasma urate concentrations. Colchicine is an alternative for those patients in whom NSAIDs are contraindicated. Allopurinol and uricosurics are not effective in treating acute gout.

For long-term control of gout in patients who have frequent acute attacks, the presence of tophi or chronic gouty arthritis, allopurinol may be used to reduce production of uric acid.

The drug should never be started during an acute attack, usually started 2-3 weeks after the attack has completely subsided. The initiation of allopurinol may precipitate an acute attack, therefore NSAID or colchicine should be used as a prophylactic and continued for at least one month after the hyperuricemia has been corrected (usually about 3 months of prophylaxis). However, if an acute attack develops during treatment, then allopurinol should continue on the same dose and acute attack should be treated. Treatment for chronic gout should be continued indefinitely to prevent further attacks of gout.

ALLOPURINOL

It acts by inhibiting synthesis of urates.

Indications: prophylaxis of gout, prophylaxis of hyperuricemia associated with cancer chemotherapy.

Adverse effects and cautions: nausea, vomiting, diarrhoea, maculo-papular skin rash, rarely exfoliate dermatitis, arthralgia and aplastic anaemia.

The drug should be used with caution in pregnancy, breast-feeding, hepatic and renal impairment.

Dose: Initially 100 mg daily as a single dose after food, gradually increased over 1-3 weeks according to the plasma or urinary uric acid concentration, to about 300 mg daily; CHILD under 15 years 10-20 mg/kg daily.

Preparation available

Allopurinol Tablets: Each tablet containing 100 mg of allopurinol is usually available.

COLCHICINE

It relieves pain and inflammation of gouty arthritis in 12-24 hours without altering the metabolism or excretion ofurates and without other analgesic effects.

Indications: acute gout.

Adverse effects and cautions: diarrhoea, nausea, vomiting, abdominal pain, rarely gastro-intestinal haemorrhage, rashes, renal and hepatic damage.

Safe use in pregnancy has not been established.

The drug should be used with caution in breast-feeding, cardiac or hepatic or renal impairment.

Dose: 1 mg initially, followed by 500 micrograms every 4 hours until relief of pain is obtained or vomiting or diarrhoea occurs. The course should not be repeated within 3 days.

Prevention of attacks during initial treatment with allopurinol or uricosuric drugs, 500 micrograms 2-3 times daily.

Preparation available

Colchicine Tablets: Each tablet containing 500 micrograms of colchicine is usually available.

PROBENECID

It is a uricosuric drug.

Indications: gouty arthritis, hyperuricemia and adjunct to therapy with penicillins.

Adverse effects and cautions: nausea and vomiting, urinary frequency, headache, flushing, dizziness, rashes, aplastic anaemia and rarely hypersensitivity.

The drug is contraindicated in acute gout attack.

Dose: Uricosuric therapy, initially 250 mg twice daily after food, increased after a week to 500 mg twice daily then up to 2 g daily in 2-4 divided doses according to plasma-uric acid concentration.

Preparation available

Probenecid Tablets: Each tablet containing 500 mg of probenecid is usually available.

SULPHINPYRAZONE

It is a uricosuric drug and can be used instead of allopurinol or in conjunction with it in cases that are resistant to treatment.

Indications: gout prophylaxis and hyperuricemia.

Adverse effects and cautions: gastrointestinal disturbances, allergic skin reactions, salt and water retention, gastrointestinal ulceration and bleeding, acute renal failure and hepatitis.

Dose: initially 100-200 mg daily with food (or milk) increasing over 2-3 weeks to 600 mg daily, continued until serum uric acid concentration normal then reduced for maintenance (maintenance dose may be as low as 200 mg daily).

Preparation available

Sulphinpyrazone Tablets: Each tablet containing 100 mg of sulphinpyrazone is usually available.

Chapter- Six

Drugs Affecting Allergic Reactions

Allergic states such as hay fever, angioneurotic oedema, urticaria, acute anaphylaxis and serum sickness can be controlled by one of the three groups of drugs viz;

6.1. Antihistamines,

6.2. Sympathomimetics,

6.3. Corticosteroids.

6.1 Antihistamines

The H_1-receptor antagonists are generally referred as antihistamines. All antihistamines are equally effective and differ mainly in the intensity of sedative and anti-muscarinic effects. The older antihistamines are relatively short acting while most of newer non-sedating are long acting.

CETIRIZINE

It is non-sedating antihistamine, but patient should be advised that it can occur. It causes less psychomotor impairment.

Indications: *see* under chlorphenamine.

Adverse effects and cautions: *see* under chlorphenamine; but incidence of sedation and antimuscarinic effects are low.

The drug should be used with caution in epilepsy, prostatic hypertrophy and glaucoma.

The drug should be avoided in pregnancy and breast-feeding.

Dose: ADULT and CHILD over 6 years, 10 mg daily or 5 mg twice daily; CHILD 2-6 years 5 mg daily or 2.5 mg twice daily.

Preparation available

CetirizineTablets: Each tablet containing 10 mg cetirizine hydrochloride is usually available.

CHLORPHENAMINE MALEATE

Chlorpheniramine maleate

This provides rapid and potent anti-allergic action without undue sedation. Effect appears within half-an-hour and lasts 4 to 8 hours.

Indications: symptomatic relief of allergy such as urticaria, hay fever, insect stings and pruritus of allergic origin.

Adverse effects and cautions: headache, psychomotor impairment, sedation is less pronounced, anticholinergic effects such as dry mouth, blurred vision and urinary retention. Some patients especially children may experience paradoxical excitement characterised by restlessness, insomnia, tremors and even seizures.

It should be used with caution in epilepsy, prostatic hypertrophy, urinary retention and glaucoma. No teratogenic potential has been shown.

Dose: 4 mg every 4-6 hours, maximum 24 mg daily; child 1-2 years 1 mg twice daily, 2-5 years 1 mg every 4-6 hours, maxmium 6 mg daily, 6-12 years 2 mg every 4-6 hours, maximum 12 mg daily; INFANT not recommended.

Preparation available

Chlorphenamine Tablets: Each tablet containing 4 mg and 8 mg of chlorphenamine maleate is usually available.

CYPROHEPTADINE

It has anti-histaminic and antiserotonergic properties. The effect of drug lasts for 8 hours.

Indications: *see* under chlorphenamine, and also migraine.

Adverse effects and cautions: see under chlorphenamine. Weight gain and increased growth in children have been observed. The drug should be used in pregnancy and breast-feeding only when clearly needed.

Dose: Allergy, usual dose 4 mg 3-4 times daily, usual range 4-20 mg daily, maximum 32 mg daily. CHILD, 2-6 years 2 mg 2-3 times daily maximum 12 mg daily; 7-14 years 4 mg 2-3 times daily, maximum 16 mg daily.

Migraine, 4 mg with a further 4 mg after 30 minutes if necessary; maintenance 4 mg every 4-6 hours.

Preparation available

Cyproheptadine Tablets: Each tablet containing the equivalent of 4 mg of anhydrous cyproheptadine hydrocloride is usually available.

DIMETHINDENE

Indications, adverse effects and cautions: *see* under chlorphenamine.

Dose: By mouth, 1-2 mg thrice daily or 2.5 mg twice daily as a sustained-release preparation.

Preparation available

Dimethindene Maleate Tablets: Each tablet containing 1 mg and 2.5 mg of dimethindene maleate is usually available.

DIPHENHYDRAMINE

The effect of drug lasts for 6-8 hours. It causes more sedation.

Indications: *see* under chlorphenamine. It is also used in motion sikness.

Adverse effects and cautions: see under chlorphenamine.

Dose: By mouth 25-50 mg 3-4 times daily. CHILD 6.25-25 mg 3-4 times a day or total daily dose of 5 mg/kg body weight may be given in divided doses.

Preparation available

Diphenhydramine Capsules: Each capsule containing 25 mg and 50 mg of diphenhydramine hydrochloride is usually available.

Diphenhydramine Oral Solution: Each 5ml containing 12.5 mg of diphenhydramine hydrochloride is usually available. It should be protected from light.

FEXOFENADINE

It is a metabolite of terfenadine but lacks the toxic effects of terfenadine. It is non-sedating antihistamine, but patient should be advised that it can occur.

Indications: *see* under chlorphenamine.

Adverse effects and cautions: *see* under cetirizine.

Dose: Allergic rhinitis, 120 mg once daily; CHILD 6-11 years 30 mg twice daily.

Chronic idiopathic urticaria, 180 mg once daily; CHILD under 12 years, not recommended.

Preparation available

Fexofenadine Tablets: Each tablet containing 120 mg and 180 mg of fexofenadine is usually available.

LEVOCETIRIZINE

It is an isomer of cetirizine.

Indications: see under cetirizine.

Adverse effects and cautions: see under cetirizine.

Dose: ADULT and CHILD over 6 years, 5 mg daily.

Preparation available

Levocetirizine Tablets: Each tablet containing 5 mg of levocetirizine hydrochloride is usually available.

LORATADINE

It is also a non-sedating antihistamine.

Indications: see under cetirizine.

Adverse effects and cautions: see under cetirizine.

Dose: ADULT and CHILD over 6 years 10 mg daily; CHILD 2-5 years 5 mg daily.

Preparation available

Loratidine Tablets: Each tablet containing 10 mg of loratidine is usually available.

PHENIRAMINE MALEATE

It causes more sedation.

Indications, adverse effects and cautions: *see* under chlorphenamine.

Dose: By mouth 25-50 mg daily in divided doses.

By intramuscular or slow intravenous injection, 25-50 mg.

Preparation available

Pheniramine Maleate Injection: Injection containing 22.75 mg per ml of pheniramine maleate is usually available.

Pheniramine Maleate Oral Solution: Each 5 ml of oral solution containing 15 mg of pheniramine maleate is usually available.

Pheniramine Maleate Tablets: Each tablet containing 22.5 mg and 45 mg of pheniramine maleate is usually available.

PROMETHAZINE HYDROCHLORIDE

It causes more sedation.

Incications: symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylatic reactions, motion sickness.

Adverse effects, cautions and drug interactions: *see* under section 1.4, anti-emetics.

TRIPROLIDINE

It is anti-histamine with less pronounced sedation. The effect of drug lasts for 4-25 hours.

Indications, adverse effects and cautions: *see* under chlorphenamine.

Dose: 10 mg early evening or 5-6 hours before retiring, increased to 20 mg daily if symptoms very severe; CHILD under 12 years not recommended.

Preparation available

Triprolidine Tablets: Each tablet containing 2.5 mg of triprolidine hydrochloride is usually available.

6.2 Sympathomimetics

Anaphylactic shock and angiooedema are dangerous conditions.

EPINEPHRINE

Adrenaline

This catecholamine has effect on many organs. This effect may be both central and peripheral. Epinephrine is a physiological antagonist to histamine and can revert the tissue to normal functioning. It is therefore useful as a life saving drug in acute emergencies, brought about by histamine release due to allergy or anaphylaxis.

Indications: acute anaphylaxis, angioedema, cardiac arrest.

Adverse effects and cautions: tachycardia, tremor, hypertension, sweating, vomiting, headache.

The drug should be used with caution in hypertension, arrhythmias, diabetes mellitus, heart disease, second stage of labour, cerebrovascular disease.

Dose: Anaphylaxis, by intramuscular injection (1:1000 solution) CHILD under 6 months 0.05 ml, 6 months – 6 years 0.12 ml, 6-12 years 0.25 ml, ADULT 0.5 ml.

6.3 Corticosteroids

Corticosteroids such as hydrocortisone, prednisolone and dexamethasone suppress or prevent almost all symptoms of inflammation associated with allergy.

DEXAMETHASONE

This is a synthetic steroid preparation used in predominantly anti-inflammatory and has no sodium retaining activity.

Indications, adverse effects, cautions, dose and preparation available: *see* under section 8.1, adrenal hormones and synthetic substitutes.

HYDROCORTISONE

This is the secretion of the adrenal cortex and has mainly glucocorticoid activity with a weak mineralocorticoid action.

Indications, adverse effects, cautions, dose and preparation available: *see* under section 8.1, adrenal hormones and synthetic substitutes.

PREDNISOLONE

This is a synthetic steroid preparation which is predominantly anti-inflammatory and has little sodium retaining activity.

Indications, adverse effects, cautions, dose and preparation available: *see* under section 8.1, adrenal hormones and synthetic substitutes.

Chapter - Seven

Drugs Used in Infections

7.1 Anthelmintics

These are the drugs used to rid the body of parasitic worms known as helminths. The term is not restricted to drugs that act locally to expel worms from the gastro-intestinal tract but they are used to combat related systemic infections.

ALBENDAZOLE

Indications: ascaris, pinworm, hookworm, whipwonn, strongyloides, *Echinococcus granulosus, E. multilocularis* infections and neurocysticercosis.

Adverse effects and cautions: gastro-intestinal discomfort, headache.

The drug should not be used during the first trimester of pregnancy and to children younger than 1 year of age.

Dose: By mouth, usually as a single dose, in the treatment of single or mixed intestinal nematode infections. The usual dose for adults and children aged 2 years or over with ascariasis, hook worm infections, or trichuriasis is 400 mg in a single dose.

In strongyloidiasis, 400 mg is given twice daily for 3 consecutive days; this may be repeated after 3 weeks if necessary.

In enterobiasis children aged 2 years or more have been given a single dose of 400 mg repeated after 14 days; the adult dose is 400 mg repeated after 14 days.

E. granulosus, 800 mg daily in divided doses for 1-6 months; CHILD, 15 mg/kg/day (maximum 800 mg) for 1-6 months.

Neurocysticercosis, ADULT over 60 kg , 800 mg daily in two divided doses for 8-30 days; ADULT less than 60 kg, 15 mg/kg daily in two divided doses (maximum 800 mg) for 8-30 days.

Preparation available

Albendazole Suspension: Suspension containing 400 mg of albendazole per 10 ml is usually available.

Albendazole Chewable Tablets: Each tablet containing 400 mg of albendazole is usually available. Albendazole tablets should be chewed before swallowing.

DIETHYLCARBAMAZINE

The drug causes rapid disappearence of microfilariae of *Wuchereria bancrofti, W. malayi* and *Loa loa* from the blood of man. The drug also causes microfilarae of *Onchocerca volvulus* to disappear from the skin but does not kill microfilariae in nodules that contain adult worms. It does not affect the microfilariae of *W. bancrofti* in a hydrocele, despite its penetration into the fluid. The drug kills the adult worms *of Loa loa* and *W. bancrofti* but has little action against adult *O. volvulus.*

Indications: filariasis, tropical pulmonary eosinophilia

Adverse effects and cautions: anorexia, nausea, headache, vomiting, skin rashes, itching, painful and tender glands, joint pain, swelling of face (especially eyes).

Low doses should be used for initial therapy, especially in onchocercosis and *Loa loa* infection to minimise the allergic adverse reactions (due to destruction of the parasites).

Dose: Bancroft's filariasis or Loiasis or Unchocerciasis, initially 1 mg/kg and increased gradually over 3 days to 6 mg/kg daily in divided doses for 21 days.

Tropical eosinophilia, 6 mg/kg once a day for 4-7 days.

Preparation available

Diethylcarbamazine Tablets: Each tablet containing 50 mg and 100 mg of diethycarbamazine citrate is usually available.

Diethylcarbamazine Oral Solution: Each 5 ml containing 50 mg and 120 mg of diethylcarbamazine citrate is usually available.

IVERMECTIN

It is effective against microfilaria but not against adult worms of *W. banerofti*. It is also effective head lice and scabies.

Indications: lymphatic filariasis.

Adverse effects and cautions: itching, headache, tachycardia, diarrhoea, dizziness, hypotension.

Dose: Lymphatic filariasis, by mouth 200 micrograms/kg as a single dose once a year with albendazole.

Preparation available

Ivermectin Tablets: Each tablet containing 3 mg and 6 mg of ivermectin is usually available.

LEVAMISOLE

It is effective against ascaris and hookworm.

Indications: ascariasis and mixed ascariasis/hookworm infections

Adverse effects and cautions: nausea, vomiting, abdominal pain, headache and dizziness.

Dose: For ascariasis 150 mg of levamisole by mouth as a single dose; CHILD 2.5 mg/kg body weight as a single dose.

Preparation available

Levamisole Oral Solution: Each 5ml of oral solution containing 50 mg of levamisole (as hydrochloride) is usually available.

Levamisole Tablets: Each tablet containing 50 mg and 150 mg of levamisole (as hydrochloride) is usually available.

MEBENDAZOLE

The drug is effective against roundworm, hookworm *(Ancylostoma* and *Necator),* pinworm *(Enterobius)* and whipworm *(Trichuris).*

Indications: ascaris, hoockworm, pinworm, whipworm infection.

Adverse effects and cautions: abdominal pain, diarrhea and rash. In heavily infected children, roundworms may be expelled through the mouth and nose, since mebendazole kills these worms slowly and cause them to migrate.

The drug should not be given to pregnant women and in children younger than 2 years of age or to patients who have experienced allergic reactions to the drug.

Dose: Thread worm, adult and CHILD 2 years, 100 mg as a single dose; if reinfection occurs second dose may be needed after 2 weeks, CHILD under 2 years, not recommended.

Roundworm and hookworm, 100 mg twice daily for 3 days.

Preparation available

Mebendazole Supension: Each 5 ml of suspension containing 100 mg of mebendazole is usually available.

Mebendazole Tablets: Each tablet containing 100 mg of mebendazole is usually available.

NICLOSAMIDE

It is effective against *Taenia solium, T. saginata, Hymenolepis nana* and *Diphyllobalhrium latum.* It is inactive against cysticercus cellulosae and danger of cysticercosis must be considered when used in *T. solium* infection.

Indications: tapeworm infection

Adverse effects and cautions: nausea, vomiting, abdominal discomfort, anorexia, diarrhoea and pruritus.

In *T. solium* infections, effective purging is essential to avoid risk of cysticercosis.

Dose: *Taenia solium*- Adult and child over 6 years 2 g as a single dose after a light breakfast or meal followed by a purgative after 2 hours; CHILD under 2 years 500 mg, 2-6 years 1 g. *T. saginata* and *Diphyllobothrium latum,* as for *T. solium* but half the dose may be taken after breakfast or meal and the remainder 1 hours later followed by a purgative 2 hours after last dose. *Hymenolepis nana,* ADULT and CHILD, over 6 years 2 g as a single dose on first day then Ig daily for 6 days; CHILD under 2 years 500 mg on first day then 250 mg daily for 6 days, 2-6 years Ig on first day then 500 mg daily for 6 days.

Preparation available

Niclosamide Tablets: Each tablet containing 500 mg of niclosamide is usually available. Niclosamide tablets should be protected from light. The tablets should be chewed thoroughly before swallowing.

PIPERAZINE

Indications: ascaris, pinworm infection.

Adverse effects and cautions: nausea, vomiting, mild diarrhoea, abdominal pain and urticaria.

The drug should be avoided in epilepsy, liver or kidney disease.

The drug is contraindicated in patients who are hypersensitive to the drug. Piperazine has been used without ill effects in pregnancy.

Drug interactions: pyrantel pamoate and piperazine have antagonistic modes of action. These drugs should not be administered concomitantly.

Dose: Ascaraisis, up to 3.5 g per day; CHILD 75 mg/kg body weight per day for two consecutive days. Treatment may be repeated after one week for heavy infection.

Enterobiasis, up to 2.5 g per day; CHILD 65 mg/kg body weight per day for seven consecutive days.

Preparation available

Piperazine Elixir: Each 5 ml containing piperazine citrate equivalent of 750 mg of piperazine hydrate is usually available.

Piperazine Tablets: Each tablet containing 300 mg of piperazine adipate equivalent to 250 mg of piperazine hydrate is usually available.

PRAZIQUANTEL

It kills both adult worms and larvae of *Taenia. solium*, *T. saginata*, *Hymenolepis nana* and *Diphyllobothrium latum*.

Indications: taeniasis *(T. solium, T. saginata),* hymenolepiasis *(H. nana),* diphylobothriasis *(D. latum)* and cysticercosis (except ocular)

Adverse effects and cautions: nausea, abdominal discomfort, headache, dizziness, drowsiness and rarely urticaria and rectal bleeding.

Praziquantel should not be used in the treatment of ocular cysticercosis because of the danger of inflammatory reactions.

Dose: *Taenia solium* 10-20 mg/kg a single dose after a light breakfast. *Hymenolepis nana* 25 mg/kg as a single dose.

Preparation available

Praziquantel Tablets: Each tablet containing 600 mg of praziquantel is usually available.

PYRANTEL PAMOATE

The drug depolarises the neuromuscular junctions of the susceptible nemotodes.

Indications: ascariasis, hookworm and pinworm infections.

Adverse effects and cautions: headache, dizziness, drowsiness and mild gastro-inteslinal disturbance.

Safe use of drug in pregnancy and children less than 2 years has not been

established.

The drug is contraindicated in patients who have experienced allergic reactions to the drug.

Drug interactions: *see* under piperazine.

Dose: Adult and CHILD over 2 years, single dose of 10 mg/kg (maximum 1 g).

For *Enterobius vermicularis,* the treatment should be repeated after 2 weeks.

Preparation available

Pyrantel Pamoate Oral Suspension: Suspension containing 25 mg and 50 mg per ml of pyrantel, as pyrantal pamoate, is usually available.

Pyrantel Pamoate Tablets: Each tablet containing the equivalent of 250 mg of pyrantel, as pyrantel pamoate, is usually available.

7.2 Antiamoebic and anti-giardial drugs

DEHYDROEMETINE

The drug is much more effective against motile forms than against cyst.

Indications: amoebic hepatitis and amoebic abscess.

Adverse effects and cautions: diarrhoea, nausea, vomiting, dizziness, hypotension, headache, precordial pain and tachycardia. The drug is cardiotoxic and the patient should remain in bed during treatment.

The drug should not be used in pregnancy and in patients with cardiac or renal disease.

DILOXANIDE FUROATE

The drug is effective against amoeba in the intestinal tract and is ineffective in amoebic abscess and hepatitis.

Indications: asymptomatic cyst passers and extra intestinal amoebiasis (together with tissue amoebicide). The drug is not reliably effective alone in the treatment of acute amoebic dysentery.

Adverse effects and cautions: vomiting, pruritus, flatulence and urticaria.

The drug should be avoided in pregnancy and breast-feeding.

Dose: 500 mg every 8 hours for 10 days. CHILD 20 mg/kg daily in 3 divided doses.

Preparation available

Diloxanide Tablets: Each tablet containing 500 mg of diloxanide furoate is usually available.

METRONIDAZOLE

The drug is effective against all forms of amoebiasis i.e. luminal, tissue and hepatic amoebic infection.

Indications: giardiasis, acute amoebic dysentery and extra-intestinal amoebiasis including amoebic liver abscess. The drug is ineffective in asymptomatic cyst passers.

The drug is also used in *Trichomonas vaginalis*, *Giardia lambia*, *Halicobacter pylori*, *Balantidium coli* and anaerobic bacterial infections. It is used in the treatment and prevention of surgical and gynaecological sepsis due to colonic anaerobes particularly Bacteroides fragilis.

Adverse effects and cautions: metallic taste, nausea, headache, furred tongue, dizziness, vertigo, dark brown urine and reversible peripheral neuropathy.

Metronidazole is carcinogenic in rats and mice but no clinical evidence of increased susceptibility to malignancy has been reported in patients.

The large dose of drug should be used during pregnancy only when clearly needed. Nursing mothers should not breast feed during treatment with high dose.

Drug interactions: disulfiram-like reactions have occurred in patients who have ingested alcohol while receiving metronidazole. Potentiation of the effects of oral anticoagulant have been reported.

Dose: Invasive intestinal amoebiasis, by mouth 800 mg every 8 hours for 5 days, CHILD 1-3 years 200 mg every 8 hours; 3-7 years 200 mg every 6 hours; 7-10 years 400 mg every 8 hours.

Extra-intestinal amoebiasis (including liver abscess) and symptomless amoebic cyst passers by mouth, 400-800 mg every 8 hours for 5-10 days, child 1-3 years 100-200 mg every 8 hours, 3-7 years 100-200 mg every 6 hours, 7-10 years 200-400 mg every 8 hours.

Giardisis, by mouth, 2 g daily for 3 days or 400 mg 3 times daily for 5 days; CHILD 1-3 years 500 mg daily for 3 days, 3-7 years 600-800 mg daily, 7-10 years 1 g daily.

Anaerobic infections (usually treated for 7 days), by mouth, 800 mg initially then 400 mg every 8 hours, by intravenous infusion, 500 mg every 8 hours; CHILD any route 7.5 mg/kg every 8 hours. Leg ulcers and pressure sores, by mouth, 400 mg every 8 hours for 7 days.

Bacterial vaginosis, by mouth, 400 mg twice daily for 5-7 days or 2 g as a single dose.

Acute ulcerative gingivitis, by mouth, 200 mg every 8 hours for 3 days; CHILD 1-3 years 50 mg every 8 hours for 3 days; 3-7 years 100 mg every 12 years, 7-10 years 100 mg every 8 hours. Acute oral infections, by mouth 200 mg every 8 hours for 3-7 days.

Surgical prophylaxis, by mouth, 400 mg started 2 hours before surgery, up to 3 further doses of 400 mg may be given every 8 hours for high-risk procedure; CHILD 7.5 mg/kg 2 hours before surgery; up to 3 further doses of 7.5 mg/kg may be given every 8 hours for hgh-risk procedures. By intravenous infusion, 500 mg shortly before surgery, CHILD 7.5 mg/kg every 8 hours.

Preparation available

Metronidazole Injection: Injection containing 500 mg of metronidazole per 100 ml is usually available.

Metronidazole Oral suspension: Each 5ml of oral suspension containing the equivalent of 100 mg and 200 mg of metronidazole, as benzoate, is usually available. Metronidazole oral suspension should be protected from light.

Metonidazole Tablets: Each tablet containing 200 mg, 400 mg and 600 mg of metronidazole is usually available.

TINIDAZOLE

It is similar to metronidazole but has a longer duration of action. It is claimed to be better tolerated orally.

Indications, adverse effects and cautions: similar to metronidazole.

Dose: Anaerobic infections, by mouth, 2 g initially, followed by 1 g daily or 500 mg twice daily, usually for 5-6 days.

Bacterial vaginosis and acute ulcerative gingivitis, a single 2 g dose.

Abdominal surgery prophylaxis, a single 2 g dose approximately 12 hours before surgery.

Intestinal amoebiasis, 2 g daily for 2-3 days; CHILD 50-60 mg/kg daily for 3 days. Amoebic involvement of liver, 1.5-2 g daily for 3-6 days; CHILD 50-60 mg/kg daily for 5 days.

Urogenital trichomoniasis and giardiasis, single 2 g dose; CHILD single dose of 50-75 mg/ kg (repeated once if necessary).

Preparation available

Tinidazole Tablets: Each tablet containing 300 mg, 500 mg and 1 g of tinidazole is usually available. They are coated.

Tinidazole Suspension: Each 5 ml containing 150 mg of tinidazole is usually available.

Tinidazole Injection: Injection containing 200 mg of tinidazole per 100 ml with 0.8% sodium chloride is usually available.

7.3 Antibacterials

7.3.1 Penicillins

AMOXICILLIN

It has the same spectrum of activity and the same level of activity against susceptible organisms as ampicillin; with the important exception that amoxicillin appears to be less effective than ampicillin for shigellosis. It is more rapidly and completely absorbed from the gastrointestinal tract than ampicillin. The absorption is not affected by the presence of food in the stomach. Clavulanic acid, a beta-lactamase inhibitor when combined with amoxicillin, increases amoxicillin activity against beta-lactamase producing strains of *H. influenzae, E. coli, Staphylococcus aureus, Klebsiella* and Bacteriodes.

Indications: urinary tract infection by *E. coli, Proteus mirabilis* and *Streptococcus faecalis;* otitis media, sinusitis, pneumonia by *H. influenzae,* pharyngitis, skin and soft tissue infections, endocarditis prophylaxis and *H. pylori* eradication.

Adverse effects and cautions: *see* under ampicillin. Diarrhoea and rash occur less frequently than with ampicillin.

Dose: By mouth, 250 mg every 8 hours, doubled in severe infections; CHILD up to 10 years, 125 mg every 8 hours, doubled in severe infections.

Otitis media, 1 g every 8 hours; CHILD 40 mg/kg daily in 3 divided doses (maximum 3 g daily)

Short-course oral therapy: dental abscess, 3g repeated after 8 hours; urinary tract infections, 3 g repeated after 10-12 hours.

By intramuscular injection, 500 mg every 8 hours; CHILD 50-100 mg/kg daily in divided doses.

By intravenous injection or infusion, 500 mg every 8 hours increased to 1 g every 6 hours; CHILD 50-100 mg/kg daily in divided doses.

Preparation available

Amoxicillin Capsules: Each capsule containing the equivalent of 250 mg and 500 mg of amoxycillin, as amoxycillin trihydrate, is usually available.

Amoxicillin Dispersible Tablets: Each tablets containing 125 mg and 250 mg of amoxycillin, as amoxicillin trihydrate is usually available.

Amoxicillin Drops: Each ml containing 100 mg of amoxycillin, as Amoxicillin trihydrate is usually available. It is prepared by dispersing dry ingredients in requisite amount of water, before use.

Amoxicillin Injection: Arnoxicillin injection is a sterile solution of amoxicillin sodium in water for injection. It is prepared by dissolving amoxicillin sodium for injection in the requisite amount of water for injection, immediately before use.

Sealed container containing the equivalent of 100 mg, 250 mg and 500 mg of amoxicyllin is usually available. The sealed container should be stored at a temperature not exceeding 25°.

Amoxicillin Oral Suspension: Amoxycillin oral suspension is a suspension of Arnoxicillin trihydrate in a suitable flavoured vehicle. It is prepared by dispersing the dry ingredients in the specified volume of water just before use. Each 5ml of oral suspension containing the equivalent of 125 mg and 250 mg of amoxicillin is usually available. The dry ingredients should be stored at a temperature not exceeding 25°. The oral suspension should be kept at the temperature and used within the period stated on the label.

AMPICILLIN

It is semisynthetic penicillin with a broader spectrum of action than benzyl penicillin. It is less active than later agent against gram positive cocci. It is inactivated by penicillinase produced by *Staphylococcus aureus* and *Escherechia coli.* It is stable in gastric acid and about 50% is absorbed following oral administration. The absorption is further decreased by the presence of food in the stomach.

Indications: urinary tract infections by *Escherechia coli* and *Proteus mirabilis,* exacerbation of chronic bronchitis and otitis media due to *Streptococcus pneumoniae* and *Haemophilus influenzae* and invasive salmonellosis.

Adverse effects and cautions: *see* under benzyl penicillin. However diarrhoea and

rash have been reported more frequently. Ampicillin shares the toxic potentials of the penicillins, including the risk of hypersensitivity reactions. There is evidence of partial cross-reactivity between penicillins and cephalosporins.

In patients with severe renal impairment, doses and/or frequency of administration of drug should be modified.

Dose: By mouth 0.25-1 g every 6 hours, at least 30 minutes before food. Urinary tract infections, 500 mg every 8 hours.

By intramuscular injection or intravenous injection or infusion, 500 mg every 4-6 hours; higher dose in meningitis.

CHILD under 10 years, any route, half adult dose.

Preparation available

Ampicillin Capsules: Each capsule containing the equivalent of 250 mg and 500 mg of ampicillin, as ampicillin trihydrate, is usually available.

Ampicillin Dispersible Tablets: Each tablet containing 125 mg of ampicillin, as ampicillin trihydrate is usually available.

Ampicillin Drops: Each ml containing 100 mg of ampicillin, as ampicillin trihydrate is usually available.

Ampicillin Injection: Ampicillin injection is a sterile solution of ampicillin sodium in water for injection. It is prepared by dissolving the content of a sealed container in the requisite amount of water for injection immediately before use.

Sealed container containing the equivalent of 100 mg, 250 mg and 500 mg of anhydrous Ampicillin are usually available. The sealed container should be stored at a temperature not exceeding 25°. Ampicillin injection should be used immediately after preparation.

Ampicillin Oral Suspension: Ampicillin oral suspension is a suspension of ampicillin or ampicillin trihydrate in a suitable flavoured vehicle. It is prepared by dispersing the dry ingredients in the specific volume of water just before use. Each 5ml of oral suspension containing the equivalent of 125 mg and 250 mg of ampicillin is usually available.

The dry ingredients should be stored at a temperature not exceeding 25°. The oral suspension should be stored at a temperature and used within the period stated on the label.

BACAMPICILLIN

It is hydrolysed *in vivo* to ampicillin and is inactive until hydrolysed, the spectrum of activity is similar to ampicillin.

Indications, adverse effects and cautions: *see* under ampicillin.

Dose: 400-800 mg 2 or 3 limes daily; CHILD over 5 years, 200 mg 3 times daily. Uncomplicated gonorrhoea a single dose of 1.6 g together with probenecid 1 g.

Preparation available

Bacampicillin Hydrochloride Tablets: Each tablet containing 400 mg bacampicillin hydrochloride is usually available.

BENZATHINE BENZYLPENICILLIN

It is given intra-muscularly to establish a depot which yields low but prolonged action.

Indications: penicillin sensitive infections particularly prophylaxis of rheumatic fever, streptococcal pharyngitis and syphilis outside the central nervous system.

Gonorrhoea should not be treated with benzathine benzylpenicillin since it does not provide adequate plasma concentrations.

Adverse effects, cautions, drug interactions: *see* under to benzyl penicillin.

Dose: by intramuscular injection, rheumatic fever prophylaxis, ADULT and CHILD over 30 kg, 1,200,000 units monthly; CHILD under 30 kg 600 000 units every 3-4 weeks.

Early syphilis, 2 400 000 units as single dose in two sites.

Late syphilis (more than one year duration), 2 400 000 units weekly for 3 weeks.

Preparation available

Benzathine Benzylpenicillin Injection: Vials containing 0.6 million IU, 1.2 million IU and 2.4 million IU of benzathine benzylpenicillin are usually available.

BENZYLPENICILLIN

Penicillin G

It is highly active against many gram-positive and gram- negative cocci. It is also highly active against *Treponema pallidum, Clostridia, Actinomycosis* and *Corynebacterium.* The drug is inactivated by bacterial penicillinase. The drug is inactivated by gastric acid and absorption from the gut is low, it is best given by injection. Following intramuscular injection, drug enters blood stream within 30 minutes but has to be given 4 to 6 hourly because of rapid excretion.

Indications: pneumococcal pneumonia, otitis media and meningitis, meningococcal meningitis and streptococcal infections.

Adverse effects and cautions: hypersensitivity accounts for the most common and potentially most serious reactions. Acute anaphylactic reactions and angioedema can occur in about 2% of patients receiving parenteral therapy. Less common hypersensitivity includes serum sickness, eosinophilia, neutropenia and diarrhoea.

Because of danger of hypersensitivity penicillin should never be used in known hypersensitivity to penicillins.

Dose : By intramuscular or by slow intravenous injection or by infusion, 2.4-4.8 g daily in 4 divided doses, PREMATURE INFANT and NEONATE, 50 mg/kg daily in 2 divided doses; INFANT 1-4 weeks, 75 mg/kg daily in 3 divided doses; CHILD 1 month-12 years, 100 mg/kg daily in 4 divided doses.

Bacterial endocarditis, by slow intravenous injection or by infusion, 7.2 g daily in 4-6 divided doses. Meningitis, by slow intravenous injection or by infusion 2.4 g every 4 hours; PREMATURE INFANT and NEONATE 100

mg/kg daily in 2 divided doses; CHILD 1 month -12 years, 180-300 mg/kg daily in 4-6 divided doses

Preparation available

Benzylpenicillin Injection: Each vial of the injection containing benzylpencillin sodium or potassium equivalent to 150 mg, 300 mg and 600 mg is usually available. The powder should be dispersed in water for injection immediately before use.

CARBENICILLIN

It is mainly indicated for the treatment of serious infections caused by *Pseudomonas aeruginosa* though it also has activity against certain other Gram-negative bacilli including *Proteus* species and *Bacterioides fragilis.*

Indications: Infections due to *Pseudomonas aeruginosa* and *Proteus* species.

Adverse effects and cautions: see under benzylpenicillin. But also hypokaelaemia, prolonged bleeding time, prolonged prothrombin time, abnormal platelet aggregation and bleeding from gastrointestinal tract has been reported.

Dose: By slow intravenous injection or rapid infusion, severe systemic infection, 5 g every 4-6 hours; CHILD 250-400 mg/kg daily in divided doses.

By intramuscular injection, urinary-tract infection, 2g every 6 hours; CHILD 50-100 mg/kg daily in divided doses.

Preparation available

Carbenicillin Injection: Carbenicillin injection is prepared by dissolving carbcnicillin sodium for injection in the requisite amount of water for injection. Scaled container containing the equivalent of 1g and 5 g of carbenicillin are usually available. The sealed container of Carbenicillin injection should be stored at a temperature of 2-8°.

Carbenicillin injection should be used immediately after preparation but; in any case, within the period recommended by the manufacturer when preparation is stored strictly in accordance with the manufacturer's instructions.

CLOXACILLIN

It is one of the semisynthetic penicillins which is resistant to staphylococcal penicillinase.

Indications: exclusively for infection caused by or suspected of being caused by penicillinase-producing staphylococci.

Benzyl penicillin is more active against other susceptible bacteria.

Adverse effects and cautions: see under benzyl penicillin.

Dose: Infections due to susceptible beta-lactamase-producing staphylococci, by mouth, ADULT 500 mg 4 times daily, doubled in severe infection; by intramuscular injection, 250 mg every 4-6 hours, doubled in severe infection; by slow intravenous injection or intravenous infusion, 1-2 g every 6 hours; CHILD up to 2 years, quarter adult dose; CHILD 2-10 years, half adult dose.

Preparation available

Cloxacillin Capsules: Each capsule containing the equivalent of 250 mg and 500 mg of cloxacillin, as cloxacillin sodium, is usually available.

Cloxacillin Injection: Cloxacillin injection is a sterile solution of cloxacillin sodium in water for injection. It is prepared by dissolving the cloxacillin sodium for injection in the required amount of water for injection.

Sealed container containing the equivalent of 250 mg and 500 mg of cloxacillin is usually available.

Cloxacillin injections should be used immediately after preparation but in any case, within the period recommended by the manufacturer when prepared and stored in accordance with manufacturer's instructions. The sealed container should be kept at a temperature not exceeding 25°.

Cloxacillin Oral Solution: Cloxacillin oral solution is a solution of cloxacillin sodium in suitable flavoured vehicle. It is prepared by dissolving the dry ingredients in the specific volume of water just before use. Each 5ml of oral solution containing the equivalent of 125 mg cloxacillin is usually available. The oral solution should be stored at the temperature and used within the period stated on the label.

FLUCLOXACILLIN

It is not inactivated by penicillin-resistant staphylococci. It is acid-stable and is well absorbed from the gut.

Indications: infections due to beta-lactamase producing staphylococci including otitis externa; adjunct in pneumonia, impetigo, osteomyelitis and staphylococcal endocarditis.

Adverse effects and cautions: see under benzylpenicillin. It also produces gastro-intestinal disturbances.

Dose: By mouth, 250-500 mg every 6 hours, at least 30 minutes before food; CHILD under 2 years, quarter adult dose, 2-10 years half adult dose.

By intramuscular injection, 250-500 mg every 6 hours; CHILD under 2 years quarter adult dose, 2-10 years half adult dose.

Endocarditis (in combination with another antibacterial) under 85 kg, 8 g daily in 4 divided doses.

Preparation available

Flucloxacillin Capsules: Each capsule containing the equivalent of 250 mg and 500 mg of cloxacillin, as flucloxacillin sodium, is usually available.

PHENOXYMETHYL PENICILLIN

Penicillin V

It has similar spectrum to benzyl penicillin but it is resistant to gastric acid, so is suitable for oral administration.

Indications: streptococcal tonsillitis and pharyngitis including scarlet fever, Streptococcal or pneumococcal sinusitis and otitis media; erysipelas,

rheumatic fever and bacterial endocarditis prophylaxis.

The drug is not suitable for high dosage therapy in severely ill patients. Because of unpredictable variation in absorption and compliance it is not appropriate for the treatment of syphilis.

Adverse effects and cautions: *see* under benzyl penicillin.

Dose: 250-500 mg every 6 hours; CHILD, every 6 hours up to 1 years 62.5 mg, 1-5 years 125 mg, 6-12 years 250 mg.

Preparation available

Phenoxymethyl Penicillin Potassium Tablets: Each tablet containing the equivalent of 62.5 mg, 125 mg, 250 mg and 500 mg of phenoxymethyl penicillin is usually available.

Phenoxymethylpenicillin Oral Suspension: Each 5 ml of oral suspension containing the equivalent of 125 mg of phenoxymethyl pencillin is usually available. The dry powder should be dispersed in requisite quantity of water before use and should be used within the time specified on the label.

PROCAINE BENZYLPENICILLIN

The drug provides therapeutic tissue concentrations for about 24 hours. Injections are virtually painless because of local anaesthetic effect of procaine. The procaine penicillin can be fortified with free benzyl penicillin (fortified procaine penicillin) to produce a high initial level.

Indications: early and late latent syphilis.

Adverse effects, cautions, drug interactions: see under benzyl penicillin.

Dose: 300 000 units every 12-24 hour; CHILD 20 000 units per kg per day; NEONATE 15 000 units per kg per day

Primary syphilis – 600 000 units once daily for 8 days. Late syphilis - 2,400,000 units once daily for 15 days.

CHILD with congenital syphilis 50 000 units/kg for 10 days.

Preparation available

Fortified Procaine Penicillin Injection: Injection containing 300 000 units of penicillin G procaine and 100 000 units of Penicillin G is usually available.

TICARCILLIN

It is highly effective against *Pseudomonas aeruginosa*. It is also effective against *Proteus* and *Bacteroides fragilis*.

It is available in combination with clavulanic acid, and is effective against beta-lactamase producing bacteria resistant to ticarcillin.

Indications: infections due to *Pseudomonas* and *Proteus.*

Adverse effects and cautions: see under benzylpenicillin. It also produces nausea, vomiting, coagulation disorders and Stevens-Johnson syndrome.

Dose: by intravenous infusion, 3.2 g every 6-8 hours increased to every 4 hours in more severe infections; CHILD 80 mg/kg every 6-8 hours (every 12 hours in neonates).

7.3.2 Sulphonamides and Trimethoprim

SULFADIMIDINE

It is one of the sulphonamides which is well absorbed and rapidly eliminated. It is excreted principally in the urine. Both the drug and its metabolite acetyl derivative are relatively soluble in urine. It is one of the safest sulphonamides

Indications: treatment and chronic suppressive therapy of urinary infections due to *E.coli* or *Proteus mirabilis* including acute and chronic cystitis, chronic infections of the upper urinary tract and asymptomatic bacilluria.

The drug is inappropriate for cases of acute pyelonephritis. The drug can also be used for prevention of recurrence of rheumatic fever in penicillin sensitive cases.

Adverse effects and cautions: nausea, vomiting, headache, malaise, rashes, agranulocytosis, granulocytopenia and haemolytic anaemia in glucoses-phosphate dehydrogenase deficiency. The risk of crystalluria is slight-because of relatively high solubility.

Treatment should be immediately stopped if rash or other manifestation of hypersensilivity occurs.

Sulphonamides are contraindicated in patients with a history of hypersensitivity to any sulphonamide or chemically related drugs (e.g. sulphonylureas and thiazides).

Sulphonamides should be used with caution and in reduced dosage in patients with impaired hepatic and renal function or urinary obstruction.

Safe use of sulphonamides during pregnancy has not been established. The drug should not be administered to nursing mothers and in children younger than 6 weeks of age, jaundice due to displacement of bilirubin from protein binding sites has occurred.

Drug interactions: The drug may potentiate the actions of coumarin anticoagulants and sulphonylureas by displacing them from protein-binding sites.

Dose: By mouth, 2 g initially then 0.5-1 g every 6-8 hours.

Preparation available

Sulfadimidine Tablets: Each tablet containing 500 mg of sulphadimidine is usually available. Sulphadimidine tablets should be protected from light.

TRIMETHOPRIM

It is a synthetic folate-antagonist anti-infective and is used alone for the treatment of urinary and respiratory-tract infections caused by *E. coli, P. mirabilia, K. pneumoniae* and *H. influenzae.*

Indications: acute uncomplicated urinary tract infections and acute and chronic bronchitis.

Adverse effects and cautions: epigastric discomfort, nausea, vomiting, rash, pruritus, neutropenia, thrombocytopenia and megaloblastic anaemia.

The drug should be used with caution in patients with impaired renal or hepatic function or with possible folate deficiency. The drug should be used during pregnancy only when the potential benefits justify the possible risk to the foetus. It is distributed into milk, the drug should be used with caution in nursing mothers.

Safety and efficacy of trimethoprim in infants under 6 weeks of age has not been established.

Dose: By mouth, acute infections, 200 mg every 12 hours, CHILD twice daily, 6 weeks-5 months 25 mg, 6 months-5 years 50 mg, 6-12 years 100 mg.

Chronic infections and prophylaxis, 100 mg at night; CHILD 1-2 mg/kg at night.

Preparation available

Trimethoprim Tablets: Each tablet containing 100 mg and 200 mg of trimethoprim is usually available.

TRIMETHOPRIM AND SULFAMETHOXAZOLE

Co-trimoxazole

A combination of sulphamethoxazole 5 parts and trimethoprim 1 part constitutes an important advancement in the therapy.

Indications: uncomplicated lower urinary tract infection, bacterial prostatitis, exacerbation of chronic bronchitis due to *H. influenzae* and *Strep. pneumoniae,* acute otitis media in children and acute maxillary sinusitis in adults due to *H. influenzae* and *Strep. pneumoniae,Pneumocystis carinii* pneumonia.

The drug is not advised in streptococcal pharyngitis as it does not eradicate the organisms. The drug is ineffective against *Treponema pallidum, Pseudomonas* and *M. tuberculosis* infections.

Adverse effects and cautions: nausea, vomiting, rashes, drug fever, erythema multiform of Stevens-johnson type, leucopenia, granulocytopenia, glossitis, stomatitis, megaloblastic anaemia and crystalluria.

Treatment should be immediately stopped if a rash or other manifestation of hypersensitivity occurs.

The drug should not be used during pregnancy and drug should be used with caution in nursing mothers. Premature and infant under 6 weeks should not be prescribed, as it may lead to jaundice.

The risk of crystalluria can be decreased by maintaining urinary output of at least 1.5 liters daily.

Dose: By mouth, 960 mg every 12 hours, CHILD every 12 hours, 6 weeks to 5 months 120 mg; 6 months to 5 years, 240 mg; 6-12 years, 480 mg.

High-dose therapy for *Pneumocystis carinii* infection, by mouth or intravenous infusion 120 mg/kg daily in 2-4 divided doses for 14 days.

Prophylaxis of *Pneumocystis carinii* by mouth, 960 mg once daily (may be reduced to 480 mg once daily) or 960 mg twice daily on alternate days; CHILD 6 weeks-5months, 120 mg twice daily on 3 consecutive or alternate days per week, 6 months – 5 years 240 mg, 6-12 years 480 mg.

Preparation available

Paediatric Co-trimoxazole Oral suspension: Each 5ml of oral suspension containing 40 mg of trimethoprim and 200 mg of sulphamethoxazole is usually available. Cotrimoxazole oral suspension should be protected from light and stored at a temperture not exceeding 30°.

Co-trimoxazole Tablets: Tablet containing 40 mg of trimethoprim and 200 mg of sulphamethaxazole, 80 mg of trimethoprim and 400 mg of sulphamethaxazole and 160 mg of trimethoprim and 800 mg of sulphamethoxazole is usually available.

Paediatric Co-trimoxazole Dispersible Tablets: Tablets containing 20 mg of trimethoprim and 100 mg of sulphamethaxazole is usually available.

7.3.3 Cephalosporins

These are semi-synthetic antibiotics and are usually bactericidal in action. Cephalosporins are generally classified by "generation" based on their spectrum of antibacterial activity. First generation cephalosporins include cefadroxil, cefazolin and cefalexin. First generation cephalosporins have the highest degree of activity against most Gram-positive bacteria including beta-lactamase (penicillinase) producing *Staphylococcus aureus* and most *Streptococci.*

Second-generation cephalosporins include cefaclor, and cefuroxime. They have enhanced activity against a greater number of Gram-negative bacteria, including *H. influenzae, N.gonorrhoeae,* indole positive *Proteus* and *Enterobacter* species. However, they have slightly less or variable activity against most Gram-positive cocci. None of the second generation has activity against *Pseudomonas aeruginosa.*They are less susceptible than first generation to inactivation by beta-lactamases.

Third-generation cephalosporins include cefotaxime, ceftazidime and ceftriaxone. They have a high degree of stability in the presence of beta-lactamases and have an expanded spectum of activity against Gram-negative bacteria compared with the first and second generation drugs. Third- generation cephalosporins are generally active against Gram negative bacteria susceptible to the first and second generation drugs and are also generally active against *Enterobacter, E.coli, Klebsiella, Neisseria, Proteus, Serratia* that may be resistant to first and second generation cephalosporins. Ceftazidime has good activity against *Pseudomonas aeruginosa.*

Fourth generation cephalosporins include cefepime and cefpirome. They are indicated for the empirical treatment of nosocomial infections where antibiotic resistance owing to extended-spectrum beta-lactamases or chromosomally induced beta-lactamases are anticipated.

CEFACLOR

This is given orally.

Indications: *see* notes above.

Adverse effects and cautions: hypersensitivity reactions including urticaria, pruritus, rash, fever, joint pain and exfoliative dermatitis. Anaphylaxis occurs rarely. The other adverse effects include nausea, vomiting, diarrhoea, positive Coomb's test, disturbances in liver enzymes levels and rarely thrombocytopenia or neutropenia. Cephalosporins have cross-allergenicity with penicillins (about 10% cases) and cephalosporins should be avoided in patients who have had hypersensitivity reaction to penicillins. Prolonged use of cephalosporins may result in the overgrowth of nonsusceptible organisms especially *Pseudomonas, Enterococci* or *Candida.*

Dose: 250 mg every 8 hours, doubled for severe infection; maximum 4g daily. CHILD over one month, 20 mg per kg daily in 3 divided doses, doubled for severe infections, maximum 1g daily.

Preparation available

Cefaclor Capsules: Each capsule containing the equivalent of 250 mg of anhydrous Cefaclor is usually available.

Cefaclor Oral Suspension: Each 5ml oral suspension containing the equivalent of 125 mg of anhydrous Cefaclor is usually available. It is prepared by dispersing the dry ingredients in the specific volume of water just before use. The dried ingredients should be kept in a well closed container and stored at a temperature and used within the period stated on the label.

CEFADROXIL

It is administered orally.

Indications: *see* notes above

Adverse effects and cautions: see under cefaclor.

Dose: 0.5-lg twice daily for patient over 40 kg; skin, soft tissue and simple urinary tract infections 1 *g* daily. CHILD under 1 year, 25 mg/kg daily in divided doses; 1 -6 years, 250 mg twice daily, over 6 years, 500 mg twice daily.

Preparation available

Cefadroxil Capsules: Each capsule containing the equivalent of 500 mg and 1000 mg anhydrous cefadoxil is usually available.

Cefadroxil Dispersible Tablets: Each dispersible tablet containing equivalent of 125 mg and 250 mg of anhydrous cefadroxil is usually available.

Cefadroxil for Oral Suspension: Each 5ml of oral suspension containing the equivalent of 125 mg and 250 mg of anhydrous cefadroxil is usually available. It is prepared by dispersing the drug ingredients in the specific volume of water just before use.

The dry ingredients should be kept in a well closed container protected from light and stored at a temperature not exceeding 25°. The oral suspension should be stored at temperature and used within the period stated on the label.

CEFALEXIN

It is administered orally.

Indications, adverse effects and cautions: *see* under cefaclor

Dose: 250 mg every 6 hours or 500 mg every 8-12 hours increased to 1-1.5g every 6-8 hours for severe infections; CHILD 25 mg/kg daily in divided doses, doubled for severe infections, maximum 100 mg/kg daily; or under 1 year, 125 mg every 12 hours; 1-5 years, 125 mg every 8 years; 6-12 hours, 250 mg every 8 hours.

Prophylaxis of recurrent urinary-tract infection, ADULT 125 mg at night.

Preparation available

Cefalexin Capsules: Each capsule containing the equivalent of 250 mg and 500 mg of anhydrous cefalexin is usually available. Cefalexin capsules should be stored at a temperature not exceeding 30°.

Cefalexin Dispersable Tablets: Each tablet containing 125 mg of cefalexin, as cefalexin monohydrate, is usually available.

Cefalexin Oral Suspension: Each 5ml of oral suspension containing the equivalent of 125 mg and 250 mg of cefalexin is usually available. It is prepared by dispersing the dry ingredients in the specific volume of water just before use.

The dry ingredients should be kept in a well closed container, protected from light and stored at a tempreture not exceeding 30°. The oral suspension should be stored at a temerature and used within the period stated on the label.

CEFAZOLIN

It is administered intramuscularly or intravenously.

Indications: see notes above. It has also been used in surgical prophylaxis.

Adverse effects and cautions: see under cefaclor.

In patients with impaired renal function, doses-and/or frequency of administration of cephazolin must be modified.

Drug interactions: *see* under cefaclor.

Dose: By intramuscular injection or intravenous injection or infusion 0.5-1g every 6-12 hours; CHILD 25-50 mg/kg daily in divided doses, increased to 100 mg/kg daily in severe infection.

Preparation available

Cefazolin Sodium Injection: Sealed container containing the equivalent of 500 mg and 1g of cefazolin is usually available. It is prepared by dissolving the content of a sealed container in the requisite amount of water for injections. Cefazolin sodium injection should be used immediately after preparation but, in any case within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

CEFEPIME

It is a fourth-generation cephalosporin. It is particularly useful for the empirical treatment of serious infections in hospitalised patients. Its activity

against *H. influenzae*, *N. gonorrhoea* and *N. meningitidis* is comparable or greater than cefotaxime. It has comparable activity to ceftazidime in *P. aeruginosa.*

Indications: see note above.

Adverse effects and cautions: *see* under cefaclor.

Dose: by intravenous injection, 2 g every 12 hours.

Preparation available

Cefepime Injection: Each vial containing 1 g and 2 g of cefepime is usually available.

CEFIXIME

It is third-generation cephalosporins. It has longer duration of action and is effective orally. It is used only in acute infections.

Indications: see under cefaclor (acute infections only).

Adverse effects and cautions: see under cefaclor.

Dose: Adult and CHILD over 10 years, 200-400 mg daily in 1-2 divided doses, CHILD over 6 years 8 mg/kg in 1-2 divided doses.

Gonorrhoea, 400 mg as a single dose.

Preparation available

Cefixime Tablets: Each tablet containing 100 mg and 200 mg of cefixime is usually available.

CEFOPERAZONE

It is a third generation cephalosporin. It is excreted primarily in the bile.

Indications: treatment of pelvic infections, urinary-tract infections, bone and joint infections.

Adverse effects and cautions: *see* under cefaclor.

Dose: By intramuscular or intravenous injection, 1-2 g (base) every 12 hours.

Preparation available

Cefoperazone Injection: Each vial containing 1 g and 2 g of cefoperazone (as sodium salt) is usually available.

CEFPODOXIME

It is third-generation cephalosporin. It is very similar in activity to the fourth-generation agent cefepime except that it is not more active against Enterobacter or Pseudomonas .

Indications: Upper and lower respiratory-tract infections, uncomplicated urinary tract infections, skin and soft tissue infections, uncomplicated gonorrhoea.

Adverse effects and cautions: *see* under cefaclor.

Dose: Upper respiratory-tract infections (but in pharyngitis and tonsillitis reserved for infections which are recurrent, chronic or resistant to other antibacterials), 100 mg twice daily (200 mg twice daily in sinusitis); CHILD

15 days- 6 months 4 mg /kg every 12 hours, 6 months- 2 years 40 mg every 12 hours, 3-8 years 80 mg every 12 hours, over 9 years 100 mg every 12 hours.

Uncomplicated urinary-tract infections, 100 mg twice daily (200 mg twice daily in uncomplicated upper urinary-tract infections); CHILD dose see under upper respiratory- tract infections

Uncomplicated gonorrhoea, 200 mg as a single dose.

Preparation available

Cefpodoxime Tablets: Each tablet containing 100 mg and 200 mg of cefpodoxime (as proxetil) is usually available.

CEFOTAXIME

It is administered intramuscularly or intravenously.

Indications: see notes above

Adverse effects and cautions: *see* under cefaclor.

Dose: By intramuscular or intravenous injection 1g every 12 hours; severe infections, 2 g every 6 hours, exceptionally, for life threatening infection due to organism less sensitive to cefotaxime, up to 12 g daily in 3-4 divided doses. Gonorrhoea 500 mg as a single dose.

NEONATE, 50 mg/kg daily 2-4 divided doses, in severe infections 150-200 mg/kg daily; CHILD, 100-150 mg/kg daily 2-4 divided doses, in severe infections, up to 200 mg/kg daily.

Preparation available

Cefotaxime Sodium Injection: Sealed container containing the equivalent of 250 mg, 500 mg and 1 g of cefotaxime as cefotaxime sodium, is usually available. It is prepared by dissoluing content of sealed container in the required amount of water for injections.

Cefotaxime sodium injection should be used immediately after preparation but, in any case, within the period recommended by the manufacturer.

CEFTAZIDIME

It is administered intramuscularly or intravenously.

Indications: *see* notes above.

Adverse effects and cautions: see under cefaclor

Dose: By deep intramuscular injection or intravenous injection or infusion, 1 g every 8 hours or 2 g every 12 hours; 2 g every 8-12 hours in severe infections. CHILD up to 2 months 25-60 mg/kg daily in 2 divided doses, over 2 months 30 -100 mg /kg daily in 2-3 divided doses, up to 150 mg/kg daily (maximum 6 g daily) in immunocompromised or meningitis.

Pseudomonal lung infection in cystic fibrosis, adult with normal renal function 100-150 mg/kg daily in 3 divided doses; CHILD up to 150 mg/kg daily (maximum 6 g daily) in 3 divided doses; intravenous route recommended for children.

Urinary tract and less severe infections, 0.5-1 g every 12 hours.

Surgical prophylaxis, prostatic surgery, 1 g at induction of anaesthesia repeated if necessary when catheter removed.

Preparation available

Ceftazidime Injection: Sealed container containing the equivalent of 250 mg, 500 mg and 1 g of anhydrous ceftazidime, as ceftazidime pentahydrate, is usually available. It is prepared by dissolving content of sealed container in the requisite amount of water for injections.

Ceftazidime injection should be used immediately after preparation but, in any case within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

CEFTRIAXONE

It is administered intramuscularly or intravenously.

Indications: *see* notes above.

Adverse effects and cautions: *see* under cefaclor.

Dose: By deep intramuscular injection, or by intravenous injection over 2-4 minutes, or by intravenous infusion, 1g daily as single dose; 2-4 g daily as a single dose in severe infection; intramuscular doses over Ig divided between more than one site.

NEONATE by intravenous infusion over 60 minutes, 20-50 mg/kg daily; INFANT and CHILD under 50 kg, by intravenous infusion or deep intramuscular injection, 20-50 mg/kg daily, up to 80 mg/kg in severe infections, doses over 50 mg/kg by intravenous infusion only.

Uncomplicated gonorrhoea, by deep intramuscular injection, 250 mg as a single dose.

Surgical prophylaxis, by deep intramuscular injection or by intravenous injection over 2-4 minutes, 1 g as a single dose at induction; colorectal surgery, by deep intramuscular injection over 2-4 minutes or by intravenous infusion, 2 g at induction, intramuscular doses over 1 g divided between more than one site.

Endocarditis (in combination with other antibacterials), by intravenous infusion, 2-4 g daily.

Preparation available

Ceftriaxone Sodium Injection: Sealed container containing the equivalent of 250 mg, 500 mg and 1 g of ceftriaxone is usually available. It is prepared by dissolving content of sealed container in the requisite amount of water for injections. Cetriaxone sodim injection should be used immidiately after preparation but in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

CEFUROXIME

It is administered both orally and intramuscularly or intravenously.

Indications: *see* notes above. It has also been used for surgical prophylaxis. It is more active against *Haemophilus influenzae* and *Neisseria gonorrhoeae*.

Adverse effects, cautions and drug interactions: see under cefaclor.

Dose: By mouth (as cefuroxime axetil), 250 mg twice daily in most infections including mild to moderate respiratory-tract infections. Urinary-tract infections, 125 mg twice daily, doubled in pyelonephritis. Gonorrhoea, 1 g as a single dose.

By intramuscular or intravenous injection or infusion 750 mg every 6-8 hours, 1.5 g every 6-8 hours in severe condition. CHILD, 60 mg/kg daily in 3-4 divided doses. Gonorrhoea, 1.5 g as a single dose by intramuscular injection, divided between two sites.

Surgical prophylaxis, 1.5 g by intravenous injection at induction; may be supplemented with 750 mg intramuscularly or intravenously 8, 16 and 24 hours later for high risk procedures.

Meningitis, 3 g by intravenous injection every 8 hours; CHILD, 200-240 mg/kg daily in 3-4 divided doses, reduced to 100 mg/kg after 3 days or clinical improvement; NEONATE, 100 mg/kg daily reduced to 50 mg/kg daily

Preparation available

Cefuroxime Sodium Injection: Sealed container containing the equivalent of 250 mg and 750 mg of cefuroxime is usually available. It is prepared by dissolving the content of a sealed container in the requisite amount of water for injections.

Cefuroxime sodium injection should be used immediately after preparation but, in any case within the period recommended by the manufacturer, when preparation is stored strictly in accordance with the manufacturer's instruction.

Cefuroxime Axetil Tablets: Each tablet containing the equivalent of 125 mg and 250 mg of cefuroxime, as cefuroxime axetil is usually available.

7.3.4 Other beta-lactam antibiotics

Imipenem and **meropenem** have broad spectrum of activity including many aerobic and anaerobic Gram-positive and Gram-negative bacteria. Imipenem is partially inactivated in the kidney by enzymatic activity, so, is given with a specific enzyme inhibitor, cilastatin. Meropenem has less seizure-inducing potential and can be used to treat central nervous system infection.

IMIPENEM

Indications: aerobic and anaerobic Gram-positive and Gram-negative infections; surgical prophylaxis, hospital-acquired septicaemia.

Adverse effects and cautions: nausea, vomiting, diarrhoea, taste disturbances, hearing loss, anaphylactic reactions, blood disorders.

The safety of drug in breast-feeding has not been established.

Dose: by deep intramuscular injection, mild to moderate infections, 500-750 mg every 12 hours.

By intravenous infusion, 1-2 g daily in 3-4 divided doses, CHILD 3 months and older 60 mg/kg (maximum 2 g) daily in 4 divided doses.

Surgical prophylaxis, by intravenous infusion, 1 g at induction repeated after 3 hours.

MEROPENEM

Indications: aerobic and anaerobic Gram-positive and Gram-negative infections.

Adverse effects and cautions: *see* under imipenem.

Dose: Meningitis, 2 g every 8 hours; CHILD 3 months-12 years 40 mg/kg every 8 hours.

7.3.5 Tetracyclines

They are broad-spectrum antibiotics but their value has decreased owing to increasing bacterial resistance.

DEMECLOCYCLINE

Indications: *see* under tetracycline.

Adverse effects and cautions: *see* under tetracycline. But photosensitivity reactions occur more frequently and more severely than other tetracyclines.

Drug interactions: *see* under tetracycline.

Dose: 150 mg every 6 hours or 300 mg every 12 hours.

Preparation available

Demeclocycline Capsules: Each capsule containing 150 mg and 300 mg of demeclocycline hydrochloride is usually available.

DOXYCYCLINE

Indications, adverse effects, cautions and drug interactions: *see* under tetracycline.

Dose: 200 mg on first day, then 100 mg daily; severe infections (including chronic urinary-tract infections) 200 mg daily.

Acne, 100 mg daily for 6-12 weeks or longer.

Early syphilis, 100 mg twice daily for 14 days; late latent syphilis 200 mg twice daily for 28 days.

Non-gonococcal urethritis, 100 mg twice daily for 7 days.

Anthrax (treatment or post-exposure prophylaxis), 100 mg twice daily; CHILD (only if alternative antibacterial cannot be given) 5 mg/kg daily in 2 divided doses (maximum 200 mg daily).

Preparation available

Doxycycline Capsules: Each capsule containing 100 mg and 200 mg of doxycycline (as hyclate) is usually available.

MINOCYCLINE

Indications: *see* under tetracycline. It has also been indicated in the treatment of asymptomatic meningococcal carriers to eliminate *Neisseria meningitidis* from the nasopharynx.

Adverse effects and cautions: *see* under tetracycline. But it may also cause dizziness, tinnitus and vertigo.

Drug interactions: *see* under tetracycline

Dose: 100 mg twice daily

Acne, 50 mg twice daily for minimum course of 6 weeks

Preparation available

Minocycline Hydrochloride Capsules: Each capsule containing the equivalent of 50 mg and 100 mg of minocycline, as hydrochloride, is usually available.

OXYTETRACYCLINE

Indications, adverse effects, cautions and drug interactions: *see* under tetracycline

Dose: 250-500 mg every 6 hours

Preparation available

Oxytetracycline Capsules: Each capsule containing 250 mg and 500 mg of oxytetracycline hydrochloride are usually available.

TETRACYCLINE

It is one of the tetracyclines, which are broad-spectrum antibiotics. These tetracyclines are now relatively less frequently used because of emergence of bacterial resistance. All of them have therapeutically similar activity.

Indications: exacerbations of chronic bronchitis, Chlamydial infections such as non-gonococcal urethritis, trachoma and lymphogranuloma venerum; acne vulgaris, brucellosis, cholera and syphilis (in patients allergic to penicillin).

Adverse effects and cautions: nausea, vomiting, diarrhoea, deposition of tetracycline in calcified tissues of bone and teeth causing yellow staining and damage to teeth and impairing bone development during foetal life and childhood, urticaria and glossitis.

All tetracyclines are to be avoided during pregnancy, lactation and in children under 12 years of age.

All tetracyclines except doxycycline and minocycline can worsen any degree of impaired renal function.

Drug interactions: food delays the absorption of all tetracyclines except doxycycline. Similarly milk and milk products, antacids can reduce the absorption of tetracyclines.

Dose: 250 mg every 6 hours, increased in severe infections to 500 mg every 6 hours.

Acne, 500 mg twice daily for 3 months reduced to 250 mg twice daily for a further 3 months.

Primary, secondary or latent syphilis, 500 mg every 6 hours for 15 days.

Non- gonococcal urethritis, 500 mg every 6 hours for 7-14 days (21 days if failure or relapse following the first course).

Preparation available

Tetracycline Capsules: Each capsule containing 250 mg and 500 mg of tetracycline hydrochloride is usually available.

7.3.6 Aminoglycosides

This is a group of bactericidal drugs active against some Gram-positive and many Gram-negative organisms. Aminoglycosides are poorly absorbed from the alimentary tract and their penetration into body tissues and fluids, including CSF, is low, but they cross the placental barrier. Serum aminoglycoside concentrations should be measured in all patients and must be determined in infants, in the elderly, if high doses given or if there is renal impairment.

AMIKACIN

It is relatively resistant to several of the enzymes that inactivate gentamicin, and it therefore can be used against some microorganisms resistant to gentamicin. It is active against *Proteus, Pseudomonas and Enterobacter.*

Indications: serious Gram-negative infections resistant to gentamicin.

Adverse effects and cautions: *see* under gentamicin but it affects auditory function more than vestibular.

Dose: For adults and children the equivalent of 15 mg of amikacin per kg body-weight daily in 2 divided doses every 12 hours by intramuscular or slow intravenous injection or infusion, up to a maximum of 1.5 g daily in adults; CHILD 15 mg/kg daily in 2 divided doses; NEONATE loading dose of 10 mg/kg then 15 mg/kg daily in 2 divided doses..

Preparation available

Amikacin Sulphate Injection: Amikacin sulphate injection is a sterile solution containing amikacin sulphate. Injection containing the equivalent of 50 mg, 125 mg and 250 mg of amikacin per ml is usually available.

GENTAMICIN

It is active against *Pseudomonas aeruginosa*, Proteus, most Enterococci and Staphylococci.

Indications: urinary tract infections due to *Pseudomonas,* meningitis and other CNS infections, septicaemia and neonatal sepsis, endocarditis (with other antibiotics).

Adverse effects and cautions: vestibular damage, reversible nephrotoxicity and respiratory paralysis. Monitoring of blood levels of gentamicin is advisable because both nephrotoxicity and ototoxicity are seen when higher doses are used, particularly in neonates, elderly and renal impaired patients.

Gentamycin should not be used during pregnancy except when essential.

Dose: By intramuscular or by slow intravenous injection over at least 3 minutes or by intravenous infusion, 3-5 mg/kg daily (in divided doses every 8 hours).

CHILD up to 2 weeks, 3 mg/kg every 12 hours; 2 weeks-12 years, 2 mg/kg every 8 hours.

By intrathecal injection, 1 mg daily (increased if necessary to 5 mg daily.

Endocarditis (in combination with other antibiotics), adult 1 mg/kg every 8 hours.

Preparation available

Gentamicin Injection: Injection containing the equivalent of 10 mg and 40 mg per ml of gentamicin (as sulfate) is usually available.

KANAMYCIN

It is toxic for parenteral administration and has limited usefulness as topical agent.

Indications: *see* notes above.

Adverse effects and cautions: see under gentamicin but it affects auditory function more than vestibular.

Dose: By intramuscular injection, 250 mg every 6 hours or 500 mg every 12 hours.

By intravenous infusion, 15-30 mg/kg daily in divided doses every 8-12 hours.

Preparation available

Kanamycin Injection: Sealed container containing 500 mg and 1 g of kanamycin acid sulfate is usually available. Kanamycin injection prepared by dissolving the content of a sealed container in water for injection. It should be used immediately after preparation but in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instruction.

NEOMYCIN

It is very toxic for parenteral administration and has widespread use as topical agent. It is used orally to reduce the bacterial population of the colon prior to bowel surgery or in hepatic failure.

Indications: bowel surgery, hepatic coma, infections of skin and mucous membranes.

Adverse effects and cautions: hypersensitivity (even with topical application) and increased salivation.

Dose: By mouth, bowel sterilisation, 1 g every hour for 4 hours, then 1 g every 4 hours for 2-3 days.

Hepatic coma, up to 4 g daily in divided doses usually for maximum 14 days.

Preparation available

Neomycin Tablets: Each tablet containing 500 mg neomycin sulfate is usually available. Neomycin tablets should be protected from light and stored at a temperature not exceeding 30°.

STREPTOMYCIN*: *see under section 7.3.10, anti-tubercular drugs.

7.3.7 Urinary-tract infections

Urinary-tract infection is more common in women than men, when it occurs in men there is frequently an underlying abnormality in the renal tract.

NALIDIXIC ACID

The drug is bactericidal to most of Gram-negative bacteria that cause urinary tract infections such as *E.coli, Proteus* and *Klebsiella. Pseudomonas* species are resistant.

Indications: urinary tract infections.

Adverse effects and cautions: nausea, vomiting, abdominal pain, allergic reactions such as pruritus, urticaria, eosinophilla and fever.

The drug should be used with caution in patients with impaired renal or hepatic function.

Dose: 900 mg every 6 hours for 7 days, reduced in chronic infection to 600 mg every 6 hours; CHILD over 3 months maximum 50 mg/kg daily in divided doses; reduced in prolonged therapy to 30 mg/kg daily.

Preparation available

Nalidixic Acid Oral Suspension: Each 5ml of oral suspension containing 300 mg of nalidixic acid is usually available.

Nalidixic Acid Tablets: Each tablet containing 500 mg of nalidixic acid is usually available. It should be protected from light.

NITROFURANTOIN

It is usually bacteriostatic and is active against gram- negative and gram-positive bacteria including *E. coli, Klebsiella, S. aureus* and S. *faecalis.* The activity of drug is greatly enhanced at pH 6.5 or less. Most species of Proteus, Pseudomonas and Enterobacter are resistant.

Indications: urinary tract infections.

Adverse effects and cautions: nausea, vomiting, diarrhoea, haemolytic anaemia in individuals with G-6 PD deficiency, allergic manifestations such as chills, fever, leucopenia, cholestatic jaundice and peripheral neuropathy.

The drug should not be used in acute pyelonephritis, infant less than 3 months old and known hypersensitive to nitrofurantoin. The drug has been used safely in pregnancy.

Dose: Acute uncomplicated infection, 50 mg every 6 hours with food for 7 days; CHILD over 3 months, 3 mg/kg daily in 4 divided doses.

Severe chronic recurrent infection, 100 mg every 6 hours with food for 7 days (dose reduced or discontinued if severe nausea).

Prophylaxis, 50-100 mg at night; CHILD over 3 months, 1 mg/kg at night.

Preparation available

Nitrofurantoin Oral Suspension: Each 5 ml containing 25 mg of nitrofurantoin is usually available.

Nitrofurantoin Tablets: Each tablet containing 50 mg and 100 mg of nitrofurantoin are usually available.

7.3.8 Quinolones

These are synthetic fluorinated analogues of nalidixic acid. Nalidixic acid, a quinolone do not achieve systemic antibacterial level and thus is used only as urinary antiseptics (*see* under section 7.3.7). Quinolones are generally not recommended in children and growing adolescents.

CIPROFLOXACIN

It is active against both Gram-positive and Gram-negative bacteria, particularly against Gram-negative bacteria including *Shigella, Salmonella, Helicohacler, Neiserria, Pseudomonas, H. influenzae* and *E. coli.* It has moderate activity against *Streptococcus pneumoniae* and *Streptococcus faecalis.* It is also active against species of *Chlamydia, Mycoplasma* and some *Mycobacterium.*

Indications: uncomplicated and complicated urinary tract infections, acute and chronic prostatitis, infective chronic airway disease, typhoid fever and gonorrhoea.

Adverse effects and cautions: nausea, vomiting, pancreatitis, tachycardia, hypotension, tinnitus, sweating.

The drug should be used with caution in patients with epilepsy or history of epilepsy, hepatic or renal impairment, pregnancy and breast-feeding.

Drug interactions: Antacids reduce absorption of ciprofloxacin, norfloxacin and ofloxacin. Concomitant use with warfarin can prolong prothrombin time.

Dose: By mouth, respiratory tract infections, 250-500 mg twice daily; Urinary-tract infections, 250-500 mg twice daily (100 mg twice daily for 3 days in acute uncomplicated cystitis in women).

Gonorrhoea, 500 mg as a single dose; chronic prostatitis, 500 mg twice daily for 28 days.

Chronic prostatitis, 500 mg twice daily for 28 days.

Most other infections, 500-750 mg twice daily.

Prophylaxis of meningococcal meningitis; 500 mg as a single dose. Surgical prophylaxis, 750 mg 60-90 minutes before procedure.

By intravenous infusion (over 30-60 minutes) 200-400 mg twice daily. Urinary-tract infections 100 mg twice daily, gonorrhoea, 100 mg as a single dose.

CHILD not recommended but when benefit outweighs risk, by mouth 10-30 mg/kg daily in 2 divided doses or by intravenous infusion 8-16 mg/kg daily in 2 divided doses.

Preparation available

Ciprofloxacin Tablets: Each tablet containing 250 mg, 500 mg and 750 mg of ciprofloxacin (as hydrochloride) is uaually available.

Ciprofloxacin Infusion: An injection containing 200 mg of ciprofloxacin per 100 ml is usually available.

LEVOFLOXACIN

It has greater activity against Streptococci than norfloxacin, ciprofloxacin and ofloxacin.

Indications: chronic prostatitis, urinary-tract infections, exacerbation of chronic bronchitis, community acquired pneumonia, skin and soft tissue infections.

Adverse effects and cautions: see under ciprofloxacin. It also causes tachycardia, hypotension, hypoglycaemia, pneumonitis.

Dose: Urinary-tract infections, 250 mg daily for 7-10 days (for 3 days in uncomplicated cases).

Exacerbation of chronic bronchitis, 250-500 mg daily for 7-10 days.

Chronic prostatitis, 500 mg once daily for 28 dayss.

Community-acquired pneumonia, 500 mg once or twice daily for 7-14 days.

Skin and soft tissue infections, 250 mg daily or 500 mg once or twice daiy for 7-14 days.

By intravenous infusion (over at least 60 minutes for 500 mg), community acquired pneumonia, 500 mg once or twice daily.

Complicated urinary-tract infections, 250 mg daily, increased in severe infections.

Preparation available

Levofloxacin Tablets: Each tablet containing 250 mg and 500 mg of levofloxacin is uaually available.

Levofloxacin Infusion: An injection containing 500 mg of levofloxacin per 100 ml is usually available.

NORFLOXACIN

Indications: uncomplicated urinary-tract infections, prophylaxis in recurrent urinary-tract infections, chronic prostatitis.

Adverse effects and cautions: see under ciprofloxacin

Drug interactions: *see* under ciprofloxacin.

Dose: Urinary-tract infections, 400 mg twice daily for 7-10 days (for 3 days in uncomplicated lower urinary-tract infections). Chronic relapsing urinary-tract infections, 400 mg twice daily for up to 12 weeks; may be reduced to 400 mg once daily if adequate suppression within first 4 weeks.

Chronic prostatitis, 400 mg twice daily for 28 days.

Preparation available

Norfloxacin Tablets: Each tablet containing 100 mg, 200 mg, 400 mg and 800 mg of norfloxacin is usually available.

OFLOXACIN

Indications: uncomplicated urinary-tract infections, acute or chronic prostatitis, infective chronic airway disease and gonorrhoea.

Adverse effects and cautions: *see* under ciprofloxacin

Drug interactions: *see* under ciprofloxacin.

Dose: By mouth, urinary-tract infections, 200-400 mg daily preferably in the morning, increased if necessary in upper urinary-tract infections to 400 mg twice daily.

Lower respiratory-tract infections, 400 mg daily preferably in the moming, increased if necessary to 400 mg twice daily.

Uncomplicated gonorrhoea, 400 mg as a single dose.

Non-gonococcal urethritis, 400 mg daily in single or divided doses for 7 days.

By intravenous infusion (over at least 30 minutes for each 200 mg), complicated urinary-tract infection, 200 mg daily.

Lower respiratory-tract infections, 200 mg twice daily.

Septicaemia, 200 mg twice daily.

Severe or complicated infections, dose may be increased to 400 mg twice daily.

Preparation available

Ofloxacin Intravenous Infusion: Intravenous infusion containing the equivalent of 200 mg per 100 ml of ofloxacin is usually available.

Ofloxacin Tablets: Each tablet containing 100 mg and 200 mg of ofloxacin is usually available.

7.3.9 Miscellaneous Drugs

AZITHROMYCIN

It is a macrolide antibiotic with slightly less activity than erythromycin against Gram- positive bacteria but enhanced activity aginst some Gram-negative bacteria including *H.influenzae*.

Indications: respiratory-tract infections, otitis media, skin and soft tissue infections, non-gonococcal urethritis, multi-drug resistant typhoid.

Adverse effects and cautions: *see* under erythromycin; also pancreatitis, constipation, headache, drowsiness.

The drug should be used in pregnancy and breast-feeding if adequate alternatives are not available.

The drug is contraindicated in impairment of hepatic function.

Dose: 500 mg once daily for 3 days; CHILD over 6 months, 10 mg/kg once daily for 3 days.

Non-gonococcal urethritis, 1 g as a single dose.

Typhoid, 500 mg once daily for 7 days.

Preparation available

Azithromycin Tablets: Each tablet containing 250 mg and 500 mg of azithromycin is usually available.

Azithromycin Dispersible Tablets: Each tablet containing 100 mg of azithromycin is usually available.

CHLORAMPHENICOL

It is a broad-spectrum antibiotic which is reserved for the treatment of life threatening infection particularly caused by *Salmonella* and *H. influenzae.* Chloramphenicol penetrates CSF and crosses the placental barrier.

Indications: typhoid fever and other *Salmonella infections, H. influenzae* meningitis, pneumonia, bacteremia and arthritis.

Adverse effects and cautions: anaemia, leucopenia, thrombocytopenia, reversible and irreversible aplastic anaemia (unrelated to dose, and duration of therapy), peripheral neuritis, nausea, vomiting and headache.

Unnecessarily prolonged treatment and repeated courses should be avoided. Periodic blood counts should be monitored. Dosage should be reduced in patients with hepatic insufficiency and in infants who have reduced ability to conjugate and excrete the drug.

Drug interactions: Chloramphenicol prolongs the half-life of phenytoin and oral hypoglycaemic agents by inhibiting hepatic microsomal enzymes.

Dose: By mouth or by intravenous injection or infusion, 50 mg/kg daily in 4[1] divided doses (exceptionally, can be doubled for severe infection such as septicaemia and meningitis, providing high doses reduced as soon as clinically indicated).

CHILD, pyogenic meningitis, 50-100 mg/ kg daily in divided doses (high doses, decreased as soon a clinically indicated). INFANT under 2 weeks 25 mg/kg daily in 4 divided doses, 2 weeks - 1 year 50 mg/kg daily in 4 divided doses.

Preparation available

Chloramphenicol Capsules: Each capsule containing 250 mg and 500 mg of chloramphenicol is usually available.

Chloramphenicol Sodium Succinate Injection: Chloramphenicol sodium succinate injection is prepared by dissolving the content of sealed container in the requisite amount of water for injection. Sealed container containing the equivalent of 1 g of chloramphenicol is usually available.

Chloramphenicol sodium succinate injection should be protected from light.

Chloramphenicol Oral Suspension: Chloramphenicol oral suspension is a suspension of chloramphenicol palmitate in a suitable flavouring vehicle. Oral suspension containing the equivalent of 125 mg of chloramphenicol per 5 ml is usually available. Chloramphenicol oral suspension should be protected from light.

CLARITHROMYCIN

It is an erythromycin derivative with slightly greater activity than the parent compound.

Indications: respiratory-tract infections, mild to moderate skin and soft tissue infections, otitis media, *H.pylori* eradication,

Adverse effects and cautions: see under erythromycin; also tooth and tongue discolouration, headache, smell and taste disturbances.

The drug should be used in pregnancy and breast-feeding if potential benefit outweighs risk.

Dose: 250 mg every 12 hours for 7 days (severe infection, 500 mg every 12 hours for up to 14 days); CHILD, 7.5 mg/kg twice daily.

Preparation available

Clarithromycin Tablets: Each tablet containing 250 mg and 500 mg of azithromycin is usually available.

ERYTHROMYCIN

Erythromycin and other macrolide antibiotics have an antibacterial spectrum similar to that of penicillin and is thus an alternative in penicillin-allergic patients. It is bacteriostatic.

Indications: alternative to penicillin in hypersensitive patients, syphilis, non-gonococcal urethritis, chronic prostatitis, diphtheria and whooping cough prophylaxis, acne vulgaris.

Adverse effects and cautions: nausea, vomiting, diarrhoea, skin rashes and fever. Choleslatic hepatitis is caused primarily by erythromycin estolate and rarely by erythromycin stearate or ethylsuccinate.

Hepatic function should be closely monitored in patients with a previous history of liver disease.

Drug interactions: Erythromycin potentiates the effects of carbamazepine, corticosteroids, digoxin, theophylline, tacrolimus and sildenafil.

Dose: ADULT and CHILD over *8* years, 250-500 mg every 6 hour; CHILD up to 2 years 125 mg every 6 hours, 2-8 years 250 mg every 6 hours, doses doubled for severe infections.

Acne, 500 mg twice daily for 3 months reduced to 250 mg twice daily for a further 3 months.

Early syphilis, 500 mg 4 times daily for 14 days.

Uncomplicated non-gonococcal urethritis, 500 mg twice daily for 14 days.

Preparation available

Erythromycin Tablets: Each tablet containing 100 mg, 250 mg and 500 mg of erythromycin estolate or erythromycin stearate is usually available.

Erythromycin Drops: Each ml containing 100 mg of erythromycin in usually available.

Erythromycin Oral Suspension: Each 5 ml containing 100 mg of erythromycin estolate or erythromycin stearate is usually available.

METRONIDAZOLE*: *see under to section 7.2, antiamoebic and anti-giardial drugs.

SPECTINOMYCIN

It is active against Gram-negative organisms but is inferior to other drugs to which such microorganisms are susceptible. It is used only as an alternative treatment for gonorrhoea in patients whose gonococci are resistant to first-line drugs or if there are contraindications to the use of these drugs.

Indications: gonorrhoea.

Adverse effects and cautions: nausea, fever and pain at sites of injection.

Dose: By deep intramuscular injection, 2 g.

Preparation available

Spectinomycin Injection: Powder for injection of spectinomycin, 2 g (as hydrochloride) is usually available.

TEICOPLANIN

It is similar to vancomycin but has longer duration of action, is given once daily. It can be given by intramuscular as well as intravenous route.

Indictions: see under vancomycin

Adverse effects and cautions: rash, bronchospasm, anaphylaxis, headache, rigors. The drug should be used with caution in pregnancy, renal or liver impairment.

Dose: By intramuscular injection or by intravenous injection or infusion, initially 400 mg (for severe infections initially 400 mg every 12 hours for 3 days) then 200 mg daily. CHILD over 2 months by intravenous injection or infusion, 10 mg/kg every 12 hours for 3 days, subsequently 6 mg/kg daily.

Preparation available

Teicoplanin Injection: Each vial containing 200 mg of teicoplanin powder for injection is usually available.

VANCOMYCIN

It is primarily active against Gram-positive bacteria. All Gram-negative bacilli and mycobacterium are resistant. It has long duration of action and can be given every 12 hours. It is not given orally since it is not significantly absorbed.

Indications: prophylaxis and treatment of endocarditis.

Adverse effects and cautions: nephrotoxicity including renal failure, ototoxicity, nausea, chills, fever, severe hypotension, shock and cardiac arrest (on rapid infusion).

The rapid infusion of the drug should be avoided. The drug should be used in pregnancy if potential benefit outweighs risk.

Plasma concentration of the drug should be monitored after 3-4 doses if renal function is normal and earlier if there is renal impairment.

Dose: By intravenous infusion, 500 mg every 6 hours or 1 g every 12 hours. ELDERLY over 65 years, 500 mg every 12 hours or 1 g once daily. NEONATE up to 1 week, 15 mg/kg initially then 10 mg/kg every 12 hours; 1-4 weeks, 15 mg/kg initially then 10 mg/kg every 8 hours; CHILD over 1 month, 10 mg/kg every 6 hours.

Preparation available

Vancomycin Injection: Powder for injection of vancomycin (as hydrochloride) 500 mg and 1 g per vial is usually available.

7.3.10 Anti-leprotic drugs

CLOFAZIMINE

It is most commonly used along with dapsone in multi-drug treatment regimen. The drug also has an anti-inflammatory use in nodosum leprosum.

Indications: multibacillary leprosy

Adverse effects and cautions: nausea, vomiting, headache, red discolouration of skin, faeces and urine.

Dose: Leprosy (with rifampicin and dapsone), 300 mg once monthly, supervised, and 50 mg daily self-administration

Preparation available

Clofazimine Capsules: Each capsule containing 50 mg and 100 mg of clofazimine is usually available.

DAPSONE

It is most commonly used sulphone.

Indications: leprosy, dermatitis herpetiformis.

Adverse effects and cautions: anorexia, nausea, vomiting, headache, pruritus, and haemolytic anaemia in individuals with glucose-6-phosphate dehydrogenase deficiency.

Dose: For multibacillary leprosy, rifampicin 600 mg and clofazimine 300 mg are both given once a month under supervision together with dapsone 100 mg and clofazimine 50 mg both daily in self administrered doses for 1 year. Doses of all 3 agents are reduced in children and in those aged 10-14 years daily dose of dapsone 50 mg or 1-2 mg/kg if their body weight is low, are given. Adult weighing less than 35 kg also receive reduced doses of rifampicin and dapsone and in such patient the dapsone dose is 50 mg or 1 - 2 mg per kg daily.

For paucibacillary leprosy, rifampicin 600 mg under supervision once a month and dapsone 100 mg self administered daily, both agents are given for 6 months. Doses are reduced in children and low weight patient as for multibacillary leprosy.

Preparation available

Dapsone Tablets: Each tablet containing 50 mg and 100 mg of dapsone is usually available.

RIFAMPICIN

It is a semisynthetic derivative of rifamycin, which is readily absorbed after oral administration. It is lipid soluble and is distributed throughout tissues and body fluid including CSF.

Indications: short course chemotherapy of tuberculosis and leprosy, prevention of meningococcal meningitis and *H.influenzae*.

Adverse effects and cautions: anorexia, nausea, vomiting, diarrhoea, "flu" like syndrome characterised by fever, malaise, headache, chills, skin reashes, transient rise in serum bilirubin and transaminases, respiratory symptoms, thrombocytopenic purpura and orange red body secretions.

Adverse effect are more likely to occur during intermittent therapy, however the monthly schedules in leprosy appears to be devoid of this risk.

Drug interactions: drug induces hepatic enzymes which accelerate the metabolism of several drugs including corticosteroids, digitalis glycosides, oestrogens and oral hypoglycaemics.

Dose: Brucellosis, legionnaire's disease and serious staphylococcal infections, in combination with other drugs, by mouth or by intravenous infusion, 0.6-1.2 g daily in 2-4 divided doses.

Tuberculosis, in combination with other drugs, ADULT (more than 50 kg) 600 mg daily for 6 months in category-I and for 8 months in category-II; CHILD 15 mg/kg daily for 6 months in category-I and for 8 months in catgory-II.

Leprosy, multibacillary leprosy (3 drugs regimen), 600 mg once monthly, supervised (450 mg for those weighing less than 35 kg.) Paucibacillary leprosy (2 drugs regimen) 600 mg once monthly supervised (450 mg for those weighing less than 35 kg).

Prophylaxis of meningococcal meningitis, 600 mg every 12 hours for 2 days; CHILD 3 months - 1 year 5 mg/kg, over 1 year 10 mg/kg every 12 hours for 2 days.

Prophylaxis of *H.influenzae* type b, 600 mg once daily for 4 days; CHILD 1-3 months 10 mg/kg once daily for 4 days, over 3 months 20 mg/kg once daily for 4 days (maximum 600 mg daily).

Preparation available

Rifampicin Capsules: Each capsule containing 150 mg, 300 mg and 450 mg of rifampicin is usually available.

Rifampicin Oral Suspension: Oral suspension containing 100 mg of rifampicin per 5 ml is usually available.

7.3.11 Anti-tubercular drugs

Amikacin, para-aminosalicylic acid, ciprofloxacin, ofloxacin, cycloserine and capreomycin are used for the treatment of multi-drug resistant tuberculosis.

CYCLOSERINE

It is used in combination with other drugs in the treatment of pulmonary or extra-pulmonary tuberculosis.

Indications: tuberculosis resistant to primary agents.

Adverse effects and cautions: headache, tremor, vertigo, confusion, irritability, psychotic stages with suicidal tendencies, tonic-clonic or absence seizures.

It is contra-indicated in severe renal impairment, epilepsy.

The drug should be used with caution in pregnancy, breast-feeding, renal or hepatic impairment, depression.

Dose: Initially 250 mg every 12 hours for 2 weeks increased according to blood concentration and response to maximum 500 mg every 12 hours; CHILD initially 10 mg/kg daily.

Preparation available

Cycloserine Capsules: Each capsule containing 250 mg of cycloserine is usually available.

ETHAMBUTOL

It has mainly bacteriostatic effect and is substantially absorbed from gastro-intestinal tract.

Indications: tuberculosis

Adverse effects and cautions: optic neuritis resulting in decrease in visual acuity and loss of ability to differentiate red from green. The effect is dose dependent and occurs rarely on dose of 15 mg/kg given daily. Recovery usually occurs when ethambutol is withdrawn. The other adverse effects are skin rash, drug fever, pruritus, joint pain and gastro-intestinal upset.

The drug is contraindicated in children under 5 years, optic neuritis and severe renal impairment.

Dose: 15 mg/kg daily.

Preparation available

Ethambutol Tablets: Each tablet containing 200 mg, 400 mg, 600 mg, 800 mg, and 1000 mg of ethambutol (as hydrochloride) is usually available.

ETHIONAMIDE

It is used as reserve drug in the treatment of tuberculosis.

Indications: tuberculosis.

Adverse effect and cautions: anorexia, nausea, vomiting, hepatitis, mental depression and drowsiness.

Dose: By mouth, in combination with other drugs, 250 mg every 12 hours increased by 12.5 mg/day every 5 days until a dose of 15-20 mg/kg/day (maximum 1 g); CHILD, in combination with other drugs 4-5 mg per kg body weight every 8 hours.

Preparation available

Ehionamide Tablets: Each tablet containing 250 mg of ethionamide is

usually available.

ISONIAZID

It is the most important drug for the treatment of all types of tuberculosis. It is bacteriostatic for 'resting' bacilli, but bactericidal for rapidly multiplying bacteria.

Indications: tuberculosis.

Adverse effects and cautions: peripheral neuritis is the most common adverse effect, higher when high doses are used; skin rash, ataxia, dizziness, optic neuritis and hepatic damage.

Patient (7-35 years of age), excessive alcohol intake and history of liver disease should be assessed monthly for hepatic-damage. Pyridoxine (6 mg) should be given per day for the prevention of peripheral neuropathy .The drug should be used with caution in patients with impaired liver and kidney function.

The drug is contraindicated in patients with previous isoniazid-induced liver disease.

Dose: 300 daily; CHILD 10 mg/kg daily (maximum 300 mg daily)

Preparation available

Isoniazid Tablets: Each tablet containing 300 mg of isoniazid is usually available.

PYRAZINAMIDE

It is bactericidal drug which is readily absorbed from gastro-intestinal tract. It is distributed in all cellular tissues and fluids including the CSF. It seems to be effective essentially in the first 8 weeks of treatment to destroy intracellular bacillary population and thus it prevents relapse. From 8 weeks onwards it is useless when rifampicin is given beyond 8 weeks in short course chemotherapy.

Indications: tuberculosis

Adverse effects and cautions: hepatotoxicity is the serious adverse effect. Anorexia, nausea, vomiting and arthralgia are less common. Rises in serum transaminase concentrations are common during the early phase of treatment and returns to normal despite continuation of treatment, in most of cases.

Dose: For first 2 months only, adult under 50 kg 1.5 g, 50 kg and over 2 g daily; CHILD 35 mg /kg daily

Preparation available

Pyrazinamide Tablets: Each tablet containing 400 mg, 500 mg, 750 mg and 1000 mg pyrazinamide is usually available.

RIFAMPICIN: *see* under section 7.3.10, anti-tubercular dugs.

STREPTOMYCIN

It is an aminoglycosides used in the treatment of tuberculosis and a few specific gram-negative infections. It has poor penetration in the CSF.

Indications: tuberculosis, brucellosis and bacterial endocarditis.

Adverse effect and cautions: vestibular damage is the main adverse effect, the risk increases with dose and age (above 40 years), skin rashes, drug fever.

The drug should be avoided during pregnancy and in patient over 40 years, whenever possible.

Dose: 0.75 g daily; CHILD 15 mg/kg/day

Preparation available

Streptomycin Injection: Each injection containing 1 g and 0.75 g streptomycin sulphate are usually available.

THIOACETAZONE

It is used in combination with isoniazid. It is readily absorbed from gastro-intestinal tract.

Indications: tuberculosis

Adverse effects and cautions: skin rashes, gastro-intestinal upset, Jaundice and bone marrow depression.

Most of the serious adverse effects occur within the first 4-7 weeks of treatment/The drug should be immediately stopped if a rash or other manifestation of hypersensitivity occurs.

Dose: 1 tablet daily

Preparation available

Thioacetazone and Isoniazid Tablets: Each tablet containing 150 mg of thioacetazone and 300 mg of isoniazid is usually available.

7.4 Anti-fungal drugs

AMPHOTERICIN B

It is poorly absorbed from the gastro-intestinal tract. It is active against *Histoplasma, Cryptococcus, Candida, Blastomyces* and other organisms producing mycotic disease in humans. Lipid formulations are significantly less toxic and are recommended when conventional formulations are contraindicated or poor in therapeutic response.

Indications: intestinal candidiasis, oral and perioral infections

Adverse effects and cautions: chills, fever, vomiting, headache, hypokalaerni'a, neurological disorders including diplopia, convulsions, peripheral neuropathy and anaphylactoid reactions. Hepatic and renal function tests, and plasma electrolyte monitoring is required.

Dose: By intravenous infusion, systemic fungal infections, initial test dose of 1 mg over 20-30 minutes then 250 micrograms/kg daily, maximum (severe infections) 1.5 mg/kg daily or on alternate days.

Preparation available

Amphotericin Injection: Injection containing 50 mg of amphotericin B per vial is usually available.

FLUCONAZOLE

It is active against Candida, Cryptococcus.

It is almost completely absorbed from the gastro-intestinal tract. It also achieves good concentrations in cerebrospinal fluid. It is an inhibitor of microsomal enzymes and significantly increases plasma concentrations of many drugs.

Indications: mucosal candidiasis (except genital), vaginal candidiasis, tinea infections, prevention of fungal infections in immunocompromised patients.

Adverse effects and cautions: diarhoea, headache, nausea, rash

The drug should be avoided in pregnanacy and breast-feeding.

The drug should be used with caution in renal impairment or liver impairment.

Dose: Vaginal candidiasis, by mouth 150 mg single dose.

Mucosal candidiasis (except genital), 50 mg daily (100 mg daily in unusually difficult infections) given for 7-14 days.

Tinea infections (pedis, corporis, cruris, versicolor and dermal) 50 mg daily for 2-4 weeks (up to 6 weeks in *Tinea pedis*).

Preparation available

Fluconazole Capsules: Each capsule containing 50 mg and 150 mg of fluconazole is usually available.

FLUCYTOSINE

It is well absorbed from the gut. It is active against yeasts only and has been used for the treatment of systemic Candida, Cryptococcus infections. It is used predominantly in combination with amphotericin B.

Indications: *see* notes above.

Adverse effects and cautions: nausea, vomiting, skin rashes, prolonged high serum level produces bone- marrow depression and abnormal liver function.

Dose: By mouth, 100-150 mg/kg daily in 4 divided doses.

Intravenous infusion (over 20-40 minutes), ADULT and CHILD 200 mg/kg daily in 4 divided doses for not more than 7 days.

Preparation available

Flucytosine Tablets: Each tablet containing 500 mg of flucytosine is usually available. Flucytosine tablets should be protected from light.

Flucytosine Injection: Flucytosine 10 mg/ml in 250-ml infusion bottle is s usually available.

GRISEOFULVIN

It is effective against tinea of hair, perineal region, body, hands and beard. It has no effect on other fungi or bacteria. The absorption of drug from small intestine is erratic.

Indications: dermatophyte infections.

Adverse effects and cautions: nausea, vomiting, headache, heartburn, photosensitivity and skin rashes. Malformations have been reported in experimental animals with high doses.

Drug interactions: griseofulvin induces microsomal enzyme in liver and decreases response to coumarin anticoagulant.

Dose: 500 mg daily in divided doses or as a single dose, in severe infection dose may be doubled, reducing when response occurs; CHILD, 10 mg/kg daily in divided doses or as a single dose.

Preparation available

Griseofulvin Tablets: Each tablet containing 125 mg and 250 mg of griseofulvin is usually available.

ITRACONAZOLE

It is systemic antifungal drug.

Indications: fungal infections.

Adverse effects and cautions: abdominal pain, diarrhoea, headache, dizziness, rash, Stevens-Johnson syndrome, menstrual disorder, hypokalaemia.

The drug should be used with caution in pregnancy, breast-feeding, renal impairment.

Dose: By mouth, oropharyngeal candidiasis, 100 mg daily (200 mg daily in AIDS or neutropenia) for 15 days.

Vulvovaginal candidiasis, 200 mg twice daily for 1 day.

Pityriasis versicolor, 200 mg daily for 7 days.

Tinea pedis, 100 mg daily for 30 days or 200 mg twice daily for 7 days.

Tinea corporis and tinea crusis, 100 mg daily for 15 days or 200 mg daily for 7 days.

By intravenous infusion, systemic aspergillosis, candidiasis and cryptococcosis including cryptococcal meningitis where other antifungal drugs inappropriate or ineffective, 200 mg every 12 hours for 2 days, then 200 mg once daily for maximum 12 days; CHILD and ELDERLY safety and efficacy not established.

Preparation available

Itraconazole Capsules: Each capsule containing 100 mg of itraconazole is usually available.

Itraconazole Concentrate for Intravenous Infusion: Solution of itraconazole 10 mg/ml in 25-ml ampoule, for dilution before use, is usually available.

KETOCONAZOLE

It is well absorbed after oral administration but CNS concentration is low. It is active against Blastomyces, Histoplasma, Candida and dermatophytes.

Indications: *see* notes above.

Adverse effects and cautions: nausea, vomiting, skin rashes, headache, elevation of serum transaminase levels, gynaecomastia and fatal liver damage.

Dose: 200 mg once daily with food, usually for 14 days; if response inadequate after 14 days continue until at least 1 week after symptoms have cleared and cultures become negative; maximum 400 mg daily. CHILD 3 mg/kg daily Chronic resistant vaginal candidiasis, 400 mg daily with food for 5 days.

Preparation available

Ketoconazole Tablets: Each tablet containing 200 mg of ketoconazole is usually available.

NYSTATIN

It is effective against many yeast and fungi but is particulrly used for *Candida albicans* infections of the skin and mucous membrane. The drug is not absorbed from gastro-intestinal tract and is very toxic for parenteral use. Nystatin is used orally for the treatment of intestinal candidiasis.

Indications: candidiasis.

Adverse effects and cautions: nausea, vomiting and diarrhoea at high doses.

Dose: By mouth-intestinal candidiasis 500,000 units every 6 hours, doubled in severe infections, CHILD 100,000 units 4 times daily.

Preparation available

Nystatin Pessaries: Pessaries containing 100 000 units of nystatin are usually available. Nystatin pessaries should be stored at a temperature not exceeding 25°.

Nystatin Tablets: Each tablet containing 500 000 units of nystatin is available. Tablets should be stored at a temperature not exceeding 25°. Nystatin tablets are coated.

7.5 Anti-leishmaniasis drugs

AMPHOTERICIN B

It is an alternative drug for the treatment of visceral leishmaniasis. Adverse effects may be reduced by using liposomal amphotericin.

Indications: visceral leishmaniasis, fungal infections.

Adverse effects and cautions: see under section 7.4, antifungal drugs.

Dose: By intravenous infusion, 1-3 mg/kg daily for 10-21 days to a cumulative dose of 21-30 mg/kg.

Preparation available

Amphotericin Injection: Each vial containing 50 mg of amphotericin is usually available.

MILTEFOSINE

It is well absorbed orally.

Indications: visceral and cutaneous leishmaniasis.

Adverse effects and cautions: vomiting, diarrhoea, rise in hepatic transaminases and serum creatinine (reversible).

The drug is contraindicated in pregnancy.

Dose: Orally, 100 mg daily (patients weighing more than 25 kg) for 28 days; CHILD 2.5 mg/kg daily.

Preparation available

Miltefosine Capsules: Each capsule containing 50 mg and 100 mg of miltefosine is usually available.

PENTAMIDINE

It is administered parenterally because it is not well absorbed from the gastro-intestinal tract. It has been used in antimony-resistant visceral leishmaniasis.

Indications: visceral leishmaniasis, *Pneumocystis carinii* pneumonia.

Adverse effects and cautions: rash, abnormal liver function tests, hypotension, hyperglycaemia, hypoglycaemia, thrombocytopenia, acute renal failure, hyperkalaemia, megaloblastic anaemia, acute pancreatitis and pain at site of injection.

The drug should be used cautiously in the presence of hypertension, hypotension, diabetes, kidney disease.

Dose: Visceral leishmaniasis, deep intramuscular injection 3-4 mg per kg of body weight on alternate days to a maximum of 10 injections; course may be repeated if necessary.

Pneumonia, *Pneumocystis carnii*, intravenous infusion, 4 mg per kg of body weight daily for at least 14 days.

Preparation available

Pentamidine Injection: Each vial containing 200 mg and 300 mg of pentamidine are usually available.

SODIUM STIBOGLUCONATE

It is an organic pentavalent antimony compound which is poorly absorbed and highly irritant to gastro-intestinal tract, so given parenterally.

Indication: leishmaniasis or kala-azar.

Adverse effect and cautions: rapid intravenous injection can result in severe cough, vomiting and even cardiovascular collapse. The other adverse effects include headache, skin rashes, vomiting and abdominal pain.

Intravenous injection should be given very slowly and care should be taken to avoid extravasation.

The drug is contraindicated in patients with severe renal impairment, breast-feeding.

Dose: 20 mg/kg daily (maximum 850 mg) for at least 20 days by intramuscular or intravenous injection. Skin lesions are treated for 10 days.

Preparation available

Sodium Stibogluconate Injection: Injection containing the equivalent of 100 mg per ml of pentavalent antimony is usually available. Sodium stibogluconate should be protected from light.

7.6 Antimalarial drugs

ARTEMETHER AND LUMEFANTRINE

Indications: uncomplicated malaria by *Plasmodium falciparum.*

Adverse effects and cautions: diarrhea, anorexia, abdominal pain, headache, dizziness, palpitation, rash.

The drug should be used with caution in first trimester of pregnancy.

The drug is contraindicated in patients with histroy of arrhythmias and in breast-feeeding.

Dose: ADULT and CHILD over 12 years, 4 tablets followed by 5 further doses of 4 tablets each at 8, 24, 36, 48 and 60 hours (total 24 tablets) with food; CHILD 5-14 kg initially 1 tablet followed by 5 further doses of 1 tablet each at 8, 24, 36, 48 and 60 hours; 15-24 kg initially 2 tablets followed by 5 further doses of 2 tablets each at 8, 24, 36, 48 and 60 hours; 25-34 kg initially 3 tablets followed by 5 further doses of 3 tablets each at 8, 24, 36, 48 and 60 hours.

Preparation available

Artemether and Lumefantrine Tablets: Each tablet containing 20 mg of artemether and 120 mg of lumefantrine is usually available.

Artemether Oily Injection: Injection containing 80 mg/ml of artemether in 1-ml ampoule is available for use in the management of severe malaria.

CHLOROQUINE

The drug is active against the asexual erythrocytic forms of most strains of *Plasmodium malariae, P. ovale, P. vivax* and many strains of *P. falciparum.* The drug is not active against pre-erythrocytic or exo-erythrocytic forms of plasmodia.

Indications: chemoprophylaxis and treatment of malaria, rheumatoid arthritis, lupus erythematosus.

Adverse effects and cautions: epigastric discomfort, anorexia, nausea, vomiting, pruritus and headache. Long term daily treatment may cause reversible visual disturbance.

Dose: Malaria prophylaxis, 300 mg base once weekly starting one week before entering malaria area and continued for 4 weeks after leaving..

Malaria treatment (presumptive and clinically suspected), 600 mg base along with 45 mg primaquine.

Malaria treatment (radical cure in relapsing malaria), 600 mg base followed by 300 mg base after 6 hours, then 300 mg base for 2 days along with 15 mg primaquine for 5 days. CHILD 10 mg base/kg for first 2 days, then 5 mg base/kg for third day.

Preparation available

Chloroquine Tablets: Each tablet containing 250 mg of chloroquine phosphate or 200 mg of chloroquine sulphate, both the preparations contain 150 mg chloroquine base.

Chloroquine Suspension: Each ml containing 40 mg of chloroquine phosphate is usually available.

MEFLOQUINE

It can be given only orally, because intense local irritation occurs with parenteral use. It is used in prophylaxis and treatment of chloroquine-resistant and multi-drug resistant falciparum malaria.

Indications: see notes above.

Adverse effects and cautions: nausea, vomiting, diarrhoea, epigastric pain, headache, dizziness, vertigo, tinnitus, bradycardia, disturbances in liver function tests and extrasystoles.

The drug is contraindicated if there is history of convulsions or psychiatric disorders including depression. The drug is also contraindicated in infants less than 3 months of age. The drug should not be used in pregnancy until potential benefit justifies the risk to the foetus.

Drug interactions: concurrent administration of mefloquine with beta-blocking agent or calcium channel blocking agents should be avoided as it may result into bradycardia.

Dose: chemoprophylaxis, 250 mg each week starting 2½ weeks before departure and continued for 4 weeks after leaving malarious area; CHILD 15-19 kg (2-5 years) quarter adult dose, 20-30 kg (6-8 years) half adult dose, 31-45 kg (9-11 years) three quarters adult dose. Longer chemoprophylaxis (more than 3 months) on individual assessment (specialist advice may need to be sought). Young children less than 15 kg not recommended.

Preparation available

Mefloquine Tablets: Each tablet containing the equivalent of 250 mg of mefloquine as mefloquine hydrochloride is usually available.

PRIMAQUINE

It is the best available drug for curative treatment of vivax malaria. It is also used against the tissue forms of *P. ovale.*

Indications: eradication of *P.vivax* and *P.ovale.*

Adverse effects and cautions: abdominal cramps, epigastric distress, anorexia, vomiting, leucocytosis and haemolytic anaemia in patients with glucose-6-phosphate dehydrogenase deficiency.

The drug should not be used in children under one year of age. The drug should always be given in conjuction with full doses of chloroquine in

order to reduce the possibility of developing drug resistant strains.

Drug interactions: should not be administered concurrently with other drugs liable to induce haemolysis or bonemarrow depression.

Dose: Presumptive cases, 45 mg single dose.

For radical cure, 15 mg daily for 5 days; CHILD 250 micrograms/kg daily

Preparation available

Primaquine Tablets: Each tablet containing 7.5 mg of primaquine phosphate in usually available.

QUININE

This drug is used for suppression of malaria caused by *P. falciparum.* But the other antimalarials like chloroquine, sulfadoxine and pyrimethamine are preferred for the prophylaxis of malaria caused by suceptible plasmodia.

The drug is used for the treatment of uncomplicated attacks of chloroquine-resistant *P. falciparum.* Quinine when used alone may control an acute attack of chloroquine resistant *P. falciparum* but it may fail to prevent recurrence. Intravenous quinine is used for severe malaria (cerebral malaria) caused by chloroquine-susceptible or resistant *P. falciparum.* Quinine is active only against asexual erythrocytic forms of plasmodia, the drug cannot provide radical cure in malaria caused by *P.vivax* and *P.ovale* since they have exoerythrocytic stage.

Indication: *P. falciparum* malaria.

Adverse effects and cautions: cinchonism including tinnitus, headache, nausea, abdominal pain, rashes, visual disturbances and hyper-sensitivity reactions.

Quinine should be avoided in patients with optic neuritis and myasthenia gravis.

Dose: By mouth, 600 mg of quinine salt every 8 hours for 7 days; CHILD 10 mg/kg every 8 hours for 7 days.

By intravenous infusion, loading dose of 20 mg/kg of quinine salt infused over 4 hours then after 8 hours maintenance dose of 10 mg/kg infusion over 4 hours every 8 hours until patient can swallow tablet to complete 7-days course.

Preparation available

Quinine Tablets: Each tablet containing 300 mg and 600 mg of quinine, as bisulfate or sulfate, is usually available.

Quinine Injcction: Each vial containing 300 mg of quinine, as dihydrochoride, is usually available.

SULFADOXINE AND PYRIMETHAMINE

This combination is effective in suppression and treatment of multi-resistant strains of *P. falciparum.* Both components are well absorbed after oral administration.

Indications: in combination with other antimalarials, malaria caused by *P. falciparum* only.

Adverse effecs and cautions: sulphonamide hypersensitivity and megaloblastic anaemia.

Dose: Treatment, adult 3 tablets, CHILD, 1.25 mg/kg body weight of pyrimethamine and 25 mg/kg of sulphadoxine.

Preparation available

Sulfadoxine and Pyrimethamine Tablets: Each tablet containing 500 mg of sulfadoxine and 25 mg of pyrimethamine is usually available.

7.7 Antiviral drugs

7.7.1 Herpes virus infection

ACYCLOVIR

It is active against herpes viruses *(Herpes simplex, Varicella zoster).* It is effective only if started as early as possible, usually within 72 hours.

Indications: herpes infections.

Adverse effects and cautions: gastrointestinal disturbances, rashes, increase in blood urea and creatinine, headache and fatigue.

The drug should be used with caution in renal impairment.

Dose: by mouth. *Herpes simplex,* treatment, 200 mg (400 mg in the immuno-compromised or if absorption is impaired) 5 times daily, usually for 5 days; CHILD under 2 years, half adult dose, over 2 years, adult dose.

Herpes simplex, prevention of recurrence, 200 mg 4 times daily or 400 mg twice daily possibly reduced to 200 mg 2 or 3 times daily and interrupted every 6-12 months.

Herpes simplex, prophylaxis in the immunocompromised, 200-400 mg 4 times daily; CHILD under 2 years, half adult dose, over 2 years, adult dose.

Varicella and Herpes zoster, treatment, 800 mg 5 times daily for 7 days;

CHILD, varicella, 20 mg/kg (max. 800 mg) 4 times daily for 5 days or under 2 years 200 mg 4 times daily, 2-5 years 400 mg 4 times daily, over 6 years 800 mg 4 times daily.

By topical application *Herpes simplex* (cream or eye ointment) every 4 hours (5 times daily) for at least 3 days after complete healing.

Preparation available

Acyclovir Injection: Injection containing 250 mg per vial is usually available.

Acyclovir Tablets: Each tablet containing 200 mg of acyclovir is usually available.

7.7.2 HIV Infections

Antiretroviral drugs do not cure HIV (human immuno-deficiency virus) infection; they only temporarily suppress viral replication and improve symptoms. Treatment is aimed at reducing the plasma viral load as much as possible and for

as long as possible; it should be started preferably before immune system is irreversibly damaged and before the onset of clinical immuno-deficiency. Commitment to treatment and strict adherance over many years are required; the regimen chosen should take into account convenience and patient's tolerance of it. The development of resistance is reduced by using a combination of 3 or 4 drugs.

Women of child bearing age receiving antiretroviral therapy must have available effective contraceptive methods to prevent unintended pregnancy.

EFAVIRENZ

It is non-nucleoside reverse transcriptase inhibitors.

The bioavailability of oral solution is lower than with capsules and tablets.

Indications: HIV infection, in combination with other drugs.

Adverse effects and cautions: rash including Stevens-Johnson syndrome, diarrhoea, vomiting, depression, anxiety, ataxia.

The drug is contraindicated in pregnancy.

The drug should be used with cautions in chronic hepatitis B or C, severe renal impairment, seizures and breast-feeding.

Dose: ADULT and CHILD 40 kg and over, 600 mg once daily.

INDINAVIR

It is protease inhibitors.

Indications: see under saquinavir.

Adevrse effecs and cautions: dry mouth, taste disturbances, headache, hyperglycaemia, dizziness, pancreatitis, paraesthesia, alopecia.

The drug shoud be used with caution in chronic hepatitis B or C, hepatic impairment, diabetes mellitus, pregnancy and breast-feeding.

Dose: 800 mg every 8 hours; CHILD 500 mg/ m^2 every 8 hours (maximum 800 mg every 8 hours).

LAMIVUDINE

It is a nucleoside reverse transcriptase inhibitor.

Indications: see under zidovudine

Adverse effects and cautions: vomiting, diarrhea, cough, headache, fatigue, insomnia, fever, rash, alopecia, peripheral neuropathy, anaemia.

The drug should be used with caution in renal impairment, chronic hepatitis B or C, liver impairment, pregnancy and breast-feeding.

Dose: ADULT 150 mg twice daily or 300 mg once daily

INFANT under 1 month, 2 mg/kg twice daily, CHILD 1 month or over 4 mg/kg twice daily (maximum 300 mg).

NEVIRAPINE

It is also non-nucleotide reverse transcriptase inhibitors.

Indications: HIV infection in combination with other drugs, prevention of mother-to-child transmission

Adverse affects and cautions: rash including Stevens-Johnson syndrome,

hepatitis, headache, fever, anaemia, arthralgia

The drug is contraindicatied in severe hepatic impairment

The drug should be used with caution in hepatic impairment (chronic hepatitis B or C, high CD_4 cell count), pregnancy and breast-feeding.

Dose: 200 mg once daily for first 14 days then 200 mg twice daily; CHILD 1 month-13 years, 120 mg/ m^2 once daily for 14 days, then 200 mg/ m^2 twice daily.

SAQUINAVIR

It is also protease inhibitors.

Indications: HIV infection in combination with other drugs.

Adverse effects and cautions: buccal and mucosal ulceration, diarrhoea, taste disturbances, vomiting, chest pain, peripheral neuropathy, fever, changes in libido.

The drug is contraindicated in severe hepatic impairment.

The drug should be used with caution in chronic hepatitis B or C, renal impairment, diabetes mellitus, pregnancy and breast-feeding.

Dose: 1 g every 12 hours within 2 hours after a meal.

CHILD: safety and efficacy in under 16 years is not established.

STAVUDINE

It is also nucleoside reverse transcriptase inhibitors.

Indications: HIV infection in combination with other drugs.

Adverse effects and cautions: peripheral neuropathy (dose-related), pancreatitis, vomiting, diarrhoea, chest pain, headache, gynaecomastia, elevated liver enzymes and serum amylase.

The drug should be used with caution in patients with history of peripheral neuropathy, pancreatitis, chronic hepatitis B or C, renal impairment, pregnancy and breast-feeding.

TENOFOVIR DISOPROXIL

It is a nucleoside reverse transcriptase inhibitor.

Indications: *see* under stavudine.

Adverse effects and cautions: gastro-intestinal disturbances including diarrhoea, vomiting, abdominal pain, anorexia, pancreatitis, headache, anorexia, neutropenia, hypophosphataemia, polyuria, renal failure.

The drug is contra-indicated in breast-feeding.

The renal function test and serum phosphate should be estimated before treatment, then every 4 weeks (more frequently if at increased risk of renal impairment) for 1 year and then every 3 months, interrupt treatment if renal function deteriorates or serum phosphate decreases.

Dose: ADULT over 18 years, 245 mg once daily.

Preparation available

Tenofovir Disoproxil Tablets: Each tablet containing 245 mg of tenofovir

disoproxil (as fumarate) is usually available.

ZIDOVUDINE (AZT)

It is also nucleoside reverse transcriptase inhibitors. It is also known as Azidothymidine.

Indications: HIV infection in combination with other drugs, prevention of mother-to-child HIV transmission.

Adverse effects and cautions: diarrhea, liver disorders, abdominal pain, pancreatitis, bone marrow depression with severe anaemia, granulo-cytopenia, and thrombo-cytopenia.

Haematological tests are best done every two weeks for first three months, and then should be done at least once a month.

The policy regarding breast feeding mother is to avoid breast feeding.

Drug interactions: concomitant use of drug with nephrotoxic and myelosuppressive drugs increases risk of toxicity.

Dose: By mouth, 500-600 mg daily in 2-3 divided doses.

CHILD over 3 months initially 360-480 mg/m^2 every 6-8 hours.

Preparation available

Zidovudine Capsules: Each capsule containing 100 mg of zidovudine is usually available.

Chapter - Eight

Drugs Used in the Disorders of the Endocrine System

8.1 Adrenal hormones and synthetic substitutes

Corticosteriods are classified into two groups. The mineralocorticoids control salt and water balance by acting on the renal tubules to cause the retention of sodium chloride and water. The glucocorticoids accelerate the formation of glucose from protein (gluconeogenesis) and have slight effect on salt and water balance.

The adrenal cortex normally secretes hydrocortisone, which has glucocorticoid activity and weak mineralcorticoid activity. It also secretes the mineralocorticoid aldosterone.

Corticosteroids are used for two main purposes:

1. For physiological replacement therapy in adrenal insufficiency as in Addison's disease, after adrenalectomy, or secondary to hypopituitarism.
2. In suppressing the manifestations of disease in a wide variety of inflammatory and allergic conditions and in reducing antibody production in a number of auto-immune diseases.

Whilst hydrocortisone is the naturally secreted product the synthetic substances in major use are prednisolone, dexamethasone, betamethasone, triamcinolone and fludrocortisone.

Dexamethasone and betamethasone have little mineralo-corticoid action and due to their longer action, these are preferred for suppressing corticotrophin secretion in congenital adrenal hyperplasia. On normal patients, a single dose of 1 mg of dexamethasone can inhibit corticotrophin secretion for 24 hours.

Indications: replacement therapy in adrenocortical insufficiency states, diagnosis of Cushing's syndrome, allergic disdorders, rheumatic disease, neoplastic diseases.

Adverse effects and cautions: hypertension, sodium retention, potassium loss, muscle weakness, diabetes, osteoporosis, dyspepsia, increased susceptibility to and severity of infection. Mental disturbance includes euphoria, psychosis, depression, aggravation of epilepsy. Peptic ulceration can lead on to haemorrhage or perforation. It may lead to suppression of growth in children.

Drug interactions: drugs such as barbiturates, phenytoin, rifampicin which induce hepatic enzymes may increase glucocorticoid metabolism and so dosage adjustment may be required. Concomitant use with alpha-blockers, angiotensin-II receptor antagonists, beta-blockers and calcium channel blockers antagonise hypotensive effect.

Relative potencies and duration of action of corticosteroids

Compounds	Relative anti-inflammatory potency	Relative sodium retaining potency	Duration of action (hours)
Hydrocortisone	1	1	8-12
Betamethasone	25	0	36-72
Dexamethasone	25	0	36-72
Methyl prednisolone	5	0.5	12-36
Prednisolone	4	1	12-36
Prednisone	4	1	12-36
Triamcinolone	5	0	12-36

BECLOMETHASONE DIPROPIONATE

Indications: prophylaxis of bronchial asthma, prophylaxis and treatment of allergic rhinitis.

Adverse effects and cautions: bronchospasm and wheezing, rash, *Candida* infections in mouth or throat.

Cautions: *see* section 3.3.1 under respiratory system.

Dose: *see* section 3.1.1 under respiratory system.

Preparation available

Beclomethasone Inhaler: Aerosol inhaler containing 50 micrograms, 100 micrograms and 200 micrograms beclomethasone dipropionate per metered dose is usually available.

BETAMETHASONE

Indications, adverse effects and cautions: *see* under section 8.1, general statement of corticosteroids and other respective sections.

Dose: By mouth, usual range 0.5-5 mg daily.

By intramuscular injection or slow intravenous injection or infusion, 4 -20 mg, repeated up to 4 times in 24 hours, CHILD, by slow intravenous injection, up to 1 year 1 mg, 1-5 years 2 mg, 6-12 years 4 mg.

Preparation available

Betamethasone Drops: Each ml containing 0.5 mg of betamethasone is usually available.

Betamethasone Injection: An injection containing 4 mg per ml of betamehtasone, as sodium phosphate, is usually available. Betamethasone injection should be stored at a temperature not exceeding 30° protected from light.

Betamethasone Tablets: Each tablet containing 0.5 mg of betamethasone is usually available. Betamethasone tablet should be protected from light.

CORTISONE ACETATE

Indications, adverse effects and cautions: *see* under section 8.1, general statement on corticosteroids.

Dose: By mouth, for replacement therapy, 25-37.5 mg in divided dose.

Preparation available

Cortisone Acetate Tablets: Each tablet containing 5 mg and 25 mg of cortisone acetate is usually available.

DEXAMETHASONE

Indications, adverse effects and cautions: see section 8.1 general statement of corticosteroids and other respective sections.

Dose: By mouth usual range 0.5-10 mg daily; CHILD 10-100 micrograms/kg daily.

By intramuscular injection or slow intravenous injection or infusion initially 0.5-24 mg; CHILD 0.2-0.4 mg/kg daily. Cerebral oedema by intravenous injection, 10 mg initially, then 4 mg by intramuscular injection every 6 hours as required for 2-4 days, then gradually reduced and stopped over 5-7 days.

Preparation available

Dexamethasone Tablets: Each tablet containing 0.5 mg of dexamethasone is usually available. Dexamethasone tablets should be protected from light.

Dexamethasone Injection: Each ml containing 4 mg dexamethasone sodium phosphate is usually available.

FLUDROCORTISONE ACETATE

It is a synthetic glucocorticoid with very potent mineralo-corticoid properties.

Indications: mineralocorticoid replacement in adrenocortical insufficiency.

Adverse effects and cautions: *see* under section 8.1, general statement of corticosteroids.

Dose: Adrenocortical insufficiency, 50-300 micrograms daily; CHILD 5 micrograms/kg daily.

Preparation available

Fludrocortisone Tablets: Each tablet containing 100 micrograms of fludrocortisone acetate is usually available.

HYDROCORTISONE

Indications, adverse effects and cautions: *see* under section 8.1, general statement of corticosteroids and other respective sections.

Dose: By intramuscular injection or slow intravenous injection or infusion, 100-500 mg, 3-4 times in 24 hours or as required; CHILD by slow intravenous injection up to 1 year 25 mg, 1-5 year 50 mg, 6-12 years 100 mg.

Preparation available

Hydrocortisone Sodium Succinate Injection: Injection containing 100 mg of hydrocortisone, as sodium succinate, is usually available.

Hydrocortisone Acetate Injection: Injection containing 25 mg/ml is usually available. Hydrocortisone injection should be protected from light. The container should be gently shaken before a dose is withdrawn.

METHYLPREDNISOLONE

It has predominantly gluco-corticoid activity.

Indications: *see* under prednisolone.

Adverse effects and cautions: *see* under prednisolone.

Dose: By mouth, usual range 2-40 mg daily.

By intramuscular injection or slow intravenous injection or infusion, initially 100-500 mg.

Preparation available

Methylprednisolone Tablets: Each tablet containing 4 mg, 8 mg and 16 mg of methylprednisolone is usually available.

Methylprednisolone Injection: Each vial containing 250 mg of methylpredisolone (as sodium succinate) of reconstitution is usually available.

PREDNISOLONE

Indications, adverse effects and cautions: see section 8.1, general statement of corticosteroids and other respective sections.

Dose: By mouth, initially up to 10-20 mg daily (severe disease, up to 60 mg daily), preferably taken in the morning after breakfast or food; can often be reduced within a few days but may need to be continued for several weeks or months.

Maintenance, usual range, 2.5-15 mg daily, but higher doses may be needed; cushingoid side effects increasingly likely with doses above 7.5 mg daily.

Preparation available

Prednisolone Tablets: Each tablet containing 5 mg, 10 mg and 20 mg of prednisolone is usually available. Prednisolone tablets should be protected from light.

TRIAMCINOLONE ACETONIDE

Indications, adverse effects and cautions: *see* section 8.1**,** general statement of corticosteroids and other respective sections.

Dose: By deep intramuscular injection, 40 mg of triamcinolone acetonide for depot effect, repeated at intervals according to the patient's response, maximum single dose 100 mg.

Preparation available

Triamcinolone acetonide injection: Injection containing 40 mg/ml of triamcinolone acetonide is usually available.

8.2 Androgens and anabolic steroids

8.2.1 Androgens

Androgens, as they are known, can be used as replacement therapy. In the normal male, they inhibit pituitary gonadotrophin secretion and depress spermatogenesis. They are useless for treatment of importence and impaired spermatogenesis unless there is associated hypogonadism.

DANAZOL

It is a synthetic derivative of ethisterone. The drug possesses weak androgenic and anabolic properties but exerts no oestrogenic or progestogenic activity. Androgenic activity is dose related.

Indications: endometriosis, palliative treatment of fibrocystic breast disease.

Adverse effects and cautions: mild hirsutism, decreased breast size, acne, weight gain, oedema, cholestatic jaundice, dizziness, headache, fatigue and tremor. Because danazol may cause fluid retention, the drug should be used with caution in patients who may be adversely affected in conditon such as migraine, seizure disorder, cardiac or renal dysfunction. Danazol is contraindicatied in patients with abnormal genital bleeding of unknown aetiology. It is also contraindicated in pregnancy.

Dose: Usual range 200-400 mg daily in up to 4 divided doses; in women all doses should start during menstruation, preferably on the first day.

Endometriosis, intially 400 mg daily in upto 4 divided doses, adjusted according to response, ususally for six months.

Menorrhagia, 200 mg daily, usually for 3 months. Benign breast cyst, 300 mg daily usually for 3 months.

Gynaecomastia, 400 mg daily in divided doses for 6 months (adolescents 200 mg daily, increased to 400 mg daily if no response after 2 months).

Preparation available

Danazol Capsules: Each capsule containing 50 mg, 100 mg and 200 mg of danazol is usually available.

FINASTERIDE

It is an antagonist of 5α-reductase, especially type II, which metabolises testosterone into more potent androgen, dihydrotestosterone. This leads to decreased concentration of dihydrotestosterone in serum and prostate, decrease in prostate volume and increased urine flow rate.

Indications: benign prostatic hyperplasia, male-pattern baldness.

Adverse effects and cautions: impotence, decreased libido, breast tenderness and enlargement, rash.

The drug is contra-indicated in children, women and adolescents.

The drug decreases serum concentration of prostate cancer markers such as prostate-specific antigen (PSA).

Dose: 5 mg daily; review treatment after 6 months.

Preparation available

Finasteride Tablets: Each tablet containing 5 mg of finasteride is usually available.

MESTEROLONE

It is an androgen.

Indications: androgen deficiency and male infertility associated with hypogonadism.

Adverse effects and cautions: prostate abnormalities and prostate cancer, headache, depression, gastro-intestinal bleeding, gynaecomastia, hypertension, male-pattern baldness, excessive frequency and duration of penile erection, weight gain, increased bone growth.

The drug is contra-indicated in breast cancer in men, prostate cancer, pregnancy, breast-feeding, hypercalcaemia, history of primary liver tumors.

The drug should be used with caution in ischaemic heart disease, hypertension, elderly, cardiac, renal or hepatic impairment, diabetes mellitus, pre-pubertal boys.

Dose: Orally, 25 mg 3-4 times daily for several months, reduced to 50-75 mg daily in divided doses for maintenance; CHILD not recommended.

Preparation available

Mesterolone Tablets: Each tablet containing 25 mg of mesterolone is usually available.

METHYLTESTOSTERONE

Indications: *see* under testosterone.

Adverse effects and cautions: see under testosterone. It is more likely to cause jaundice.

Dose: hypogonadism, orally 10-50 mg per day.
Breast cancer, 50 mg one to four times a day.

TESTOSTERONE

It is the principal endogenous androgens.

Indications: hypogonadism, breast cancer in females.

Adverse effects and cautions: headache, nausea, prostate abnormalities and prostate cancer, changes in libido, gynaecomastia, oedema, priapism, nausea, hypercalcaemia, precocious sexual development and premature closure of epiphyses in pre-pubertal males.

Testosterone should be used with caution in patients with cardiac, renal or hepatic impairment, ischaemic heart disease, diabetes mellitus and hypertension. The drug should be used with extreme caution in children.

Testosterone is contraindicated in males with carcinoma of the breast or prostate. The drug is also contraindicated in pregnancy and breast-feeding.

Dose: Hypogonadism, testosterone propionate, by intramuscular injection 50 mg twice or thrice weekly.
Testosterone enanthate, by slow intramuscular injection 250 mg every 2-3 weeks.
Breast cancer in women, testosterone propionate, 100 mg 2-3 times weekly; testosterone enanthate, 250 mg every 2-3 weeks.

Preparation available

Testosterone Enanthate Injection: Injection containing 100 mg of testosterone enanthate is usually available.

Testosterone Propionate Injection: Injection containing 25 mg of testosterone propionate is usually available.

8.2.2 Anabolic steroids

All anabolic steroids have some androgenic activity but cause less virilisation in women. They reverse catabolic processes and negative nitrogen balance by promoting protein anabolism and stimulating appetite if there is concurrently a proper intake of calories and proteins. Some of these drugs increase production of erythropoietin. All anabolic steroids are approximately equal in efficacy. Use of anabolic steroids by athletes is not recommended.

NANDROLONE

Indications: aplastic anaemia, antineoplastic.

Adverse effects and cautions: virilism, oedema, acne, amenorrhoea, inhibition of spermatogenesis, liver tumour with prolonged treatment.

This drug is contraindicated during pregnancy, breast-feeding and prostate cancer.

The drug should be used with caution in cardiac, hepatic and renal impairment, in children and adolescents because of possible premature epiphyseal closure, precocious sexual development in males and virilisation in females.

Dose: By deep intramuscular injection, 50 mg every 3 weeks.

Preparation available

Nandrolone Decanoate Injection: Injection containing 25 mg/ml and 50 mg/ml nandrolone decanoate is usually available. Nandrolone decanoate injection should be protected from light. This injection is for intramuscular only.

Nandrolone Phenylpropionate Injection: Injection containing 25 mg per ml of nandrolone phenylpropionate is usually available. Nandrolone phenylpropionate injection should be protected from light. This injection is for intramuscular only.

OXYMETHOLONE

Indications: aplastic anaemia.
Adverse effects and cautions: see under nandrolone.
Dose: 1-5 mg/kg daily in divided doses; CHILD 0.175 mg/kg daily as a single dose.

Preparation available

Oxymetholone Tablets: Each tablet containing 50 mg of oxymetholone is usally available. Oxymetholone tablets should be protected from light.

STANOZOLOL

Indications: *see* under dose.
Adverse effects and cautions: *see* under nandrolone
Dose: Hereditary angioedema, by mouth initially 2-4 mg daily.

Preparation available

Stanozolol Tablets: Each tablet containing 2 mg of stanozolol is usually available. Stanozol tablets should be protected from light.

8.3 Oestrogens

These are necessary for the development of female secondary sexual characteristics. They also bring about the proliferation of the endometrium, growth of the uterine muscle and increase the duct tissue in the breast.

DIETHYLSTILBESTROL

Stilboestrol

The pharmacological effects of stilboestrol are similar to those of natural oestrogens.

Indications, adverse effects and cautions: breast cancer in post-menopausal women, rarely in prostate cancer.

Dose: Breast cancer, 10-20 mg daily.

Prostate cancer, 1-3 mg daily.

Preparation available

Diethylstilboestrol Tablets: Each tablet containing 1 mg of diethylstilbestrol diphosphate is usually available. Diethylstilbestrol tablets should be protected from light.

ESTRADIOL

It is the principal and most active endogenous oestrogen. Its activity differs following oral or parenteral administration.

Indications, adverse effects and cautions: *see* under ethinylestradiol.
Dose: Menopausal symptoms, 1-2 mg daily.

OESTROGENS, CONJUGATED

The pharmacological effects of conjugated oestrogens are similar to those of endogenous oestrogens.
Indications, adverse effects and cautions: *see* under ethinyloestradiol.
Dose: menopausal symptoms, 0.625-1.25 mg daily.

Preparation available

Oestrogens, Conjugated Tablets: Each tablet containing 625 micrograms and 1.25 mg of oestrogens, conjugated is usually available.

ETHINYLESTRADIOL

This preparation of oestrogen is in widespread use. It is about twenty times more active than oestradiol following oral administration.

Indications: vasomotor symptoms of menopause, menstrual disorders, female hypogonadism, palliative treatment of carcinoma of prostate.

Adverse effects and cautions: nausea and vomiting; weight gain, jaundice, rashes, depression, headache, breast enlargement and tenderness, withdrawal bleeding. Impotence and gynaecomastia in men.

The drug is contraindicated in pregnancy, history of arterial and venous thrombosis, transient cerebral ischaemic attacks, migraine.

The drug should be used with caution in risk factors for venous thromboembolism, arterial disease, history of severe depression.

Dose: Menopausal symptoms, 10-50 micrograms daily.

Prostate cancer (palliative) 0.15-1.5 mg daily.

Preparation available

Ethinylestradiol Tablets: Each tablet containing 50 micrograms of ethinyloestradiol is usually available. Tablets should be protected from light.

MESTRANOL

It is a 3-methyl ester of ethinyl oestradiol and is slightly less active than ethinyloestradiol.
Indications, adverse effects and cautions: see under ethinyloestradiol
Dose: Menopausal symptoms, if uterus intact 1 tablet daily.

Preparation available

Mestranol Tablets: Each tablet containing 50 micrograms and 35 micrograms of mestranol is usually available.

8.4 Progestogens

Progestogens are derivatives of testosterone or progesterone. These modify some of the effects of oestrogens and act on tissues sensitised by oestrogens. This group of drugs causes further thickening and development of the secretory phase in the endometrium. Progesterone is the natural hormone but is effective only parenterally. There are however a number of orally active synthetic progestogens.

DYDROGESTERONE

It is an analogue of the naturally occuring progesterone and does not cause virilisation.

Indications, adverse effects and cautions: see under norethisterone.

Dose: Endometriosis, 10 mg 2-3 times daily from 5th to 25th day of cycle or continuously.

Dysfunctional uterine bleeding, 10 mg twice daily (together with an oestrogen) for 5-7 days to arrest bleeding; 10 mg twice daily (together with an oestrogen) from 11th to 25th day of cycle to prevent bleeding.

Dysmenorrhoea, 10 mg twice daily from 5 to 25 day of cycle.

Amenorrhoea, 10 mg twice daily from 11th to 25th day of cycle with oestrogen therapy from 1st to 25th day of cycle.

Hormone replacement therapy, with continuous oestrogen therapy, 10 mg daily from 15-28 days of each 28-day hormone replacement therapy (HRT) cycle.

Preparationp available

Dydrogesterone Tablets: Each tablet containing 5 mg of dydrogesterone is usuallly available.

HYDROXYPROGESTERONE

This is a derivative of progesterone. It is more potent than progesterone and has longer duration of action (7-14 days).

Indications: amenorrhoea, dysfunctional uterine bleeding, induction of menses.

Adverse effects and cautions: see under norethisterone.

Dose: Amenorrhoea or dysfunctional uterine bleeding, by intramuscular injection, 375 mg.

Induction of menses, intramuscular injection, 125-250 mg on day 10 of the menstrual cycle.

Preparation available

Hydroxyprogesterone Injection: Injection containing 250 mg and 500 mg of hydroxyprogesterone caproate is usually available. Hydroxyprogesterone injection should be protected from light. Hydroxyprogesterone injection is for intramuscular injection only.

LEVONORGESTREL

It is effective if dose is taken within 72 hours of unprotected sex. Hormonal emergency contraception is less effective than insertion of an intra-uterine device.

Indications: emergency contraceptive.

Adverse effects and cautions: nausea, low abdominal pain, headache, dizziness, menstrual irregularities.

Dose: Contraceptive, by subdermal implantation, set of 2 capsules, each containing 750 micrograms of levonorgestrel inserted preferably on first day of cycle.

Emergency contraceptive, 1.5 mg as a single dose as soon as possible after sex (preferably within 12 hours but not later than after 72 hours)

Preparation available

Levonorgestrel Implants: Each capsule containing 75 mg of levonorgestrel is usually available.

Levonorgestrel Tablets: Set of two tablets, each tablet containing 750 micrograms of levonorgestrel is usually available.

MEDROXYPROGESTERONE

This is a derivative of progesterone and has less androgenic activity.

Indications: contraceptive (long acting), secondary amenorrhoea, dysfunctional uterine bleeding, mild to moderate endometriosis.

Adverse effects and cautions: see under norethisterone.

Dose: For contraception, by deep intramuscular injection, 150 mg within first 5 days of cycle or within first 5 days after parturition (delay until 6 weeks after parturition if breast-feeding); for long-term contraception, repeated every 3 months.

Dysfunctional uterine bleeding and secondary amenorrhoea, by mouth, 2.5-10 mg daily for 5-10 days beginning on 16-21 day of cycle, repeated for 2 cycles in dysfunctional uterine bleeding and 3 cycles in secondary amenorrhoea.

Mild to moderate endometriosis, 10 mg 3 times daily for 90 consecutive days, beginning on day 1 of cycle.

Preparation available

Medroxyprogesterone Injection: Each ml containing 150 mg of medroxyprogesterone acetate is usually available.

Medroxyprogesterone Tablets: Each tablet containing 10 mg of medroxyprogesterone acetate is usually available.

NORETHISTERONE

It is a testosterone derivative and has some androgenic activity. It is a potent oral progestin.

Indications: contraceptive, endometriosis, premenstrual syndrome, postponement of menstruation.

Adverse effects and cautions: more virilising effects and the greater possibility of liver disturbances and jaundice, urticaria, gastrointestinal disturbances, oedema, weight gain, breast discomfort and irregular menstrual cycles.

This drug should be used with caution in patients with conditions that might be aggravated by fluid retention (cardiac or renal dysfunction, or epilepsy or hypertension), diabetes, impaired liver function.

The drug is contraindicated in pregnancy and patients with genital or breast cancer.

Dose: Endometriosis, 10-15 mg daily starting 5th day of cycle for 4-6 months (increased if spotting occurs to 20-25 mg daily, reduced once bleeding has stopped).

Postponement of menstruation, 5 mg 3 times daily starting 3 day before anticipated onset (mestruation occurs 2-3 days after stopping).

Preparation available

Norethisterone Tablets: Each tablet containing 5 mg of norethistreone is usually available. Norethisterone tablets should be protected from light.

8.5 Anti-oestrogens

CHORIONIC GONADOTROPHIN

Human Chorionic Gonadotrophin; HCG

It mimics the action of luteinising hormone (LH), is obtained from the urine of pregnant women.

Indications: treatment of infertility in women.

Adverse effects and cautions: headache, tiredness, mood changes, multiple pregnancy.

The drug should be used with caution in cardiac or renal impairment, epilepsy, asthma, migraine.

Dose: By subcutaneous or intramuscular injection, according to patient's response.

Preparation available

Chorionic Gonadotrophin Injection: Each vial containing 1500 unit and 5000 unit, as powder for reconstitution, is usually available.

CLOMIPHENE

It is a nonsteroidal compound with oestrogenic and antioestrogenie properties. Mechanism in stimulating ovulation is unknown but is believed to be related to its antioestrogenic properties. It occupies oestrogen receptors in hypothalamus, thereby interfering with feedback mechanism; causes increased secretion of LH and FSH resulting into maturation of ovarian follicles and development of corpus luteum.

Indications: anovulatory infertility in females.

Adverse effects and cautions: ovarian enlargement or cyst formation, vasomotor symptoms such as hot flushes, transient blurring of vision, diplopia, abdominal or pelvic discomfort, nausea, vomiting, heavier menses, breast discomfort, weght gain, endometriosis and headache.

Clomiphene should not be used in presence of ovarian cysts. Patients receiving the drug should be cautioned against performing hazardous tasks requiring mental alertness because of possible visual disturbances with the drug. The drug should be used with caution in uterine fibroids, ectopic pregnancy.

The drug is contraindicated in patients with liver disease or abnormal uterine bleeding. The drug is contraindicated during pregnancy.

Dose: 50 mg daily for 5 days, starting within about 5 days of onset of menstruation (preferably on 2nd day) or at any time if cycles have ceased; second course of 100 mg daily for 5 days may be given in absence of ovulation; most patients who are going to respond will do so to first course; 3 courses should constitute adequate therapeutic trial, long term cyclical therapy not recommended.

Preparation available

Clomiphene Tablets: Each tablet containing 25 mg and 50 mg of clomiphene citrate in usually available. Clomiphene tablet should be protected from light stored at a temperature not exceeding 40°.

TAMOXIFEN

See under section 11.3.3, hormone antagonist.

8.6 Drugs used in diabetes

8.6.1 Insulin

Insulin plays an important role in the body's regulation of carbodydrate, fat and protein metabolism. Diabetes mellitus occurs because of a lack of insulin or resistance to its action. The rise in blood sugar level is a result of the decreased utilization and increased production of glucose. Insulin stimulates carbohydrate metabolism in skeletal and adipose tissue by facilitating transport of glucose into these cells. Nerve tissues, erythrocytes, and cells of the intestines, liver, and kidney tubules do not require insulin for transfer of glucose. Insulin also has a direct effect on fat and protein metabolism. The hormone stimulates lipogenesis and protein synthesis. Insulin also promotes an intracellular shift of potassium and magnesium and thereby temporarily decreases elevated blood concentrations of these ions.

Insulin when given by mouth is inactivated by gastro-intestinal enzymes. So it must be administered parenterally. Insulin preparations are of mainly three types.

1. Short duration with relatively rapid action, e.g. insulin injection (soluble), insulin lispro and insulin aspart.
2. Intermediate duration of action e.g. isophane insulin (NPH) injection and insulin zinc suspension (lente).
3. Those whose action are slow in onset and last for long period e.g. protamine zinc insulin and insulin zinc suspension (ultralente).

Insulin is extracted from pork pancreas and purified by crystallisation. Human insulin can also be produced biosynthetically by recombinant DNA technology using bacteria or yeast or semisynthetically by enzymatic modification of porcine insulin. All insulin preparations including human insulins are equally immunogenic.

INSULIN INJECTION (SOLUBLE)

This is a clear solution of insulin which when given subcutaneously has a maximal effect in 2-4 hours and effect lasts up to 8 hours. In maintenance regimens it is usually given 15 to 30 minutes before meals. When given intravenously its effect disappears within 30 minutes. Human insulin analogues have faster onset but have shorter duration of action than soluble insulin.

Indications: diabetic ketoacidosis, diabetes mellitus.

Adverse effects and cautions: hypoglycaemia localised allergic reactions, fat hypertrophy at injection sites.

Dose: By subcutaneous, intramuscular or intravenous injection, according to patient's requirements.

Preparation available

Soluble Insulin Injection: Soluble insulin injection is a sterile solution of porcine insulin or of human insulin. Injection containing 40 units and 100 units of soluble insulin per ml is usually available.

ISOPHANE INSULIN (NPH)

This is neutral insulin of intermediate action. Its duration of action is less than that of protamine zinc insulin. It will not give control of diabetes throughout the 24 hours by itself, but it is of value when combined with soluble insulin. Its onset of action is 1-2 hours, maximal effect 8-12 hours and effect lasts for 18-24 hours. Biphasic insulin preparations (containing soluble insulin and isophane or insulin aspart or insulin lispro) are available.

Indications: diabetes mellitus.

Adverse effects and cautions: *see* under soluble insulin.

Dose: By subcutaneous injection, according to patient's requirements.

Preparation available

Isophane Insulin Injection: Isophane insulin injection is a sterile suspension of porcine insulin or of human insulin in the form of a complex obtained by the addition of protamine sulphate or another suitable protamine. Injection containing 40 units/ml of isophane insulin is usually available.

INSULIN ZINC SUSPENSION

The amorphous form (insulin semilente) has a relatively quick action and the crystalline form (insulin ultralente) has a slow action. The action of semilente starts at about one hour and reaches its peak in approximately 5 to 7 hours and persists for approximately 12 to 16 hours. Ultralente insulin is a long acting form of insulin; its effect is evident in approximately 4 to 8 hours, reaches its peak in approximately 16 to 18 hours and persists for more than 36 hours.

Indications: diabetes mellitus.

Adverse effects and cautions: *see* under soluble insulin.

Dose: By subcutaneous injection, according to patient's requirements.

Preparation available

Insulin Zinc Suspension: Insulin zinc suspension is a sterile, neutral suspension of porcine insulin or of human insulin in the form of a complex obtained by the addition of a suitable zinc salt; the insulin is in a form insoluble in water. When prepared from insulin it contains either beef or pork insulin or a mixture of beef and pork insulin. Insulin containing 40 units/ml of insulin zinc suspension is usually available.

INSULIN ASPART

It is a human insulin analogue, which has faster onset and shorter duration of action than soluble insulin. Compared to soluble insulin, fasting and preprandial blood-glucose concentration is a little higher, postprandial blood-glucose is a little lower and hypoglycaemia occurs slightly less frequently.

Indications: diabetes mellitus

Adverse effects and cautions: see under soluble insulin

Dose: By subcutaneous injection, immediately before meals or when necessary shortly after meals, according to requirements.

By intravenous injection or infusion according to requirements.

INSULIN GLARGINE

It is a human insulin analogue and has a prolonged duration of action. Unlike traditional insulin preparations, the site of administration does not influence the time-action profile of the drug.

Indications: diabetes mellitus.

Adverse effects and cautions: see under soluble insulin.

Dose: By subcutaneous injections, ADULT and CHILD over 6 years, according to requirements.

INSULIN LISPRO

It is also a human insulin analogue. It is also faster acting and short acting drug than soluble insulin.

Indications: diabetes mellitus.

Adverse effects and cautions: *see* under soluble insulin

Dose: *see* under insulin aspart.

PROTAMINE ZINC INSULIN (PZI)

This is a long acting form of insulin; its effect is evident in approximately 4 to 8 hours, reaches its peak in approximately 14 to 20 hours and persists for approximately 36 hours. It was designed as to produce a "one shot-a-day" form of treatment. However, the delay in the commencement of its action and the prolongation of its action to more than 30 hours make it unsuitable for this. In combination with soluble insulin it forms a most useful mixture and many patients

have been controlled by this means for long periods of time.

Indications: diabetes mellitus.

Adverse effects and cautions: see under soluble insulin.

Dose: By subcutaneous injection according to patient's requirement.

Preparation available

Protamine Zinc Insulin Injection: Injection containing 100 units per ml of protamine zinc is usually available.

8.6.2 Oral antidiabetic drugs

Oral antidiabetic agents are used for non-insulin dependent (type 2) diabetes. They should be used only when patients are not adequately responding to carbohydrate intake and an increase in physical activity. There are two main types of oral antidiabetic agents, the biguanides and the sulphonylureas. Sulphonylureas act mainly by augmenting insulin secretion and biguanides act mainly by decreasing gluconeogenesis and by increasing peripheral utilisation of glucose.

ACARBOSE

It acts by inhibiting intestinal alpha-glucosidases, which delays the digestion and absorption of starch and sucrose. It does not enhance insulin secretion, so does not cause hypoglycaemia when used alone. It has small but significant effect in lowering blood glucose and is used as an adjunct to metformin or to sulphonylureas when they prove inadequate.

Indications: type 2 diabetes mellitus.

Adverse effects and cautions: abdominal pain, flatulence, diarrhoea, jaundice.

The drug is contraindicated in pregnancy, breast-feeding, hepatic impairment, severe renal impairment.

The drug should be used with caution with insulin and sulphonylureas (enhanced hypoglycaemia).

Dose: Initially, 50 mg daily, increased to 50 mg 3 times daily then increased if necessary after 6-8 weeks to 100 mg 3 times daily; maximum 200 mg 3 times daily; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Acarbose Tablets: Each tablet containing 50 mg of acarbose is usually available.

CHLORPROPAMIDE

This is an oral antidiabetic agent of the sulphonylureas group. Chlorpropamide has a prolonged action and can be given once daily.

Indications: type 2 diabetes mellitus.

Adverse effects and cautions: hypoglycaemia, nausea, vomiting, diarrhoea and disulfiram like reaction after drining alcohol. The antidiuretic action may result in the symptoms and signs of water intoxication (mental confusion, decreased sodium concentration, dizziness etc).

The drug is contraindicated in patients with ketoacidosis or diabetic coma or severe infection. The drug is also contraindicated in patients with severe impairment of kidney or liver function. Safety of drug during pregnancy and breast-feeding has not been established.

Dose: Initially 250 mg daily adjusted according to response, maximum 500 mg daily taken with breakfast or meal.

Preparation available

Chlorpropamide Tablets: Each tablet containing 250 mg of chlorpropamide is usually available.

GLIBENCLAMIDE

This is a sulphonylurea. Glibenclamide has longer duration of action.

Indications: type 2 iabetes mellitus.

Adverse effects and cautions: hypoglycaemia, nausea, vomiting, diarrhoea and constipation.

Cautions: *see* under chlorpropamide.

Drug interactions: warning signs of hypoglycaemia (such as tremor) with antidiabetic may be masked when given with beta-blockers.

Dose: Initially 5 mg daily (ELDERLY patient 2.5 mg), adjusted according to response; maximum 15 mg daily; taken with breakfast or meal.

Preparation available

Glibenclamide Tablets: Each tablet containing 2.5 mg and 5 mg of glibenclamide is usually available.

GLICLAZIDE

This is an oral hypoglycaemic agent of second generation sulphonylurea. The second generation sulphonylureas have short half-lives but their hypoglycaemic effects are evident for 12-24 hours.

Indications: type 2 diabetes mellitus.

Adverse effects and cautions: *see* under glibenclamide.

Dose: Initially, 40-80 mg daily, adjusted according to response; up to 160 mg as a single dose, with breakfast or meal; higher doses divided; maximum 320 mg daily.

Preparation available

Gliclazide Tablets: Each tablet containing 80 mg of gliclazide is usually available.

GLIPIZIDE

Indications, adverse effects and cautions: see under glibenclamide.

Dose: Initially 2.5-5 mg daily, adjusted according to response; maximum 20 mg daily, up to 15 mg may be given as a single dose before breakfast or meal; higher doses divided.

Preparation available

Glipizide Tablets: Each tablet containing 5 mg of glipizide is usually available.

METFORMIN

This is a biguanides. This group of drugs do not stimulate the secretion of insulin by the pancreas. It is the drug of choice in overweight patients in whom strict dieting has failed to control diabetes.

Indications: type 2 diabetes mellitus.

Adverse effects and cautions: anorexia, nausea, vomiting, diarrhoea, metallic taste and lactic acidosis (rarely).

It is contraindicated in patients with renal impairment, hepatic impairment, recent myocardial infarction.

Dose: ADULT and CHILD over 10 years, initially 500 mg with breakfast for at least 1 week then 500 mg every 12 hours with or after food for at least 1 week, maximum 2 g daily in divided doses.

Preparation available

Metformin Tablets: Each tablet containing 500 mg and 850 mg of metfonnin hydrochloride is usually available. They are coated.

PIOGLITAZONE

It is related to rosiglitazone. Like rosiglitazone, it can also lower haemoglobin A1c levels by 1% to 1.5% in patients with type 2 diabetes mellitus.

Indications: see under rosiglitazone.

Adverse effects and cautions: *see* under rosiglitazone.

Dose: Initially 15-30 mg once daily increased to 45 mg once daily according to response.

Preparation available

Pioglitazone Tablets: Each tablet containing 15 mg and 30 mg of pioglitazone hydrochloride is usually available.

REPAGLINIDE

It stimulates insulin release.

Indications: type 2 diabetes mellitus.

Adverse effects and cautions: hypoglycaemia, diarrhoea, constipation, abdominal pain, nausea, vomiting.

The drug is contraindicated in ketoacidosis, pregnancy, breast-feeding, severe hepatic impairment.

The drug should be used with caution in myocardial infarction, infection, coma, during surgery, renal impairment.

Dose: Initially 500 micrograms within 30 minutes before main meals, adjusted according to response at intervals of 1-2 weeks; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Repaglinide Tablets: Each tablet containing 500 micrograms, 1 mg and 2 mg of repaglinide is usually available.

ROSIGLITAZONE

It is one of the thiazolidinediones and acts by decreasing insulin resistance at peripheral sites. This results in increased insulin-dependent glucose disposal and decreased hepatic glucose output. It is used in combination with metformin or sulphonylureas in patients in whom either metformin or sulphonylureas is contraindicated. It is used as monotherapy adjunctive to diet and exercise.

Indictions: type 2 diabetes mellitus.

Adverse effects and cautions: peripheral oedema, headache, anaemia, weight gain, dizziness, impotence.

The drug is contraindicated in hepatic impairment, pregnancy, breast-feeding and history of heart failure.

The drug should be used with caution in hepatic impairment (monitor liver function before treatment and periodically there after), renal impairment.

Dose: Initially 4 mg daily, if used alone or in combination with metformin, may increase to 8 mg daily (in 1 or 2 divided doses) after 8 weeks according to response; CHILD and ADOLESCENT under 18 years not recommended.

Preparation available

Rosiglitazone Tablets: Each tablet containing 4 mg and 8 mg of rosiglitazone (as maleate) is usually available.

8.6.3 Treatment of hypoglycaemia

Initially glucose 10-20 g is given by mouth. If necessary this may be repeated in 10-15 minutes. Hypoglycaemia which causes unconsciousness is an emergency. It should be treated with glucagon or 50 ml of glucose intravenous infusion 20% into large vein.

GLUCAGON

Glucagon is produced by the alpha cells of the islet of Langerhans in the pancreas. It is a polypeptide hormone and its action is to raise the blood glucose concentration by increasing the release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to elicit an antihypoglycaemic effect.

Indications: acute hypoglycaemia.

Adverse effects and cautions: nausea, vomiting, hypotension, hypokalaemia.

It should be used with caution in patients with history of insulinoma, starvation.

Dose: By subcutaneous, intramuscular, or intravenous injection ADULT and CHILD over 8 years 1 mg, if no response after 15 minutes intravenous glucose should be given.

Preparation available

Glucagon Injection: Glucagon injection is a sterile solution of glucagon with hydrochloric acid and lactose in a suitable liquid. Glucagon injection should be used immediately after preparation but, in any case within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instruction. If it shows any signs of gel formation or insoluble matter it should be discarded. Sealed container for injection containing 1 unit (1mg) vial of glucagon is usually available. The sealed container should be protected from light and stored at a temperature not exceeding 25°.

8.7 Thyroid and antithyroid drugs

8.7.1 Thyroid Hormones

LEVOTHYROXINE

L-thyroxine

Thyroxine is the major component of normal secretions of the thyroid gland. The principal pharmacological effect of exogenous thyroid hormones is to increase the metabolic rate of body tissues. Although the precise mechanism of action by which thyroid hormones affect metabolism and cellular growth and diffentiation is not clearly established.

Indications: hypothyroidism.

Adverse effects and cautions: palpitation, tachycardia, diarrhoea, cardiac arrhythmias, tremor, weight loss, sweating, insomnia, angina pain and increased appetite. Adverse effects result from overdose.

The drug should be used with extreme caution and in reduced dosage in patients with angina pectoris or other cardiovascular disease including hypertension, diabetes mellitus, pregnancy and breast-feeding.

The drug is contraindicated in presence of thyrotoxicosis.

Dose: The initial dose should not exceed 50-100 micrograms daily, preferably before morning meal or breakfast, or 25-50 micrograms in elderly patients or those with cardiac disease, increased by 50 micrograms at intervals of at least 3-4 weeks.

NEONATE up to 1 month a daily dose of 5-10 micrograms/kg; CHILD over 1 month initially 5 micrograms/kg, adjusted in steps of 25 micrograms every 2-4 weeks until mild toxic symptoms appear then reduce dose slightly.

Preparation available

Levothyroxine Tablets: Each tablet contaning 100 micrograms of levothyroxine sodium is usually available.Levothyroxine tablets should be protected from light.

8.7.2 Anti-thyroid drugs

CARBIMAZOLE

This is an antithyroid drug which inhibits the formation of thyroid hormones by interfering with incorporation of oxidised iodine into tyrosine residues of thyroglobulin. It also inhibits the coupling of iodotyrosine residues to form iodothyronines. The drug also makes the gland more vascular. Response to treatment takes several weeks, and it is usually 1-2 months before the patient becomes euthyroid.

Indications: hyperthyroidism.

Adverse effects and cautions: rashes, nausea, headache, arthralgia, agranulocytosis and pruritus.

The patient should be asked to report sore throat; WBC count should be performed if there is clinical evidence of infection.

The drug should be used with caution in pregnancy, breast-feeding and liver disorders.

Dose: 15-40 mg daily in divided doses, until patient becomes euthyroid (usually 4-8weeks), then reduced to a maintenance dose of 5-15 mg for 12-18 months.

Preparation available

Carbimazole Tablets: Each tablet containing 5 mg of carbimazole is usually available.

IODINE

Indications: prevention and treatment of iodine deficiency.

Adverse effects and cautions: goitre, hypothyroidism, hyperthyroidism, hypersensitivity.

The drug is contraindicated in breast-feeding.

The drug should be used with caution in pregnancy, nodular goitre, over 45 years of age.

Dose: Iodine deficiency, by intramuscular injection, INFANT, 190 mg; CHILD and ADULT 380 mg (aged over 45 years or with nodular goitre 76 mg). It provides protection up to 3 years.

Iodine deficiency, by mouth, ADULT (except during pregnancy) and CHILD above 6 years, 400 mg once a year; ADULT during pregnancy, single dose of 200 mg; INFANT under 1 year, single dose of 100 mg; CHILD 1-5 years, 200 mg once a year.

Endemic moderate to severe iodine deficiency, by intramuscular injection, ADULT woman of child-bearing age, including any stage of pregnancy, 480 mg once each year.

Preparation available

Iodised Oil Injection: Injection containing 480 mg of iodine per ml is usually available.

LUGOL'S IODINE

This is an aqueous solution containing 5% iodine and 10% potassium iodide.

Indications: thyrotoxicosis (pre-operative).

Adverse effects and cautions: hypersensitivity reactions manifested by angioedema, fever, arthralgia, urticaria, metallic taste, headache, swelling and tenderness of the salivary glands.

The drug is contraindicated in breast-feeding. It should be used with caution in pregnancy and children.

Dose: Aqueous iodine oral solution should be taken 0.1-0.3 ml 3 times daily well diluted with water or milk.

Preparation available

Aqueous Iodine Oral Solution (Lugol's solution): It contains 5% w/v of iodine and 10% w/v of potassium iodide.

Aqueous iodine oral solution should be kept in well closed container, the material of which is resistant to iodine.

PROPRANOLOL

This is useful for quick relief of thyrotoxic symptoms. It is used together with antithyroid drugs or as an adjunct to radioactive iodine.

Adverse effects, cautions and preparation available: *see* under section 2.1.2, beta- blockers.

PROPYLTHIOURACIL

This is an antithyroid drug. The mechanism of action is similar to carbimazole.

Indications: see under carbimazole.

Adverse effects and cautions: see under carbimazole. The drug may cause thrombocytopenia, aplastic anaemia, hypoprothrombinaemia and bleeding.

Dose: 200-400 mg daily and maintained on this dose until the patient becomes euthyroid, the dose may then be gradually reduced to maintenance of 50 to 150 mg daily.

Preparation available

Propylthiouracil Tablets: Each tablet containing 50 mg of propylthiouracil is usually available.

8.8 Posterior pituitary hormone

DESMOPRESSIN

Indications: diabetes insipidus, primary nocturnal enuresis.

Adverse effects and cautions: fluid retention, headache, nausea, vomiting, epistaxis, allergic reaction. Less pressor activity, but still need for considerable caution in renal impairment, cardiovascular disease and hypertension.

The drug is contraindicated in cadiac insufficiency.

Dose: By mouth, diabetes insipidus treatment, ADULT and CHILD, initially 300 micrograms daily (in three divided doses); maintenance, 300-600 micrograms daily in three divided doses; range 0.2-1.2 mg daily.

Primary nocturnal enuresis, ADULT and CHILD over 5 years, 200 micrograms at bedtime, increased to 400 micrograms if lower dose not effective.

Postoperative polyuria/polydipsia adjust dose according to urine osmolality.

By injection, diabetes insipidus, diagnosis (subcutaneous or intramuscular ADULT and CHILD, 2 micrograms; treatment (subcutaneous, intramuscular or intravenous) ADULT 1-4 micrograms daily, CHILD 400 nanogram.

Renal function testing (subcutaneous or intramuscular) ADULT and CHILD, 2 micrograms.

Preparation available

Desmopressin Tablets: Each tablet containing 100 micrograms and 200 micrograms of desmopressin acetate is usually available.

Desmopressin Injection: Injection containing 4 micrograms of desmopressin is usually available.

VASOPRESSIN (ANTIDIURETIC HORMONE)

Exogenous vasopressin elicits all the pharmacological responses usually produced by endogenous vasopressin. The oxytocic properties of vasopressin are minimal but in large doses the drug may stimulate uterine contractions.

Indications: diabetes insipidus, bleeding oesophageal varices.

Adverse effects and cautions: nausea, vomiting, abdominal cramps, belching, fluid retention, sweating, tremor, constriction of coronary arteries and desire to defaecate.

The drug is contraindicated in vascular disease (especially disease of coronary arteries).

The drug should be used with caution in patients with asthma, heart failure, pregnancy and renal disease.

Dose: By subcutaneous or intramuscular injection, diabetes insipidus, 5-20 units every four hours.

By intravenous infusion, initial control of variceal bleeding 20 units over 15 minutes.

Preparation available

Vasopressin Injection: Injection containing 20 units/ml is usually available.

8.9 Drugs affecting bone metabolism

SODIUM ALENDRONATE

It is one of the second generation bisphosphonates. It inhibits bone resorption due to direct inhibitory effects on osteoclasts.

Indications: prevention and treatment of post-menopausal osteoporosis, osteoporosis in men, prevention and treatment of corticosteroid-induced osteoporosis.

Adverse effects and cautions: oesophageal reactions (oesophagitis, oesophageal ulcers, oesophageal stricture and oesophageal erosions), dyspepsia, abdominal pain and distension, regurgitation, diarrhoea or constipation, melaena, headache, peptic ulceration, severe skin reactions including Stevens-Johnson syndrome.

The drug is contraindicated in pregnancy, breast-feeding, stricture or achalasia of oesophagus.

The drug should be used with caution in patients with history of ulcers, active gastro-intestinal bleeding, renal impairment, gastritis.

Dose: Prevention of post-menopausal osteoporosis, 5 mg daily.

Treatment of post-menopausal osteoporosis and osteoporosis in men, 10 mg daily or (in post-menopausal osteoporosis) 70 mg once weekly.

Prevention and treatment of corticosteroid-induced osteoporosis, 5 mg daily (post-menopausal woman not receiving hormone replacement therapy, 10 mg daily).

Preparation available

Sodium Alendronate Tablets: Each tablet containing sodium alendronate equivalent to 5 mg, 10 mg, 35 mg and 70 mg of alendronoic acid is usually available.

Chapter - Nine

Drugs Used in Anaesthesia

9.1 General anaesthetics

General anaesthesia is a state of drug-induced loss of consciousness whereby surgical procedures can be carried out painlessly.

9.1.1 Inhalational anaesthetics

DIETHYL ETHER

Ether

Induction and recovery from anaesthesia is slow, due to its high blood solubility. Its margin of safety is high. Muscular relaxation is good in the presence of adequate respiration. It is irritant to the airway and increases bronchial and salivary secretion. It stimulates respiration by central action. Heart rate is increased and blood pressure is maintained even in deep anaesthesia due to increased sympathetic activity.

Indications: *see* notes above.

Adverse effects and cautions: nausea and vomiting, acidosis, dehydration and fever in children may predispose to convulsions under ether anaesthesia.

Dose: Open drop, 12 drops/min for 2 minutes, then 1 drop until patient loses consciousness (usually within 5 minutes). The rate is subsequently adjusted to provide the required depth of anaesthesia. Administration from vaporisers: not exceeding 15% during induction and then 5-10% during maintenance.

HALOTHANE

Anaesthesia with halothane can be induced rapidly because of its high potency and it is non-irritating to inhale. Recovery from anaesthesia is also rapid. It is used for induction and maintenance of anaesthesia in major surgery with oxygen or nitrous oxide-oxygen mixtures. It causes respiratory depression, more so in volume than rate. Halothane depresses heart and causes a fall in blood pressure proportional to the depth of anaesthesia. Ventricular dysrhythmia under halothane anaesthesia bears direct relationship to hypoxia.

Halothane produces moderate muscle relaxation but this may be inadequate for major abdominal surgery and specific muscle relaxants are used. Halothane readily crosses the placental barrier and depresses foetal respiration.

Indications: *see* notes above.

Adverse effects and cautions: nausea, vomiting, fall in blood pressure, bradycardia, shivering (heat loss due to peripheral vasodilatation) and hepatitis.

The risk of severe hepatotoxicity appears to be increased by repeated exposures within a short time interval, but even after a long interval (sometimes of several years) susceptible patients have been reported to develop jaundice. Following precautions are recommended prior to use of halothane:

- avoid repeated exposure to halothane in less than three months unless under certain circumstances.
- careful anaesthetic history to determine previous exposure and previous reaction to halothane.
- history of unexplained jaundice or pyrexia in a patient following exposure to halothane is an absolute contraindication to its use.

Use of halothane may cause excessive bleeding during caesarean section and post-partum haemorrhage.

Dose: Using a special calibrated vaporiser, induction, increased gradually to 2-4% in oxygen or nitrous oxide-oxygen; child 1.5-2%; maintenance, 0.5-2%.

Preparation available

Halothane Liquid: Bottle containing 50 ml, 200 ml and 250 ml of halothane are usually available.

ISOFLURANE

Heart rhythm is generally stable during isoflurane anaesthesia, but heart-rate may rise, particularly in younger patients. Systemic arterial pressure may fall, due to a decrease in systemic vascular resistance and with less decrease in cardiac output than occurs with halothane. Respiration is depressed. Muscle relaxation is produced and muscle relaxant drugs potentiated.

Indications, adverse effects and cautions: *see* notes above. Hepatotoxicity is smaller than halothane.

Dose: Using a special calibrated vaporiser, induction, increased gradually form 0.5 % to 3%, in oxygen or nitrous oxide-oxygen. Maintenance, 1-2.5% in nitrous oxide-oxygen; an additional 0.5 -1% may be required when given with oxygen alone. Caesarean section, 0.5-0.75% in nitrous oxide-oxygien.

NITROUS OXIDE

It is used for maintenance of anaesthesia. Nitrous oxide has analgesic properties and at sub-anaesthetic concentration (50%) with oxygen, is used frequently to provide analgesia in obstetrics. It is a weak anaesthetic. For anaesthesia it is commonly used in a concentration of 50 to 70% in oxygen in association with other inhalational or intravenous agents. Nitrous oxide is a weak respiratory stimulant. It depresses myocardium but it stimulates sympathetic nervous activity by central action, and this tends to antagonise direct myocardial depression.

Indications: *see* notes above.

Adverse effects and cautions: megaloblastic anaemia, bone-marrow depression. Nitrous oxide may have a deleterious effect if used in patients with an air-containing closed space since nitrous oxide diffuses into such a space with a resulting build up of pressure. Exposure of anaesthetists and theatre staff should be minimised to avoid its adverse effects.

Dose: Using a suitable anaesthetic apparatus, a mixture with 25-30% oxygen for maintenance of light anaesthesia; analgesic, as a mixture with 50% oxygen, according to the patient's needs.

9.1.2 Intravenous anaesthetics

DIAZEPAM: *see* under section 9.1.3, benzodiazepines.

KETAMINE

It is a rapidly acting general anaesthetic. It is used mainly for paediatric anaesthesia. Ketamine produces a somnolent state in which some patients appear to be awake but dissociated from their environment, unresponsive to pain, and having no recall. Somatic pain appears to be more effectively blocked than visceral pain. It produces no muscle relaxation but may produce generalised extensor spasm during emergence from anaesthesia. In 2 mg per kg dose given intravenously or 10 mg/kg dose intra-muscularly, a feeling of dissociation becomes apparent in about 15 seconds; unconsciousness occurs in about 50 seconds and lasts for 10-15 minutes. Ketamine causes transient depression of the respiratory centre. It causes an increase of systolic and diastolic blood pressure and heart rate.

Indications: induction and maintenance of anaesthesia for minor surgical or diagnostic procedures.

Adverse effects and cautions: tachycardia, hallucinations, nightmares, increased salivation, increased arterial pressure.

The incidence of delirium and hallucinations are much less significant in children. Diazepam and lorazepam have been recommended for their reduction or elimination. Ketamine is contraindicated in patients with epilepsy, hypertension and in patients with increased intracranial pressure.

Dose: By intramuscular injection, short procedures, initially 6.5-13 mg/kg (10 mg/kg usually produces 12-25 minutes of surgical anaesthesia).

Diagnostic manoeuvers and procedures not involving intense pain, initially 4 mg /kg. By intravenous injection over at least 60 seconds, short procedures, initially 1-4.5 mg/kg (2 mg/kg usually produces 5-10 minutes of surgical anaesthesia). By intravenous infusion of a solution containing 1 mg/ml, longer procedures, induction, total dose of 0.5-2 mg/kg; maintenance (using microdrip infusion), 10-45 micrograms/kg/minute, rate adjusted according to response.

Preparation available

Ketamine Hydrochloride Injection: Injection containing 10 mg and 100 mg of ketamine hydrochloride per ml is usually available.

PROPOFOL

Loss of consciousness occurs rapidly and smoothly, usually within 40 seconds (one arm-brain ciculation time) and recovery from anaesthesia is rapid (wihin 8 minutes) with minimal psychomotor impairment.

Indications: induction and maintenance of anaesthesia, sedation for surgical and diagnostic procedures.

Adverse effects and cautions: bradycardia, hypotension, apnoea, involuntary muscle movements, nausea, vomiting, hiccups.

The drug is contraindicated for sedation of ventilated children and adolescents under 17 years.

The drug should be used with caution in pregnancy.

Dose: Induction of anaesthesia, by intravenous infusion or injection, 1.5-2.5 mg/kg (less in those over 55 years) at a rate of 20-40 mg every 10 seconds; CHILD over 8 years 2.5 mg/kg.

Maintenane of anaesthesia, by intravenous injection, 25-50 mg repeated according to response or by intravenous infusion, 4-12 mg/kg/hour; CHILD over 3 years, by intravenous infusion, 9-15 mg/kg/hour.

Sedation for surgical and diagnostic procedures, initially by intravenous injection over 1-5 minutes,0.5-1 mg/kg; maintenance, by intravenous infusion, 1.5-4.5 mg/kg/hour; CHILD and ADOLESCENT under 17 yrars nor recommended.

Preparation available

Propofol Injection: Injection containing 10 mg and 20 mg of propofol per ml, as emulsion, is usually available.

THIOPENTAL SODIUM

Thiopentone sodium

It is the most widely used intravenous anaesthetic, but lacks analgesic effect. After a single intravenous anaesthetic dose, consciousness is lost in 10-20 seconds and returns in about 20-30 minutes. Induction is generally smooth. This short-lasting anaesthetic effect is caused by redistribution of the drug from the brain (which it enters rapidly and where the initial concentration is high), to the other tissues of the body (such as adipose and muscle).

Thiopentone causes dose-related respiratory depression. It depresses the respiratory centre rapidly. Reduction of myocardial contractility leading to decrease of cardiac output and hypotension may occur immediately after rapid intravenous injection.

Indications: induction of general anaesthesia, anaesthesia of short duration in minor surgical procedures.

Adverse effects and cautions: arrhythmias, cough, laryngeal spasm, myocardial depression, rash.

Anaesthesia is deeper whenever the protein binding is less. The amount of drugs administered should be reduced in patients with liver disease. It should be used with caution in pregnancy. Extravasation should be avoided.

The drug is contraindicated in porphyria and breast-feeding.

Dose: By intravenous injection, in fit premedicated adult, initially 100-150 mg (4-6 ml of 2.5% solution) over 10-15 seconds, repeated if necessary according to response after 30-60 seconds; or up to 4 mg/kg; CHILD induction 2-7 mg/kg.

Preparation available

Thiopental Injection: Sealed container of thiopental sodium for injection containing 500 mg and 1 g of thiopental sodium (2.5% when dissoloved in water for injection) is usually available.

Thiopental injection should be used immediately but in any case, within the period recommended by the manufacturer, when prepared and stored strictly in accordance with the manufacturer's instructions.

9.1.3 Pre-anaesthetic medication drugs

These drugs are given to dry bronchial and salivary secretions which are increased by intubation, surgery to upper airways and inhalational anaesthetics. These drugs are also used to allay the apprehension of the patient in the pre-operative period (including the night before operation), to relieve pain and discomfort when present, and to augment the action of subsequent anaesthetic agents.

ANTIMUSCARINIC DRUGS

Atropine is used to prevent or treat reflex slowing of heart during anaesthesia. It is given preoperatively. Hyoscine (scopolamine) is a good sedative and produces retrograde amnesia. It is more effective drying agent for secretions than atropine, but less effective as a vagolytic agent. Glycopyrronium, unlike atropine and hyoscine, this drug does not cross the blood-brain barrier, hence does not produce central sedation or post operative delirium. Tachycardia is less pronounced than with atropine.

Antimuscarinics may not be prescribed routinely in the preoperative medication, because secretions are no longer a major problem unless ether is used. It is better to give the drug intravenously as the need arises.

ATROPINE

Dose: Premedication, by intravenous injection, 300-600 micrograms immediately before induction of anesthesia; CHILD 20 micrograms/kg (maximum 600 micrograms).

By intramuscular injection, 300-600 micrograms 30-60 minutes before induction; CHILD 20 micrograms/kg.

For control of muscarinic side effects of neostigmine in reversal of competitive neuromuscular block, by intravenous injection, 0.6-1.2 mg; CHILD under 12 years, 20 micrograms/kg (maximum 600 micrograms).

Bradycardia, particularly complicated by hypotension after myocardial infarction, intravenous injection of 300 micrograms, increasing to 1 mg if necessary.

Preparation available

Atropine Sulfate Injection: Atropine sulfate injection is a sterile solution of aropine sulfate in water for injection. Injection containing 1 mg in 1 ml is usually available.

BENZODIAZEPINES

Benzodiazepines are frequently used for premedication by oral or intramuscular or intravenous routes. They produce relief of anxiety, sedation and amnesia. (*see* under section 4.4, anxiolytics).

DIAZEPAM

Dose: By mouth, 5 mg at night before minor or dental surgery then 5 mg 2 hours before procedure; ELDERLY half adult dose.

By intravenous injection, into a large vein 10-20 mg over 2-4 minutes as sedative cover for minor surgical and medical procedures; premedication 100-200 micrograms/kg.

LORAZEPAM

Dose: By mouth, 2-3 mg the night before operation; 2-4 mg 1-2 hours before operation.

By slow intravenous injection, preferably diluted with an equal volume of sodium chloride (0.9%), 50 micrograms/kg 30-45 minutes before operation.

MIDAZOLAM

Recovery is faster than from diazepam. Midazolam is associated with marked sedation when high doses are given intravenously or used with certain other drugs.

Dose: Premedication, by deep intramuscular injection, 70-100 micrograms/kg (ELDERLY 25-50 micrograms/kg) 20-60 minutes before induction; CHILD 1-15 years 80-200 micrograms/kg.

Induction, by slow intravenous injection with premedication 150-200 micrograms/kg (ELDERLY 100-200 micrograms/kg); without premedication, 300-350 micrograms/kg (ELDERLY 150-300 micrograms/kg); doses increased in steps not greater than 5 mg every 2 minutes; maximum 600 micrograms/kg; CHILD over 7 years 150 micrograms/kg.

GLYCOPYRRONIUM BROMIDE

Dose: Premedication, by intramuscular or intravenous injection, 200-400 micrograms, or 4-5 micrograms/kg to a maximum of 400 micrograms; CHILD, by intramuscular or intravenous injection 4-8 micrograms/kg to a maximum of 200 micrograms; intra-operative use, by intravenous injection, as for premedication.

For control of muscarinic side effects of neostigmine in reversal of competitive neuromuscular block, by intravenous injection 10-15 micrograms/kg with 50 micrograms/kg neostigmine; CHILD 10 micrograms/kg with 50 micrograms/kg neostigmine.

Preparation available

Glycopyrronium Bromide Injection: Injection cantaining 200 micrograms per ml of glycopyrronium bromide is usually available.

OPIOID ANALGESICS

They are prescribed in premedication or with induction to reduce the dose of some drugs used during anaesthesia. (*see* section 4.1 opioid analgesic)

FENTANYL

It is an opioid analgesic. Analgesic effect is seen within 1-2 minutes and effect lasts for 30-60 minutes with intravenous administration of the drug.

Dose: By intravenous injection, with spontaneous respiration, 50-100 micrograms, then 50 micrograms as required; CHILD 3-5 micrograms/kg, then 1 micrograms/kg as required.

With assisted ventilation, 0.3-3.5 mg, then 100-200 micrograms as required; CHILD 15 micrograms/kg, then 1-3 micrograms/kg as required.

PROMETHAZINE HYDROCHLORIDE

It it used as pre-operative sedative and antiemetic, see section 1.4 anti-emetics for detail.

Dose: Premedication, by mouth CHILD 2-5 years 15-20 mg, 5-10 years 20-25 mg.

By deep intramuscular injection, 25-50 mg, 1 hour before operation, CHILD 5-10 years, 6.25-12.5 mg. CHILD under 2 years not recommended.

9.1.4 Muscle relaxants

Muscle relaxants are used in anaesthesia to bring adequate relaxation of` the muscles of the abdomen and diaphragm. They also relax the vocal cords and allow the passage of a tracheal tube. These muscles relaxants are also known as neuromuscular blocking drugs. These drugs can be classified into competitive muscle relaxants (non-depolarising muscle relaxants) and depolarising muscle relaxants. Competitive muscle relaxants competitively block the depolarising action of acetylcholine on the receptor (in the end-plate), and this block can be reversed by increasing the concentration of acetylcholine, with anticholinesterases such as neostigmine.

Depolarising muscle relaxants cause initial depolarisation of the end-plate like acetylcholine, but unlike acetylcholine, they persist at the neuromuscular junction and prolong depolarisation, during which the end-plate is unable to respond to acetylcholine or nerve stimulation. Anticholinesterase agents do not reverse such blockade, rather may potentiate it.

ATRACURIUM

It is a non-depolarising muscle relaxant. It is metabolised by non-enzymatic mechanism which is independent of liver and kidney function, thus it can be used in hepatic or renal impairment. It causes histamine release. It has intermediate duration of action.

Indications: competitive muscle relaxation.

Adverse effects and cautions: *see* under pancuronium.

Dose: Surgery or intubation, ADULT and CHILD over 1 month, by intravenous injection, initially 300-600 micrograms/kg; maintenance, by intravenous injection, 100-200 micrograms/kg as required or by intravenous infusion, 5-10 micrograms /kg/minute.

Preparation available

Atracurium Injection: Atracurium besilate 10 mg/ml in 2.5-ml vial is usually available.

GALLAMINE

It has intermediate duration of action. It has an atropine like effect, blocks cardiac vagus, and may cause sinus tachycardia and occasionally increased cardiac output and hypertension. Its blocking effect is diminished by respiratory acidosis and enhanced by alkalosis. It is excreted solely by the kidney. Action of drug may be reversed with anticholinesterase such as neostigmine.

Indications:competitive muscle relaxation.

Adverse effects and cautions: tachycardia.

Gallamine should be used in reduced dose in renal impairment and should be avoided in patients with moderate renal impairment. The drug should be avoided in myasthenia gravis.

Drug interactions: potentiation or prolongation of effects with many antibiotics e.g. aminoglycosides (streptomycin, neomycin, kanamycin, gentamicin, amikacin), and tetracyclines. Nifedipine, verapamil, quinidine, beta-blockers also potentiate gallamine effect.

Dose: By intravenous injection, 80-120 mg, then 20-40 mg as required; NEONATE, 600 micrograms/kg; CHILD, 1.5 mg/kg.

Preparation available

Gallamine Injection: An injection containing 40 mg of gallamine triethiodide per ml is usually available. Gallamine injection should be protected from light.

NEOSTIGMINE

Neostigmine is anticholinesterase. It reverses the effects of the non-depolarising (competitive) muscle relaxant drugs such as pancuronium, vecuronium but prolong the action of depolarising muscle relaxant drug suxamethonium. It acts within one minute of intravenous injection and lasts for 20 to 30 minutes. Atropine or glycopyrronium should be given before or with neostigmine in order prevent bradycardia, excessive salivation and other muscarinc actions of neostigmine.

Indications: reversal of non-depolarising block, myasthenia gravis.

Adverse effects and caution: increased salivation, increased bronchial secretion, sweating, diarrhoea, abdominal pain.

The drug is contraindicated in recent intestinal or bladder surgery, after suxamethonium.

The drug should be used with caution in pregnancy, breast-feeding, epilepsy, renal impairment, bradycardia.

Dose: Reversal of non-depolarising neuromuscular blockade, by intravenous injection over 1 minute, 50-70 micrograms/kg (maximum 5 mg) after or with atropine sulphate 0.6-1.2 mg.

Myasthenia gravis, by mouth, neostigmine bromide 15-30 mg at suitable intervals throughout day, total daily dose 75-300 mg. NEONATE 1-2 mg every 4 hours, half an hour before feeds, CHILD up to 6 years initially 7.5 mg, 6-12 years initially 15 mg, usual total daily dose 15-90 mg.

By subcutaneous or intramuscular injection, neostigmine methylsulphate 1-2.5 mg at suitable intervals throughout day (usual total daily dose 5-20 mg); NEONATE 50-250 micrograms every 4 hours half hour before foods, CHILD 200-500 micrograms as required.

PANCURONIUM

It has long duration of action. This drug does not cause ganglion blockage, and rarely histamine release. Bronchospasm and hypotension are not observed. It may increase heart rate, cardiac output and arterial pressure primarily due to vagolytic and sympathomimetic actions. Action of drug may be reversed with anticholinesterase such as neostigmine.

Indications: competitive muscle relaxation.

Adverse effects and cautions: tachycardia, hypertension. Pancuronium should be used with caution in pregnancy, breast-feeding and liver impairment. The drug should be used in reduced dose in renal impairment. The drug should be avoided in myasthenia gravis.

Dose: For intubation, by intravenous injection, initially, 50-100 micrograms/kg then 10-20 micrograms/kg as required; CHILD initially 60-100 micrograms/kg then 10-20 micrograms/kg. NEONATE 30-40 micrograms/kg initially then 10-20 micrograms/kg.

Intensive care, by intravenous injection 60 micrograms/kg every 1-1.5 hours.

Preparation available

Pancuronium Injection: Injections containing 2 mg/ml of pancuronium bromide is usually available. Pancuronium injection should be stored at a temperature of 2°-8°.

ROCURONIUM

It is a non-depolarising muscle relaxant and produces its effects within 2 minutes.

It has minimal cardiovascular effect and produces mild vagolytic activity at high doses.

Indications: *see* under atracurium.

Adverse effects and cautions: *see* under atracurium.

Dose: For intubation, ADULT and CHILD over 1 month, by intravenous injection, initially, 600 micrograms/kg; maintenance by intravenous injection, 150 micrograms/kg (ELDERLY 75-100 micrograms/kg) or maintenance by intravenous infusion, 300-600 micrograms/kg/hour.

Intensive care, by intravenous injection, initially 600 micrograms/kg; maintenance by intravenous infusion, 300-600 micrograms/kg/hour for first hour, then adjusted according to response.

Preparation available

Rocuronium Injection: Injections containing 10 mg/ml of rocuronium bromide in 5-ml or 10-ml vial is usually available.

SUXAMETHONIUM CHLORIDE

Succinylcholine chloride

It is the only depolarising muscle relaxant that is commonly used at present. Succinylcholine has a rapid onset (1 minute) and short duration (2-6 minutes). The flaccid paralysis is preceded by transient muscle fasciculations; especially visible over cheeks and abdomen. Paralysis then develops over arm, neck and leg muscles. Weakness of respiratory muscles follows. Prolonged muscle paralysis may occur in patients with low or atypical plasma pseudocholinesterase enzymes.

Indications: depolarising muscle relaxation.

Adverse effects and cautions: tachycardia, post-operative muscle pain, nodal and ventricular arrhythmias, prolonged apnoea, malignant hyperthermia (when given as an adjuvant to a volatile general anaesthetic) and myoglobinuria.

The drug is contraindicated in severe liver disease (including low plasma cholinesterase), severe burns.

The drug should be used with caution in pregnancy, severe trauma, breast-feeding.

Dose: By intravenous injection, initially, 1 mg/kg, maintenance, usually 0.5 -1 mg/kg at 5-10 minutes intervals. NEONATE and INFANT 2 mg/kg; CHILD over 1 year, 1 mg/kg.

By intravenous infusion, as a 0.1% solution, 2-5 mg/minute (2-5 ml/minute).

Preparation available

Suxamethonium Chloride Injection: Injection containing 50 mg per ml of suxamethonium chloride in water for injection is usually available. Suxamethonium chloride injection should be stored at a temperature of 2-8°. It should not be allowed to freeze.

VECURONIUM

It is a non-depolarising muscle relaxant and has shorter duration of action (20-30 minutes). It does not produce histamine release and lacks cardiovascular effects.

Indications: muscle relaxation.

Advere effects and cautions: rarely bronchospasm, hypotension, tachycardia, pruritus.

The drug is contraindicated in myasthenia gravis, dehydrated or severely ill patients.

The drug should be used with cautions in pregnancy, breast-feeding, hepatic impairment.

Dose: By intravenous injection, intubation, 80-100 micrograms/kg; maintenance 20-30 micrograms/kg according to response; NEONATE and INFANT up to 4 months, initially 10-20 micrograms/kg then incremental doses to achieve response; CHILD over 5 months, as adult dose.

By intravenous infusion, 0.8-1.4 micrograms/kg/minute (after initial intravenous injection of 40-100 micrograms/kg).

9.2 Local anaesthetics

Local anaesthetics are agents that, when applied locally to nerve tissue in appropriate concentrations, they can act on any part of the nervous system and on every type of nerve fiber. These drugs act by blocking the activation (opening) of sodium channels induced by depolarisation of the nerves.

The drugs used vary widely in their potency, duration of action, toxicity, solubility in water and ability to penetrate mucous membranes. These variations determine their use by various routes, e.g. surface (topical), infiltration, epidural or spinal blocks. The addition of adrenaline diminishes local blood flow, slows the rate of absorption of local anaesthetic and prolongs its local effects, but should not be used in digits and appendages.

BUPIVACAINE

It has a slow onset and long duration of action. It is suitable for epidural analgesia in labour and lumbar epidural blockade.

Indications: local infiltration, peripheral nerve block, epidural block, sympathetic block.

Adverse effects and cautions: headache, bradycardia, hypotension, cardiac arrhythmias, cardiac arrest, anxiety, restlessness, tremor, dizziness, respiratory arrest, hypersensitivity reactions manifested by oedema, status asthmaticus or anaphylactoid reaction.

The drug should be used with caution in severely debilitated patients and in those with liver disease, renal impairment, pregnancy, impaired cardiac condition. It should also be used with caution in patients with myasthenia gravis and severe shock. Local anaesthetic solutions containing vasoconstrictor such as adrenaline (epinephrine) should be used with caution, in geriatric patients and in patients with cardiovascular diseases including hypertension, peripheral vascular disease, diabetes and hyperthyroidism. Vasoconstrictor should not be used in conjunction with anaesthesia of digits, ears, nose or penis.

Dose: Adjusted according to site of operation and response of patient, local infiltration, 0.25% (up to 60 ml). Peripheral nerve block 0.25% (maximum 60 ml), 0.5% (maximum 30 ml).

Epidural block surgery, lumbar, 0.5% (maximum 20 ml); caudal, 0.5% (maximum 30 ml); labour, lumbar, 0.25-0.5% (maximum 12 ml of either).

Preparation available

Bupivacaine Injection: An injection containing the equivalent of 5 mg per ml of anhydrous bupivacaine hydrochloride is usually available.

LIDOCAINE

Lignocaine

When used for block or infiltration or surface anaesthesia its duration of action is longer (90 minutes) with adrenaline. Adrenaline must be used in low concentration (1:200 000).

Indications, adverse effects and cautions: *see* under bupivacaine.

Dose: Adjusted according to site of operation and response of patient. Infiltration, by injection, maximum dose 200 mg (or 500 mg with solution which also contains adrenaline). Maximum dose of adrenaline 500 µg.

Nerve blocks with adrenaline 1 in 200,000, 1% to a maximum of 40 ml.

Surface anaesthesia, usual strength 4% for mouth, throat and upper gastro-intestinal tract maximum 200 mg.

Surface anaesthesia of urethra, 4% solution, maximum 400 mg.

Preparation available

Lignocaine Gel: Gel containing the equivalent of 2% w/v of anhydrous lignocaine hydrochloride is usually available. Lignocaine should be stored at a temperature of 8-15°. Any of the gel not used in a single application should be discarded.

Lignocaine Injection: Injection containing 1% and 2% w/v of lignocaine hydrochloride is usually available.

PRILOCAINE HYDROCHLORIDE

When used for block for infiltration without adrenaline (epinephrine), the duration of anaesthesia is longer than that of equal dose of lidocaine. When adrenaline is added to both drugs, the duration of lidocaine action is lengthened to a greater extent than that of prilocaine.

Indications: infiltration for dentistry, nerve block.

Adverse effects and cautions: *see* under lidocaine.

Dose: Adjusted according to site of operation and response of patient, 100-200 mg/minute to maximum 400 mg.

Preparation available

Prilocaine Injection: Injection containing 3% of prilocaine hydrochloride is usually available.

PROCAINE HYDROCHLORIDE

Procaine generally has an onset of action of 2 to 5 minutes and duration of action of about an hour.

Indications: infiltration, peripheral nerve block, sympathetic nerve block, spinal anaesthesia.

Adverse effects and cautions: see under bupivacaine.

Dose: Adjusted according to site of operation and patient's rseponse. By injection, up to 1g (200 ml of 0.5% solution or 100 ml of 1% solution).

Preparation available

Procaine Hydrochloride Injection: Injection containing 2% w/v (20 mg/ml) of procaine hydrochloride is usually available.

Chapter -Ten

Drugs Used as Antidotes and Other Substances Used in Poisoning

Hospital admission is generally what should be done for all patients who show features of poisoning. Persons who have taken substances which have a delayed action e.g. salicylates, iron, paracetamol, tricyclic antidepressants, lithium or even sustained-release capsules or tablets should also be admitted.

In most cases the identity of the poison and the size of the dose is often difficult to establish with certainty. This is important in symptomatic management. Only a few patients require active removal of the drug. In most cases one treats the clinical state as it presents. However if one has an idea of what the poison taken is, then one can plan ones course of action. Patients' reports are generally of little help for they are usually confused or can only say that they have taken an undefined amount, possibly of mixed drugs. Some parents may think that their child has taken something which might be poisonous and may exaggerate or underplay the risks out of anxiety or guilt.

10.1 Clues to poisoning

The fixed dilated pupil: a fixed dilated pupil may be a sign of death, but it could be due to atropine, tricyclic antidepressants, antihistamines. Therefore, even in the presence of acute respiratory or cardiac arrest, resuscitation should be attempted.

Pinpoint pupils: may be a sign of pontine haemorrhage, but consider opiate poisoning, mushroom, organophosphorous insecticide or other cholinergic poisoning.

Atypical convulsions: a dazed look and oculogyric spasms. Always think of phenothiazine overdose (iatrogenic or otherwise).

Patient looks drunk: may be hypoglycaemic, but consider all hypnotics, sedatives and antipsychotics.

Metabolic acidosis: may be diabetic or severe gastro-enteritis, but do not forget salicylate poisoning.

10.2 Prevention of absorption and active elimination of drugs

Activated charcoal can bind many poisons in gastro-intestinal system thereby reduce their absorption. It may be effective up to 1 hour after ingestion of poison, sooner the better. It is particularly useful for the prevention of absorption of poisons which are toxic in small amounts e.g. antidepressants. Repeated doses

of activated charcoal enhance the elimination of some drugs e.g. carbamazepine, dapsone, phenobarbital, quinine, theophylline etc. after they have been absorbed.

Adverse effects and cautions: black stools, vomiting.

Vomiting should be treated with an anti-emetic since it may reduce the efficacy of charcoal treatment.

The drug should not be used for poisoning with corrosives, alcohols, DDT, malathion, iron, lithium and petroleum distillates.

The drug should be used with caution in drowsy or comatosed patients and reduced gastro-intestinal motility.

Dose: reduction of absorption, 50 g, repeated if necessary; CHILD under 12 years 25 g.

Active eliminaton, 50 g initially then 50 g every 4 hours.

10.3 Removal of the poison from the stomach

Attempting to remove the poison from the stomach can be a risky undertaking. Gastric lavage is rarely required and should only be considered if a life-threatening amount of a substance that cannot be removed effectively by other means (e.g. iron) has been ingested within the previous hour.

The chief danger of gastric aspiration and lavage is inhalation of stomach contents and it should not be tried in drowsy or comatose patients unless there is a cough reflex or the airway can be protected adequately. Stomach tube should not be aspirated after corrosive poisoning or hydrocarbon products.

Gastric lavage may be considered in patients who have ingested iron or lithium. Induction of emesis for the treatment of poisoning is not recommended.

10.4 Symptomatic and supportive treatment

When the nature of the poison is not known, then the treatment is essentially symptomatic as given below:

Respiratory depression: the airway should be cleared and if necessary, respiration should be assisted. Analeptics should not be used.

Shock: raise the foot of the bed. Intravenous fluids to expand intravascular volume - the central venous pressure should be carefully monitored when necessary. The urine flow should also be monitored, a catheter being inserted into the bladder if necessary. Drugs for the raising of blood pressure are rarely required.

Convulsions: these may be controlled by intravenous diazepam or lorazapam.

Pain: in corrosive poisoning or for burns, pethidine or other analgesic should be given.

Cardiac conduction defects and arrhythmias: arrhythmias often respond to correction of underlying hypoxia, acidosis or other biochemical abnormalities.

Fluid and electrolyte balance: an intravenous drip is always useful, especially if an open route for drug administration is required. Hypotonic electrolyte solutions such as half-strength Lactated Ringer's, half-strength Darrow's Solution or Paediatric Electrolyte Mixture are safe. Care should be taken

not to overload the circulation. Forced alkaline diuresis is not recommended.

Hypothermia: in children, a low-reading thermometer is essential for detecting hypothermia. Wrapping the patient or electric blankets are reasonable safe means of raising the temperature. Hot water bottles have caused burns too often and should be abandoned.

Skin contamination: certain poisons, particularly organophosphorous insecticides, are absorbed via the intact skin. Attendants should wear latex gloves, strip the patient of his clothes and wash the skin with warm water and soap.

Dialysis: haemodialysis for brake fluid (ethylene glycol), salicylates, methyl alcohol and lithium poisoning.

10.5 List of poisons and antidotes

ACIDS (HYDROCHLORIC, SULPHURIC AND NITRIC ACID)

Never lavage in corrosive poisoning and do not prescribe emetics. The treatment of choice is dilution with water or milk; analgesics for pain. Cortisone has been suggested to prevent stricture. Dilatation of the oesophagus may begin on the fourth or fifth day.

ALKALIS (AMMONIA, CAUSTIC SODA, CAUSTIC POTASH)

Never lavage in corrosive poisoning and never use emetics. Analgesics may be given as required. Oesophagoscopy shortly after admission to determine if bum is present. The treatment of choice is dilution with water or milk.

ALUMINIUM PHOSPHIDE

Phosphine gas is released from tablets of aluminium phosphide in presence of atmospheric moisture. Severe pulmonary irritation and pulmonary oedema are the main toxic effects of phosphine. It can also produce hepatic and myocardial injury. Breathlessness and cyanosis may develop up to 36 hours after exposure. Death may occur. Patients are kept under observation and those who develop oedema are given oxygen. Assisted ventilation may be necessary in the most serious cases.

ASPIRIN (SALICYLATE)

Activated charcoal should be given in repeated doses (50 g 4 hourly). Fluid and electrolyte replacement to maintain normal potassium concentration should be done. Ensure that urine is alkaline by giving sodium bicarbonate. The most effective treatment is haemodialysis.

ATROPINE AND BELLADONNA

Physostigmine, an anticholinesterase drug which prolongs and intensifies the acetylcholine is used. Physostigmine crosses the blood-brain barrier and therefore, reverses both the central and peripheral action of anticholinergic drugs

such as atropine, belladonna, certain antihistaminics and tricyclic antidepressants notably amitriptyline.

Dose: The basic adult dose of this is 2 mg I.M. or I.V. or subcutaneously, followed by 1 mg every 20 to 30 minutes until the desired effect is obtained (up to 4 mg). The effect lasts less than an hour; therefore the dose should be repeated.

BARBITURATES

Treatment for overdose of this is by stomach washout. If the patient is in coma, an intratracheal tube should be inserted to prevent aspiration and for assisted respiration. Blood gases and serum electrolytes should be closely monitored. Haemodialysis in severe cases. The majority of patients survive with supportive measures alone. Pulmonary complications (oedema, bronchopneumonia) and renal failure are likely fatal complications of severe poisoning.

BENZODIAZEPINES

Benzodiazepines have a large therapeutic index. Management consists of simple supportive treatment in most cases.

CARBAMATE INSECTICIDES

The carbmate insecticides propoxur (Baygon), aldicarb produce symptoms closely resembling those of oganophosphates. They are reversible acetylcholinesterase inhibitors. Atropine is given in the treatment but pralidoxime is not recommended for the treatment.

CARBON MONOXIDE

Fresh air and 100% oxygen inhalations will be adequate. Supplementary care includes correction of hypotension and acidosis. The patient should be admitted because complications may arise after a delay of hours or days. Cerebral oedema should be anticipated.

CHLORINATED HYDROCARBON INSECTICIDES

Includes DDT, BHC (benzene hexachloride), chlordane, aldrin, dieldrin, gamma BHC, heptachlor and many others. They may be absorbed percutaneously, through the lungs or bowel. All act primarily on CNS and result in excitation. For convulsions diazepam drip until excitability and tremors controlled. Avoid milk and oils as these facilitate absorption. Renal tubular damage and hepatocellular necrosis may occur.

INSECT STINGS

Stings from ants, bees and wasps cause local pain and swelling but seldom cause severe toxicity. The stings from these insects are usually treated by cleansing the area, applying a cooling lotion and giving an antihistamine orally.

Bee stings should be removed by scraping them off with a finger nail or knife before cleansing the area. Anaphylactic reactions require treatment with adrenaline.

KEROSENE

Gastric lavage is contraindicated. Pulmonary oedema if occurs, should be treated with furosemide (25-100 mg intravenously) or by mechanical ventilation. Antibiotic treatment is unnecessary unless bacterial pneumonia develops.

METHANOL

Symptomatic support of respiration and circulation is augmented by correction of metabolic acidosis with intravenous bicarbonate infusion and control of seizures with diazepam. Ethanol inhibits metabolism of methanol. Ethanol may be given orally or intravenously. Dialysis is recommended if more than 30 ml of (pure) methanol is ingested.

MORPHINE AND OTHER OPIOIDS

Naloxone antagonizes the action of morphine and others such as pethidine, codeine, diphenoxylate, propoxyphene and pentazocine. Within 1-2 minutes after an intravenous injection there is an improvement in respiration, the pin-point pupils return to normal and the patient awakes. The action lasts for 1 to 4 hours, therefore the dose should be repeated to prevent relapse.

The chief advantage of naloxone is that it has no agonist action of its own. Therefore if it is given in error to a patient who has not taken opioid it will do no harm.

Dose: The basic adult dose is 0.4-2 mg I.V. Repeat every 2 to 3 minutes to a maximum of 10 mg.

MUSHROOM

Symptomatic and supportive treatment is the therapeutic mainstay. Because the severity of toxicity and treatment strategies for poisoning depend on species ingested, their identification should be sought.

ORGANOPHOSPHORUS INSECTICIDES

All inhibit cholinesterase, resulting in symptoms of parasympathomimetic overactivity. Keep airway clear. Must repeatedly aspirate secretions and if necessary do intubation and artificial ventilation. Atropine 2-4 mg every 15 to 30 minutes until symptoms under control and then less frequently ("toxic" dose of atropine must be given). Atropine is very effective in reducing tracheo-bronchial secretions and bronchial constriction and is not effective in decreasing central respiratory depression. It is ineffective against action of insecticides on peripheral neuromuscular junction and paralysis. **Pralidoxime (PAM)**, a cholinesterase reactivator is very effective at skeletal neuromuscular junctions to reduce paralysis. It is not very effective at autonomic effector sites or the CNS.

Adverse effects and cautions: The drug may cause tachycardia, headache, drowsiness, respiratory depression. The drug has few beneficial effects if given more than 48 hours after insecticide ingestion.

Dose: Pralidoxine, a dose of 30 mg/kg diluted to 10-15 ml with water for injection, by slow intravenous injection over 5-10 minutes followed by 8 mg/kg/hour by infusion until clinical recovery.

PARACETAMOL

Ingestion of single dose as low as 7.5 g in adults or 150 mg/kg in a child can cause severe hepatocellular necrosis and less frequently renal tubular necrosis. Serum paracetamol levels in excess of 200 mg/litre at 4 hours and 25 mg/litre at 16 hours post ingestion often results in hepatotoxicity. Activated charcoal may be given. Antidotes such as methionine and ***acetylcysteine*** protects the liver if given within 16 hours of paracetamol ingestion.

Adverse effects and cautions: Adverse effects of acetylcysteine are rashes and anaphylaxis.

Dose: Acetylcysteine, intravenously 150 mg/kg in 200 ml glucose 5% over 15 minutes, then 50 mg/kg in 500 ml glucose 5% over 4 hours, then 100 mg/kg in 1 litre glucose 5% over 16 hours.

TRICYCLIC ANTIDEPRESSANTS

Poisoning with tricylic antidepressants such as imipramine, amitriptyline is dangerous. Give activated charcoal, sodium bicarbonate (100 ml 4.2% solution) over about 15-20 minutes for cardiac arrhythmias. Direct current cardioversion may sometimes be required. Sustained seizures should be treated with diazepam.

ZINC PHOSPHIDE

It reacts with water and hydrochloric acid in the stomach to produce phosphine, which produces severe gastro-intestinal irritations. Hepatic necrosis may develop after initial phase. Patients are kept under observation.

Chapter – Eleven

Drugs Used in Malignant Disease and Immunsuppressives

11.1 Immunosuppressive drugs

Drugs in this group are used in organ transplant recipients and to treat chronic inflammatory and auto-immune diseases. Because of their toxic effects on the bone marrow it is necessary to do periodic blood counts. Furthermore patients on such drugs are liable to suffer from other atypical infections e.g. fungal infections.

Drugs in this group include azathioprine, ciclosporin, tacrolimus and corticosteroids.

AZATHIOPRINE

It is in use as an immunosuppressant to treat a number of auto-immune conditions when corticosteroid therapy alone has not been effective. It is also used in transplant recipients. Inside the body this drug is metabolised to mercaptopurine.

Indications: *see* notes above; rheumatoid arthritis.

Adverse effects and cautions: hepatotoxicity can occur with this drug. Its major toxic effect is myelosuppression. The other adverse effects include vomiting, diarrhoea, fever, rash.

Dose: Auto-immune conditions, by mouth 1-3 mg/kg daily, adjust according to response (withdrawal if no improvement in 3 months).

Suppression of transplant rejection, initially, by mouth or intravenously (over at least 1 minute and followed by 50 ml sodium chloride solution) up to 5mg/kg; then l-4mg/kg daily according to response.

Note: Intravenous injections is alkaline and very irritant

Preparation available

Azathioprine Tablets: Each tablet containing 25 mg and 50 mg of azathioprine is usually available. Azathioprine tablets should be protected from light.

Azathioprine Injection: Each vial containing 50 mg of azathioprine (as sodium salt), in the form of powder for reconstitution, is usually available.

CICLOSPORIN

It is a potent immunosuppressant which is virtually non-myelotoxic but is markedly nephrotoxic. The dose of drug is adjusted according to plasma-ciclosporin concentrations and renal function.

Indications: to prevent organ and tissue rejection in transplant recipients, rheumatoid arthritis, nephrotic syndrome.

Adverse effects and cautions: dose-related and reversible increases in serum-creatinine and urea during first few weeks, hypertension (especially in heart transplant patients), hepatic dysfunction, gingival hypertrophy, burning sensation in hands and feet (usually during first week), hyperkalaemia, hyperglycaemia, oedema, tremor, pancreatitis, increased susceptibility to infections, hypertrichosis.

The drug should be used with caution in pregnancy, breast-feeding. Kidney function, liver function, blood pressure, serum potassium should be monitored.

Dose: Organ transplantation used alone, ADULT and CHILD over 3 months 10-15 mg/kg by mouth 4-12 hours before transplantation followed by 10-15 mg/kg daily for 1-2 weeks postoperatively, then reduced gradually to 2-6 mg/kg daily for maintenance.

Nephrotic syndrome, by mouth, 5 mg/kg daily in 2 divided doses; CHILD 6 mg/kg in 2 divided doses; maintenance treatment reduce to lowest effective dose according to proteinuria and serum creatinine measurements.

TACROLIMUS

It produces more neurotoxicity and nephrotoxicity than ciclosporin.

Indications: primary immunosuppression in liver and kidney allograft recipients and allograft rejection resistant to conventional immunosuppressive regimens.

Advese effects and cautions: *see* under ciclosporin. It also produces cardiomyopathy, visual and hearing abnormalities.

The concurrent use should be avoided with ciclosporin.

Dose: Renal transplantation, starting within 24 hours of transplantation, by mouth 150-300 micrograms/kg daily in 2 divided doses.

Preparation available

Tacrolimus Capsules: Each capsule containing 500 micrograms and 1 mg of tacrolimus is usually available.

INTERFERON BETA

Interferons (IFNs) are potent cytokines that possess antiviral, immunomodulating and antiproliferative activities. These proteins are synthesised by host cells in response to various inducers and, in turn, cause biochemical changes leading to an antiviral state in cells.

Inductions: multiple sclerosis.

Adverse effects and cautions: irritation at injection site, influenza-like symptoms (fever, chills, myalgia), nausea, vomiting, hypersensitivity reactions, menstrual disorders.

He drug is contra-indicated in patients with history of severe depressive illness, inadequately controlled epilepsy or decompensated hepatic impairment, pregnancy, breast-feeding.

The drug should be used with caution in cardiac disorders or myelosuppression.

11.2 Cytotoxic drugs

Limitation of this group of drugs is that they not only affect the neoplastic cells but also have potential to damage normal tissue. This group has alkylating agents, antimetabolites, and others.

BLEOMYCIN

It is an antineoplatic antibiotic and is used against solid tumours and lymphomas.

Indications: Hodgkin's disease and non-Hodgkin's lymphomas, carcinomas of the head, neck, larynx, cervix, penis, testicles, malignant effusions.

Adverse effects and cautions: dermatological toxicity is common, increased pigmentation in those areas subject to friction or pressure, chills and fever, and progressive pulmonary fibrosis. It causes no bone-marrow suppression.

The drug is contraindicated in pregnancy and breast-feeding.

The drug should be used with caution in renal impairment.

Preparation available

Bleomycin Injection: Injection containing 15 000 international unit of bleomycin (as sulphate) per ampoule is usually available.

BUSULFAN

Busulphan

This is an alkylating agent.

Indications: chronic myeloid leukaemia, haematopoietic stem-cell transplantation in adults.

Adverse effects and cautions: thrombocytopenia, leucopenia, anaemia, hyperuricemia, glossitis, skin hyperpigmentation and hepatitis. The drug is highly toxic with a low therapeutic index.

The drug is contraindicated during pregnancy and breast-feeding.

Dose: Chronic myeloid leukaemia, induction of remission, 60 micrograms/kg to maximum 4 mg daily; maintenance, 0.5- 2 mg daily.

Preparation available

Busulfan Tablets: Each tablet containing 0.5 mg and 2 mg of busulfan is usually available. Busulphan tablets are coated.

CALCIUM FOLINATE

Leucovorin Calcium

It is used to counteract the folate-antagonist action of methotrexate. It does not counteract the antibacterial activity of trimethoprim.

Indications: *see* dose.

Adverse effects and cautions: allergic reactions, rarely pyrexia after parenteral administration.

Dose: As an andidote to methotrexate (started 24 hours after the beginning of methotrexate infusion) in general up to 120 mg in divided doses over 12-24 hours by intramuscular or intravenous injection or infusion, followed by 12-15 mg intramuscularly or 15 mg by mouth every 6 hours for the next 48-72 hours.

Suspected methotrexate over dosage, immediate administration at a rate not exceeding 160 mg/minute in a dose equal or higher dose of methotrexate.

Preparation available

Calcium Folinate Tablets: Each tablet containing 15 mg of folinic acid (as calcium salt) is usually available.

Calcium Folinate Injection: Injection containing 3 mg folinic acid per ml (as calcium salt) is usually available.

CHLORAMBUCIL

This drug, derivative of nitrogen mustard, also possesses some immunosuppressive activity, principally due to its suppression of lymphocytes. The drug is slowest acting and generally least toxic of presently available nitrogen mustard derivatives. This drug is used in chronic lymphocytic leukaemia, Hodgkin's disease and non-Hodgkin's lymphoma.

Indications: *see* notes above.

Adverse effects and cautions: bone-marrow suppression, rashes and Stevens-Johnson syndrome.

The drug is contraindicated in pregnancy and breast-feeding.

The drug should be used with caution in severe hepatic impairment and renal impairment.

Dose: Non-Hodgkin's lymphoma used alone, usually 100-200 micrograms/kg daily for 4-8 weeks.

Chronic lymphocytic leukaemia, initially 150 micrograms/kg daily; maintenance 100 micrograms/kg daily.

Preparation available

Chlorambucil Tablets: Each tablet containing 2 mg and 5 mg of chlorambucil is usually available. Chlorambucil tablets are coated.

CISPLATIN

The drug is used alone or in combination for the treatment of testicular, lung, bladder, head and neck, cervical and ovarian carcinoma.

Indications: *see* notes above.

Adverse effects and cautions: nephrotoxicity, nausea and vomiting, ototoxicity, hypokalaemia, hypocalcemia, peripheral neuropathy, leukopenia, thrombocytopenia and anaemia.

Monitoring renal function is essential.

The drug is contraindicated during pregnancy and breast-feeding.

The drug should be used with caution in renal impairment.

Dose: Usually given 20 mg per m^2 body surface, per day for five days, intravenously.

Preparation available

Cisplatin Injection: An injection containting 10 mg of cisplatin per vial is usually available.

CYCLOPHOSPHAMIDE

This is an alkylating agent. It is indicated in malignant lymphomas like adenocarcinoma of ovary, breast cancer, Hodgkin's disease, lymphocytic lymphoma, Burkitt's lymphoma; multiple myeloma. Administration is by oral and intravenous routes. However it is inactive until it has been metabolised by the liver. About 14% of the drug given is excreted unchanged in the urine.

Indications: *see* notes above.

Adverse effects and cautions: important adverse effects are leucopenia which is ordinarily used as a guide to therapy, thrombocytopenia, anaemia, anorexia, nausea, vomiting and alopecia. These disorders are always reversible when therapy is interrupted.

Cyclophosphamide should be administered with caution to patients with impaired hepatic or renal function.

The drug is contraindicated during pregnancy and breast-feeding.

Preparation available

Cyclophosphamide Injection: Each vial containing 200 mg, 500 mg and 1 g of cyclophosphamide, in the form of powder for reconstitution, is usually available. It is prepared by dissolving the content of the vial in the requisite amount of water for injection immediately before use.

Cyclophosphamide Tablets: Each tablet containing 50 mg of cyclophosphamide is usually available.

CYTARABINE

It is an antimetabolite. This drug is used principally as a component of chemotherapeutic regimens for chronic myeloid leukaemia, acute lymphoblastic leukemia and non-Hodgkin's lymphomas.

Indications: *see* notes above.

Adverse effects and cautions: myelosuppression manifested by leukopenia, thrombocytopenia and anaemia, nausea and vomiting, anorexia, diarrhoea, fever, rash and alopecia.

The drug should be used with caution in hepatic impairment.

The drug is contraindicated in pregnancy and breast-feeding.

Preparation available

Cytarabine Injection: Injection containing 100 mg, 500 mg and 1 g of cytarabine is usually available.

DACARBAZINE

It is used in metastatic melanoma, and combination therapy in soft tissue sarcomas and Hodgkin's disease.

Indications: *see* notes above.

Adverse effects and cautions: myelosuppression, severe nausea and vomiting, liver nacrosis.

Preparation available

Dacarbazine Injection: Each vial containing 100 mg, 200 mg and 500 mg of dacarbazine (as citrate) powder for reconstitution is usually available.

DACTINOMYCIN

Actinomycin-D

It is an antineoplastic antibiotic and is used for the treatment of paediatric neoplasia like Wilm's tumour, rhabdomyosarcoma and Ewing's sarcoma.

Indications: *see* notes above.

Adverse effects and cautions: leucopenia, thrombocytopenia, anaemia, anorexia, vomiting, proctitis, alopecia, local necrosis and erythema.

The drug is contraindicated in pregnancy and breast-feeding.

Preparation available

Dactinomycin Injection: Each vial containing 500 micrograms of dactinomycin is usually available. The injection is prepared by dissolving the content of a sealed container in the requisite amount of water for injection immediately before use.

DOXORUBICIN

It is very effective antineoplastic antibiotic in use against acute leukaemias, lymphomas and other solid tumours.

Indications: *see* notes above.

Adverse effects and cautions: nausea and vomiting, myelosuppression and alopecia. Cardiomyopathy, cardiac arrhythmias and facial flushes.

The drug should be used with caution in hepatic impairment.

Its use during pregnancy and breast-feeding should be avoided.

Dose: The recommended dose is 60-75 mg per square meter of the body surface.

Preparation available

Doxorubicin Hydrochloride Injection: Each vial containing 10 mg doxorubicin hydrochloride in sually available.

FLUOROURACIL

This fluorinated pyrimidine analogue is converted inside the body to the active metabolites. It can be given orally but absorption is unpredictable. It is given in the treatment of carcinoma of breast and gastro-intestinal tract. It can be used topically for certain malignant and pre-malignant skin conditions.

Indications: *see* notes above.

Adverse effects and cautions: anorexia, nausea, vomiting stomatitis, proctitis, depression of bone marrow and alopecia.

The drug has a very low therapeutic index.

Safe use of fluorouracil during pregnancy and breast-feeding has not been established.

Dose: By mouth, maintenance 15 mg/kg weekly; maximum in one day 1 g.

Preparation available

Fluorouracil Injection: An injection containing 50 mg/ml of fluorouracil (as sodium salt) is usually available. Fluorouracil injection should be protected from light and stored at a temperature of 15- 25°.

Fluorouracil Capsules: Each capsule containing 250 mg of fluorouracil is usually available.

LOMUSTINE

It is an alkylating drug and is given by mouth. It is mainly used to treat Hodgkin's disease and certain solid tumours. Bone marrow toxicity is delayed, and the drug is given at intervals of 4 to 6 weeks. Permanent bone marrow damage may occur with prolonged use. Nausea and vomiting are common.

Indications, adverse effects and cautions: *see* notes above.

Dose: used alone, 120-130 mg/m^2 body surface every 6-8 weeks.

Preparation available

Lomustine Capsules: Each capsule containing 10 mg of lomustine is usually available.

MELPHALAN

It is also an alkylating agent and is used to treat multiple myeloma and advanced ovarian adenocarcimoma and advanced breast cancer. It is usually given by mouth, but may also be given intravenously. Marrow toxicity, pulmonary fibrosis are importat adverse effects.

Indications, adverse effects and cautions: *see* notes above.

Dose: Advanced breast cancer, by mouth 150 micrograms/kg daily for 5-6 days, repeated every 6 weeks.

Preparation available

Melphalan Tablets: Each tablet containing 2 mg and 5 mg of melphalan is usually available.

Melphalan Injection: Powder for injection containing 50 mg of malphalan, as hydrochloride, is usually available.

MERCAPTOPURINE

This is also an antimetabolite. It is indicated in the treatment of acute leukaemias.

Indications: *see* notes above.

Adverse effects and cautions: leucopenia, anaemia, thrombocytopenia, hepatotoxicity, nausea and vomiting.

The drug has low therapeutic index. The drug is contraindicated in pregnancy and breast-feeding.

The drug should be used with cautions in renal or hepatic impairment.

Dose: Initially 2.5 mg /kg daily.

Preparation available

Mercaptopurine Tablets: Each tablet containing 50 mg of mercaptopurine is usually available. Mercaptopurine tablets should be protected from light.

METHOTREXATE

This is also an antimetabolite. It is used for the treatment of acute lymphoblastic leukaemia in children, choriocarcinoma, non-Hodgkin's lymphoma, carcinoma of breast, head and neck, lung, psoriasis and rheumatoid arthritis.

Indications: see notes above.

Adverse effects and cautions: ulcerative stomatitis, leucopenia, thrombocytopenia, nausea, abdominal distress, anaemia, hepatotoxicity, erythematous rashes and headache.

The drug is contraindicated in pregnancy and breast-feeding.

The drug should be used with caution in hepatic or renal impairment.

Dose: By mouth, leukaemia in children (maintenance) 15 mg/m^2 weekly in combination with other drugs.

Preparation available

Methotrexate Injection: Injection containing 25 mg per ml of methotrexate is usually available. Methotrexate injection should be protected from light. This injection is not intended for intrathecal injection.

Methotrexate Tablets: Each tablet containing 2.5 mg of methotrexate is usually available.

MITOMYCIN

This is an antineoplastic antibiotic. The drug is used in the treatment of upper gastro-intesinal and breast cancers.

Indications: *see* notes above.

Adverse effects and cautions: myelosuppression manifested by thrombocytopenia and leukopenia; nausea and vomiting, mouth ulcers, alopecia, pain on injection, thrombophlebitis, renal toxicity and lung firbosis. It causes delayed bone-marrow toxicity and therefore usually administered at 6-weekly intervals.

Safe use of drug in pregnancy and breast-feeding has not been established.

Dose: By intravenous infusion usually at 6-weekly.

Preparation available

Mitomycin Injection: Injection containing 2 mg and 10 mg of mitomycin is usually available.

PACLITAXEL

It is a member of taxane group of drugs.

Indications: treatment of metastatic ovarian, breast, lung and head and neck cancers.

Adverse effects and caution: neutropenia, myalgias, mucositis, hypersensitivity, asymptomatic bradycardia, peripheral neuropathy.

The drug is contraindicated in pregnancy, breast-feeding, severe hepatic impairment.

Preparation available

Paclitaxel Concentrate for Intravenous Infusion: Each vial containing 6 mg/ml of paclitaxel is usually available.

PROCARBAZINE

The drug is used in the treatment of Hodgkin's disease, non-Hodgkin's lymphomas. Various regimens have been used in combination therapy.

Indications: *see* notes above.

Adverse effects and cautions: bone-marrow depression, severe nausea and vomiting, paresthesia, neuropathies, mental depression, ascites, oedema and cough.

The drug should be used with caution in liver or renal impairment.

The drug should not be used in pregnancy and breast-feeding.

Drug interactions: use of alcohol may result into disulfiram like reaction.

Dose: Used alone, intially, 50 mg daily, increased by 50 mg daily to 250-300 mg daily in divided doses; maintenance (on remission) 50-150 mg daily to cumulative total of at least 6 g.

Preparation available

Procarbazine Hydrochloride Capsules: Each tablet containing 50 mg of procarbazine, as hydrochloride, is usually available.

VINBLASTINE

It is used in disseminated Hodgkin's disease and non-Hodgkin's lyphomas, advanced carcinoma of testes, Kaposi's sarcoma.

Indications: *see* notes above.

Adverse effects and cautions: leucopenia, thrombocytopenia, nausea and vomiting, anorexia, diarrhoea, constipation, neurotoxicity occasionally, especially with high doses or prolonged therapy, but less frequently than with vincristine.

It is contraindicated during pregnancy and breast-feeding.

The drug should be used with caution in hepatic impairment.

Preparation available

Vinblastine Injection: Injection containing 1 mg/ml of vinblastine sulphate in 10 ml vial is usually available. Vinblastine injection is prepared by dissolving the content of vial in the requisite amount of sodium chloride solution.

Vinblastine injection should be used immediately after preparation but in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

VINCRISTINE

This is a Vinca alkaloid and is used in acute lymphoblastic leukaemia, Wilm tumour, Hodgkin's and non-Hodgkin's lymphomas, Ewing sarcoma, breast and lung cancer.

Indications: *see* notes above.

Adverse effects and cautions: Neurotoxicity mostly peripheral neuropathy and CNS toxicity, alopecia, nausea, vomiting and diarrhoea.

Safe use of vincristine during pregnancy and breast-feeding has not been established.

The drug should be used with caution in hepatic impairment and neuromuscular disease.

Preparation available

Vincristine Injection: Injection containing 1 mg/ml of vincristine sulfate in 1ml, 2 ml and 5 ml vial is usually available. Vincristine injection is prepared by dissolving the vincristine sulphate powder for injection in the requisite amount of sodium chloride solution. Vincristine injection should be used immediately after preparation but, in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instruction. Vincristine sulfate for injection should be stored at a temperature of 2-8°.

11.3 Hormones and antihormones

11.3.1 Corticosteroids

Chief use is in acute lymphoblastic leukaemia, Hodgkin's disease, non-Hodgkin's lymphomas and haematological malignancies.

Prednisolone is widely used in oncology, though no evidence for its therapeutic superiority over dexamethasone or hydrocortisone has been found. (*see* section 8.1, adrenal hormones)

11.3.2 Sex Hormones

Some of the neoplasms of prostate, endometrium and breast are hormone dependent.

The oestrogens used are stilboestrol and ethinylestradiol. The progestogens like norethisterone, medroxyprogesterone are used in endometrial cancer.

(*see* sections, 8.3, oestrogens and 8.4, progestogens)

11.3.3 Hormone antagonist

TAMOXIFEN

It is an antioestrogen and is used in breast cancer.

Indications: early breast cancer in peri-menopausal, pre-menopausal and post-menopausal women, advanced breast cancer in post-menopausal women, anovulatory infertility.

Adverse effects and cautions: hot flushes, nausea, vomiting, menstrual irregularities, rash, vaginal bleeding and vaginal discharge and headache are reported. Hypercalcemia may occur during initial tamoxifen therapy in patients with bone metastases.

The drug is contraindicated in pregnancy and should be used with caution in breast-feeding.

Dose: Breast cancer, 20 mg daily as a single dose or in 2 divided doses.

Anovulatory infertility, 20 mg daily on second to fifth day of cycle; if necessary increased to 40 mg daily then 80 mg daily for subsequent courses; if cycle irregular, start initial course on any day, with subsequent course starting 45 days later or an second day of cycle if menstruation occurs.

Preparation available

Tamoxifen Tablets: Each tablet containing 10 mg and 20 mg of tamoxifen is usually available. Tamoxifen tablets should be protected from light.

11.4 Medicines used in palliative care

Palliative care includes both pain relief and symptomatic relief of conditions including anorexia, constipation, nausea, vomiting, insomnia and dyspnoea etc.

Most patients with cancer pain can obtain effective relief if treated correctly. Pain is best treated with a combination of drug and non-drug measures. Some types of pain respond well to a combination of a non-opioid and opioid analgesic. Neuropathic pain often show little response to non-opioids and opioids, but often respond to tricyclic antidepressants e.g. amitriptyline and anticonvulsants like carbamazepine and valproic acid.

Cancer patients often have fears and anxieties and may become depressed and these patients may need an appropriate drug in addition to an analgesic.

The first step to reduce pain is to give a non-opioid analgesic such as aspirin, paracetamol or ibuprofen. If this does not relieve the pain, an opioid such as codeine should be added. If this combination fails to relieve pain, morphine should substitute it.

The range for oral morphine can be as little as 5 mg to more than 100 mg every 4 hours. Sustained release morphine tablets are available for dosing every 12 hours.

Chapter - Twelve

Drugs Affecting Nutrition and Blood

12.1 Anti-anaemics

12.1.1 Iron

A common form of anaemia in Nepal is due to lack of iron. Such anaemia may be due to blood loss, increased requirement, inadequate intake or occasionally malabsorption. Ferrous iron is better absorbed than ferric. They however can cause gastro-intestinal upsets such as nausea, abdominal pain, constipation or diarrhoea. These side effects are reduced by giving iron with food or by reducing the dose or by changing to a preparation containing less elemental iron. Infants, especially those who are premature or those who are weaned late, may suffer from iron deficiency and supplement of iron should therefore be given.

The treatment with oral iron is continued until the haemoglobin is normal and then for a further three months, to completely replenish stores. Ferrous sulfate in tablet form is the preparation of choice amongst the oral iron preparations. Iron is given routinely in pregnancy because of the increased requirement due to the presence of the foetus. Addition of Vitamin C, to iron preparations may improve the absorption of iron, but the extra cost of the preparation does not justify the slightly shorter time taken to replenish stores.

There is no justification for the inclusion of other ingredients such as vitamin B complex (except folic acid) for pregnant women.

FERROUS FUMARATE

200 mg of ferrous fumarate contains 65 mg of elemental iron.

Indications: iron deficiency anaemia.

Adverse effects and cautions: diarrhoea or constipation, nausea, epigastric pain and heart bum.

Drug interactions: concurrent administration of antacids and tetracyclines with oral iron preparation will inhibit absorption of tetracyclines and iron.

Dose: Prophylaxis, 200 mg daily before food.

Treatment, 400-600 mg daily, in divided doses, before food.

FERROUS GLUCONATE

300 mg of ferrous gluconate contains 35 mg of iron.

Indications, adverse effects, cautions and drug interactions: *see* under ferrous fumarate.

Dose: Prophylaxis, 600 mg daily before food.

Treatment, 1.2-1.8 g daily in divided doses before food.

FERROUS SUCCINATE

100 mg of ferrous succinate contains 35 mg of iron.

Indications, adverse effects, cautions and drug interactions: *see* under ferrous fumarate.

Dose: Prophylaxis, 200 mg daily.

Treatment, 400-600 mg daily in divided doses.

FERROUS SULFATE

300 mg of ferrous sulfate contains 60 mg of elemental iron and 200 mg of dried ferrous sulfate contains 65 mg of elemental iron.

Indications, adverse effects, cautions and drug interactions: *see* under ferrous fumarate.

Dose: Prophylaxis, 200 mg dried ferrous sulfate daily after food.

Treatment, 400-600 mg daily in divided doses after food.

IRON AND FOLIC ACID

The preparations are used during pregnancy in women who are at risk of developing iron and folic acid deficiency.

Preparation available: *see* folic acid.

IRON DEXTRAN INJECTION

It is recommended only when oral administration has been found unsatisfactory or impossible. It contains 5% w/v of iron.

Indications: iron deficiency anaemia.

Adverse effects and cautions: nausea, vomiting, abdominal pain, arthralgia, fever, urticaria, pain, anaphylactoid reactions, headache and hypotension.

The drug should be used with caution in pregnancy and patients with hepatic or renal impairment.

The drug is contraindicated in allergic disorders including asthma, infection and active rheumatoid arthritis.

Preparation available

Iron Dextran Injection: A complex of ferric hydroxide with dextran, containing 50 mg of elemental iron per ml is usually available.

12.1.2 Vitamins

For megaloblastic anaemias of pregnancy, infancy, antiepileptics, nutritional and certain malabsorption syndrome, folic acid will have to be given. Once Vitamin B_{12} has been excluded as the cause of megaloblastic anaemia, folic acid is given. It should never be administered without vitamin B_{12} in undiagnosed anaemia.

VITAMIN B_{12}

Disorder due to vitamin B_{12} deficiency result more commonly from dietary deficiency or lack of gastric intrinsic factor.

Vitamin B_{12} will have to be given by injection for pernicious anaemia and also for other deficiency states of this vitamin occurring in conditions such as resection of stomach or lower ileum, and malabsorption.

Hydroxocobalamin is used more commonly because it is retained in the body longer than **cyanocobalamin**.

Indications: pernicious anaemia and other macrocytic anaemia.

Adverse effects and cautions: rarely diarrhoea, itching, urticaria, headache, nausea.

Dose: Cyanocobalamin, by mouth, vitamin B_{12} deficiency of dietary origin, 50-150 micrograms or more daily taken between meals, CHILD 25-50 micrograms twice daily.

By intramuscular injection, initially 1 mg repeated 10 times at intervals of 2-3 days, maintenance 1 mg every month.

Hydroxocobalamin, pernicious anaemia and other macrocytic anaemias without neurological involvement, by intramuscular injection, initially 1 mg repeated 5 times at intervals of 2 days, then 1 mg every 3 months; CHILD dosage as for adult.

Preparation available

Cyanocobalamin Injection: Injection containing 1 mg cyanocobalamin per ml is usually available.

Cyanocobalamin Tablets: Each tablet containing 50 micrograms of cyanocobalamin is usually available.

Hydroxocobalamin Injection : Injection containing 1 mg hydroxocobalamin is usually available.

FOLIC ACID

Water soluble and obtained from animal and vegetable sources e.g. green vegetables, liver, kidney are the best sources. Milk, egg and meat are poor in folic acid. Considerable losses occur when vegetable are boiled for longer time.

Deficiency of this vitamin causes megaloblastic anaemia especially in pregnancy and infancy, when requirements are increased. An adequate intake of folic acid before conception and during early pregnancy (first trimester) reduces the risk of neural tube defects in babies. It must never be given without vitamin B_{12} in Addisonian or other B_{12} deficiency anaemias because it can aggravate or precipitate the neurological features of Vitamin B_{12} deficiency.

Indications: folic acid deficiency anaemia, prevention of neural tube defects in pregnancy.

Adverse effects and cautions: rareley rash, itching and bronchospasm.

It should not be given in cases of undiagnosed megaloblastic anaemia without vitamin B_{12} as there is risk of precipitating subacute combined degeneration of the spinal cord.

Dose: Initially, 5 mg daily for 4 months; maintenance, 5 mg every 1-7 days depending on underlying disease; CHILD up to 1 year, 500 micrograms/kg daily, over 1 year as adult dose.

Prevention of neural tube defects, 400-500 micrograms daily before conception and during the first 12 weeks of pregnancy.

Preparation available

Folic acid Tablets: Each tablet containing 5 mg of folic acid is usually available.

Ferrous Sulfate and Folic Acid Tablets: Each tablet containng ferrous sulfate equivalent to 60 mg of elemental iron and 400 micrograms of folic acid is usually available.

12.1.3 Erythropoietin

It is one of the growth factors responsible for erythropoiesis. In its absence, severe anaemia is invariably present.

Recombinant human erythropoietins (epoetin alfa and beta) are used. The clinical efficacy of epoetin alfa and epoetin beta is similar.

Indications: anaemia associated with chronic renal failure on haemodialysis, anaemia associated with chronic renal failure in adults on peritoneal dialysis, anaemia in adults receiving cancer chemotherapy.

Adverse effecs and cautions: headache, increase in blood pressure or aggravation of hypertension, increase in platelet count (thrombocytosis rare), thromboembolic events, hypertensive crisis with encephalopathy-like symptoms and generalised tonic-clonic seizures, pure red cell aplasia, hyperkalaemia.

The drug is contraindicated in uncontrolled hypertension, pure red cell aplasia.

The drug should be used with caution in patients with inadequately treated or poorly controlled blood pressure, epilepsy, malignant disease, chronic liver failure, pregnancy, breast-feeding.

Subcutaneous injection is contraindicated in patients with chronic renal failure.

Dose: Severe symptomatic anaemia of renal origin in adults with renal insufficiency not yet on dialysis, by intravenous injection over 1-5 minutes, initallly 50 units/kg 3 times weekly increased according to response in steps of 25 units/kg 3 times weekly at intervals of at least 4 weeks; maintenance dose, 17-33 units/kg 3 times weekly; maximum 200 units/kg 3 times weekly.

12.2 Blood products and plasma substitutes

ALBUMIN, HUMAN

It is prepared from whole blood, contains soluble proteins and electrolytes but no clotting factors, blood group antibodies or plasma cholinesterases. The protein contains at least 95% albumin.

Indications: severe hypoalbuminaemia associated with low plasma volume and generalised oedema where salt and water restriction with plasma volume expansion are required, adjunct in the treatment of hyperbilirubinaemia by

exchange transfusion in new born, acute or sub-acute loss of plasma volume (burns, trauma, pancreatitis).

Adverse effects and cautions: hypersensitivity reactions (including anaphylaxis) with nausea, vomiting, increased salivation, hypotension, fever.

It should be given with caution to patients with history of cardiac or circulatory diseases.

It is contraindicated in severe anaemia, cardiac failure.

Preparation available

Human Albumin Concentrated Solution: Solution containing 20% or 25% of protein derived from plasma, serum or normal placentas in 100 ml bottle is usually available. Protein contains at least 95% of albumin.

DEXTRAN

Dextran 40 and Dextran 70 are macromolecular substances. Dextran 40 differs from dextran 70 in molecular weight and indications. Dextran 70 is used for volume expansion. Dextran 40 is used to improve peripheral blood flow.

Indications: plasma expansion in cases of shock from bums or septicaemia; ischaemic disease of the limbs.

Adverse effects and cautions: mild urticarial reactions, rarely severe anaphylactoid reactions manifested by generalised urticaria, tightness of chest, wheezing, nausea, vomiting and hypothermia.

Patients should be closely observed during the first few minutes of infusion because severe reactions have been reported in some cases.

They are contraindicated in shock due to sodium and water depletion, burns or peritonitis of several days or weeks.

They should be used with caution in cardiac or liver or renal impairment. Dextrans may interfere with blood groups cross-matching or biochemical measurements.

Dose: Dextran 70, by intravenous infusion, after moderate to severe haemorrhage or shock of burn (initial 48 hours) 500-1000 ml rapidly followed by 500 ml later if necessary, total dose should not exceed 20 ml/kg during initial 24 hours, CHILD total dose should not exeeed 20 ml/kg.

Preparation available

Dextan Infusion: Low molecular weight dextran with average molecular weight 40 000 and 70 000 in 5% dextrose or 0.9% sodium chloride is usually available.

POLYGELINE

It is a gelatin (hydrolysed collagen) with an average molecular weight 30000.

Indications: low blood volume.

Adverse effects and cautions: *see* under dextran; increased risk of hyper-sensitivity.

Dose: By intravenous infusion, initially 500-1000 ml of a 3.5% solution.

Preparation available

Polygeline Intravenous Infusion: 3.5% solution of polygeline (gelatin derivative, average molecular weight 30 000), along with appropriate amount of Na+, K+,Ca2+ and Cl- in 500 ml bottle is usually available.

12.3 Vitamins and minerals

Vitamins are used for the prevention and treatment of specific deficiency states. They should not be used as dietary supplements.

The preparations containing vitamin A or D may be harmful if patients take more than the prescribed dose.

12.3.1 Vitamins

ASCORBIC ACID

Vitamin C

It is water soluble and found in fruits especially citrus, tomatoes and leafy green vegetables. Deficiency of this vitamin leads to scurvy. It has a low renal threshold and any excess above the plasma saturation level is rapidly excreted in the urine.

Indications: prevention and treatment of scurvy.

Adverse effects and cautions: nausea, vomiting, headache, heartburn and with large doses diarrhoea.

Dose: Prophylactic, 25-75 mg daily; therapeutic, not less than 250 mg daily in divided doses.

Preparation available

Ascorbic Acid Tablets: Each tablet containing 150 mg and 500 mg of ascorbic acid is usually available.

CHOLECALCIFEROL, ERGOCALCIFEROL, CALCITRIOL

Vitamin D

Vitamin D includes ergocalciferol (vitamin D_2) and cholecalciferol (vitamin D_3) which is formed in the skin after exposure to ultraviolet light. Vitamin D is fat soluble and its other sources are liver, fatty fish and egg yolk. Milk has a very small content of vitamin D. Deficiency of the vitamin causes osteomalacia and if growth is taking place, the clinical picture of rickets is produced. Minimum daily requirement for infants and children is 400 IU. Pregnant or lactating mothers need not less than 1000 IU/day. Calcitriol is the active form of vitamin D.

Indications: prevention and treatment of rickets, post-menopausal osteoporosis.

Adverse effects and cautions: loss of appetite, gastro-intestinal disturbances, sweating, headache, and thirst.

It is contraindicated in hypercalcaemia.

The drug should be used with caution in patients receiving high doses and in renal impairment.

Dose: Post-menopausal osteoporosis, calcitriol 250 nanograms twice daily (monitor plasma calcium concentration and creatinine).

NICOTINAMIDE

It is water soluble and found in yeast, meat, milk, fish, eggs and green vegetables. It is preferred to nicotinic acid as it does not cause vasodilatation.

Indications: treatment of pellagra.

Adverse effects and cautions: very rarely cause flushing, pruritus, nausea, vomiting, tachycardia and diarrhoea.

Dose: ADULT up to 500 mg daily in divided doses.

PYRIDOXINE HYDROCHLORIDE

Vitamin B_6

It is water soluble and found in liver, meat, yeast, legumes, vegetables and cereals. It is concerned with amino acid metabolism. The pyridoxal hydrochloride is converted into its active form pyridoxal phosphate which serves as a co-enzyme for various metabolic functions affecting proteins, carbohydrates and lipid. In patients receiving anti-tubercular therapy with isoniazid, the INH blocks the conversion of Vitamin 85 into its co-enzyme. Supplementation is therefore necessary to prevent INH induced peripheral neuritis.

Indications: deficiency states causing peripheral neuritis, patients on anti-tuberculous therapy with isoniazid, pre-menstrual symdrome.

Adverse effects and cautions: nausea, headache and paraesthesia.

Dose: Deficiency states, 20-50 mg up to 3 times daily.

Isoniazid neuropathy, prophylaxis 10 mg daily, therapeutic, 50 mg three times daily.

Premenstrual syndrome, 50-100 mg daily.

Preparation available

Pyridoxine Tablets: Each tablet containing 10 mg, 20 mg and 50 mg of pyridoxine hydrochloride are usually available.

RETINOL

Vitamin A

The natural vitamin A is a fat soluble oily liquid present in dairy products such as milk, butter, cream, fish liver oils and eggs. Deficiency of vitamin A is associated with xerophthalmia and increased susceptibility to infections.

Indications: prevention and treatment of vitamin A deficiency, prevention of complications of diarrhoea and measles in children.

Adverse effects and cautions: hypervitaminosis A on excessive administration.

The drug should be used with caution in pregnancy and breast-feeding.

Dose: Treatment of xerophthalmia, INFANTS (6-11 months) 100 000 units (3 drops) on diagnosis, repeated next day and then after one month; CHILD over one year and ADULT (except women of child-bearing age) 200 000 units on diagnosis, repeated next day and then after one month.

Prevention of vitamin A deficiency, CHILD age 6 months to 5 years, one dose every 6 months (for dose see treatment of xerophthalmia).

All measles cases, one dose on diagnosis, repeated next day.

Prolonged diarrhoea of more than 14 days, one dose on diagnosis.

Newly delivered mothers, one dose at delivery or in the first 6 weeks.

Severe malnutrition, one dose on diagnosis.

Preparation available

Retinol Capsules: Each capsule containing 200,000 units of vitamin A is usually available.

Retinol with DL-alpha-Tocopherol Soft Gel Capsules: Each soft gel capsule containing retinol (as palmitate) 200 000 units and DL-alpha-tocopherol or tocopheryl acetate 40 units is usually available.

RIBOFLAVIN

Vitamin B_2

It is water soluble and found in vegetables, milk, meat and eggs. Deficiency causes angular stomatitis and other cutaneous manifestations.

Indications: prophylaxis and treatment of deficiency.

Adverse effects and cautions: non-toxic, large doses may cause yellow discolouration of urine.

Dose: Treatment, ADULT and CHILD up to 30 mg daily in divided doses.

Prophylaxis, ADULT and CHILD, 1-2 mg daily.

THIAMINE HYDROCHLORIDE

Vitamin B_1

It is water soluble and obtained from whole grains, peas, beans, yeast and meat. Steaming or exposure to moist heat reduces the thiamine content of the foods. Deficiency of this vitamin causes beri-beri.

Indications: Beri-beri (dry/wet), Wemickes's encephalopathy.

Adverse effects and cautions: Non-toxic but may cause allergic reactions, sweating, weakness, feeling of warmth and tingling.

Dose: Mild chronic deficiency, 10-25 mg daily severe deficiency, 200-300 mg daily.

Preparation available

Thiamine Tablets: Each tablet containing 10 mg of thiamine hydrochloride is usually available.

TOCOPHEROL

Vitamin E

Vitamin E is considered an essential nutritional element, although its exact function is unknown. It has never been proven effective for treatment of infertility, habitual abortion, cancer, loss of hair, heart disease, peptic ulcer, bums and prevention of arteriosclerosis.

Indications: *see* notes above.

Adverse effects and cautions: usually non-toxic, however large doses may cause diarrhoea, dizziness, headache and intestinal cramps.

12.3.2 Minerals

IRON: *see* under section 12.1 antianaemics.

CALCIUM

The daily requirement varies with the age and is greater in childhood, pregnancy, lactation and old age. In osteoporosis, a calcium intake which is double the recommended daily amount reduces rate of bone loss.

Indications: hypocalcaemia in tetany, osteoporosis.

Adverse effects and cautions: constipation, bradycardia, cardiac arrhythmia, hypotension and irritation after parenteral administration.

Drug interactions: calcium salts reduce absorption of ciprofloxacin, tetracycline, iron, bisphosphonates.

Dose: 1-2 g between meals.

Acute hypocalcaemia, by slow intravenous injection, ADULT 1-2 g.

Preparation available

Calcium Carbonate Tablets: Each tablet containing 1.25 g of calcium carbonate (equivalent to 500 mg calcium) is usually available.

Calcium Gluconate Injection: Injection containing 500 mg in 5-ml and 1 g in 10-ml ampoule is usually available.

Calcium Chloride Injection: Injection containing 100 mg of calcium chloride per ml in 10-ml ampoule is usually available.

IODINE

It is among the body's essential trace elements. The daily recommended intakae is 150 micrograms (200 micrograms in pregnant and breast-feeding mothers), 50 micrograms for under 1 year, 90 micrograms for 2-6 yeas and 120 microgrms for 7-12 years. Control of iodine deficiency largely depends upon salt iodization with potassium iodide or potassium iodate.

Indications: prevention and treatment of iodine deficiency.

Adverse effects and cautions: *see* section 8.7.2 under endocrine system.

PHOSPHATES

Indications: treatment of hypophosphatemia.

Adverse effects and cautions: diarrhoea, nausea, vomiting, fluid retention, and hypocalcaemia.

SODIUM FLUORIDE

Availability of fluoride confers significant resistance to dental caries. Where the drinking water has less than 700 micrograms per litre (0.7 parts per million), it is advisable to institute artificial fluoridation. It is now considered that the topical action of fluoride on enamel and plague is more important than the systemic effect.

Indications: prevention of dental caries.

Adverse effects and cautions: yellowish brown discolouration of teeth (more than recommended doses), white flakes on teeth with recommended doses.

It is contraindicated in infants under 6 months of age.

Dose: Water content less than 0.3 ppm, CHILD up to 6 months none; 6 months-3 years 250 micrograms daily; 3-6 years 500 micrograms daily; over 6 years 1 mg daily.

Water content 0.3-0.7 ppm, CHILD up to 3 years none; 3-6 years 250 micrograms daily, over 6 years 500 micrograms daily.

Water content above 0.7 ppm, supplements not advised.

Prevention of dental caries, as oral rinse, CHILD over 6 years 10 ml 0.05% solution daily or 10 ml 0.2% solution weekly.

Preparation available

Sodium fluoride Tablets: Each tablet containing 2.2 mg of sodium fluoride is usually available.

Sodium Fluoride Mouth Wash: 0.05% and 0.2% solution of sodium fluoride is usually available.

ZINC

Zinc deficiency can occur as a result of inadequate diet or malabsorption.

Indications: zinc deficiency.

Adverse effects and cautions: dyspepsia, abdominal pain, headache, nausea, vomiting, gastritis.

The drug should be used with caution in acute renal failure.

Dose: Adjunct to oral rehydraton solution in acute diarrhoea, under 6 months 10 mg (elemental zinc) daily for 10 days; 6 months – 5 years 20 mg daily for 10 days.

Preparation available

Zinc Sulfate Dispersible Tablets: Dispersible tablets of zinc sulfate containing equivalent of 10 mg and 20 mg zinc are usually available.

12.4 Intravenous fluids and electrolytes

Solutions of electrolytes are given intravenously to meet normal fluid and electrolyte requirements or to replenish substantial deficits.

Sodium is the major cation of extracellular fluid and functions principally in the control of water distribution, fluid and electrolyte balance and osmotic pressure of body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of acid-base balance.

Chloride, the major extracellular anion, closely follows the physiologic disposition of sodium, and changes in the acid-base balance of the body are reflected by change in serum chloride concentration. Potassium is the major cation of intracellular fluid and is essential for maintenance of acid-base balance, isotonicity, and electrodynamic characteristics of the cell. Potassium is essential to a number of physiologic processes including transmission of nerve impulses;

contraction of cardiac, smooth and skeletal muscles; gastric secretion and renal function.

CALCIUM CHLORIDE: *see* under section 12.3.2, minerals.

COMPOUND SODIUM LACTATE INTRAVENOUS INFUSION

Ringer-Lactate Solution for Injection, Hartmann's Solution for Injection

Compound Sodium Lactate Intravenous Infusion contains sodium chloride 0.6% sodium lactate 0.25%, potassium chloride 0.04% calcium chloride 0.027%. Sodium lactate is an alkalinising agent whose activity depends on conversion to bicarbonate. Sodium lactate is oxidised in the liver to bicarbonate and glycogen.

It is the best commercially available solution and can be used in all age groups to treat dehydration due to acute diarrhoea of any cause. Compound sodium lactate solution can be used instead of isotonic sodium chloride solution during surgery or in the initial management of the injured or wounded.

Indications: *see* notes above.

Adverse effects and cautions: oedema, metabolic alkalosis, reactions including fever, infection at the site of injection, venous thrombosis or phlebitis and extravasation.

Changes in fluid balance, electrolyte concentrations, and acid-base balance should be evaluated clinically and by periodic laboratory determination during prolonged therapy and in patients whose condition warrants such evaluation.

Sodium lactate should be used with extreme caution in patients with congestive heart failure or other oedematous or sodium-retaining conditions, in patients with renal impairment, hypertension, pulmonary oedema, toxaemia of pregnancy.

DEXTROSE INJECTION

Glucose Injection

Dextrose injections are used as a source of calories and water for hydration. 5% Dextrose injection are administred by intravenous infusion to provide calories and water for hydration. Hypertonic dextrose injections (concentration greater than 5%) are used to provide adequate calories in a minimal volume of water. 50% Dextrose injections are frequently used in adults and children to restore blood glucose concentrations in the treatment of hypoglycaemia.

Indications: fluid replacement witout significant electrolyte deficit, hypoglycaemia.

Adverse effects and cautions: reactions (because of contamination) including fever, infection at the site of injection, venous thrombosis or bhiebitis, and extravasation.

Changes in fluid balance, electrolyte concentrations, and acid base balance should be evaluated clinically and by periodic laboratory determinations during prolonged therapy and in patients whose condition warrants such evaluation.

Dextrose solutions should be used with caution in patients with overt or known subclinical diabetes mellitus or with carbohydrate intolerance for any reason Intravenous administration of dextrose may cause fluid and/or solute overload resulting in dilution of serum electrolytes, overhydration, congestive conditions or pulmonary oedema.

SODIUM CHLORIDE INJECTION

Solutions of sodium chloride closely approximate the composition of the extracellular fluid of the body. A 0.9% solution of sodium chloride (isotonic) has approximately the same osmotic pressure as body fluids. Sodium chloride injection is capable of inducing diuresis depending on the volume administered and the clinical condition of the patient. 0.9% sodium chloride will not haemolyse erythrocytes.

Sodium chloride injections are used as a source of sodium chloride and water for hydration. Sodium chloride is also used to treat deficiencies of sodium and chloride caused by excessive diuresis or excessive salt restriction. 0.9% sodium chloride injection is used for extracellular fluid replacement and in the management of metabolic alkalosis in the presence of fluid loss and mild sodium depletion.

Indications: electrolyte imbalance, wound irrigation, oral hygiene.

Adverse effects and cautions: reaction (because of contamination) including fever, infection at the site of injection, venous thrombosis or phlebitis, and extavasation. Excessive administration of sodium chloride may result in hypematramia and large amounts of chloride may cause a loss of bicarbonate with an acidifying effect.

Changes in fluid balance, electrolyte concentrations, and acid-base balance should be evaluated clinically and by periodic laboratory determinations during prolonged therapy with sodium chloride and in patients whose condition warrants such evalution. Sodium chloride should be used with extreme caution, if at all, in patients with congestive heart failure or other oedematous or sodium retaining conditions, in patients with impaired renal function, hypertension, pulmonary oedema, toxaemia of pregnancy.

SODIUM CHLORIDE AND DEXTROSE INJECTION

Solutions containing sodium chloride and glucose are indicated when there is combined water and sodium depletion. A 1:1 mixture of isotonic sodium chloride and 5% glucose allow some of the water (free of sodium) to enter body cells which suffer most from dehydration while the sodium salt with a volume of water determined by the normal plasma sodium remains extracellular.

Indications: fluid and electrolyte replacement.

Adverse effects and cautions: *see* under sodium chloride

POTASSIUM CHLORIDE INJECTION

Potassium supplements are used as a source of potassium cation for treatment or prevention of potassium depletion because of dietary or other conditions resulting in potassium deficiency. Potassium chloride is usually the salt

of choice in the treatment of potassium depletion, since the chloride ion is required to correct hypochloremia which frequently accompanies potassium deficiency.

Indications: electrolyte imbalance.

Adverse effects and cautions: hyperkalemia, nausea, vomiting, diarrhoea, and abdominal discomfort. Pain at the site of injection and phlebitis may occur during intravenous administration.

Potassium supplements should be administered with caution in patients with cardiac disease, renal impairment.

Potassium supplements concentration should not usually exceed 3.2 g (43 mmol/litre). Initial potassium replacement should not be given with glucose; glucose may cause a further decrease in the plasma potassium concentration.

SODIUM BICARBONATE INJECTION

Sodium bicarbonate is an alkalinising agent which dissociates to provide bicarbonate ion. In the body fluids, there are many buffers, including haemoglobin, proteins and phosphates, however, the principal extracellular buffer is the bicarbonate. Sodium bicarbonate is used as an alkalinising agent in the treatment of metabolic acidosis.

Indications: metabolic acidosis.

Adverse effects and cautions: metabolic alkalosis, sodium and water retention when given in large doses or to patients with renal insufficiency. Serum potassium concentration may decrease during bicarbonate therapy.

Periodic laboratory determinations of the patient's acid-base status are recommended to minimise the risk of overdose.

Sodium bicarbonate should be used with caution in patients with congestive heart failure or other oedematous conditions; in patients with impaired renal function, toxemia of pregnancy.

The drug is contraindicated in metabolic or respiratory alkalosis, hypocalcaemia.

Chapter - Thirteen

Drugs Acting on the Skin

The topical applications generally consist of an active drug in a base or vehicle. The type of topical application to be used depends on the type and stage of skin disease. The type of base used is important and consists of one or a combination of powder, water and grease.

Ointments: These may be water soluble, emulsifying ointments containing either lanolin or mineral oil and emulsifying wax, and non-emulsifying ointments with paraffin as base. The ointments are especially useful for treatment of dry, cracked or lichenified skin lesions such as chronic topic eczema, psoriasis, ichthyosis and chapping of hands.

Creams: These are emulsions which may be either water dispersed in oil (e.g. oily cream) or oil dispersed in water (e.g. aqueous cream). Generally, creams are cosmetically more acceptable than ointment because they are less greasy and easier to apply.

Paste: These are the preparations in which powder is suspended in an ointment e.g. zinc oxide paste. They are used to protect subacutely inflammed, lichenified or excoriated skin as well as to prevent the spreading of active ingredients.

Lotions: They are used in acutely inflammed, wet and oozing skin surface (e.g. weeping eczema and other bullous disease) for drying, soothing and cooling affect, e.g. calamine lotion. They are preferred to ointments or creams for application over a hairy area.

Dusting powders: These are used to lessen the friction between skin surfaces and drying agents. They are used especially if soreness and moistness exist. They are to be avoided in moist areas because they can cake and abrade the skin.

13.1 Anti-fungal drugs

Most localised fungal infections are treated with topical preparations. Systemic therapy is necessary for nail or scalp or if the skin infection is widespread.

AMPHOTERICIN B: *see* under section 7.4, anti-fungal drugs.

BENZOIC ACID AND SALICYLIC ACID

This is generally used as Whitfield's ointment containing benzoic acid 6% and salicylic acid 3% in emulsifying ointment. Generally used to treat patches of ringworm on the body.

Benzoic acid is fungistatic and salicylic acid is keratolytic.

Indications: *see* notes above.

Adverse effects and cautions: rarely induces mild inflammatory action. No special precautions are needed.

Dose: Apply twice daily until the infected skin is shed (usually at least 4 weeks).

Preparation available

Compound Benzoic Acid Ointment (Benzoic Acid and Salicylic Acid Ointment, Whitfield Ointment): Compound benzoic acid ointment contains 6.0%w/w of benzoic acid and 3.0% w/w of salicylic acid in a suitable base.

CLOTRIMAZOLE

The drug inhibits or kills many genera of fungi, including *Candida* and dermatophytes.

Indications: *Tinea pedis*, *T. cruris*, *T. carports*, *T. versicolor*, cutaneous candidasis, vaginal candidiasis.

Adverse effects and cautions: rarely erythema, edema, pruritus, urticaria and mild burning with vaginal tablets.

Clotrimazole is contraindicated in patients who are hypersensitive to the drug. Contact with eyes and mucous membranes should be avoided.

Dose: Apply 2-3 times daily.

Preparation available

Clotrimazole Cream: Clotrimazole cream contains clotrimazole in a suitable base. Cream containing l%w/w clotrimazole is usually available.

Clotrimazole Pessaries: Clotrimazole pessaries contain clotrimazole in a suitable base. Pessaries containing 100 mg of clotrimazole is usually available.

Clotrimazole Solution: Solution containing l%w/w clotrimazole is usually available.

ECONAZOLE

It is usually fungistatic in action but may be fungicidal in high concentrations or against very susceptible organisms. The drug is active against many genera of fungi including dermatophytes and *Candida*.

Indications: *see* under clotrimazole.

Adverse effects and cautions: pruritus, erythema, burning.

Cautions: see under clotrimazole.

Dose: Apply 2 times daily; nail infections, apply once daily under occlusive dressing.

Preparation available

Econazole Cream: Cream containing 1 % of econazole nitrate in a suitable base is usually available.

Econazole Pessaries: Pessaries containing 150 mg of econazole nitrate in a suitable base is usually available.

GENTIAN VIOLET

It inhibits the growth of many genera of fungi, including dermatophytes. The drug has been reported to be effective against *Candida, Cryptococcus* and *Trichophyton.* Gentian violet is also active against some Gram-positive bacteria, especially *Staphylococcus* species.

Indications: cutaneous or mucocutaneous infections caused by *Candida albicans.*

Adverse effects and cautions: irritation or sensitivity reactions and ulcerations of mucous membranes.

The drug is contraindicated in patients with ulcerated lesions, broken skin and mucous membranes.

Dose: Apply locally, 2-3 imes daily.

Preparation available

Getian Violet Paint: Gentian violet paint contains 1% w/v of gentian violet in freshly boiled and cooled water.

GRISEOFULVIN: *see* under section 7.4, antifungal drugs.

MICONAZOLE NITRATE

It is fungistatic and is fungicidal at higher concentration to *Candida* and dermatophytes. In the treatment of vaginal candidiasis, miconazole is considerably superior to nystatin.

Indications: fungal skin infections, oral fungal infection, vaginal candidiasis.

Adverse effects and cautions: local irritation and burning.

Dose: Skin infection, apply twice daily for 10 days.

Preparation available

Miconazole Ointment: Ointment containing 2% w/w of miconazole nitrate is usually available.

Miconazole Ovule: Each ovule containing 200 mg of miconazole nitrate is usually available.

NYSTATIN: *see* under section 7.4, antifungal drugs.

SELENIUM SULFIDE

It is an anti-infective agent having antibacterial and mild antifungal activity.

Indications: relieve itching and flaking of the scalp with dandruff, *Tinea versicolor*.

Adverse effects and cautions: local irritation, tremors, pain in lower abdomen, vomiting.

Because of the risk of systemic toxicity, selenium sulfide should not be applied to damaged skin.

Safety of drug in under 5 years has not been established.

Dose: Seborrhoeic dermatitis and dandruff, apply twice weekly for 2 weeks then once weekly for 2 weeks and then as necessary.

Preparation available

Selenium Sulfide Scalp Application: Scalp application containing 2.5% w/v of selenium sulfide is usually available.

SODIUM THIOSULFATE

Indications: *Tinea versicolor* infection.

Adverse effects and cautions: the drug should be discontinued if irritation or sensitivity occurs. It should not be applied to or near the eyes.

Dose: Apply twice daily for 4 weeks.

Preparation available

Sodium Thiosulfate Solution: Sodium thiosulfate 15% solution in freshly boiled and cooled water.

TOLNAFTATE

The drug is effective against dermatophytes but is ineffective against *Candida*.

Indications: *Tinea pedis*, *T. cruris*, *T. corporis*, *T. versicolor* infection.

Adverse effects and cautions: slight skin irritation.

Tolnaftate preparations should not come in contact with the eyes.

Dose: Locally twice daily.

Preparation available

Tolnaftate Cream: Cream containing 1 % tolnaftate is usually available.

KETOCONAZOLE: *see* under section 7.4, antifungal drugs.

13.2 Anti-bacterial drugs

In all skin infections, an important part of treatment is cleansing and thorough drying. Washing with soap and water will often help to prevent infection. To minimise the development of resistant organisms it is advisable to limit the choice of antibacterials applied topically to those not used systemically.

BACITRACIN

It is bactericidal or bacteriostatic in action depending on the concentration of the drug attained at the site of infection and the susceptibility of the infecting organism. It is active against gram-positive organisms such as *Staphylococci* (including some penicillin resistant *Staphylococci*) and *Streptococci.* The activity of bacitracin is not impaired by blood, pus, necrotic tissue or large inocula.

Indications: topically alone or in combination with other anti-infectives for the treatment of superficial skin infection caused by susceptible organisms.

Adverse effects and cautions: hypersensitivity reactions.

Topical corticosteroids, when used in combination with topical anti-infectives including bacitracin, may mask the clinical signs of bacterial,

fungal or viral infections, or may suppress hypersensitivity reactions to the antibiotics or any other ingredients in the formulations.

Preparation available

Bacitracin Powder: Powder for skin use containing 250 units of bacitracin zinc per g is usually available.

Bacitracin Skin Ointment: Ointnment containing 250 units of bacitracin zinc per g is usually available.

GENTAMICIN

It is bactericidal and is active against many aerobic Gram-negative bacteria and some aerobic Gram-positive bacteria.

Indications: topically in the treatment of superficial infections on the skin caused by susceptible bacteria.

Adverse effects and cautions: erythema and pruritus.

The use of gentamicin may result in overgrowth of non-susceptible organisms including fungi.

Topical gentamicin is contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulations.

Preparation available

Gentamicin Cream: A cream containing the equivalent of 0.3% w/w of gentamicin, as sulfate is usually available.

Gentamicin Ointment: Ointment containing the equivalent of 0.3% w/w of gentamicin, as sulfate, is usually available.

IODINE

It is a local irritant and has bactericidal activity against Gram-positive and Gram-negative bacteria. Povidone iodine is effective against bacteria, fungi, viruses, spores and significantly reduces surgical wound infections.

Indications: povidone iodine solution and tincture iodine are used topically as antiseptic in the management of minor superficial skin wounds and disinfect the skin preoperatively

Adverse effects and cautions: skin stain, iodine burn, sensitisation to iodine.

Povidone iodine should be avoided in neonates and should be used with caution in pregnancy, breast-feeding and severe renal impairment.

Preparation available

Alcoholic Iodine Solution: It is an alcoholic solution containing 2.5% w/v of iodine and 2.5% w/v of potassium iodide. Alcoholic iodine solution should be kept in well closed container, the materials of which are resistant to iodine.

Povidone Iodine Solution: Solution containing 5%, 7.5% and 10% of povidone iodine is usually available.

NEOMYCIN

It is usually bactericidal and is active against many aerobic Gram-negative bacteria and some aerobic Gram-positive bacteria. The drug is inactive against fungi, viruses and most anaerobic bacteria.

Indications: topically alone or in combination with other anti-infectives for the treatment of superficial infections of the skin caused by susceptible bacteria.

Adverse effects and cautions: sensitivity to topical neomycin has been reported in 5 to 15 percent of patients. Rash, urticaria, burning, contact dermatitis, ototoxicity, nephrotoxicity and neuromuscular blockade have occurred following topical application.

Because of the possibility of ototoxicity, nephrotoxicity and neuromuscular blockade, neomycin should be used with caution for the topical treatment of extensive bums.extensive dermatologic conditions where rapid absorption of the drug is possible.

The use of neomycin may result in overgrowth of nonsusceptible organisms including fungi. The drug is contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulations. Cross allergenicity among aminoglycosides have been demonstrated.

Dose: ADULT and CHILD over 2 years, apply up to 3 times daily.

NITROFURAZONE

It is used topically in patients with second and third degree bums, other skin and mucous membrane infections caused by susceptible bacteria.

Indications: *see* notes above.

Adverse effects and cautions: allergic contact dermatitis.

Preparation available

Nitrofurazone Cream: Cream containing 0.2% w/w of nitrofurazone is usually available.

Nitrofurazone Ointment: Ointment containing 0.2% w/w of nitrofurazone is usually available.

Nitrofurazone Powder: Containing 0.2%w/w of nitrofurazone is usually available.

POLYMYXIN B

It is active against Gram-negative bacteria, including *Pseudomonas aeruginosa.* It is very toxic for parenteral administration and is not absorbed from the gut.

Indications: bacterial skin infections.

Adverse effects and cautions: rarely hypersensitivity to topical application.

Dose: Apply twice daily or more frequently if required.

Preparation available

Skin Ointment: Skin ointment containing polymyxin B sulfate, neomycin sulfate and bacitracin zinc is usually available.

Dusting Powder: Powder containing polymxin B sulfate, neomycin sulfate and bacitracin zinc is usually available.

SILVER SULFADIAZINE

It is in widespread use especially for Gram-negative infections e.g. *Pseudomonas* in prophylaxis and treatment of infection in burn wounds. Also for chronic infected leg ulcers and pressure sores.

Indiactions: see notes above.

Adverse effects and cautions: rashes, burning or itching have been reported following applications of drug.

Do not use in cases known to be hypersensitive to sulphonamides, and in pregnancy, breast-feeding and neonates.

It should be used with caution in hepatic or renal impairment.

Dose: Apply daily or more frequently if very exudative.

Preparation available

Silver Sulfadiazine Cream: Silver sulfadiazine cream contains l% w/w of silver sulfadiazine in a suitable cream base.

13.3 Anti-inflammatory and antipruritic drugs

These are indicated to provide symptomatic relief of inflammation associated with acute and chronic corticosteroid responsive disorders. They are not curative and on discontinuation a rebound exacerbation of the condition may occur. The location of skin lesion to be treated should be considered in selecting a formulation. In area with thinner skin, such as facial, eye and intertriginous areas, low-potency corticosteroid are preferred for long term therapy. Potency of a topical corticosteroid preparation is as a result of the formulation as well as the corticosteroid.

BECLOMETHASONE

It is ranked as medium to very high potency corticosteroid depending upon type of esters. Benzoate and valerate containing preparations are ranked moderate whereas dipropionate is ranked potent.

Indications: *see* under hydrocortisore.

Adverse effects and cautions: *see* under hydrocortisone.

Preparation available

Beclomethasone Cream: Cream containing 0.25% beclomethasone dipropionate is usually available. Beclomethasone cream should be protected from light.

Beclomethasone Ointment: An ointment containing 0.25% of beclomethasone dipropionate is usually available. Beclomethasone ointment should be protected from light.

BETAMETHASONE

It is ranked as potent corticosteroids.

Indications, adverse effects and cautions: *see* under hydrocortisone.

Preparation available

Betamethasone Valerate Scalp Application: The scalp application contains 0.12% of betamethasone valerate. Scalp application should be protected from light.

Betamethasone Cream: Betamethasone cream contains betamethasone valerate or dipropionate in a suitable base. Cream containing 0.1% of betamethasone valerate or 0.05% of betamethasone dipropionate is usually available. Betamethasone cream should be protected from light.

CALAMINE LOTION

Calamine lotion is used as antipruritic and is often ineffective.

Indications: *see* notes above.

Preparation available

Calamine Lotion: Calamine lotion contains calamine 15%, zinc oxide 5%, glycerol 5%, bentonite 3%, sodium citrate 0.5%, and liquified phenol 0.5% in freshly boiled and cooled water.

Calamine Lotion, Oily: It contains calamine 5%, arachis oil 50%, oleic acid 0.5% wool fat 1% in calcium hydroxide solution.

CLOBETASOL

It is ranked as very potent corticosteroid.

Indications, adverse effects and cautions: *see* under hydrocortisone.

Dose: Apply thinly 1-2 times daily for up to 4 weeks.

Preparation available

Clobetasol Cream: Cream containing 0.05% w/w of clobetasol propionate is usually available.

CLOBETASONE

It is ranked as moderate potent corticosteroid.

Indications, adverse effects and cautions: *see* under hydrocortisone.

Dose: Apply thinly 1-2 times daily.

Preparation available

Clobetasone Cream: Clobetasone cream containing 0.05% w/w of clobetasone butyrate is usually available.

FLUOCINOLONE

It is ranked as mild potent corticosteroid except 0.025 percent cream which is ranked as potent preparation.

Indications, adverse effects and cautions: *see* under hydrocortisone.
Dose: Apply thinly 1-2 times daily, reducing strength as condition responds.

Preparation available

Fluocinolone Ointment: Fluocinolone ointment contains fluocinolone acetonide or fluocinolone acetonide dihydrate in a suitable base. An ointment containing the equivalent of 0.025 % of fluocinolone acetonide is usually available.

FLUOCINONIDE

It is ranked as potent corticosteroid.
Indications, adverse effects and cautions: *see* under hydrocortisone.
Dose: Apply thinly 1-2 times daily.

Preparation available

Fluocinonide Cream: Cream containing 0.05 % of fluocinonide is usually available.

Fluocinonide Ointment: An ointment containing 0.05% of fluocinonide is usually available.

HALCINONIDE

It is ranked as very potent corticosteroid.
Indications, adverse effects and cautions: *see* under hydrocortisone.
Dose: Apply thinly 1-2 times daily.

Preparation available

Halcinonide Cream: Cream containing 0.10% w/w halcinonide is usually available.

HYDROCORTISONE

Indications: corticosteroid responsive dermatoses.
Adverse effects and cautions: exacerbation of local infection, atrophic striae, depigmentation, hypertrichosis.

Local adverse effects occur most frequently with occlusive dressing especially with prolonged therapy. Topical corticosteroid therapy in children under 2 years should be limited to the minimum amount necessary for therapeutic efficacy; chronic therapy may interfere with growth and development.

Use on the face for more than 7 days should be avoided.

The drug is contraindicated in untreated skin infections, acne and broken skin.

Preparation available

Hydrocortisone Cream: Cream containg 0.1, 0.5, 1.0 and 2.5% w/w of hydrocortisone is usually available.

TRIAMCINOLONE

It is ranked as potent preparation.
Indications, adverse effects and cautions: *see* under hydrocortisone.

Preparation available

Triamcinolone Ointment: Ointment containing 0.1% triamcinolone acetonide in a suitable base is usually available.

13.4 Astringent drugs

ALUMINIUM DIACETATE

It acts by precipitating protein. It is used as lotion containing 0.65% aluminium diactetate.
Indications: eczematous skin lesions, suppurative superficial wounds, tropical ulcers.

13.5 Drugs affecting skin differentiation and proliferation

BENZOYL PEROXIDE

It is a keratolytic drug with bacteriostatic activity against propionibacterium acnes. Both comedones and inflamed lesions respond well to the drug. The lower concentrations seem to be as effective as higher concentrations in reducing inflammation. Treatment is usually started with a lower strength and increased as tolerance develops to the initial irritant action.

Indications: acne vulgaris.

Adverse effects and cautions: skin irritation, may bleach hair and clothing.

The drug should be avoided contact with eyes, mouth and mucous membranes, excessive exposure to sunlight.

Dose: Apply 1-2 times daily preferably after washing with soap and water.

Preparation available

Benzoyl Peroxide Gel: Aqueous gel containing 5% of benzoyl peroxide is usually avilble.

COAL TAR

It has anti-inflammatory and antiscaling properties.
Indications: psoriasis, chronic atopic eczema.

Adverse effects and cautions: skin irritations, photosensitivity.

It may stain skin, hair and fabric.

Coal tar preparations should be avoided in the eyes. It should not be applied to acutely inflammed or broken skin. Coal tar preparations are contraindicated in presence of infection.

Dose: Apply 1-3 times daily starting with low strength preparations.

Preparation available

Coal Tar Paste: Paste containing 7.5% w/w of strong coal tar in compound zinc paste is usually available.

Coal Tar Solution: Solution containing 20% w/v of coal tar in ethanol (96 percent) is usually available. Coal tar solution should be kept in well closed container.

DITHRANOL

It restores the normal rate of epidermal cell proliferation and karatinisation.

Indications: psoriasis.

Adverse effects and cautions: local irritation, allergic reactions (skin rash) or redness. Severe conjunctivitis, keratitis or comeal opacity may occur if medication comes in contact with the eye.

The drug should be avoided in hypersensitive patients.

Preparation available

Dithranol Ointment: An ointment containing 0.1% and 1% w/w of dithranol is usually available. Dithranol ointment should be protected from light.

ICHTHAMMOL

It is used in lichenification which results from repeated scratching.

Indications: chronic lichenified eczema.

Adverse effects and cautions: skin irritation.

Dose: Apply 1-3 times daily.

SALICYLIC ACID

It has potent kerotolytic action when applied topically to the skin.

Indications: warts and calluses, acne.

Adverse effects and cautions: local irritation, salicylism on excessive application or treatment of large areas.

The drug is contraindicated in children uner 2 years, broken or inflammed skin.

The drug should be used with caution in significant peripheral neuopathy; contact with eyes, mouth and mucous membranes should be avoided.

TRETINOIN AND ISOTRETINOIN

They are first generation retinoids. They are useful in comedonal acne.

Indications: acne vulgaris.

Adverse effects and cautions: peeling skin, burning or redness.

The drugs should be avoided in severe acne involving large areas, since the drug may produce severe irritation of eczematous skin. Exposure to ultraviolet light increase the intensity of the inflammtory reaction. The drug should not come in contact with the eyes, mouth, mucous membranes or open wounds.

The drug is contraindicated in pregnancy, women of child bearing age, breast-feeding.

Application: Apply thinly 1-2 times daily.

Dose: 500 micrograms/kg daily increased if necessary to 1 mg/kg (1-2 divided doses) for 16-24 weeks; CHILD not recommended.

Preparation available

Tretinoin Cream: Cream containing 0.025% and 0.05% of tretinoin in a suitable base is usually available.

Isotretinion capsules: Each capsule containing 10 mg and 20 mg of isotretinoin is usually available.

13.6 Scabicides and pediculocides

Benzyl benzoate application is effective for scabies. It is necessary to treat all members of the family at the same time. The clothes and sheets should be changed after treatment. Benzyl benzoate is unsuitable for babies owing to its irritating properties. It is removed by washing. Lindane application is effective in the treatment of scabies and pediculosis. Some resistant strains have now emerged.

BENZYL BENZOATE

It is toxic to the parasite arthropod *Sarcoptes scabei*.

Indications: scabies.

Adverse effects and cautions: when applied in appropriate dosage, slight local irritation (especially of the male genitalia), rashes may occur.

In patients with scabies pruritus frequently persists for one to several weeks following treatment with the drug, this does not indicate treatment failure and is not an indication for further treatment.

Contact with the face, eyes, mucous membranes and urethral meatus should be avoided. Benzyl benzoate should not be applied to acutely inflammed skin or raw, weeping surfaces.

Breast-feeding should be avoided until product has been washed off.

Dose: Apply over the whole body; repeat without bathing on the following day and wash off after 24 hours. Third application may be required in some cases.

Preparation available

Benzyl Benzoate Application: Benzyl benzoate application contains 25% w/w of Benzyl benzoate in a suitable oil-in-water emulsified base. Benzyl benzoate application should be shaken before use.

CROTAMITON

It is less effective in scabies.

Indications: scabies.

Adverse effects and cautions: local irritation.

Pruritus, caused by an acquired sensitivity to mites and their products, frequently persists for one to several weeks following treatment with the drug, this does not indicate treatment failure and is not an indication for further treatment. Crotamiton should not be applied to acutely inflammed skin or raw, weeping surfaces.

Preparation available

Crotamiton Cream: Crotamiton cream containing 10% w/w of crotamiton in a suitable base is usually available.

Crotamiton Lotion: Crotamiton lotion containing 10% w/v of crotamiton in a suitable vehicle is usually available.

LINDANE

Gamma Benzene Hexachloride

It is toxic to parasite arthropod *Sarcoptes scabei* and their eggs. It is also toxic to *Pediculus capitis, Pediculus corporis* and *Phthirus pubis.*

Indications: scabies, pediculosis

Adverse effects and cautions: local irritation, contact dermatitis. Inhalation of lindane vapour may produce headache, nausea, vomiting and irritation of eyes, nose and throat.

Contact with the face, eyes, mucous membranes and urethral meatus should be avoided. If accidental contact with the eyes occurs, the eye should be flushed thoroughly with water.

Lindane is contraindicated in patients with a history of sensitivity to the drug or any ingredients in the products. Lindane should be used with caution in infants and small children since the potential for CNS toxicity (ataxia, clonic and tonic seizures, restlessness etc), is greater in this age group.

Dose: Scabies, apply over whole body, omitting head and neck, wash of using cool water after 24 hours, repeat if necessary after 7 days. Pediculosis, lotion or cream is applied, wash off after 8-12 hours.

Pareparation available

Lindane Application: Application containing 1 % w/v of lindane is usually available.

Lindane Cream: Cream containing 1 % w/v of lindane is usually available.

PERMETHRIN

It is effective for scabies, head and body lice.

Indications: *see* notes above.

Adverse effects and cautions: local irritations, rashes, itching.

The drug should avoid contact with eyes, inflammed or broken skin.

Dose: Scabies and body lice, apply cream over whole body and wash off after 8-12 hours; if hands washed with soap within 8 hours of application for treating scabies, treat again.

Head lice, apply lotion to clean damp hair and rinse after 10 minutes.

Preparation available

Permethrin Cream: cream containing 5% of permethrin is usually available.

Permethrin Lotion: Lotion containing 1% of permethrin is usually available.

13.7 Depigmenting and pigmenting agents

HYDROQUINONE

Topical application of hydroquinone produces reversible depigmentation of the skin.

Indications: melasma, solar lentigines.

Adverse effects and cautions: burning, allergic dermatitis.

Hydroquinone is contraindicaled in patients with a history of sensitivity or allergic reactions to the drug or any ingredients in the available preparation.

Preparation available

Hydroquinone Cream: Cream containing 2% w/w of hydroquinone is usually available.

METHOXSALEN

Ammoidin

Photochemotherapy combining long-wave ultraviolet A radiation with a psoralen (like methoxsalen) i.e. PUVA is effective in most forms of psoriasis.

Indications: vitiligo, psoriasis.

Adverse effects and cautions: nausea, painful erythema and blistering and pruritus. The drug may produce severe burns if used improperly. Long term toxic reactionsinclude skin ageing, neoplastic skin lasion.

Dose: By mouth, 0.4-0.6 mg/kg, 1.5-2 hours before UVA exposure.

Preparation available

Methoxsalen Capsules: Each capsule containing 10 mg of methoxsalen is usually available.

Methoxsalen Topical Solution: Solution containing 1 % methoxsalen is usually available.

13.8 Sunscreen agents

The medium wavelength (290-320nm or UVB) ultraviolet radiation cause sunburn and contribute to the long-term changes responsible for skin cancer and ageing. UVA (320-400 nm) not cause sunburn, but are responsible for photosensitivity eactions and photo-dermatoses.

AMINOBENZOIC ACID

PABA

Indications: prevent sunburn

Adverse effects and cautions: contact dermatitis. Even when using a sunscreen, prolonged sunlight exposure should be avoided. PABA containing sunscreens may permanently stain light colourd clothing.

Preparation available

Aminobenzoic Acid Cream: Cream containing 10% aminobenzoic acid is

usually available. Aminobenzoic acid cream should be protected from light.

TITANIUM DIOXIDE

Indications, adverse effects and cautions: *see* under PABA, but it protects UVA.

Preparation available

Titanium Dioxide Paste: It contains titanium dioxide 200g, chlorocresol 1 g, red ferric oxide of commerce 20g, light kaolin or light kaolin (natural) sterilised 10 g, zinc oxide, fine 250 g, glycerol 150 g per kg of paste in aqueous base.

ZINC OXIDE

Indication, adverse effects and cautions: *see* under PABA, but it protects UVA.

Preparation available

Zinc Oxide Ointment: Ointment containing 15% w/w of zinc oxide in a suitable emulsifying base is available.

Chapter - Fourteen

Drugs Acting on the Eye

Eye preparations should be sterile and may contain suitable preservatives.

Eye preparations are mainly presented in the following dosage forms:

Eye Lotions: These are solutions to flush out irritants or foreign bodies by irrigation of the conjunctival sac.

Sodium chloride (0.9%) eye lotion is a sterile preparation and used widely. The preparation should be used once only from unopened container for first aid and for treatment it should be used within 24 hours after the container is opened. Tap water can be used directly from the main supply. Stored water should not be used even in emergency.

Eye Drops and Eye Ointments: When eye drops are administered into the pocket formed by gently pulling down the lower eyelid and keeping the eye closed for as long as possible after application. One drop is needed. The drugs penetrate the eye ball probably through the cornea. Eye ointments are generally applied similar to eye drops.

When two different eye drops are required to be administered same time, dilution and overflow may occur when one is immediately followed by the other. So the patient should administer the drugs at an interval of 5 minutes.

Eye drops should be instilled very frequently, at least every two hours until infection is controlled. At night time it is advisable to use eye ointments because of its longer action.

Subconjunctival Injection: Drugs such as anti-infectives or corticosteroids may be administered by subconjunctival injection. By this route the dose volume is usually not more than 1ml.

14.1 Anti-infective preparations

14.1.1 Anti-bacterial preparations

Antibiotics with a broad spectrum of activity are chloramphenicol, framycetin, neomycin, polymyxin etc. For infection due to *Pseudomonas aeruginosa,* gentamicin, ciprofloxacin, ofloxacin are effective.

CHLORAMPHENICOL

It is usually bacteriostatic in action, but may be bactericidal in high concentrations or against highly susceptible organisms.

Indications: superficial infections of the eye.

Adverse effects and cautions: itching or burning.

Topical corticosteroids, when used in combination with chloramphenicol may mask the clinical signs of bacterial, fungal or viral infections, or may suppress hypersensitivity reactions to the antibiotic or other ingredients in the formulations. They should not be prescribed for undiagnosed 'red eye'.

Preparation available

Chloramphenicol Eye Drops: Eye drops conaining 0.5% w/v of chloramphenicol is usually available. Chloramphenicol eye drops should be protected from light.

Chloramphenicol Eye Ointment: Eye ointments containing 1% w/w of chloramohenicol is usually available.

CIPROFLOXACIN

Indications: superficial bacterial infections, corneal ulcers.

Adverse effects and cautions: corneal staining, local burning and itching, lacrimation, photophobia.

Dose: Corneal ulcer, eye drops, day 1 apply every 15 minutes for 6 hours then every 30 minutes, day 2 apply every hour, days 3-14 apply every 4 hours (maximum duration of treatment 21 days).

Apply ointment throughout day and night; apply 1.25 cm ointment every 1-2 hours for 2 days then every 4 hours for next 12 days.

Preparation available

Ciprofloxacin Eye Drops: Eye drops containing 0.3% of ciprofloxacin (as hydrochloride) is usually available.

Ciprofloxacin Eye Ointment: Eye ointment containing 0.3% of ciprofloxacin (as hydrochloride) is usually available.

FRAMYCETIN

Indications: superficial infections of the eye.

Adverse effects and cautions: irritation and burning.

Cautions and contraindications: *see* under neomycin.

Preparation available

Framycetin Drops: Eye drops containing 0.5% w/v of framycetin sulfate is usually available.

GENTAMICIN

It is usually bactericidal in action.

Indications: superficial infections of the eye including *Pseudomonas.*

Adverse effects and cautions: transient irritation, burning, itching.

The use of gentamicin may result in overgrowth of nonsusceptible organisms including fungi.

Topical preparations are contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulations. Cross-allergenicity among the aminoglycosides has been demonstrated.

Preparation available

Gentamicin Eye Drops: Eye drops containing the equivalent of 0.3% w/v of gentamicin (as sulphate) is usually available.

NEOMYCIN

It is usually bactericidal in action.

Indications: superficial infections of the eye.

Adverse effects and cautions: contact conjunctivitis, burning, rash and urticaria.

Topical corticosteroids, when used in combination with neomycin may mask the clinical signs of bacterial, fungal or viral infections, or may suppress hypersensitivity reactions to the antibiotic or other ingredients in the formulations. The use of neomycin may result in overgrowth of nonsusceptible organisms including fungi.

Neomycin preparations are contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulations. Cross-allergenicity among the aminoglycosides has been demonstrated.

Preparation available

Neomycin Eye Drops: Eye drops containing 0.25 % (1700 units per ml) is usually available. Neomycin eye drops should be protected from light.

OFLOXACIN

Indications: *see* under ciprofloxacin.

Adverse effects and cautions: photophobia, nausea, headache, dizziness.

The drug should not be used for more than 10 days.

Dose: *see* under ciprofloxacin.

Preparation available

Ofloxacin Eye Drops: Eye drops containing 0.3% of ofloxacin is usually available.

POLYMYXIN B

It is bactericidal in action.

Indications: superficial infections of the eye.

Adverse effects and cautions: irritations and contact dermatitis.

Cautions and contraindications: see under neomycin.

Preparation available

Polymyxin B Eye Ointments: Eye ointment containing polymyxin B sulfate190 000 units and baxitracin zinc 500 units per g is usually available.

SULPHACETAMIDE

It is bacteriostatic in action.

Indications: superficial infections of the eye.

Adverse effects and cautions: burning, rash, urticaria.

The use of sulphacetamide may result in overgrowth of non susceptible organisms including fungi. Topical preparations are contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulations.

Dose: 1-2 drops 3-4 times a day.

Preparation available

Sulphacetamide Eye Drops: Eye drops containing 10%, 20% of sulphacetamide sodium is usually available.

TETRACYCLINE

It is usually bacteriostatic in action but may be bactericidal in high concentrations or against highly susceptible organisms. It is active against *Rickettsia, Chlamydia, Mycoplasma.*

Indications: superficial bacterial infections and chlamydial infections of the eye.

Adverse effects and cautions: dermatitis, increased lacrimation and transient burning sensation.

Topical use of tetracycline may result in overgrowth of nonsusceptible organisms including fungi.

Topical corticosteroids, when used in combination with topical tetracycline may mask the clinical signs of bacterial, fungal or viral infections or may suppress hypersensitivity reactions to the antibiotics or other ingredients in the formulations.

Topical preparations are contraindicated in patients who are hypersensitive to the drug or any ingredients in the formulation.

Preparation available

Tetracycline Eye Ointment: Eye ointment containing 1% of tetracycline hydrochloride is usually available.

14.1.2 Fungal infections of the eye

In hot and humid climate especially after agriculture injuries, fungal infections of the cornea are common. Orbital mycosis is rare, but may occur due to direct spread of infection from the paranasal sinuses. Many different fungi are capable of producing ocular infection.

NATAMYCIN

Following topical application, natamycin is retained in the conjunctival fomices so that significant drug concentrations are usually not attained in ocular fluids or in the deep comeal stroma.

Indications: fungal blepharitis and conjunctivitis caused by susceptible organisms, fungal keratitis caused by susceptible organisms including *Fusarium solani.*

Adverse effects and cautions: eye irritation.

The drug should not be used in patients who are allergic to natamycin.

Peparation available

Natamycin Ophthalmic Suspension: A 5% suspension of natamycin is ususlly available.

14.1.3 Viral infections of the eye

ACICLOVIR

Indications: corneal ulcer produced by *Herpes simplex.*

Adverse effects and cautions: local irritation, inflammation.

Dose: Apply 5 times daily (continue for at least 3 days after complete healing)

Preparation available

Aciclovir Eye Ointment: Aciclovir 3% ointment in suitable base in usually available.

GANCICLOVIR

Indications: acute herpetic keratitis.

Adverse effects and cautions: irritation and visual disturbances.

The drug should be used with caution in pregnancy and breast-feeding.

Dose: Apply 5 times daily until complete corneal re-epithelisation, then 3 times daily for 7 days (usual duration of treatment 21 days).

14.2 Anti-inflammatory agents

Corticosteroids administered locally or by mouth are impotant in treatment of anterior segment inflammation, including from sugery. There are three main dangers with their use - aggravation of 'red eye' condition due to herpes simplex leading to corneal ulceration with possible damage to vision and even loss of the eye, steroid glaucoma and steroid cataract.

BETAMETHASONE

Indications: local treatment of inflammation.

Adverse effects and cautions: blurred vision, posterior capsular cataract, glaucoma, secondary infection.

The drug is contraindicated in patients with acute, untreated purulent bacterial, viral or fungal infections. Patients receiving prolonged therapy, intraocular pressure should be checked frequently.

Dose: Apply eye drops every 1-2 hours until controlled then reduce frequency.

Preparation available

Betamethasone Eye Drops: Eye drops containing 0.1 % of betamethasone sodium phosphate is usually available. Betamethasone eye drops should be protected from light and stored at a temperature not exceeding 25°.

DEXAMETHASONE

Indications, adverse effects and cautions: *see* under betamethasone.

Dose: Apply eye drops 4-6 times daily; severe conditions every 30-60 minutes until controlled then reduce frequency.

Preparation available

Dexamethasone Eye Drops: Eye drops containing 0.1% of dexamethasone sodium phosphate is usually available.

DICLOFENAC, FLURBIPROFEN AND KETOROLAC

Diclofenac, flurbiprofen and ketorolac are used in the treatment of ocular diseases.

DICLOFENAC

Indications: inhibition of intra-operative miosis during cataract surgery, post-operative inflammation in cataract surgery, seasonal allergic conjunctivitis.

Adverse effects and cautions: occasionally corneal perforations, especially in older patients with ocular surface disease, such as dry eye syndrome.

Preparation available

Diclofenac Eye Drops: Eye drop containing 0.1% of diclofenac sodium is usually available.

FLURBIPROFEN

Indications: *see* under diclofenac.

Adverse effects and cautions: *see* under diclofenac.

Preparation available

Flurfiprofen Eye Drops: Eye drops contiang 0.3% of flurbiprofen is usually available.

KETOROLAC

Indications: prophylaxis and reduction of inflammation and associated symptoms following ocular surgery.

Preparation available

Ketorolac Eye Drops: Eye drop containing 0.5% of ketorolac trometamol is usually available.

HYDROCORTISONE

Indications, adverse effects and cautions: *see* under betamethasone

Preparation available

Hydrocortisone Eye Drops: Eye drops containing 1% of hydrocortisone acetate is usually available.

KETOTIFEN

It is an antihistamine.

Indications: allergic conjunctivitis, allergic rhinitis.

Adverse effects and cautions: transient burning or stinging, photophobia, headache, skin reactions.

Dose: ADULT and CHILD over 3 years, apply twice daily.

Preparation available

Ketotifen Eye Drops: Eye drops containing 250 micrograms/ml of ketotifen (as fumarate) is usually available.

MEDRYSONE

Indications, adverse effects and cautions: *see* under betamethasone

Preparation available

Medrysone Ophthalmic Suspension: Ophthalmic suspension containing 1 % of medrysone is usually available.

PREDNISOLONE

Indications, adverse effects and cautions: *see* under betamethasone.

Dose: Apply eye drops every 1-2 hours until controlled then reduce frequency.

Preparation available

Prednisolone Eye Drops: Eye drops containing 1% of prednisolone acetate is usually available.

SODIUM CROMOGLICATE

It inhibits mast cell release of histamine, leukotriens and other substances that cause hypersensitivity reactions. It is used as eye ointment or eye drops.

Indications: allergic conjunctivitis, allergic keratoconjunctivitis

Adverse effects and cautions: burning or stinging.

Dose: ADULT and CHILD, apply 4 times daily.

Preparation available

Sodium Cromoglicate Eye Drops: Eye drops containing 2% of sodium cromoglicate is usually available.

14.3 Local Anaesthetics

LIDOCAINE

Lignocaine

As topical local anaesthetic, it is injected into the eyelids for minor surgery, while a retrobulbar or peribulbar injection may be used for major eye surgery.

Indications: *see* notes above.

Adverse effects and cautions: burning, skin rash, itching, redness and lacrimation. Excessive doses of topically applied drug can produce systemic adverse effects.

Dose and prepartion available: *see* under section 9.2, local anaesthetics.

TETRACAINE

Instillation of a 0.5% solution of drug into the eye produces local anaesthesia within 25 seconds. The duration of action is up to 15 minutes or longer.

Indications: minor surgical procedures.

Adverse effects and cautions: *see* under lidocaine.

14.4 Miotics and antiglaucoma drugs

A high intra-ocular pressure, glaucoma, may result in blindness. The rise in the pressure is due to reduced outflow of aqueous humour, the inflow remaining almost constant. Probably the commonest condition is chronic simple or open angle glaucoma where the obstruction is in the trabecular meshwork. Narrow angle glaucoma or acute closed angle glaucoma is due to blockage of aqueous humour flow into anterior chamber and is a medical emergency.

Glaucoma may be treated by the aplication of eye drops containing miotics, adrenaline, or beta-adrenoceptor blocking drugs such as timolol. Other drug such as acetazolamide is given by mouth.

The small pupil is an unfortunate side effect of these drugs, except when pilocarpine is used temporarily while patient awaits operation for close angle glaucoma, the main factor is the opening up of the inefficient drainage channels in the trabecular meshwork resulting from contraction or spasm of the ciliary muscle. This also produces accommodation spasm, which is a disadvantage especially in patients under 40 years of age.

ACETAZOLAMIDE

It has a significant place in the treatment of glaucoma. It is used systemically. It inhibits carbonic anhydrase, hence reducing the formation of hydrogen and bicarbonate in aqueous humour and the water secreted with it, resulting in a fall in the intraocular pressure.

Indications: open angle glaucoma, angle-closure glaucoma.

Adverse effects and cautions: anorexia, nausea, vomiting paresthesia, hypokalaemia, drowsiness, depression, rashes, blood disorders manifested by aplastic anaemia, thrombocytopenia or leucopenia.

lectrolyte balance should be maintained in patients receiving acetazolamide. Respiratory acidosis may be precipitated or increased in patients with severe loss of respiratory capacity.

Preparation available

Acetazolamide Tablets: Each tablet containing 250 mg of acetazolamide is usually available.

LATANOPROST

It is a prostaglandin analogue. It acts by facilitating aqueous outflow through the accessory uveosceleral outflow pathway.

Indications: raised intraocular pressure in open-angle glaucoma, ocular hypertension.

Adverse effects and cautions: brown pigmentation, blepharitis, ocular irritation and pain, conjunctival hyperaemia, skin rash, dyspnoea, exacerbation of asthma, chest pain.

The drug should be used with caution in pregnancy, breast-feeding, aphakia.

Dose: Apply once daily, preferably in the evening; CHILD not recommended.

Preparation available

Latanoprost Eye Drop: Eye drop containing 50 micrograms of latanoprost per ml is usually available.

PHYSOSTIGMINE

Eserine

Following topical application of a 0.25-1% solution or ointment to the conjunctival sac, miosis occurs within 10 to 30 minutes and persists for 12 to 48 hours.

Indications: open - angle glaucoma.

Adverse effects and cautions: blurring of vision, ocular or brow pain, burning, lacrimation, hypersensitivity reactions such as allergic conjunctivitis and dermatitis. Because of the spasm of accomodation and poor vision in dim light, patients receiving miotic therapy, particularly geriatric patients or those with lens opacities should avoid driving at night.

Miotics should be used with caution in patients with comeal abrasion to avoid excessive penetration and systemic toxicity.

Dose: Apply 2-6 times daily.

Preparation available

Physostigmine Eye Drops: Eye drops containing 0.25% of physostigmine sulphate is usually available.

PILOCARPINE

Following topical application of a 1% solution of pilocarpine to the conjunctival sac, miosis occurs within 10 to 30 minutes and persists for 4 to 8 hours or rarely upto 20 hours.

Indications: open-angle glaucoma, acute angle -closure glaucoma.

Advese effects and cautions: headache, browache, burning, itching.

The drug is contraindicated in acute iritis, acute uveitis, acute inflammatory disease of the anterior segment.

The drug should be used with caution in retinal disease, conjunctival or corneal damage.

Administration: Apply eye-drops 3-4 times daily

Preparation available

Pilocarpine Eye Drops: Eye drops containing 1%, 2% and 4% of pilocarpine nitrate is usually available.

TIMOLOL

It is a non-selective beta-adrenergic blocking agent. It lowers intraocular pressure by reducing aqueous humour production.

Indications: open-angle glaucoma, glaucoma in aphakic eyes.

Adverse effects and cautions: allergic reactions (skin rash, itching), conjunctivitis or keratitis, burning of eye, pain, systemic absorption of drug may produce chest pain, anxiety, diarrhoea, nausea or vomiting and wheezing.

Beta-blocker eye drops are contraindicated in patients with asthma or a history of obstructive airways disease, bradycardia, heart block.

Dose: Apply drops twice daily.

Preparation available

Timolol Eye Drops: Eye drops containing the equivalent of 0.25 % w/v and 0.5% w/v of timolol (as maleate) is usually available.

14.5 Mydriatics

Antimuscarinic drugs when applied topically produce dilatation of the pupil and paralysis of the ciliary muscles.

ATROPINE

It has a slower onset of mydriatic and cycloplegic action and more prolonged ocular effects than most other antimuscarinic drugs. The maximum mydriatic effect occurs in about 30 to 40 minutes following topical application to the eye. Maximum cycloplegic occurs in several hours. Mydriasis generally lasts for about 7 to 12 days and cycloplegic persists for upto 14 days or longer.

Indications: refraction procedures in children up to 5 years of age, uveitis to prevent posterior synachiae.

Adverse effects and cautions: local irritation, raised intraocular pressure, dermatitis, systemic effects manifested by flushing, dryness of the skin and blurred vision etc.

Atropine is contraindicated in patients with known or suspected angle-closure glaucoma. The drug is contraindicated in patients with known hypersensitivity to the drug or any ingredient in the formulation.

Preparation available

Atropine Eye Drops: Eye drops containing 1% w/v of atropine sulphate is usually available.

Atropine Eye Ointment: Eye ointments containing 1 % of of atropine sulphate w/w is ususally available.

CYCLOPENTOLATE

It has a rapid onset of action and a shorter duration of action than atropine or homatropine. Maximum mydriatic and cycloplegic effects occur within about 15 to 60 minutes following topical application to the eye. Mydriasis and cycloplegic generally last about 24 hours.

Indications: *see* under atropine.

Adverse effects and cautions: *see* under atropine.

Preparation available

Cyclopentolate Eye Drops: Cyclopentolate eye drops are a sterile solution of cyclopentolate hydrochloride in purified water. Eye drops containing 1 % w/v of cyclopentolate hydrochloride is usually available.

EPINEPHRINE

Adrenaline

It acts on alpha-adrenergic receptors in the conjunctiva to produce vasoconstriction and haemostasis in bleeding from small vessels. It contracts the dilator muscle of the pupil by acting on alpha-adrenergic receptors, resulting in dilatation of the pupil. Cycloplegia does not occur. It lowers intraocular pressure probably by decreasing production of aqueous humour and increase in outflow. It is used as eye drops containing 1 % adrenaline.

Indications: open angle glaucoma.

Adverse effects and cautions: headache or browache, blurred vision, eye pain, burning, watering and macular oedema in aphakic eyes.

The drug should be used with caution in patients with vascular hypertension or cardiac disorders including arrhythmias and cardio-vascular disease.

Epinephrine is contraindicated in patients with angle closure glucoma.

HOMATROPINE

It is relatively short acting mydriatic and cycloplegic agent and has a shorter duration of action than atropine. The maximum mydriatic effect occurs in about 10 to 30 minutes, and the maximum cyclopegic effect in about 30 to 90 minutes. Mydriasis may last 6 hours to 4 days and cycloplegia may persist for 10 to 48 hours. It is used as eye drop containing 1% and 2% Hormatropine hydrobromide.

Indications: refraction procedures, uveitis.

Adverse effects and cautions: *see* under atropine.

Preparation available

Homatropine Eye Drops: Eye drops containing 2% homatropine hydromide is usually available.

PHENYLEPHRINE

It acts on alpha-adrenergic receptors in the dilator muscle of the pupil producing contraction. It also acts on alpha-adrenergic receptors in the arterioles of the conjunctiva, producing constriction. Cycloplegia does not occur.

Indications: refraction procedures, uveitis to prevent posterior synechiae.

Adverse effects and cautions: burning, eye pain, blurred vision, allergic conjunctivitis or dermatitis and systemic sympathomimetic effects.

The drug should be used with caution in patients with hypertension, cardiac disorders, diabetes mellitus, children and elderly.

The drug is contraindicated in patients with angle-closure glaucoma.

HYOSCINE

Scopolamine

It has more rapid onset of mydriatic and cycloplegic action and less prolonged ocular effects than atropine. Maximum mydriatic effect occurs in about 15 to 30 minutes following topical application to the eye. Maximum cycloplegia occurs within 30 to 45 minutes. Mydriasis generally lasts for several days and cycloplegia persists for upto 7 days.

Indications: refraction procedures, uveitis.

Adverse effects and cautions: *see* under atropine.

Preparation available

Hyoscine Eye Drops: Eye drops containing 0.25% of hyoscine hydrobromide is usually available.

TROPICAMIDE

It produces rapid and less prolonged mydriasis than that produced by most other mydriatic drugs. The maximum mydriatic effect appears in about 20 to 40 minutes, and the maximum cycloplegic occurs within 20 to 35 minutes. Mydriasis generally lasts about 6 to 7 hours and cycloplegia persists for 50 minutes to 6 hours.

Indications: refraction procedures.

Adverse effects and cautions: increased intraocular pressure, burning, photophobia, allergic reactions and systemic effects. The drug is contraindicated in patients with known or suspected angle-closure glaucoma. The drug is also contraindicated in patients hypersensitive to the drug or any ingredient in the formulation.

Preparation available

Tropicamide Eye Drops: Eye drops containing 1 % of tropicamide is usually available. Tropicamide eye drops should be stored at a temperature of 8-15°.

14.5 Miscellaneous ophthalmic preparations

14.5.1 Preparation for tear deficiency and astringent

HYPROMELLOSE

It promotes comeal wetting by stabilizing and thickening the precomeal tear film and prolonging the tear film break up time, which is usually shortened in dry eye conditions. It also acts to lubricate and protect the eye.

Indications: tear deficiency

Adverse effects and cautions: eye irritation, blurred vision, stickiness of eye lashes.

Preparation available

Hypromellose Eye Drops: Eye drops containing 0.3% and l%w/v of hypromellose is usually available. They are isotonic with tear secretion.

HYDROXYPROPYL CELLULOSE

It acts in the similar way to hypromellose.

Indications: see under hypromellose.

Adverse effects and cautions: *see* under hypromellose.

POLYVINYL ALCOHOL

It increases the persistence of the tear film and is useful when the ocular surface mucin is reduced.

Indications: tear deficiency.

Adverse effects and cautions: *see* under hypromellose.

Preparation availabele

Polyvinyl Alcohol Eye Drops: Eye drop containing 1.4% polyvinyl alcohol is usually available.

SODIUM CHLORIDE

0.9% drops are useful in tear deficincy, as "comfort drops" in lens wearers and facilitation of lens removal.

Indications: *see* notes above.

ZINC SULFATE

It has astringent activity. The eye drops contain 0.25% zinc sulfate.

Indications: minor eye irritation.

14.5.2 Diagnostic preparations

FLUORESCEIN SODIUM

It is used to locate damaged areas of the cornea due to injury or disease.

Indications: detection of corneal lesions and foreign bodies.

Preparation available

Fluorescein Eye Drops: Eye drops containing 1% and 2 % w/v of fluorescein sodium is usually available. Fluorescein eye drops should be protected from light.

ROSE BENGAL

Indications: see under fluorescein.

Preparation available

Rose Bengal Eye Drops: Eye drops containing 1% rose bengal is usually available.

Chapter - Fifteen

Drugs Acting on the Ear, Nose and Oropharynx

The drugs used vary from local preparations to those which can and must be used on a systemic basis. The specific preparations for the different areas and their classification are given below.

15.1 Drugs acting on the ear

Uncomplicated cases of acute infection of the middle ear require no antibiotics. Topical treatment of acute otitis media is ineffective and there is no place for drops containing a local anaesthetic. In chronic suppurative otitis media, the initial treatment is directed at measures for producing a healthy nose and paranasal sinuses. Acute exacerbations of chronic infection may require systemic antibiotics.

One major concern regarding ears is the removal of ear wax. However, the ear-wax is a normal body secretion which provides a protective film on meatal skin and should be removed only if it causes deafness or blocks a proper view of the ear drum. In certain patients this wax may need to be softened with a topical solution such as sodium bicarbonate ear-drops or olive or almond oil before the actual syringing. Then the removal of wax can be done by syringing with warm water. Ear drops containing organic solvents can cause irritation of the meatal skin.

15.1.1 Antibacterial preparations

ACETIC ACID

It has antifungal and antibacterial activity.

Indications: mild otitis externa.

ALUMINIUM ACETATE

It is a topical astringent.

Indications: inflammation in otitis externa.

Dose: Apply on ribbon gauze dressing or sponge wick saturated with the ear drop.

CHLORAMPHENICOL

Indications: bacterial infection in otitis externa.

Adverse effects and cautions: sensitivity reactions. For details, *see* under section 14.1.1, antibacterial preparations.

Preparation available

Chloramphenical Ear Drops: Ear drops containing 5% w/v of chloramphenicol is usually available. Chloramphenicol ear drops should be protected from light.

GENTAMICIN

Indications: bacterial infection in otitis externa.

Adverse effects and cautions: local sensitivity reactions.

Avoid prolonged use. Risk of ototoxicity in perforated eardrum.

Preparation available

Gentamicin Ear Drops: Ear drop containing 0.3% gentamicin (as sulfate) is usually available.

ICHTHAMMOL

It has mild antiseptic and antipruritic effect and modifies keratinisation. Ear drops containing ichthammol 10% and glycerin 5% is usually available.

NEOMYCIN SULFATE

Indications: bacterial infections in otitis extema.

Adverse effects and cautions: local sensitivity reaction. Avoid prolonged use.

Slight risk of ototoxicity in perforated ear drum. For details, *see* under section 14.1.1, antibacterial preparations.

TETRACYCLINE HYDROCHLORIDE

Indications: otitis externa

Adverse effects and cautions: local sensitivity, stains skin and clothing. Avoid prolonged use.

15.1.2 Anti-fungal drugs

CLIOQUINOL

It is applied as 1 % solution.

Indications: mild bacterial or fungal infections in otitis externa.

Adverse effects and cautions: local sensitivity, stains skin and clothing. Prolonged use should be avoided. It should be avoided in perforated ear drum.

CLOTRIMAZOLE

It is applied as 1 % solution in polyethylene glycol.

Indications: fungal infection in otitis externa.

Adverse effects and cautions: occasionally skin irritation or sensitivity.

15.1.3 Anti-inflammatory drugs

BETAMETHASONE SODIUM PHOSPHATE

It is applied as 0.1 % solution.

Indications: eczematous inflammation in otitis externa.

Adverse effect and cautions: local sensitivity reactions.

It is contraindicated in untreated infection and should not be used for prolonged period.

Preparation available

Betamethasone Sodium Phosphate Ear, Eye and Nasal Drops: Drops containing 0.1% of betamethasoe sodium phosphate is usually availabele.

DEXAMETHASONE

Indications: eczematous inflammation in otitis externa.

Adverse effects and cautions: *see* under betamethasone.

HYDROCORTISONE

Indications: eczematous inflammation in otitis externa.

Adverse effects and cautions: *see* under betamethasone.

Preparation available

Hydrocortisone Ear Drops: Ear drops containing 1% of hydrocortisone acetate is usually available.

PREDNISOLONE SODIUM PHOSPHATE

It is applied as 0.5% solution.

Indications: eczematous inflammation in otitis externa.

Adverse effect and cautions: *see* under betamethasone.

Preparation available

Prednisolone Ear Drops: Ear drops containing 0.5% of prednisolone sodium phosphate is usually available.

15.2 Drugs acting on the nose

15.2.1 Decongestants

Repeated use of topical nasal decongestants may cause rebound congestion of the nasal mucous or a chemical rhinitis. The nasal decongestants and antihistaminic combinations are available. Systemic nasal decongestants are of doubtful value. Sodium chloride 0.9% given as nasal drops may relieve nasal congestion by helping to liquify mucous secretion.

As they generally contain sympathomimetics, they should be used with caution in patients with hypertension, hyperthyroidism, coronary heart disease or

diabetes. There is no evidence that nasal preparations containing antibiotics and anti-infective agents have any therapeutic value.

EPHEDRINE HYDROCHLORIDE

Is is the safest preparation and can give relief for several hours.

Indications: nasal congestion.

Adverse effects and cautions: local irritation, headache, nausea, cardiovascular effects.

After excessive use there may be tolerance with diminished effect, prolonged use may cause rebound congestion of the nasal mucosa and chemical rhinitis.

The drug should be used with caution in infants under three months.

Dose: 1-2 drops into each nostril up to 3-4 times daily; CHILD over 3 months, 1-2 drops into each nostril 3-4 times daily; maximum 7 days.

Preparation available

Ephedrine Nasal Drops: Nasal drops containing 0.5% w/v of ephedrine hydrochloride is usually available.

OXYMETAZOLINE HYDROCHLORIDE

It is more likely than ephedrine to cause rebound effects.

Indications: nasal congestion

Adverse effects and cautions: *see* under ephedrine hydrochloride.

Dose: 0.05% solution, 2-3 drops into each nostril 2-3 times daily when required, maximum duration 7 days.

0.025% solution CHILD over 3 months, 1-2 drops into each nostril 2 times a day, morning and evening; dosage has not been established for children below 3 months of age, maximum duration 7 days.

Preparation available

Oxymetazoline Nasal Drops: Oxymetazoline hydrochloride 0.05% solution is usually available.

Oxyroetazoline Nasal Drops, Paediatric: Oxymetazoline hydrochloride 0.025% solution is usually available.

SODIUM CROMOGLICATE

Indications: prophylaxis of allergic rhinits.

Adverse effects and cautions: local irritation, rarely transient bronchospasm.

Preparation available

Sodium Cromoglicate Nasal Drops and Spray: Nasal drops or nasal spray containing 2% of sodium cromoglicate is usually available.

XYLOMETAZOLINE HYDROCHLORIDE

It is also more likely than ephedrine to cause rebound effects.

Indications: nasal congestion

Adverse effects and cautions: *see* under ephedrine hydrochloride.

Preparation available

Xylometazoline Nasal Drops: Nasal drops containing 0.1% xylometazoline hydrochloride is usually available.

Xylometazoline Nasal Drops, Paediatric: Nasal drops containing 0.05% xylometazoline hydrochloride is usually available

15.2.2 Corticosteriods

In allergic rhinitis, topical preparations of corticosteroids and sodium cromoglycate have a well-established role. Beclomethasone, betamethasone, budesonide, mometasone and triamcinolone have a useful role in the prophylaxis and treatment of allergic rhinitis.

BETAMETHASONE

Indications: prophylaxis and treatment of allergic rhinitis.

Adverse effects and cautions: irritation of nose and throat, dryness, headache, smell and taste disturbances, bronchospasm.

The drug should be avoided in the presence of untreated nasal infections, after nasal surgery. Systemic absorption may occur on nasal administration particularly if high doses are used or if treatment is prolonged. The risk of systemic effects may be greater with nasal drops than with nasal sprays.

Dose: ADULT and CHILD over 6 years 100 micrograms into each nostril twice daily; maximum 400 micrograms daily; when symptoms controlled, dose reduced to 50 micrograms into each nostril twice daily.

Preparation available: *see* under section 15.1.3, anti-inflammatory drugs.

BUDESONIDE

Indications: *see* under betamethasone.

Adverse effects and cautions: *see* under betamethasone.

Dose: ADULT and CHILD over 12 years, apply 2 sprays into each nostril once daily in the morning or 1 spray into each nostril twice daily; when control achieved reduce to 1 spray into each nostril once daily.

Preparation available

Budesonide Nasal Spray: Spray delivering budesonide 100 micrograms per metered spray is usually available.

DEXAMETHASONE

Indocations: treatment of allergic rhinitis.

Adverse effects and cautions: *see* under betamethasone.

Dose: ADULT and CHILD over 12 years, 1 spray into each nostril 2-3 times daily, maximum 6 times daily; maximum duration 14 days; CHILD 5-12 years,1 spray into each nostril up to twice daily; under 5 years not recommended.

Preparation available

Dexamethasone Isonicotinate Nasal Spray: Nasal spray delivering dexamethasone isonicotinate 20 micrograms per metered spray is usually available.

15.3 Drugs acting on the oropharynx

A saline mouthwash may relieve the pain of traumatic ulceration. Use of chlorhexidine or povidone iodine mouthwash is often beneficial and may accelerate healing of recurring aphthae. Topical corticosteroids may be used for some forms of oral ulceration.

Local anaesthetic is generally used for the relief of pain in oral lesions. There is no convincing evidence that antiseptic logenzes and sprays have beneficial action and they sometimes irritate and cause sore tongue and lips. Patients with an unexplained mouth ulcer of more than 3 weeks duration require urgent referral to hospital to exclude oral cancer.

CHOLINE SALICYLATES

Indications: mild oral and perioral lesions.

Adverse effects and cautions: salicylate poisoning in childern if frequently used.

The drug should not be applied to dentures, leave at least 30 minutes before re-insertion of denture.

Dose: Apply ½ inch of gel with gentle massage not more often than every 3 hours; CHILD over 4 months, ¼ inch of gel not more often than every 3 hours.

Preparation available

Choline Salicylate Dental Gel: Oral gel containing 8.7% of choline salicylate is usually available.

CORTICOSTEROIDS

Indications: oral and perioral lesions.

Adverse effects and cautions: exacerbation of local infections, thrush or other candidal infections.

It is contraindicated in untreated oral infections.

LIDOCAINE

Indications: relief of pain in oral lesions.

Adverse effects and cautions: chocking.

The drug should be used with caution before meals as this might lead to chocking due to anaesthesia of pharynx.

15.4 Miscellaneous

BETAHISTINE DIHYDROCHLORIDE

Indications: Meniere's disease, vertigo

Adverse effects and cautions: rashes, pruritus, headache, gastro-intestinal disturbances.

The drug should be used with caution in pregnancy, breast-feeding, asthma and peptic ulcer.

Dose: Initially 16 mg 3 times daily, preferably with food; maintenance 24-48 mg daily; CHILD not recommended.

Peparation available

Betahistine Tablets: Each tablet containing 8 mg of betahistine dihydrochloride is usually available.

Chapter - Sixteen

Immunologicals

16.1 Diagnostic Agents

TUBERCULIN, PURIFIED PROTEIN DERIVATIVE (PPD)

It has limited diagnostic value.

Tuberculin PPD is made from the heat-treated products of growth and lysis of the appropriate species of Mycobacteria. Mantoux positive indicates previous exposure to mycobacterium antigens through infection with tubercle bacilli or BCG vaccination. An inflammed area of induration to intradermal testing with PPD denotes a positive reaction.

Adverse effects and cautions: headache, rash, nausea, malaise.

It should not be used within 4 weeks of receiving a live viral vaccine.

16.2 Sera and immunoglobulins

ANTI-RABIES HYPERIMMUNE SERUM

It should be given at the same time as the vaccine when the exposure has been certain and severe. As it is a serum preparation, enquiry should be made for any history of allergy. Skin test must be done prior to giving the sera.

ANTI-D IMMUNOGLOBULIN (HUMAN)

This is given to a rhesus-negative woman following the birth of a rhesus positive infant, and sometimes after abortion. If it is injected within 72 hours of the birth or abortion, the vaccine prevents the formation of antibodies and thus children to be born in the future are protected from the dangers of haemolytic anaemia.

Dose: By deep intramuscular injection, to rhesus-negative woman for prevention of D sensitisation:

Following abortion or birth of rhesus-positive infant, 500 units immediately or within 72 hours; for transplacental bleed in excess of 5 ml foetal red cells, extra 100-125 units per ml foetal red cells.

Following any potentially sensitising episode (e.g. still birth) up to 20 weeks gestation 250 units per episode (after 20 weeks, 500 units) immediately or within 72 hours.

Following Rho (D) incompatible blood transfusion, 100-125 units per ml transfused rhesus-positive red cells.

Preparation available

Anti-D Immunoglobulin Injection: Injection containing 300 micrograms per 2 ml is usually available.

DIPTHERIA ANTITOXIN

This is a refined globulin from horses that have been immunised with diphtheria toxin. Like other sera it causes passive protection only and is likely to cause reactions in certain individuals. It should be used with caution in individuals with a history of allergy. Initial skin test must be done prior to its use. If the amount to be given is large e.g. over 30 000 units then it is usual to give this I.M. and the rest I.V. after a little while.

Dose: Therapeutic use, pharyngeal or laryngeal diphtheria, by intravenous infusion, 20 000 to 40 000 units; CHILD under 10 years half adult dose.

Preparation available

Diphtheria Antitoxin: Each vial containing 10 000 units and 20 000 units are usually available.

HEPATITIS B IMMUNOGLOBULIN

It is recommended for use in association with hepatitis B vaccine for prevention of infection in health care workers dealing with blood products and also for persons who have been accidently inoculated. It is also given to babies of mothers who have become infected with this virus in pregnancy. (see hepatitis B vaccine).

Hepatitis A virus vaccine is still in the developmental stage. However immunoglobulins are given to travellers going to areas where the disease is highly endemic.

Dose: By intramuscular injection (as soon as possible after exposure), ADULT and CHILD over 10 years, 500 units; CHILD under 5 years 200 units, 5-9 years 300 units, NEONATE 200 units as soon as possible after birth.

Preparation available

Hepatitis B Immunoglobulin Injection: Each ml containing 250 units of Anti-HBs in usually available.

NORMAL HUMAN IMMUNOGLOBULIN

The normal human immunoglubulin is prepared from the pooled plasma of a minimum of 1000 donors. The screening involved and the processing now undertaken ensures that AIDS is not transmitted by this preparation.

Normal immunoglobulin may interfere with the immune response to live virus vaccination. It should only be given at least 3 weeks before or 3 months after an injection of normal immunoglobulin.

SNAKE ANTIVENOM SERUM

Snake Venom Antiserum

This is a horse serum preparation and so precaution must be taken in its use as untoward reaction, can lead to death. It is impearative to do a sensitivity test prior to giving the serum. It is necessary to check that the antivenum serum that is being used is effective against the bites of those types of snakes that are found in that region.

Antivenom sera should never be injected into a finger or toe. If it is given intramuscularly it should be injected into a large muscle mass such as the gluteal region. However one must avoid nerve trunks.

16.3 Vaccines

BACILLUS CALMETTE GUERIN VACCINE

BCG Vaccine

This is a live attenuated strain of *Mycobacterium tuberculosis* which is in a freeze-dried state. It is reconstituted and then given intradermally just above the insertion of the deltoid muscle. A small papule forms after about a week and a small ulcer after about three weeks. No dressing is necessary for this ulcer and it heals in a few weeks. BCG vaccine may be given simultaneously with another live vaccine, but if they are not given at the same time, an interval of 4 weeks should normally be allowed. BCG vaccine is normally given to newborns and certainly by the 6^{th} week when other vaccines are started.

Adverse effects and cautions: It is contraindicated in infants known to be HIV infected, immunodeficiency.

Dose: INFANTS up to 12 months 0.05 ml by intradermal injection.

CHOLERA VACCINE

This is inactivated vaccine.

WHO has recommended it for prevention and not for containing outbreaks. Protection is obtained 7 days after completing the course and lasts for at least 6 months.

Adverse effects: mild transient gastro-intestinal disturbances.

Dose: By mouth, ADULT and CHILD over 2 years, 2 doses each separated by 1 week.

DIPHTHERIA, TETANUS VACCINE

DT Vaccine

This is used mainly as a vaccine which is given as a booster dose at time of school entry viz. around 7 years of age.

Dose: Primary immunisation of children, 0.5 ml by intramuscular injection at 6 weeks, followed by second dose after 4 weeks and third dose after another 4 weeks.

DIPTHERIA, TETANUS AND PERTUSSIS VACCINE

DTP Vaccine

This vaccine is a combination of the diphtheria formol toxoid, tetanus formol toxoid and the pertussis vaccine with a mineral carrier. It is used for primary immunisation for children. The first dose is given at 6 weeks with subsequent two doses at 4 weeks intervals. In the National schedule currently in use, the initial dose is being given at 6 weeks and a total of 3 doses by one year.

The immunisation schedule followed by the Expanded Programme of Immunisation (EPI) is given at the end of this section.

Dose: primary immunisation of children, 0.5 ml by intramuscular injection at 6 weeks followed by second dose after 4 weeks and third dose after another 4 weeks.

DIPTHERIA, TETANUS, PERTUSSIS AND HEPATITIS B VACCINE

DTP, Hep B Vaccine

Diphtheria, tetanus, pertussis (acellular, component) and hepatitis B (rdna) vaccine (adsorbed) is a combined vaccine composed of: diphtheria formol toxoid; tetanus formol toxoid; individually purified antigenic components of *Bordella pertussis*; hepatitis B surface antigen; a mineral adsorbent such as aluminium hydroxide or hydrated aluminium phosphate.

The immunisation schedule followed by the Expanded Programme of Immunisation (EPI) is given at the end of this section.

DIPTHERIA, TETANUS, PERTUSSIS, HEPATITIS B AND HAEMOPHILIS INFLUENZA B VACCINE

DTP, Hep B, Hib Vaccine

Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rdna) and haemophilus type b conjugate vaccine (adsorbed) is a combined vaccine composed of: diphtheria formol toxoid; tetanus formol toxoid; individually purified antigenic components of *Bordetella pertussis*; hepatitis B surface antigen (hbsag).

The immunisation schedule followed by the Expanded Programme of Immunisation (EPI) is given at the end of this section.

HEPATITIS B VACCINE

The hepatitis B vaccine is a recombinant vaccine.

A single course of hepatitis B vaccine with a single booster 5 years after the primary course may be sufficient to maintain immunity.

Immunisation takes upto six months to confer adequate protection.

Dose: By intramuscular injection, 3 doses of 1 ml, the second 1 month and the third 6 months after the first dose; CHILD birth to 15 years 3 doses of 0.5 ml, INFANTS born to HBsAg positive mothers, 4 doses of 0.5 ml, first dose at birth with hepatitis B immunoglobulin injection (separate site), second 1 month, the third 2 months and the fourth 12 months after the first dose.

Note: The deltoid muscle is the preferred site of injection in adults and older children; the anterolateral thigh is the preferred site in infants and children; the buttock must not be used because vaccine efficacy is reduced. The subcutaneous route is used for patients with bleeding disorder.

Preparation available

Hepatitis-B Surface Antigen Vaccine: Each ml containing 20 micrograms of hepatitis-B-surface antigen protein is usually available.

JAPANESE ENCEPHALITIS VACCINE

Three types of vaccines are available. The recommended schedule varies between vaccines. Live vaccine is contraindicated in immunosuppression and pregnancy.

MEASLES VACCINE

This is a live attenuated strain of measles virus vaccine. Currently it is given at nine months of age. The child may experience a mild measles like syndrome with a rash and pyerexia which comes in about a week after the injection of the vaccine. As the vaccine starts protecting the child after seven days, it is better to vaccine a child within 48 hours, who has not been immunised, has come in contact with a case.

It can be used to immunize HIV infected infants (unless severely immunocompromised).

MENINGOCOCCAL VACCINE

This vaccine has been in more general use since the epidemic of 1984 when it was used as a measure for the control of the disease.

Meningococcal vaccines are available as combinations of capsular polysaccharide antigens.

POLIOMYELITIS VACCINE (LIVE ATTENUATED)

This vaccine is a trivalent one containing a mixture of attenuated strains of virus types 1, 2 and 3. It is given as two drops orally on 3 occasions together with the DTP vaccine.

The vaccine is contraindicated in primary immunodeficiency or immunosuppression.

Preparation available

Poliomyelitis Vaccine, Live (Oral): A suspension of suitable live attenuated strains of poliomyelitis virus, type 1, 2 and 3 is usually available.

RABIES VACCINE

This vaccine is used for pre-exposure and post-exposure prophylaxis. Human diploid cell vaccine (HDCV) and purified chick embryo cell vaccine are

cell-derived. Vaccines of nerve cell tissue are less potent and are frequently associated with adverse effects.

Dose: Pre-exposure prophylaxis, by deep subcutaneous or intramuscular injection in the deltoid region, 1 ml on days 0, 7 and 28; also booster doses every 2-3 years.

Post-exposure, by deep subcutaneous or intramuscular injection, 1 ml on days 0, 3, 7, 14, and 30 days.

TETANUS TOXOID

This is a single monovalent type of vaccine and is available as adsorbed vaccine. It should not be given more frequently than five years since the last booster dose.

With the concept of preventing the occurance of tetanus neonatarum and also preventing tetanus in the post partum state, it has become customary to immunise against tetanus or to give booster doses of tetanus toxoid to women during the course of pregnancy.

Dose: Primary immunization, 0.5 ml by intramuscular injection followed after 4 weeks by a second dose and after a further 6 months by a third dose; 2 re-inforcing doses of 0.5 ml the first at least 1 year after and secondat least one year later.

Unimmunised pregnant women 0.5 ml by intramuscular injection followed after at least 4 weeks by a second dose.

Preparation available

Tetanus Toxoid Absorbed Vaccine: Vial containing 0.5 ml and 5 ml are usually available.

TYPHOID VACCINE

Oral typhoid vaccine is commonly used. Protection lasts about 3 years. Four doses of oral typhoid vaccines are given, each 2 days apart to ADULT and CHILD over 5 years.

YELLOW FEVER VACCINE

This is a live attenuated yellow fever virus (17 D strain) vaccine. It should not be given to CHILDREN under eight months as it can lead to encephalitis. It should not also be given to pregnant women. Immunity is probably life-long but booster doses recommended every ten years. Immunity starts 10 days after primary vaccination and immediately after revaccination.

Dose: 0.5 ml by subcutaneous injection.

Preparation available

Yellow Fever Vaccine: Suspension of chick embryo proteins containing attenuated 17 D strain of yellow fever virus is usually available.

16.4 Pregnancy and vaccination

1. Live vaccines should be avoided because of possible harm to foetus.
2. Inactivated and killed vaccines can be administered.

Note: Live vaccines are: Yellow fever, measles, mumps, rubella, polio and BCG.

16.5 National Immunization Schedule

Vaccine	Doses	Age	Minimum interval
BCG	One	Birth or first contact with health institution	-
DTP, HepB, Hib	Three	6 weeks, 10 weeks, 14 weeks	4 weeks each
Oral polio	Three	6 weeks, 10 weeks, 14 weeks	4 weeks each
Measles	One	9 months	-
TT	Two	Pregnant women	4 weeks

Chapter - Seventeen

Drugs Acting on Uterus

17.1 Uterine Stimulants

CARBOPROST

It is a prostaglandin F2α analogue.

Indications: postpartum haemorrhage due to uterine atony in patients unresponsive to ergometrine and oxytocin.

Adverse effects and cautions: hypertension, bronchospasm, nausea, vomiting, diarrhoea, hyperthermia and flushing, pulmonary oedema.

The drug is contra-indicated in untreated pelvic infection, cardiac, renal, pulmonary or hepatic disease.

The drug should be used with caution in glaucoma, asthma, hypertension, hypotension, diabetes, epilepsy, uterine scars

Dose: By deep intramuscular injection, 250 micrograms, repeated if necessary at intervals of 1 ½ hours (in severe cases the interval may be reduced but should not be less than 15 minutes); total dose should not exceed 2 mg.

Preparation available

Carboprost Injection: Injection containing 250 micrograms of carboprost (as trometamol salt) in 1-ml vial is usually available.

ERGOMETRINE AND *METHYLERGOMETRINE*

It directly stimulates the uterine muscle to increase force and frequency of contractions. With small doses, contractions are increased in force or frequency or both but followed by normal degree of relaxation; with larger doses, basal uterine tone is elevated and the relaxation periods will be decreased. Methylergometrine has an action on uterus similar to ergometrine.

Indications: prevention and treatment of postpartum and post-abortal haemorrhage.

Oxytocin is now recommended for routine use in postpartum and post-abortion haemorrhage, since oxytocin is more stable than ergometrine. Oxytocin does not require transport by cold chain.

Adverse effects and cautions: nausea, vomiting, abdominal pain, dizziness, transient hypertension, chest pain and tachycardia.

The drug should be used with caution in cardiac disease, hypertension, hepatic and renal impairment, multiple pregnancy.

The drug is contraindicated for induction of labour, first and second stage of labour, severe cardiac disease, severe cardiac and renal impairment, severe hypertension and eclampsia.

Dose: Prevention and treatment of post-partum haemorrhage, by intramuscular injection, 200 micrograms when the anterior shoulder is delivered or immediately after birth.

Excessive uterine bleeding, by slow intravenous injection, 250-500 micrograms when the anterior shoulder is delivered.

Preparation available

Ergometrine Injection: Injection containing ergometrine maleate 200 micrograms and 500 micrograms per ml is usually available.

Ergometrine Tablets: Each tablet containing 500 micrograms of ergometrine maleate is usually available.

Methylergometrine Maleate Injection: Injection containing 200 micrograms of methylergometine maleate per ml in light resistant vial is usually available.

MISOPROSTOL

It is a prostaglandin which is used as a low-dose vaginal tablet.

Indications: induction of labour, medical termination of pregnancy of up to 63 days gestation.

Adverse effects and cautions: uterine hyperstimulation, uterine rupture, foetal distress, diarrhoea, abdominal pain, rashes, dizziness.

The drug is contraindicated in placenta praevia, major cephalopelvic disproportion, foetal malpresentation, foetal distress, history of caesarean section, multiple pregnancy.

The drug should be used with caution in hypertension. Oxytocin should not be started for 6 hours following administration of vaginal dose.

Dose: Induction of labour, by vagina, 25 micrograms repeated after 6 hours if necessary, if still no response increase to 50 micrograms every 6 hours for up to 4 doses.

Medical termination of intra-uterine pregnanancy of up to 63 days gestation, by mouth mifepristone 200 mg as a single dose, followed 36-48 hours later (unless abortion already complete) by misoprostol 800 micrograms by vagina and individual observed for at least 6 hours (or until bleeding or pain at acceptable level) with follow-up visit 10-15 days later to verify complete expulsion (if treatment fails, it is essential that pregnancy be terminated by another method).

Preparation available

Misoprostol Tablets: Each tablet containing 25 micrograms and 200 micrograms of misoprostol is usually available.

Mifepristone – Misoprostol Tablets: A combi-pack of one tablet mifepristone (200 mg) and 4 tablets of misoprostol each tablet containing 200 micrograms is available.

MIFEPRISTONE

It is an antiprogestogenic steroid, which sensitises the myometrium to prostaglandin-induced contractions. It softens and dilates the cervix. Abortion occurs in shorter time and with a lower dose of prostaglandin.

Indications: medical termination of intra-uterine pregnancy of up to 63 days gestation.

Adverse effects and cautions: uterine contractions, vaginal bleeding (sometimes severe), nausea, vomiting, rash, dizziness, headache.

The drug is contraindicated in suspected ectopic pregnancy, uncontrolled severe asthma.

The drug should be used with caution in hepatic or renal impairment, breast-feeding, asthma, mothers aged over 35 years.

Dose: *see* under misoprorstol.

Preparation available: *see* under misoprostol.

OXYTOCIN

It stimulates the frequency and force of contraction of uterine smooth muscle. The uterine myometrium contains receptors specific to oxytocin. Amplitude and duration of uterine contractions are increased, leading to dilation and effacement of the cervix. The number of oxytocin receptors and, therefore, uterine response to oxytocin increases gradually throughout pregnancy, reaching its peak at term.

It also stimulates smooth muscle to facilitate ejection of milk from breast. Oxytocin does not increase milk production.

Indications: induction of labour, incomplete or inevitable or missed abortion, prevention and treatment of postpartum and post-abortion haemorrhage.

Adverse effects and cautions: nausea, vomiting, high dose cause violent uterine contractions leading to rupture, foetal distress, asphyxia and death, arrhythmias, rashes, water intoxication and anaphylactoid reactions.

The drug should be used with caution in hypertension, abnormal presentation, previous caesarean section, caudal block anaesthesia.

The drug is contraindicated in mechanical obstruction to delivery, severe pre-eclamptic toxaemia, foetal distress, hypertonic uterine contraction and placenta praevia.

Dose: By slow intravenous infusion, induction of labour and augmentation of labour in hypotonic uterine inertia, a solution containing 1 unit per litre, 0.001-0.002 units/minute, increased at intervals of at least 30 minutes, until a maximum of 3-4 contractions occur every 10 minutes, maximum rate 0.02 units/ minute.

Incomplete, inevitable or missed abortion, by slow intravenous infusion, 5 units followed if necessary, by intravenous infusion, 0.02-0.04 units/minute.

Prevention of post-partum haemorrhage after delivery of anterior shoulder, by slow intravenous infusion, 5 units. Treament of post-postum haemorrhage, by slow inravenous injection, 5-10 units.

Preparation available

Oxytocin Injection: Injection containing 1 unit/ml of oxytocin in 5-ml vial is usually available.

17.2 Uterine Relaxants (Tocolytics)

B-2 receptor agonists relax the uterus and are employed to inhibit premature labour. However, these drugs may not have clinically significant benefits on perinatal mortality and may actually increase maternal morbidity. Nifedipine has longer postponement of delivery and fewer adverse effects.

ISOXSUPRINE HYDROCHLORIDE

It is a vasodilator which also stimulates beta-adrenergic receptors. It causes direct relaxation of vascular and uterine smooth muscle. Isoxsuprine hydrochloride has been used to arrest premature labour.

Indication: *see* notes above.

Adverse effects and cautions: transient flushing, hypotension, tachycardia, rashes and gastrointestinal disturbances. Maternal pulmonary oedema and foetal tachycardia have been reported following intravenous administration in premature labour.

Isoxsuprine is contra-indicated following recent arterial haemorrhage. It should not be administered parenterally to patients with heart disease or severe anaemia.

It should not be given where there is premature detachment of the placenta or immediately post partum, nor should be used for premature labour if there is infection.

Dose: To arrest premature labour, by intravenous infusion, 200-300 micrograms per minute, adjust according to patient's response, until control is achieved. Prophylaxis, by month, 40-80 mg daily.

Preparaion available

Isoxsuprine Hydrochloride Injection: Injection containing 5 mg of isoxsuprine hydrochloride per ml is usually available.

Isoxsuprine Hydrochloride Tablets: Each tablet containing 10 mg, 20 mg and 40 mg of isoxsuprine hydrochloride is usually available.

NIFEDIPINE

It is a calcium-channel blocker.

Indications: uncomplicated premature labour between 24-33 weeks gestation.

Adverse effects and cautions: tachycardia, flushing, headache, oedema, constipation or diarrhoea, tremor, urticaria.

The drug is contraindicated within 1 month of myocardial infarction, cardiogenic shock, unstable or acute attacks of angina.

The drug should be used with caution in severe hypotension, diabetes mellitus, breast-feeding, heart failure.

Dose: Sublingually (immediate-release tablets) 10 mg every 15 minutes if necessary, maximum 40 mg in the first hour then by mouth (sustained

release tablets) 60-160 mg daily in 3-4 divided doses adjusted to uterine activity.

RITODRINE

It is used for inhibiting uncomplicated premature labour between 24 and 33 weeks of gestation. It may permit a delay in delivery of 48 hours.

Indications: *see* notes above.

Adverse effects and cautions: nausea, vomiting, sweating, tremor, tachycardia, palpitations, hypokalaemia, chest pain or tightness, arrhythmias, uterine bleeding, over-hydration.

The drug should be used with caution in hypertension, hypokalaemia, hyperthyroidism, diabetes mellitus, mild to moderate pre-eclampsia.

The drug is contraindicated in cardiac disease, eclampsia- severe pre-eclampsia, intrauterine foetal death, placenta praevia, cord compression, and intra-uterine infection.

Dose: By intravenous injection, initially 50 micrograms/minute, gradually increased by 50 micrograms/minute every 10 minutes, until contractions stop or maternal heart rate reaches 100/minute, to 150-350 micrograms/minute, continue for 12-48 hours after contractions have ceased. Then by mouth, 10 mg, 30 minutes before termination of intravenous infusion, repeated every 2 hours for 24 hours, followed by 10-20 mg every 4-6 hours, maximum dose 120 mg daily.

Preparation available

Ritodrine Tablets: Each tablet containing 10 mg of rotodrine hydrochloride is usually available.

Ritodrine Injection: Injection containing 10 mg of ritodrine hydrochloride per ml is usually available.

SALBUTAMOL

Indications: uncomplicated premature labour.

Adverse effects, cautions, and contraindications: see under ritodrine.

Dose: By intravenous infusion, 10 micrograms/minute increased gradually according to response at 10-minute intervals until contractions cease, to maximum of 45 micrograms/minute. Maintain rate for 1 hour after contractions have stopped, then gradually reduce by 50% every 6 hours, then by mouth 4 mg every 6-8 hours.

Preparations available

Salbutamol Injection: Injection containing 50 micrograms and 500 micrograms of salbutamol (as sulfate) per ml is usually available.

Salbutamol Tablets: Each tablet containing 2 mg, 4 mg and 8 mg of salbutamol (as sulfate) is usually available.

TERBUTALINE SULFATE

Indications: uncomplicated premature labour.

Adverse effects, cautions and contraindications: *see* under ritodrine.

Dose: By intravenous infusion, 5 micrograms/minute for 20 minutes, gradually increased every 20 minutes to 10 micrograms/minute (maximum 20 micrograms/minute rarely needed), continue for 1 hour then decrease every 20 minutes in steps of 2.5 micrograms/minute tp lowest dose that maintains suppression, continue at this level for 12 hours and then by mouth, 5 mg every 8 hours for as long as desirable to prolong pregnancy.

Preparation available

Terbutaline Injection: Injection containing terbutaline sulfate 500 micrograms/ml is usually available.

Terbutaline Tablets: Each tablet containing 2.5 mg and 5 mg of terbutaline sulfate is usually available.

17.3 Contraceptives

17.3.1 Combined Oral Contraceptives

Oestrogen-progestin combinations are oral contraceptive combinations containing oestrogenic and progestinic steroids. The oestrogenic component of oral contraceptive combinations is mostly ethinylestradiol or mestranol. Mestranol, the methyl ester of ethinylestradiol is slightly less active than ethinyl-estradiol.

Low strength preparations (containing ethinylestradiol 20 micrograms) are appropriate for women with risk factors and standard preparations (containing ethinylestradiol 30 or 35 micrograms) are appropriate for standard use.

Oestrogen-progestin combinations produce a contraceptive effect mainly by suppressing the hypothalamic-pituitary system resulting in prevention of ovulation; in addition changes in endometrium make it unreceptive to implantation. The oestrogen acts mainly by suppressing secretion of follicle-stimulating hormone (FSH), and progestin appears to act mainly by inhibiting the preovulatory rise of LH. In addition, changes in cervical mucous may prevent sperm penetration.

Ovulation usually resumes within 3 menstrual cycles after oral contraceptives have been discontinued; anovulation and amenorrhoea persisting for 6 months or longer requires investigation and appropriate treatment.

Indications: contraception, menstrual symptoms.

Adverse effects and cautions : nausea, vomiting, abdominal cramps, diarrhoea, constipation, chloasma, breast tenderness, mental depression, headache, oedema, thromboembolic disorders, bleeding irregularities including breakthrough bleeding, spotting and menstrual irregularities, changes in libido, depression, impairment of liver function, hepatic tumors.

Oral contraceptives should be used with caution in patients with risk factors for venous thromboembolism, arterial disease, migraine.

Oral contraceptives are contraindicated in women with known or suspected pregnancy, undiagnosed genital bleeding, diplopia, active liver disease or history of cholestatic jaundice.The drugs are also contraindicated during breast-feeding, women who have or had thrombophlebitis or

thromboembolic disorders, cerebrovascular or coronary artery disease, carcinoma of the breast or genital carcinoma.

The combination should be stopped immediately if following symptoms occur: sudden severe chest pain, severe pain in calf of one leg, severe stomach pain, blood pressure above 160 mmHg systolic and diastolic 100 mmHg, hepatitis, jaundice, liver enlargement, severe prolonged headache, sudden partial or complete loss of vision.

Drug interactions: Rifampicin and other known inducers of hepatic microsomal enzymes including carbamazepine, phenytoin decrease contraceptive efficacy and increase break through bleeding during concomitant use with oral contraceptives.

Preparation available

Ethinylestradiol + Norethisterone Tablets: Each tablet containing 35 micrograms of ethinylestradiol and 1 mg of norethisterone is usually available. The first course is usually started on 1st day of cycle and one tablet daily is taken for 21 days, followed by 7-day interval during which withdrawal bleeding occurs.

Ethinylestradiol + Levonorgestrel tablets: Each tablet containing 30 micrograms of ethinylestradiol and 150 micrograms of levonorgestrel is usually available.

17.3.2 Progestogen-only contraceptives

Progestogen-only contraception may offer a suitable alternative when oestrogens are contraindicated, but have a higher failure rate than combined preparations. A three month depot intramuscular injection is an alternative. Subcutaneous implants that release hormone for several years (e.g. Norplant) are in use; they can be removed surgically if adverse effects develop or pregnancy is desired. Intramuscular progestogen is equal in efficacy to the combined pill.

Progestogen-only contraception is particularly appropriate to older women, women having an absolute contraindication for oestrogen, e.g. history of thromboembolism, heavy smokers, diabetics, hypertension, migraine and lactating women (it interfers with milk less than the combined pill). Adverse effects such as reduced amount of menstrual bleeding, menorrhagia are common and tend to resolve on long term treatment.

Medroxyprogestrone is used with caution in diabetes, hypertension.

Preparation available

Levonorgestrel Implant: It has comparable efficacy to injectable medroxyprogesterone acetate but lasts for 7 years. Unlike the injectable preparations the method is immediately reversible on removal of the implants. Two-rod levonorgestrel-releasing implant, each rod containing 75 mg of levonorgestrel (150 mg total) is usually available.

Medroxyprogesterone Acetate Injection: It is aqueous suspension containing 150 mg of medroxyprogesterone acetate per ml. 150 mg is given by deep intramuscular injection in first 7 days of cycle or within first 5 days after

parturition or delay until 6 weeks after parturition if breast-feeding, for long-term contraception and has to be repeated every 3 months.

17.3.3 Spermicidal contraceptives

Vaginal preparations to immobilise or kill spermatozoa are used to add safety to various mechanical contraceptives. They are very unreliable and should be used alone only in an emergency. Substances used include nonoxinols as pessary, cream, gel or foam.

17.3.4 Intrauterine devices

Copper intrauterine devices are recommended as a long-term contraceptive method, primarily for older parous women and young nulliparous women with no history of pelvic inflammatory disease. Intrauterine devices do not protect against sexually transmitted diseases including human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS).

The copper intrauterine device prevents pregnancy in 96 to 99% of users in the first year of use, depending on the specific device. The precise mechanism of action has not been fully established; a number of mechanisms may contribute to the contraceptive effect. The devices produce cellular reactions which result in interference with sperm migration, fertilisation and, to a lesser extent, with implantation.

Local contraceptive action begins immediately after insertion and action terminates quickly on removal. Manufacturers recommend IUD replacement within the following time periods:

Copper - T 300	:	5 years
Copper-T 380 A	:	8 years

Indications: contraception, emergency contraception.

Adverse effects and cautions: uterine or cervical perforation, pelvic infection may be exacerbated, heavy menses, dysmenorrhoea, and allergy. Some pain, bleeding, epileptic seizures and vasovagal attack on insertion may be encountered.

The devices are contraindicated in pregnancy, severe anaemia, very heavy menses, recent sexually transmitted infection, history of ectopic pregnancy or tubal surgery, distorted or small uterine cavity, pelvic inflammatory disease, genital malignancy, immunosuppressive therapy and copper allergy.

Administration: contraception, can be inserted any time between day 4 and day 12 after start of menstrual bleeding.

Emergency contraception, device may be inserted up to 120 hours (5 days) after unprotected intercourse.

Appendix - I

Drug Interaction

In the following table the symbol * with **bold** letter indicates a **potentially hazardous interaction** and the combined administration of the drugs involved should be **avoided**, or only taken with caution and appropriate monitoring. Interactions with no symbol do not usually have serious consequences.

Abacavir

Methadone: Plasma concentration of methadone possibly reduced
Phenobarbital: Plasma concentration of abacavir possibly reduced
Phenytoin: Plasma concentration of abacavir possibly reduced
Rifampicin: Plasma concentration of abacavir possibly reduced

Acetazolamide

Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
Amlodipine: Enhanced hypotensive effect
Aspirin: Increased risk of toxicity when given with high-dose aspirin
Atenolol: Enhanced hypotensive effect
***Carbamazepine:** Increased risk of hyponatraemia; acetazolamide increases plasmacarbamazepine concentration
Chlorpromazine: Enhanced hypotensive effect
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Contraceptives, Oral: Antagonism of diuretic effect by estrogens
Dexamethasone: Increased risk of hypokalaemia; antagonism of diuretic effect
Diazepam: Enhanced hypotensive effect
***Digoxin:** Hypokalaemia caused by acetazolamide increases cardiac toxicity of digoxin
***Enalapril:** Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Increased risk of hypokalaemia
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Increased risk of hypokalaemia

Hydrocortisone: Increased risk of hypokalaemia; antagonism of diuretic effect
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
***Lidocaine:** Hypokalaemia caused by acetazolamide antagonises action of lidocaine (interaction less likely when lidocaine used topically)
***Lithium:** Excretion of lithium increased
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Phenobarbital: Increased risk of osteomalacia
Phenytoin: Increased risk of osteomalacia
Prednisolone: Increased risk of hypokalaemia; antagonism of diuretic effect
Propranolol: Enhanced hypotensive effect
***Quinidine:** Cardiac toxicity of quinidine increased if hypokalaemia occurs; acetazolamide possibly reduces excretion of quinidine (increased plasma concentration)
Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol
Sodium nitroprusside: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Acetylsalicylic acid: *see* Aspirin

Aciclovir

Ciclosporin: Increased risk of nephrotoxicity

Adrenaline: *see* Ephinephrine

Albendazole

Dexamethasone: Plasma-albendazole concentration possibly increased
Praziquantel: Increased plasma concentration of active metabolite of albendazole

Alcohol

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
***Amitriptyline:** Enhanced sedative effect
Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

Carbamazepine: Possibly enhanced CNS adverse effects of carbamazepine

Chlorphenamine: Enhanced sedative effect

Chlorpromazine: Enhanced sedative effect

***Clomipramine:** Enhanced sedative effect

Codeine: Enhanced sedative and hypotensive effect

***Cycloserine:** Increased risk of convulsions

Diazepam: Enhanced sedative effect

Enalapril: Enhanced hypotensive effect

Fluphenazine: Enhanced sedative effect

Furosemide: Enhanced hypotensive effect

Glibenclamide: Enhanced hypoglycaemic effect

Glyceryl trinitrate: Enhanced hypotensive effect

Griseofulvin: Possibly enhanced effects of alcohol

Haloperidol: Enhanced sedative effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Insulins: Enhanced hypoglycaemic effect

Isosorbide dinitrate: Enhanced hypotensive effect

Levamisole: Possibility of disulfiram-like reaction

Metformin: Enhanced hypoglycaemic effect; increased risk of lactic acidosis

Methadone: Enhanced hypotensive and sedative effects

Methyldopa: Enhanced hypotensive effect

Metronidazole: Disulfiram-like reaction

Morphine: Enhanced sedative and hypotensive effect

Nifedipine: Enhanced hypotensive effect

Phenobarbital: Enhanced sedative effect

Phenytoin: Plasma-phenytoin concentration reduced with regular large amounts of alcohol

Procarbazine: Disulfiram-like reaction

Promethazine: Enhanced sedative effect

Propranolol: Enhanced hypotensive effect

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Verapamil: Enhanced hypotensive effect; plasma concentration of alcohol possibly increased by verapamil

***Warfarin:** Enhanced anticoagulant effect with large amounts of alcohol; major changes in alcohol consumption may affect anticoagulant control

Alcuronium

***Amikacin:** Enhanced effects of alcuronium

Carbamazepine: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)

***Clindamycin:** Enhanced muscle relaxant effect

***Gentamicin:** Enhanced muscle relaxant effect

Halothane: Effects of alcuronium enhanced

Lithium: Enhanced muscle relaxant effect

Magnesium (parenteral): Enhanced muscle relaxant effect

Neostigmine: Antagonism of muscle relaxant effect

Nifedipine: Enhanced muscle relaxant effect

Phenytoin: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)

***Procainamide:** Enhanced muscle relaxant effect

Propranolol: Enhanced muscle relaxant effect

Pyridostigmine: Antagonism of muscle relaxant effect

***Quinidine:** Enhanced muscle relaxant effect

***Streptomycin:** Enhanced muscle relaxant effect

Verapamil: Enhanced muscle relaxant effect

Allopurinol

Amoxicillin: Increased risk of rash

Ampicillin: Increased risk of rash

***Azathioprine:** Effects of azathioprine enhanced and toxicity increased, reduce dose of azathioprine

Ciclosporin: Plasma-ciclosporin concentration possibly increased (risk of nephrotoxicity)

Didanosine: Possibly increased plasma concentration of didanosine

Hydrochlorothiazide: Increased risk of hypersensitivity, especially in renal impairment

***Mercaptopurine:** Effects of mercaptopurine enhanced and toxicity increased, reduce dose of mercaptopurine

Warfarin: Anticoagulant effect possibly enhanced

Aluminium hydroxide: *see* Antacids

Amikacin

***Alcuronium:** Enhanced effects of alcuronium

Amphotericin B: Increased risk of nephrotoxicity

Capreomycin: Increased risk of nephrotoxicity and ototoxicity

***Ciclosporin:** Increased risk of nephrotoxicity

***Cisplatin:** Increased risk of nephrotoxicity and possibly of ototoxicity

***Furosemide:** Increased risk of ototoxicity

***Neostigmine:** Antagonism of effects of neostigmine

***Pyridostigmine:** Antagonism of effects of pyridostigmine

***Suxamethonium:** Enhanced effects of suxamethonium

Vancomycin: Increased risk of nephrotoxicity and ototoxicity

***Vecuronium:** Enhanced effects of vecuronium

Amiloride

Alcohol: Enhanced hypotensive effect

Amitriptyline: Increased risk of postural hypotension

Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

Carbamazepine: Increased risk of hyponatraemia

Chlorpromazine: Enhanced hypotensive effect

***Ciclosporin:** Increased risk of hyperkalaemia

Cisplatin: Increased risk of nephrotoxicity and ototoxicity

Clomipramine: Increased risk of postural hypotension

Contraceptives, Oral: Antagonism of diuretic effect by estrogens

Dexamethasone: Antagonism of diuretic effect

Diazepam: Enhanced hypotensive effect

***Enalapril:** Enhanced hypotensive effect; increased risk of severe hyperkalaemia

Fluphenazine: Enhanced hypotensive effect

Glyceryl trinitrate; Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrocortisone: Antagonism of diuretic effect

Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

***Lithium:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)

Methyldopa: Enhanced hypotensive effect

Nifedipine: Enhanced hypotensive effect

Nitrous oxide Enhanced hypotensive effect

***Potassium salts:** Increased risk of hyperkalaemia

Prednisolone: Antagonism of diuretic effect

Propranolol: Enhanced hypotensive effect

Sodium nitroprusside: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Verapamil: Enhanced hypotensive effect

Amitriptyline

Acetazolamide: Increased risk of postural hypotension

***Alcohol**: Enhanced sedative effect

Amiloride: Increased risk of postural hypotension

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Atropine: Increased antimuscarinic adverse effects

Biperiden: Increased antimuscarinic adverse effects

***Carbamazepine:** Antagonism of anticonvulsant effect (convulsive threshold lowered); accelerated metabolism of amitriptyline (reduced plasma concentration; reduced antidepressant effect)

Chlorphenamine: Increased antimuscarinic and sedative effects

***Chlorpromazine:** Increased risk of antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Codeine: Possibly increased sedation

Contraceptives, Oral: Antagonism of antidepressant effect by estrogens but adverse effects of amitriptyline possibly increased due to increased plasma concentration of amitriptyline

Diazepam: Enhanced sedative effect

***Epinephrine**: Increased risk of hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)

***Ethosuximide:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Fluphenazine:** Increased risk of antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Furosemide: Increased risk of postural hypotension

Glyceryl trinitrate: Reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under tongue owing to dry mouth)

***Haloperidol:** Increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Halothane: Increased risk of arrhythmias and hypotension

Hydrochlorothiazide: Increased risk of postural hypotension

Isosorbide dinitrate: Reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under tongue owing to dry mouth)

Ketamine: Increased risk of arrhythmias and hypotension

Levothyroxine: Enhanced effects of amitriptyline

Lithium: Risk of toxicity

Methadone: Sedative effects possibly increased

Morphine: Possibly increased sedation

Nitrous oxide: Increased risk of arrhythmias and hypotension

***Phenobarbital:** Antagonism of anticonvulsant effect (convulsive

threshold lowered); metabolism of amitriptyline possibly accelerated (reduced plasma concentration)

***Phenytoin:** Antagonism of anticonvulsant effect (convulsive threshold lowered); possibly reduced plasma-amitriptyline concentration

***Procainamide:** Increased risk of ventricular arrhythmias

Promethazine: Increased antimuscarinic and sedative effects

***Quinidine:** Increased risk of ventricular arrhythmias

Rifampicin: Plasma concentration of amitriptyline possibly reduced

***Ritonavir:** Plasma concentration possibly increased by ritonavir

Spironolactone: Increased risk of postural hypotension

Thiopental: Increased risk of arrhythmias and hypotension

***Valproate:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Verapamil: Possibly increased plasma concentration of amitriptyline

***Warfarin:** Enhanced or reduced anticoagulant effect

Amlodipine

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

Amiloride: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

Carbamazepine: Probably reduced effect of amlodipine

Chlorpromazine: Enhanced hypotensive effect

Contraceptives, Oral: Antagonism of hypotensive effects by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

Enalapril: Enhanced hypotensive effect

Fluphenazine: Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

Haloperidol: Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

Mefloquine: Possible increased risk of bradycardia

Methyldopa: Enhanced hypotensive effect

Nitrous oxide: Enhanced hypotensive effect

***Phenobarbital:** Probably reduced effect of amlodipine

Phenytoin: Probably reduced effect of amlodipine

Prednisolone Antagonism of hypotensive effect

Propranolol: Enhanced hypotensive effect

***Ritonavir:** Possibly increased plasma concentration of amlodipine

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Chlorpromazine: Plasma concentration of chlorpromazine increased (consider reducing chlorpromazine dose)

Amoxicillin

Allopurinol: Increased risk of rash

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

Warfarin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of amoxicillin

Amoxicillin + Clavulanic acid: *see* Amoxicillin

Amphotericin B

NOTE. Close monitoring required with concomitant administration of nephrotoxic drugs or cytotoxics

Amikacin: Increased risk of nephrotoxicity

***Ciclosporin:** Increased risk of nephrotoxicity

***Dexamethasone:** Increased risk of hypokalaemia (avoid concomitant use unless dexamethasone needed to control reactions)

***Digoxin:** Hypokalaemia caused by amphotericin B increases cardiac toxicity of digoxin

Fluconazole: Possible antagonism of effect of amphotericin B

Flucytosine: Renal excretion of flucytosine decreased and cellular uptake increased (flucytosine toxicity possibly increased)

Furosemide: Increased risk of hypokalaemia

Gentamicin: Increased risk of nephrotoxicity

Hydrochlorothiazide: Increased risk of hypokalaemia

***Hydrocortisone:** Increased risk of hypokalaemia (avoid concomitant use unless hydrocortisone needed to control reactions)

Miconazole: Possibly antagonism of effects of amphotericin B

Pentamidine: Possibly increased risk of nephrotoxicity

***Prednisolone:** Increased risk of hypokalaemia (avoid concomitant use

unless prednisolone needed to control reactions)
Streptomycin: Increased risk of nephrotoxicity
Vancomycin: Possibly increased risk of nephrotoxicity

Ampicillin

Allopurinol: Increased risk of rash
Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)
Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)
Warfarin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of ampicillin

Antacids (Aluminium hydroxide; Magnesium hydroxide)

NOTE. Antacids should preferably not be taken at the same time as other drugs since they may impair absorption
Aspirin: Excretion of acetylsalicylic acid increased by alkaline urine
Azithromycin: Reduced absorption of azithromycin
Chloroquine: Reduced absorption of chloroquine
Chlorpromazine: Reduced absorption of chlorpromazine
Ciprofloxacin: Reduced absorption of ciprofloxacin
Digoxin: Possibly reduced absorption of digoxin
Doxycycline: Reduced absorption of doxycycline
Enalapril: Absorption of enalapril reduced
Fluphenazine: Reduced absorption of fluphenazine
Isoniazid: Reduced absorption of isoniazid
Levofloxacin: Reduced absorption of levofloxacin
Ofloxacin: Reduced absorption of ofloxacin
Penicillamine: Reduced absorption of penicillamine
Phenytoin: Reduced absorption of phenytoin
Quinidine: Reduced quinidine excretion in alkaline urine (plasma-quinidine concentration occasionally increased)
Rifampicin: Reduced absorption of rifampicin

Artemether+Lumefantrine

***Amitriptyline**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Azithromycin:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Chloroquine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Chlorpromazine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ciprofloxacin**: Manufacturer of artemether with lumefantrine advises avoid concomitant use

***Clomipramine**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Erythromycin:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Fluconazole:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Fluphenazine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Grapefruit Juice:** Metabolism of artemether and lumefantrine may be inhibited (avoid concomitant use)
***Haloperidol**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Indinavir:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Levofloxacin:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Lopinavir:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Mefloquine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Nelfinavir:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ofloxacin**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Primaquine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Procainamide:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
***Proguanil:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Pyrimethamine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Quinidine:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
***Quinine:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
***Ritonavir:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Saquinavir:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
Sulfadoxine +Pyrimethamine: Manufacturer of artemether with lumefantrine advises avoid concomitant use

Asparaginase

Vaccine, Live: Avoid use of live vaccines with asparaginase (impairment of immune response)

Aspirin

Acetazolamide: Increased risk of toxicity when given with high-dose aspirin

Antacids (Aluminium hydroxide; Magnesium hydroxide): Excretion of acetylsalicylic acid increased by alkaline urine

Dexamethasone: Increased risk of gastrointestinal bleeding and ulceration; dexamethasone reduces plasmasalicylate concentration

Enalapril: Antagonism of hypotensive effect; risk of renal impairment when acetylsalicylic acid given in doses of over 300 mg daily

***Heparin:** Enhanced anticoagulant effect of heparin

Hydrocortisone: Increased risk of gastrointestinal bleeding and ulceration; hydrocortisone reduces plasmasalicylate concentration

***Ibuprofen:** Avoid concomitant use (increased adverse effects); antiplatelet effect of acetylsalicylic acid possibly reduced

***Methotrexate:** Reduced excretion of methotrexate (increased toxicity)

Metoclopramide: Enhanced effect of acetylsalicylic acid (increased rate of absorption)

Mifepristone: Manufacturer of mifepristone advises avoid concomitant use

Phenytoin: Enhancement of effect of phenytoin

Prednisolone: Increased risk of gastrointestinal bleeding and ulceration; prednisolone reduces plasmasalicylate concentration

Spironolactone: Antagonism of diuretic effect

Valproate: Enhancement of effect of valproate

***Warfarin**: Increased risk of bleeding due to antiplatelet effect

Atenolol

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

Amiloride: Enhanced hypotensive effect

Amlodipine: Enhanced hypotensive effect

Chlorpromazine: Enhanced hypotensive effect

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

Digoxin: Increased risk of AV block and bradycardia

Enalapril: Enhanced hypotensive effect

***Epinephrine:** Severe hypertension

Fluphenazine: Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glibenclamide: Atenolol may mask warning signs of hypoglycaemia such as tremor

Glyceryl trinitrate: Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Insulins: Enhanced hypoglycaemic effect; atenolol may mask warning signs of hypoglycaemia such as tremor

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

***Lidocaine:** Increased myocardial depression (interaction less likely when lidocaine used topically)

Mefloquine: Increased risk of bradycardia

Metformin: Atenolol may mask warning signs of hypoglycaemia such as tremor

Methyldopa: Enhanced hypotensive effect

***Nifedipine:** Enhanced hypotensive effect. Possibly severe hypotension and heart failure

Nitrous oxide: Enhanced hypotensive effect

Pilocarpine: Increased risk of arrhythmias

Prednisolone: Antagonism of hypotensive effect

***Procainamide**: Increased myocardial depression

***Quinidine:** Increased myocardial depression

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

***Verapamil:** Asystole, severe hypotension and heart failure

Atropine

NOTE. Many drugs have antimuscarinic effects; concomitant use of 2 or more such drugs can increase adverse effects such as dry mouth, urine retention, and constipation, and can also lead to confusion in the elderly.

Amitriptyline: Increased antimuscarinic adverse effects

Chlorphenamine: Increased antimuscarinic adverse effects

Chlorpromazine: Increased antimuscarinic adverse effects (but reduced plasma- chlorpromazine concentration)

Clomipramine: Increased antimuscarinic adverse effects

Fluphenazine: Increased antimuscarinic adverse effects (but reduced plasma-fluphenazine concentration)

Glyceryl trinitrate: Possibly reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)

Haloperidol: Possibly reduced effects of haloperidol

Isosorbide dinitrate: Possibly reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)

Levodopa: Absorption of levodopa possibly reduced
Metoclopramide: Antagonism of effects of metoclopramide on gastrointestinal activity
Neostigmine: Antagonism of effects of neostigmine
Pilocarpine: Antagonism of effects of pilocarpine
Promethazine: Increased antimuscarinic adverse effects
Pyridostigmine: Antagonism of effects of pyridostigmine

Azathioprine

***Allopurinol**: Effects of azathioprine enhanced and toxicity increased, reduce dose of azathioprine
Phenytoin: Possibly reduced absorption of phenytoin
***Sulfamethoxazole +Trimethoprim:** Increased risk of haematological toxicity
Sulfasalazine: Possibly increased risk of leukopenia
***Trimethoprim:** Increased risk of haematological toxicity
***Vaccine, Live:** Avoid use of live vaccines with azathioprine (impairment of immune response)
***Warfarin:** Anticoagulant effect possibly reduced

Azithromycin

Antacids: Reduced absorption of azithromycin
***Artemether with lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ciclosporin:** Possible inhibition of metabolism of ciclosporin (increased plasma concentration)
Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)
Digoxin: Increased plasma concentration of digoxin (increased risk of toxicity)
Ritonavir: Plasma concentration of azithromycin possibly increased
***Warfarin:** Possibly enhanced anticoagulant effect of warfarin

Beclometasone

Mifepristone: Possibly reduced effects of inhaled beclometasone for 3–4 days

Benzathine benzylpenicillin *see* Benzylpenicillin

Benzylpenicillin

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)
Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

BCG vaccine: *see* Vaccine, live

Biperiden

NOTE. Many drugs have antimuscarinic effects; concomitant use of 2 or more such drugs can increase adverse effects such as dry mouth, urine retention, and constipation, and can also lead to confusion in the elderly.

Amitriptyline: Increased antimuscarinic adverse effects
Chlorphenamine: Increased antimuscarinic adverse effects
Chlorpromazine: Increased antimuscarinic adverse effects (but reduced plasma-chlorpromazine concentration)
Clomipramine: Increased antimuscarinic adverse effects
Fluphenazine: Increased antimuscarinic adverse effects (but reduced plasma-fluphenazine concentration)
Glyceryl trinitrate: Possibly reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Haloperidol: Possibly reduced effects of haloperidol
Isosorbide dinitrate: Possibly reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Levodopa: Absorption of levodopa possibly reduced
Metoclopramide: Antagonism of effects of metoclopramide on gastrointestinal activity
Neostigmine: Antagonism of effects of neostigmine
Pilocarpine: Antagonism of effects of pilocarpine
Promethazine: Increased antimuscarinic adverse effects
Pyridostigmine: Antagonism of effects of pyridostigmine

Bleomycin

***Cisplatin:** Increased pulmonary toxicity
***Oxygen:** Serious pulmonary toxicity in patients exposed to conventional oxygen concentrations during anaesthesia
Phenytoin: Possibly reduced absorption of phenytoin
Vaccine, Live: Avoid use of live vaccines with bleomycin (impairment of immune response)
***Vinblastine:** Increased risk of cardiovascular toxicity

Bupivacaine

Lidocaine: Increased myocardial depression (interaction less likely when lidocaine used topically)
Procainamide: Increased myocardial depression
***Propranolol:** Increased risk of bupivacaine toxicity
Quinidine: Increased myocardial depression

Calcium folinate: *see* Folic acid and Folinic acid

Calcium gluconate: *see* Calcium salts

Calcium salts

Ciprofloxacin: Reduced absorption of ciprofloxacin

Dexamethasone Reduced absorption of calcium salts

Digoxin: Large intravenous doses of calcium salts can precipitate arrhythmias

Ferrous salts: Reduced absorption of oral ferrous salts

Hydrochlorothiazide: Increased risk of hypercalcaemia

Hydrocortisone: Reduced absorption of calcium salts

Levothyroxine: Reduced absorption of levothyroxine

Prednisolone: Reduced absorption of calcium salts

Sodium fluoride: Reduced absorption of sodium fluoride

Zinc sulfate: Reduced absorption of zinc sulfate

Capreomycin

Amikacin: Increased risk of nephrotoxicity and ototoxicity

Gentamicin: Increased risk of nephrotoxicity and ototoxicity

Streptomycin: Increased risk of nephrotoxicity and ototoxicity

Vancomycin: Increased risk of nephrotoxicity and ototoxicity

Carbamazepine

***Acetazolamide**: Increased risk of hyponatraemia; acetazolamide increases plasma-carbamazepine concentration

Alcohol: Possibly enhanced CNS adverse effects of carbamazepine

Alcuronium: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)

Amiloride: Increased risk of hyponatraemia

***Amitriptyline:** Antagonism of anticonvulsant effect (convulsive threshold lowered); accelerated metabolism of amitriptyline (reduced plasma concentration; reduced antidepressant effect)

Amlodipine: Probably reduced effect of amlodipine

Chloroquine: Possibly increased risk of convulsions

***Chlorpromazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Ciclosporin:** Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

***Clomipramine:** Antagonism of anticonvulsant effect (convulsive threshold lowered); accelerated metabolism of clomipramine (reduced plasma concentration; reduced antidepressant effect)

***Contraceptives, Oral:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

***Dexamethasone**: Accelerated metabolism of dexamethasone (reduced effect)

Doxycycline: Accelerated metabolism of doxycycline (reduced effect)

Ergocalciferol: Ergocalciferol requirements possibly increased

*** Erythromycin**: Increased plasma-carbamazepine concentration

Ethosuximide: May tration of ethosuximide possibly reduced

***Fluphenazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered) be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concen

Furosemide: Increased risk of hyponatraemia

***Haloperidol:** Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)

Hydrochlorothiazide: Increased risk of hyponatraemia

***Hydrocortisone:** Accelerated metabolism of hydrocortisone (reduced effect)

Indinavir: Possibly reduced plasma-indinavir concentration

***Isoniazid:** Increased plasma-carbamazepine concentration (also isoniazid hepatotoxicity possibly increased)

***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)

Lithium: Neurotoxicity may occur without increased plasma-lithium concentration

***Lopinavir**: Possibly reduced plasma-lopinavir concentration

Mebendazole: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

***Medroxyprogesterone:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

***Mefloquine:** Antagonism of anticonvulsant effect

Methadone: Reduced plasma concentration of methadone

Miconazole: Plasma concentration of carbamazepine possibly increased

Nelfinavir: Possibly reduced plasma-nelfinavir concentration

Nifedipine- Probably reduced effect of nifedipine

***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)

Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; reduced plasma concentration of carbamazepine

***Phenytoin:** May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; reduced plasma concentration of carbamazepine often lowered

Praziquantel: Plasma-praziquantel concentration reduced

***Prednisolone:** Accelerated metabolism of prednisolone (reduced effect)

***Ritonavir:** Plasma concentration possibly increased by ritonavir

Saquinavir: Possibly reduced plasma-saquinavir concentration

Spironolactone: Increased risk of hyponatraemia.

Valproate: May be enhanced toxicity without corresponding increase in antiepileptic effect; reduced plasma concentration of valproate; plasma concentration of active metabolite of carbamazepine increased

Vecuronium: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)

***Verapamil:** Enhanced effect of carbamazepine

***Warfarin**: Accelerated metabolism of warfarin (reduced anticoagulant effect)

Cefixime

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Warfarin: Possibly enhanced anticoagulant effect

Ceftazidime

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Warfarin:** Possibly enhanced anticoagulant effect

Ceftriaxone

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Warfarin:** Possibly enhanced anticoagulant effect

Chlorambucil

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with chlorambucil (impairment of immune response)

Chloramphenicol

***Ciclosporin:** Plasma concentration of ciclosporin possibly increased

***Glibenclamide**: Enhanced effect of glibenclamide

Hydroxocobalamin: Response to hydroxocobalamin reduced

***Phenobarbital:** Metabolism of chloramphenicol accelerated (reduced chloramphenicol concentration)

***Phenytoin:** Plasma-phenytoin concentration increased (increased risk of toxicity)

Rifampicin: Accelerated metabolism of chloramphenicol (reduced plasma-chloramphenicol concentration)

***Warfarin:** Enhanced anticoagulant effect

Chlormethine

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with chlormethine (impairment of immune response)

Chloroquine

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of chloroquine

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Carbamazepine: Possible increased risk of convulsions

***Ciclosporin:** Increased plasma-ciclosporin concentration (increased risk of toxicity)

***Digoxin:** Plasma-digoxin concentration possibly increased

Ethosuximide: Possible increased risk of convulsions

***Mefloquine**: Increased risk of convulsions

Neostigmine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of neostigmine

Phenytoin: Possible increased risk of convulsions

Praziquantel: Plasma-praziquantel concentration possibly reduced

Pyridostigmine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of pyridostigmine

Quinidine: Increased risk of ventricular arrhythmias

Quinine: Increased risk of ventricular arrhythmias

Valproate: Possible increased risk of convulsions

Chlorphenamine

Alcohol: Enhanced sedative effect

Amitriptyline: Increased antimuscarinic and sedative effects

Atropine: Increased antimuscarinic adverse effects

Biperiden: Increased antimuscarinic adverse effects

Clomipramine: Increased antimuscarinic and sedative effects

Diazepam: Enhanced sedative effect

Lopinavir: Possibly increased plasma concentration of chlorphenamine

Chlorpromazine

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced sedative effect

Amiloride: Enhanced hypotensive effect

***Amitriptyline:** Increased risk of antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Amlodipine: Enhanced hypotensive effect

Amodiaquine: Plasma concentration of chlorpromazine increased (consider reducing chlorpromazine dose)

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of chlorpromazine

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Atenolol: Enhanced hypotensive effect

Atropine: Increased antimuscarinic adverse effects (but reduced plasma-chlorpromazine concentration)

Biperiden: Increased antimuscarinic adverse effects (but reduced plasma-chlorpromazine concentration)

***Carbamazepine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Clomipramine:** Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias

Codeine: Enhanced sedative and hypotensive effect

Diazepam: Enhanced sedative effect

Dopamine: Antagonism of hypertensive effect

Enalapril: Enhanced hypotensive effect

Ephedrine: Antagonism of hypertensive effect

Epinephrine: Antagonism of hypertensive effect

***Ethosuximide:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Furosemide: Enhanced hypotensive effect

Glibenclamide: Possible antagonism of hypoglycaemic effect

Glyceryl trinitrate: Enhanced hypotensive effect

***Halothane:** Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Isosorbide dinitrate: Enhanced hypotensive effect

***Ketamine:** Enhanced hypotensive effect

Levodopa: Antagonism of effects of levodopa

Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity

Methadone: Enhanced hypotensive and sedative effects

Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects

Metoclopramide: Increased risk of extrapyramidal effects

Morphine: Enhanced sedative and hypotensive effect

Nifedipine: Enhanced hypotensive effect

***Nitrous oxide:** Enhanced hypotensive effect

***Phenobarbital:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Procainamide: Increased risk of ventricular arrhythmias

***Propranolol:** Concomitant administration may increase plasma concentration of both drugs; enhanced hypotensive effect

***Quinidine:** Increased risk of ventricular arrhythmias

***Ritonavir:** Plasma concentration possibly increased by ritonavir

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

***Thiopental:** Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

***Valproate:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Verapamil: Enhanced hypotensive effect

Ciclosporin

Aciclovir: Increased risk of nephrotoxicity

Allopurinol: Plasma-ciclosporin concentration possibly increased (risk of nephrotoxicity)

***Amikacin:** Increased risk of nephrotoxicity

***Amiloride:** Increased risk of hyperkalaemia

***Amphotericin B:** Increased risk of nephrotoxicity

***Azithromycin:** Plasma concentration of ciclosporin possibly increased

***Carbamazepine:** Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

***Chloramphenicol:** Plasma concentration of ciclosporin possibly increased

***Chloroquine**: Increased plasma-ciclosporin concentration (increased risk of toxicity)

***Ciprofloxacin:** Increased risk of nephrotoxicity

***Contraceptives, Oral:** Plasma-ciclosporin concentration increased by progestogens and possibly increased by estrogens

***Digoxin:** Increased plasma concentration of digoxin (increased risk of toxicity)

***Doxorubicin:** Increased risk of neurotoxicity

***Doxycycline:** Possibly increased plasma-ciclosporin concentration

***Enalapril:** Increased risk of hyperkalaemia

***Erythromycin:** Increased plasma-ciclosporin concentration (inhibition of metabolism of ciclosporin)

Etoposide: Possibly increased plasma concentration of etoposide (increased risk of toxicity)

***Fluconazole:** Metabolism of ciclosporin inhibited (increased plasma concentration)

***Gentamicin:** Increased risk of nephrotoxicity

***Grapefruit Juice:** Increased plasma-ciclosporin concentration (risk of toxicity)

Griseofulvin: Plasma-ciclosporin concentration possibly reduced

Hydrochlorothiazide: Increased risk of nephrotoxicity and possibly hypermagnesaemia

***Ibuprofen:** Increased risk of nephrotoxicity

***Levofloxacin**: Increased risk of nephrotoxicity

***Levonorgestrel:** Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)

***Medroxyprogesterone:** Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)

***Methotrexate**: Increased toxicity

***Metoclopramide:** Plasma-ciclosporin concentration increased

***Nelfinavir:** Possibly increased plasma-ciclosporin concentration

Nifedipine; Possibly increased plasma-nifedipine concentration (increased risk of adverse effects such as gingival hyperplasia)

***Norethisterone:** Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)

***Ofloxacin:** Increased risk of nephrotoxicity

***Phenobarbital:** Metabolism of ciclosporin accelerated (reduced effect)

***Phenytoin:** Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

***Potassium salts:** Increased risk of hyperkalaemia

Prednisolone: Increased plasma concentration of prednisolone

***Rifampicin:** Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

***Ritonavir:** Plasma concentration possibly increased by ritonavir

***Saquinavir:** Plasma concentration of both ciclosporin and saquinavir increased

***Silver sulfadiazine:** Increased risk of nephrotoxicity; possibly reduced plasma concentration of ciclosporin

***Spironolactone:** Increased risk of hyperkalaemia

***Streptomycin:** Increased risk of nephrotoxicity

***Sulfadiazine:** Plasma-ciclosporin concentration possibly reduced; increased risk of nephrotoxicity

***Sulfadoxine +Pyrimethamine:** Increased risk of nephrotoxicity

***Sulfamethoxazole +Trimethoprim:** Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim

***Trimethoprim:** Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim

***Vaccine, Live:** Avoid use of live vaccines with ciclosporin (impairment of immune response)

***Vancomycin:** Increased risk of nephrotoxicity

***Verapamil:** Increased plasma-ciclosporin concentration

Ciprofloxacin

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of ciprofloxacin

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Calcium salts: Reduced absorption of ciprofloxacin

***Ciclosporin:** Increased risk of nephrotoxicity

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Dairy products: Reduced absorption of ciprofloxacin

Ferrous salts: Absorption of ciprofloxacin reduced by oral ferrous salts

Glibenclamide: Possibly enhanced effect of glibenclamide

***Ibuprofen:** Possibly increased risk of convulsions

Morphine: Manufacturer of ciprofloxacin advises avoid premedication with morphine (reduced plasma-ciprofloxacin concentration) when ciprofloxacin used for surgical prophylaxis

Phenytoin: Plasma-phenytoin concentration can be increased or decreased by ciprofloxacin

***Warfarin:** Enhanced anticoagulant effect

Zinc sulfate: Reduced absorption of ciprofloxacin

Cisplatin

Acetazolamide: Increased risk of nephrotoxicity and ototoxicity

***Amikacin**: Increased risk of nephrotoxicity and possibly of ototoxicity

Amiloride: Increased risk of nephrotoxicity and ototoxicity

***Bleomycin:** Increased pulmonary toxicity

Furosemide: Increased risk of nephrotoxicity and ototoxicity

***Gentamicin:** Increased risk of nephrotoxicity and possibly of ototoxicity

Hydrochlorothiazide: Increased risk of nephrotoxicity and ototoxicity

***Methotrexate:** Risk of pulmonary toxicity

Phenytoin: Reduced absorption of phenytoin

Spironolactone: Increased risk of nephrotoxicity and ototoxicity

***Streptomycin**: Increased risk of nephrotoxicity and possibly of ototoxicity

Vaccine, Live: Avoid use of live vaccines with cisplatin (impairment of immune response)

Vancomycin: Increased risk of nephrotoxicity and possibly of ototoxicity

Clindamycin

***Alcuronium:** Enhanced muscle relaxant effect

Neostigmine: Antagonism of effects of neostigmine

Pyridostigmine: Antagonism of effects of pyridostigmine

***Suxamethonium:** Enhanced effects of suxamethonium

***Vecuronium:** Enhanced muscle relaxant effect

Clomipramine

Acetazolamide: Increased risk of postural hypotension

***Alcohol:** Enhanced sedative effect

Amiloride: Increased risk of postural hypotension

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Atropine: Increased antimuscarinic adverse effects

Biperiden: Increased antimuscarinic adverse effects

***Carbamazepine:** Antagonism of anticonvulsant effect (convulsive threshold lowered); accelerated metabolism of clomipramine (reduced plasma concentration; reduced antidepressant effect)

Chlorphenamine: Increased antimuscarinic and sedative effects

***Chlorpromazine:** Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of

ventricular arrhythmias

Codeine: Possibly increased sedation

Contraceptives, Oral: Antagonism of antidepressant effect by estrogens but adverse effects of clomipramine possibly increased due to increased plasma concentration of clomipramine

Diazepam: Enhanced sedative effect

***Epinephrine:** Increased risk of hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)

***Ethosuximide:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Fluphenazine:** Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias

Furosemide: Increased risk of postural hypotension

Glyceryl trinitrate: Reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)

***Haloperidol:** Increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias

Halothane: Increased risk of arrhythmias and hypotension

Hydrochlorothiazide: Increased risk of postural hypotension Reduced effect of sublingual

Isosorbide dinitrate: isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)

Ketamine: Increased risk of arrhythmias and hypotension

Levothyroxine: Possibly enhanced effects of clomipramine

Lithium: Risk of toxicity

Methadone: Sedative effects possibly increased

Morphine: Possibly increased sedation

Nitrous oxide: Increased risk of arrhythmias and hypotension

***Phenobarbital:** Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of clomipramine possibly accelerated (reduced plasma concentration)

***Phenytoin:** Antagonism of anticonvulsant effect (convulsive threshold lowered); possibly reduced plasma-clomipramine concentration

***Procainamide:** Increased risk of ventricular arrhythmias

Promethazine: Increased antimuscarinic and sedative effects

***Quinidine:** Increased risk of ventricular arrhythmias

Rifampicin: Plasma concentration of clomipramine possibly reduced

***Ritonavir:** Plasma concentration possibly increased by ritonavir

Spironolactone: Increased risk of postural hypotension

Thiopental: Increased risk of arrhythmias and hypotension

***Valproate:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Verapamil: Possibly increased plasma concentration of clomipramine

***Warfarin:** Enhanced or reduced anticoagulant effect

Cloxacillin: *see* Benzylpenicillin

Codeine

Alcohol: Enhanced sedative and hypotensive effect

Amitriptyline: Possibly increased sedation

Chlorpromazine: Enhanced sedative and hypotensive effect

Clomipramine: Possibly increased sedation

Diazepam: Enhanced sedative effect

Fluphenazine: Enhanced sedative and hypotensive effect

Haloperidol: Enhanced sedative and hypotensive effect

Metoclopramide: Antagonism of effect of metoclopramide on gastrointestinal activity

***Ritonavir:** Ritonavir possibly increases plasma concentration of codeine

Contraceptives, Oral

NOTE. Interactions also apply to ethinylestradiol taken alone. In hormone replacement therapy low dose unlikely to induce interactions

Acetazolamide: Antagonism of diuretic effect by estrogens

Amiloride: Antagonism of diuretic effect by estrogens

Amitriptyline: Antagonism of antidepressant effect by estrogens but adverse effects of amitriptyline possibly increased due to increased plasma concentration of amitriptyline

Amlodipine: Antagonism of hypotensive effect by estrogens

Amoxicillin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Ampicillin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Atenolol: Antagonism of hypotensive effect by estrogens

Azithromycin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Benzylpenicillin: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Carbamazepine:** Accelerated metabolism ofestro gens and progestogens (reduced contraceptive effect)

Cefixime: Contraceptive effect of estrogens possibly reduced (risk probably small)

Ceftazidime: Contraceptive effect of estrogens possibly reduced (risk probably small)

Ceftriaxone: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Ciclosporin:** Plasma-ciclosporin concentration increased by progestogens and possibly increased by estrogens

Ciprofloxacin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Clomipramine: Antagonism of antidepressant effect by estrogens but adverse effects of clomipramine possibly increased due to increased plasma concentration of clomipramine

Dexamethasone: Oral contraceptives containing estrogens increase plasma concentration of dexamethasone

Doxycycline: Contraceptive effect of estrogens possibly reduced (risk probably small)

Efavirenz: Efficacy of estrogen-containing oral contraceptives possibly reduced

Enalapril: Antagonism of hypotensive effect by estrogens

Erythromycin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Fluconazole: Anecdotal reports of failure of estrogen-containing contraceptives

Furosemide: Antagonism of diuretic effect by estrogens

Glibenclamide: Antagonism of hypoglycaemic effect by estrogens and progestogens

Glyceryl trinitrate: Antagonism of hypotensive effect by estrogens

***Griseofulvin**: Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Hydralazine: Antagonism of hypotensive effect by estrogens

Hydrochlorothiazide: Antagonism of diuretic effect by estrogens

Hydrocortisone: Oral contraceptives containing estrogens increase plasma concentration of hydrocortisone

Imipenem + Cilastatin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Insulins: Antagonism of hypoglycaemic effect by estrogens and progestogens

Isosorbide dinitrate: Antagonism of hypotensive effect by estrogens

Levofloxacin: Contraceptive effect of estrogens possibly reduced (risk probably small)

Metformin: Antagonism of hypoglycaemic effect by estrogens and progestogens

Methyldopa: Antagonism of hypotensive effect by estrogens

Metronidazole: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Nelfinavir:** Accelerated metabolism of estrogens (reduced contraceptive effect); nelfinavir possibly reduces contraceptive effect of progestogens

***Nevirapine:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Nifedipine: Antagonism of hypotensive effect by estrogens

Ofloxacin: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Phenobarbital:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Phenoxymethylpenicillin: Contraceptive effect of estrogens possibly reduced (risk probably small)

***Phenytoin:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Prednisolone: Oral contraceptives containing estrogens increase plasma concentration of prednisolone

Propranolol: Antagonism of hypotensive effect by estrogens

***Rifampicin:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

***Ritonavir:** Accelerated metabolism of estrogens (reduced contraceptive effect)

Sodium nitroprusside: Antagonism of hypotensive effect by estrogens

Spironolactone: Antagonism of diuretic effect by estrogens

Verapamil: Antagonism of hypotensive effect by estrogens

***Warfarin**: Antagonism of anticoagulant effect by estrogens and progestogens

Cyclophosphamide

Phenytoin: Possibly reduced absorption of phenytoin

Suxamethonium: Enhanced effect of suxamethonium

Vaccine, Live: Avoid use of live vaccines with cyclophosphamide (impairment of immune response)

Cycloserine

***Alcohol:** Increased risk of convulsions

Isoniazid: Increased risk of CNS toxicitiy

Cytarabine

Flucytosine: Plasma-flucytosine concentration possibly reduced

Phenytoin: Reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with cytarabine (impairment of immune response)

Dacarbazine

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with dacarbazine (impairment of immune response)

Dactinomycin

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with dactinomycin (impairment of immune response)

Dairy products

Ciprofloxacin: Reduced absorption of ciprofloxacin

Dapsone

Rifampicin: Reduced plasma-dapsone concentration

Sulfamethoxazole +Trimethoprim: Plasma concentration of both dapsone and trimethoprim may increase with concomitant use

Trimethoprim: Plasma concentration of both dapsone and trimethoprim may increase with concomitant use

Daunorubicin

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with daunorubicin (impairment of immune response)

Dexamethasone

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect

Albendazole: Plasma-albendazole concentration possibly increased

Amiloride: Antagonism of diuretic effect

Amlodipine: Antagonism of hypotensive effect

***Amphotericin B:** Increased risk of hypokalaemia (avoid concomitant use unless dexamethasone needed to control reactions)

Aspirin: Increased risk of gastrointestinal bleeding and ulceration; dexamethasone reduces plasma-salicylate concentration

Atenolol: Antagonism of hypotensive effect

Calcium salts: Reduced absorption of calcium salts

***Carbamazepine:** Accelerated metabolism of dexamethasone (reduced effect)

Contraceptives, Oral: Oral contraceptives containing estrogens increase plasma concentration of dexamethasone

Digoxin: Increased risk of hypokalaemia

Enalapril: Antagonism of hypotensive effect

Ephedrine: Metabolism of dexamethasone accelerated

Erythromycin: Erythromycin possibly inhibits metabolism of dexamethasone

Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia

Glibenclamide: Antagonism of hypoglycaemic effect

Glyceryl trinitrate: Antagonism of hypotensive effect

Hydralazine: Antagonism of hypotensive effect

Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia

Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration

Indinavir: Possibly reduced plasmaindinavir concentration

Insulins: Antagonism of hypoglycaemic effect

Isosorbide dinitrate: Antagonism of hypotensive effect

***Lopinavir:** Possibly reduced plasmalopinavir concentration

Metformin: Antagonism of hypoglycaemic effect

***Methotrexate**: Increased risk of haematological toxicity

Methyldopa: Antagonism of hypotensive effect

Mifepristone: Possibly reduced effects of dexamethasone for 3–4 days

Nifedipine: Antagonism of hypotensive effect

***Phenobarbital:** Metabolism of dexamethasone accelerated (reduced effect)

***Phenytoin:** Metabolism of dexamethasone accelerated (reduced effect)

Praziquantel: Plasma-praziquantel concentration reduced

Propranolol: Antagonism of hypotensive effect

***Rifampicin:** Accelerated metabolism of dexamethasone (reduced effect)

Ritonavir: Plasma concentration possibly increased by ritonavir

Salbutamol: Increased risk of hypokalaemia if high doses of salbutamol given with dexamethasone

Saquinavir: Possibly reduced plasma-saquinavir concentration

Sodium nitroprusside: Antagonism of hypotensive effect

Spironolactone: Antagonism of diuretic effect

Vaccine, Influenza: High doses of dexamethasone impair immune response

***Vaccine, Live:** High doses of dexamethasone impair immune response; avoid use of live vaccines

Verapamil: Antagonism of hypotensive effect

***Warfarin:** Anticoagulant effect possibly enhanced or reduced (high-dose dexamethasone enhances anticoagulant effect)

Diazepam

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced sedative effect

Amiloride: Enhanced hypotensive effect

Amitriptyline: Enhanced sedative effect

Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

Chlorphenamine: Enhanced sedative effect

Chlorpromazine: Enhanced sedative effect

Clomipramine: Enhanced sedative effect

Codeine: Enhanced sedative effect

Enalapril: Enhanced hypotensive effect

Fluphenazine: Enhanced sedative effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

Halothane: Enhanced sedative effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Isoniazid: Metabolism of diazepam inhibited

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced sedative effect

Levodopa: Possibly antagonism of levodopa effects

Methadone: Increased sedative effect
Methyldopa: Enhanced hypotensive effect
Morphine: Enhanced sedative effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced sedative effect
Phenytoin: Plasma-phenytoin concentrations possibly increased or decreased by diazepam
Promethazine: Enhanced sedative effect
Propranolol: Enhanced hypotensive effect
Rifampicin: Metabolism of diazepam accelerated (reduced plasma concentration)
***Ritonavir:** Plasma concentration possibly increased by ritonavir (risk of extreme sedation and respiratory depression—avoid concomitant use)
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced sedative effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Didanosine

NOTE. Antacids present in buffered tablet formulation may affect absorption of other drugs; *see also* Antacids
Allopurinol: Possibly increased plasma concentration of didanosine
***Stavudine:** Increased risk of adverse effects

Digoxin

***Acetazolamide:** Hypokalaemia caused by acetazolamide increases cardiac toxicity of digoxin
***Amphotericin B:** Hypokalaemia caused by amphotericin B increases cardiac toxicity of digoxin
Antacids (Aluminium hydroxide; Magnesium hydroxide): Possibly reduced absorption of digoxin
Atenolol: Increased risk of AV block and bradycardia
Azithromycin: Increased plasma concentration of digoxin (increased risk of toxicity)
Calcium salts: Large intravenous doses of calcium salts can precipitate arrhythmias
***Chloroquine:** Plasma-digoxin concentration possibly increased
***Ciclosporin:** Increased plasma concentration of digoxin (increased risk of toxicity)
Dexamethasone: Increased risk of hypokalaemia
Erythromycin: Increased plasma concentration of digoxin (increased risk of toxicity)
***Furosemide:** Hypokalaemia caused by furosemide increases cardiac toxicity of digoxin
Gentamicin: Possibly increased plasma concentration of digoxin

***Hydrochlorothiazide:** Hypokalaemia caused by hydrochlorothiazide increases cardiac toxicity of digoxin
Hydrocortisone: Increased risk of hypokalaemia
Ibuprofen: Possibly exacerbation of heart failure, reduced renal function, and increased plasma-digoxin concentration
Mefloquine: Possibly increased risk of bradycardia
***Nifedipine:** Possibly increased plasma concentration of digoxin
Penicillamine: Plasma concentration of digoxin possibly reduced
Phenytoin: Plasma concentration of digoxin possibly reduced
Prednisolone: Increased risk of hypokalaemia
Propranolol: Increased risk of AV block and bradycardia
***Quinidine:** Plasma concentration of digoxin increased (halve dose of digoxin)
***Quinine**: Plasma concentration of digoxin increased
Rifampicin: Plasma concentration of digoxin possibly reduced
Salbutamol: Possibly reduced plasma concentration of digoxin
***Spironolactone:** Plasma concentration of digoxin increased
Sulfamethoxazole +Trimethoprim: Plasma concentration of digoxin possibly increased
Sulfasalazine: Absorption of digoxin possibly reduced
Suxamethonium: Risk of ventricular arrhythmias
Timolol: Increased AV block and bradycardia
Trimethoprim: Plasma concentration of digoxin possibly increased
***Verapamil:** Increased plasma concentration of digoxin; increased AV block and bradycardia

Dimercaprol

***Ferrous salts:** Avoid concomitant use

Dopamine

Chlorpromazine: Antagonism of hypertensive effect
Ergometrine: Increased risk of ergotism
Fluphenazine: Antagonism of hypertensive effect
Haloperidol: Antagonism of hypertensive effect

Doxorubicin

***Ciclosporin:** Increased risk of neurotoxicity
Phenytoin: Possibly reduced absorption of phenytoin
Stavudine: Doxorubicin may inhibit effect of stavudine
Vaccine, Live: Avoid use of live vaccines with doxorubicin (impairment of immune response)

Doxycycline

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of doxycycline

Carbamazepine: Accelerated metabolism of doxycycline (reduced effect)

***Ciclosporin:** Possibly increased plasma-ciclosporin concentration

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Ferrous salts: Absorption of oral ferrous salts reduced by doxycycline; absorption of doxycycline reduced by oral ferrous salts

Methotrexate: Increased risk of methotrexate toxicity

Phenobarbital: Metabolism of doxycycline accelerated (reduced plasma concentration)

Phenytoin: Increased metabolism of doxycycline (reduced plasma concentration)

Rifampicin: Plasma-doxycycline concentration possibly reduced

***Warfarin**: Anticoagulant effect possibly enhanced

Efavirenz

Contraceptives, Oral: Efficacy of estrogen-containing oral contraceptives possibly reduced

***Ergometrine:** Increased risk of ergotism (avoid concomitant use)

Grapefruit Juice: Plasma concentration of efavirenz possibly increased

Indinavir: Efavirenz reduces plasma concentration of indinavir

Lopinavir: Plasma concentration of lopinavir reduced

Methadone: Reduced plasma concentration of methadone

Nevirapine: Plasma-efavirenz concentration reduced

Rifampicin: Reduced plasma concentration of efavirenz (increase efavirenz dose)

Ritonavir: Increased risk of toxicity (monitor liver function tests)

Saquinavir: Efavirenz significantly reduces plasma concentration of saquinavir

Enalapril

***Acetazolamide:** Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

***Amiloride:** Enhanced hypotensive effect; increased risk of severe hyperkalaemia

Amlodipine: Enhanced hypotensive effect

Antacids (Aluminium hydroxide; Magnesium hydroxide): Absorption of enalapril reduced

Aspirin: Antagonism of hypotensive effect; risk of renal impairment when acetylsalicylic acid given in doses of over 300 mg daily

Atenolol: Enhanced hypotensive effect

Chlorpromazine: Enhanced hypotensive effect

***Ciclosporin:** Increased risk of hyperkalaemia

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

Fluphenazine: Enhanced hypotensive effect

***Furosemide:** Enhanced hypotensive effect

Glibenclamide: Hypoglycaemic effect possibly enhanced

Glyceryl trinitrate: Enhanced hypotensive effect

Haloperidol: Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Heparin: Increased risk of hyperkalaemia

Hydralazine: Enhanced hypotensive effect

***Hydrochlorothiazide**: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect, increased risk of renal impairment

Insulins: Hypoglycaemic effect possibly enhanced

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

***Lithium:** Enalapril reduces excretion of lithium (increased plasma-lithium concentration)

Metformin: Hypoglycaemic effect possibly enhanced

Methyldopa: Enhanced hypotensive effect

Nifedipine: Enhanced hypotensive effect

Nitrous oxide: Enhanced hypotensive effect

***Potassium salts:** Increased risk of severe hyperkalaemia

Prednisolone: Antagonism of hypotensive effect

Propranolol: Enhanced hypotensive effect

Sodium nitroprusside: Enhanced hypotensive effect

***Spironolactone:** Enhanced hypotensive effect; increased risk of severe hyperkalaemia (monitor plasma-potassium concentration with low-dose spironolactone in heart failure)

Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Verapamil: Enhanced hypotensive effect

Ephedrine

Chlorpromazine: Antagonism of hypertensive effect

Dexamethasone: Metabolism of dexamethasone accelerated

Fluphenazine: Antagonism of hypertensive effect

Haloperidol: Antagonism of hypertensive effect

Oxytocin: Risk of hypertension due to enhanced vasopressor effect of ephedrine

Epinephrine (Adrenaline)

***Amitriptyline:** Increased risk of hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)

***Atenolol:** Severe hypertension

Chlorpromazine: Antagonism of hypertensive effect

***Clomipramine:** Increased risk of hypertension and arrhythmias (but local anaesthetics with epinephrine appear to be safe)

Fluphenazine: Antagonism of hypertensive effect

Haloperidol: Antagonism of hypertensive effect

***Halothane:** Risk of arrhythmias

Oxytocin: Risk of hypertension due to enhanced vasopressor effect of epinephrine

***Propranolol:** Severe hypertension

***Timolol:** Severe hypertension

Ergocalciferol

Carbamazepine: Ergocalciferol requirements possibly increased

Hydrochlorothiazide: Increased risk of hypercalcaemia

Phenobarbital: Ergocalciferol requirements possibly increased

Phenytoin: Ergocalciferol requirements possibly increased

Dopamine: Increased risk of ergotism

Ergometrine

***Efavirenz:** Increased risk of ergotism (avoid concomitant use)

Halothane: Reduced effect of ergometrine on parturient uterus

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

***Carbamazepine:** Increased plasma-carbamazepine concentration

***Ciclosporin:** Increased plasma-ciclosporin concentration (inhibition of metabolism of ciclosporin)

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Dexamethasone: Erythromycin possibly inhibits metabolism of dexamethasone

Digoxin: Increased plasma concentration of digoxin (increased risk of toxicity)

Hydrocortisone: Erythromycin possibly inhibits metabolism of hydrocortisone

Prednisolone: Erythromycin possibly inhibits metabolism of prednisolone

***Quinidine:** Increased risk of ventricular arrhythmias with parenteral erythromycin

Ritonavir: Plasma concentration possibly increased by ritonavir

Valproate: Metabolism of valproate possibly inhibited (increased plasma concentration)

***Verapamil:** Possible inhibition of metabolism of verapamil (increased risk of toxicity)

***Vinblastine:** Increased toxicity of vinblastine (avoid concomitant use)

***Warfarin:** Enhanced anticoagulant effect

Ethinylestradiol: *see* Contraceptives, Oral

Ethosuximide

***Amitriptyline**: Antagonism of anticonvulsant effect (convulsive threshold lowered)

Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; possibly reduced plasma concentration of ethosuximide

Chloroquine: Possible increased risk of convulsions

***Chlorpromazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Clomipramine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Fluphenazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Haloperidol:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Isoniazid:** Metabolism of ethosuximide inhibited (increased plasma-ethosuximide concentration and risk of toxicity)

***Mefloquine**: Antagonism of anticonvulsant effect

Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; possibly reduced plasma concentration of ethosuximide

***Phenytoin**: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin possibly increased; plasma concentration of ethosuximide possibly reduced

Valproate: May be enhanced toxicity without corresponding increase in antiepileptic effect; possibly increased plasma concentration of ethosuximide

Etoposide

Ciclosporin: Possibly increased plasma concentration of etoposide (increased risk of toxicity)

Phenobarbital: Possibly reduced plasma concentration of etoposide

Phenytoin: Possibly reduced absorption of phenytoin and possibly reduced plasma concentration of etoposide

Vaccine, Live: Avoid use of live vaccines with etoposide (impairment of immune response)

***Warfarin:** Possibly enhanced anticoagulant effect

Ferrous salts

Calcium salts: Reduced absorption of oral ferrous salts

Ciprofloxacin: Absorption of ciprofloxacin reduced by oral ferrous salts

***Dimercaprol:** Avoid concomitant use

Doxycycline: Absorption of oral ferrous salts reduced by doxycycline; absorption of doxycycline reduced by oral ferrous salts
Levodopa: Absorption of levodopa may be reduced by oral ferrous salts
Levofloxacin: Absorption of levofloxacin reduced by oral ferrous salts
Levothyroxine: Absorption of levothyroxine reduced by oral ferrous salts (give at least 2 hours apart)
Methyldopa: Oral ferrous salts reduce hypotensive effect of methyldopa
Ofloxacin: Absorption of ofloxacin reduced by oral ferrous salts
Penicillamine: Oral ferrous salts reduce absorption of penicillamine
Zinc sulfate: Absorption of zinc and of oral ferrous salts reduced

Ferrous salt and Folic acid: *see* Ferrous salts; Folic acid

Fluconazole

Amphotericin B: Possible antagonism of effect of amphotericin
***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
Ciclosporin: Metabolism of ciclosporin inhibited (increased plasma concentration)
Contraceptives, Oral: Anecdotal reports of failure of estrogen-containing contraceptives
***Glibenclamide:** Plasma concentration of glibenclamide increased
Hydrochlorothiazide: Plasma concentration of fluconazole increased
***Nevirapine:** Increased plasma concentration of nevirapine
***Phenytoin:** Plasma concentration of phenytoin increased (consider reducing dose of phenytoin)
***Rifampicin:** Accelerated metabolism of fluconazole (reduced plasma concentration)
Ritonavir: Plasma concentration of fluconazole increased by ritonavir
Saquinavir: Plasma concentration of saquinavir possibly increased
***Warfarin:** Enhanced anticoagulant effect
***Zidovudine**: Increased plasma concentration of zidovudine (increased risk of toxicity)

Flucytosine

Amphotericin B: Renal excretion of flucytosine decreased and cellular uptake increased (flucytosine toxicity possibly increased)
Cytarabine: Plasma-flucytosine concentration possibly reduced

Fluorouracil

Metronidazole: Metabolism of fluorouracil inhibited (increased toxicity)
Phenytoin: Metabolism of phenytoin possibly inhibited (increased risk of toxicity)
Vaccine, Live: Avoid use of live vaccines with fluorouracil (impairment of immune response)
***Warfarin:** Anticoagulant effect possibly enhanced

Fluphenazine

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced sedative effect
Amiloride: Enhanced hypotensive effect
***Amitriptyline:** Increased risk of antimuscarinic adverse effects; increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias
Amlodipine: Enhanced hypotensive effect
Antacids: Reduced absorption of fluphenazine
***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
Atenolol: Enhanced hypotensive effect
Atropine: Increased antimuscarinic adverse effects (but reduced plasma-fluphenazine concentration)
Biperiden: Increased antimuscarinic adverse effects (but reduced plasma-fluphenazine concentration)
***Carbamazepine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Clomipramine:** Increased antimuscarinic adverse effects; increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias
Codeine: Enhanced sedative and hypotensive effect
Diazepam: Enhanced sedative effect
Dopamine: Antagonism of hypertensive effect
Enalapril: Enhanced hypotensive effect
Ephedrine: Antagonism of hypertensive effect
Epinephrine: Antagonism of hypertensive effect
***Ethosuximide:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
Furosemide: Enhanced hypotensive effect
Glibenclamide: Possible antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
***Halothane:** Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
***Ketamine:** Enhanced hypotensive effect
Levodopa: Antagonism of effects of levodopa
Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity
Methadone: Enhanced hypotensive and sedative effects
Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects
Metoclopramide: Increased risk of extrapyramidal effects
Morphine: Enhanced sedative and hypotensive effect

Nifedipine: Enhanced hypotensive effect
***Nitrous oxide:** Enhanced hypotensive effect
***Phenobarbital:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Phenytoin:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Procainamide:** Increased risk of ventricular arrhythmias
Propranolol: Enhanced hypotensive effect
***Quinidine:** Increased risk of ventricular arrhythmias
***Ritonavir:** Plasma concentration possibly increased by ritonavir
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
***Thiopental**: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
***Valproate:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
Verapamil: Enhanced hypotensive effect

Folic acid and Folinic acid

Phenobarbital: Plasma concentration of phenobarbital possibly reduced
Phenytoin: Plasma-phenytoin concentration possibly reduced
Sulfasalazine: Possibly reduced absorption of folic acid

Furosemide

Acetazolamide: Increased risk of hypokalaemia
Alcohol: Enhanced hypotensive effect
***Amikacin:** Increased risk of ototoxicity
Amitriptyline: Increased risk of postural hypotension
Amlodipine: Enhanced hypotensive effect
Amphotericin B: Increased risk of hypokalaemia
Atenolol: Enhanced hypotensive effect
Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Contraceptives, Oral: Antagonism of diuretic effect by estrogens
Dexamethasone: Antagonism of diuretic effect; increased risk of hypokalaemia
Diazepam: Enhanced hypotensive effect
***Digoxin:** Hypokalaemia caused by furosemide increases cardiac toxicity of digoxin
***Enalapril:** Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
***Gentamicin:** Increased risk of ototoxicity

Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Increased risk of hypokalaemia
Hydrocortisone: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of iuretic effect
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
***Lidocaine:** Action of lidocaine antagonized by hypokalaemia caused by furosemide (interaction less likely when lidocaine used topically)
***Lithium:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide
Metformin: Antagonism of hypoglycaemic effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of diuretic effect; increased risk of hypokalaemia
Propranolol: Enhanced hypotensive effect
***Quinidine**: Cardiac toxicity of quinidine increased by hypokalaemia caused by furosemide
Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol
Sodium nitroprusside: Enhanced hypotensive effect
***Streptomycin**: Increased risk of ototoxicity
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
***Vancomycin:** Increased risk of ototoxicity
Verapamil: Enhanced hypotensive effect

Gentamicin

***Alcuronium:** Enhanced muscle relaxant effect
Amphotericin B: Increased risk of nephrotoxicity
Capreomycin: Increased risk of nephrotoxicity and ototoxicity
***Ciclosporin:** Increased risk of nephrotoxicity
***Cisplatin:** Increased risk of nephrotoxicity and possibly of ototoxicity
Digoxin: Possibly increased plasma concentration of digoxin
***Furosemide**: Increased risk of ototoxicity
***Neostigmine:** Antagonism of effect of neostigmine
***Pyridostigmine:** Antagonism of effect of pyridostigmine

***Suxamethonium:** Enhanced muscle relaxant effect
Vancomycin: Increased risk of nephrotoxicity and ototoxicity
***Vecuronium**: Enhanced muscle relaxant effect

Glibenclamide

Alcohol: Enhanced hypoglycaemic effect
Atenolol: Atenolol may mask warning signs of hypoglycaemia such as tremor
***Chloramphenicol:** Enhanced effect of glibenclamide
Chlorpromazine: Possible antagonism of hypoglycaemic effect
Ciprofloxacin: Possibly enhanced effect of glibenclamide
Contraceptives, Oral: Antagonism of hypoglycaemic effect by estrogens and progestogens
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
***Fluconazole:** Plasma concentration of glibenclamide increased
Fluphenazine: Possible antagonism of hypoglycaemic effect
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
***Ibuprofen:** Possibly enhanced effect of glibenclamide
Levonorgestrel: Antagonism of hypoglycaemic effect
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Propranalol may mask warning signs of hypoglycaemia such as tremor
***Rifampicin:** Possibly accelerated metabolism (reduced effect) of glibenclamide
Silver sulfadiazine: Effects of glibencamide rarely enhanced
Sulfadiazine: Effect of glibenclamide rarely enhanced
Sulfadoxine +Pyrimethamine: Effect of glibenclamide rarely enhanced
Sulfamethoxazole +Trimethoprim: Effect of glibenclamide rarely enhanced
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Timolol may mask warning signs of hypoglycaemia such as tremor
Trimethoprim: Effects of glibencamide rarely enhanced
***Warfarin:** Possibly enhanced hypoglycaemic effects and changes to anticoagulant effect

Glyceryl trinitrate

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect

Amitriptyline: Reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Atropine: Possibly reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Biperiden: Possibly reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Reduced effect of sublingual glyceryl trinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Contraceptives, Oral: Antagonism of hypotensive effect by estrogens
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
***Heparin:** Anticoagulant effects reduced by infusion of glyceryl trinitrate
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen Antagonism of hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Grapefruit Juice

Artemether +Lumefantrine: Metabolism of artemether and lumefantrine may be inhibited (manufacturer advises avoid)
***Ciclosporin:** Increased plasma-ciclosporin concentration (risk of toxicity)
Efavirenz: Plasma concentration of efavirenz possibly increased
Nifedipine: Increased plasma-nifedipine concentration
Verapamil: Increased plasma-verapamil concentration

Griseofulvin

Alcohol: Possibly enhanced effects of alcohol

Ciclosporin: Plasma-ciclosporin concentration possibly reduced

***Contraceptives, Oral:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

***Medroxyprogesterone:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

***Norethisterone**: Accelerated metabolism of norethisterone (reduced contraceptive effect)

Phenobarbital: Reduction in absorption of griseofulvin (reduced effect)

***Warfarin:** Reduced anticoagulant effect

Haloperidol

Alcohol: Enhanced sedative effect

***Amitriptyline:** Increased plasma-amitriptyline concentration; possibly increased risk of ventricular arrhythmias

Amlodipine: Enhanced hypotensive effect

***Artemether +Lumefantrine:** Maufacturer of artemether with lumefantrine advises avoid concomitant use

Atropine: Possibly reduced effects of haloperidol

Biperiden: Possibly reduced effects of haloperidol

***Carbamazepine:** Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)

***Clomipramine:** Increased plasma-clomipramine concentration; possibly increased risk of ventricular arrhythmias

Codeine: Enhanced sedative and hypotensive effect

Diazepam: Enhanced sedative effect

Dopamine: Antagonism of hypertensive effect

Enalapril: Enhanced hypotensive effect

Ephedrine: Antagonism of hypertensive effect

Epinephrine: Antagonism of hypertensive effect

***Ethosuximide:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Halothane:** Enhanced hypotensive effect

***Ketamine:** Enhanced hypotensive effect

Levodopa: Antagonism of effects of levodopa

Lithium: Increased risk of extrapyramidal effects and possibility of neurotoxicity

Methadone: Enhanced hypotensive and sedative effects

Methyldopa: Enhanced hypotensive effect; increased risk of extrapyramidal effects

Metoclopramide: Increased risk of extrapyramidal effects

Morphine: Enhanced sedative and hypotensive effect

Nifedipine: Enhanced hypotensive effect

***Nitrous oxide:** Enhanced hypotensive effect

***Phenobarbital:** Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)

***Phenytoin:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Procainamide:** Increased risk of ventricular arrhythmias

***Quinidine:** Increased risk of ventricular arrhythmias

***Rifampicin:** Accelerated metabolism of haloperidol (reduced plasmahaloperidol concentration)

***Ritonavir:** Plasma concentration possibly increased by ritonavir

***Thiopental:** Enhanced hypotensive effect

***Valproate:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Verapamil: Enhanced hypotensive effect

Halothane

Acetazolamide: Enhanced hypotensive effect

Alcuronium: Effects of alcuronium enhanced

Amiloride: Enhanced hypotensive effect

Amitriptyline: Increased risk of arrhythmias and hypotension

Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

***Chlorpromazine:** Enhanced hypotensive effect

Clomipramine: Increased risk of arrhythmias and hypotension

Diazepam: Enhanced sedative effect

Enalapril: Enhanced hypotensive effect

***Epinephrine:** Risk of arrhythmias

Ergometrine: Reduced effect of ergometrine on parturient uterus

***Fluphenazine:** Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

***Haloperidol:** Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Isoniazid: Possible potentiation of isoniazid hepatotoxicity

Isosorbide dinitrate: Enhanced hypotensive effect

***Levodopa:** Risk of arrhythmias

Methyldopa: Enhanced hypotensive effect

Nifedipine: Enhanced hypotensive effect

Oxytocin: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias

Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Suxamethonium: Enhanced effects of suxamethonium
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
Vecuronium: Enhanced effects of vecuronium
***Verapamil:** Enhanced hypotensive effect and AV delay

Heparin

***Aspirin:** Enhanced anticoagulant effect of heparin
Enalapril: Increased risk of hyperkalaemia
***Glyceryl trinitrate:** Anticoagulant effects reduced by infusion of glyceryl trinitrate
Ibuprofen: Possibly increased risk of bleeding

Hydralazine

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect by estrogens
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Hydrochlorothiazide

Acetazolamide: Increased risk of hypokalaemia
Alcohol: Enhanced hypotensive effect
Allopurinol: Increased risk of hypersensitivity, especially in renal impairment
Amitriptyline: Increased risk of postural hypotension
Amlodipine: Enhanced hypotensive effect
Amphotericin B: Increased risk of hypokalaemia
Atenolol: Enhanced hypotensive effect
Calcium salts: Increased risk of hypercalcaemia
Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
Ciclosporin: Increased risk of nephrotoxicity and possibly hypermagnesaemia
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension
Contraceptives, Oral: Antagonism of diuretic effect by estrogens
Dexamethasone: Antagonism of diuretic effect; increased risk of hypokalaemia
Diazepam: Enhanced hypotensive effect
***Digoxin:** Hypokalaemia caused by hydrochlorothiazide increases cardiac toxicity of digoxin
***Enalapril:** Enhanced hypotensive effect
Ergocalciferol: Increased risk of hypercalcaemia
Fluconazole: Plasma concentration of fluconazole increased
Fluphenazine: Enhanced hypotensive effect
Furosemide: Increased risk of hypokalaemia
Glibenclamide: Antagonism of hypoglycaemic effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrocortisone: Antagonism of diuretic effect; increased risk of hypokalaemia
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Insulins: Antagonism of hypoglycaemic effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
***Lidocaine:** Action of lidocaine antagonized by hypokalaemia caused by hydrochlorothiazide (interaction less likely when lidocaine used topically)

***Lithium:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide

Metformin: Antagonism of hypoglycaemic effect

Methyldopa: Enhanced hypotensive effect

Nifedipine: Enhanced hypotensive effect

Nitrous oxide: Enhanced hypotensive effect

Prednisolone: Antagonism of diuretic effect; increased risk of hypokalaemia

Propranolol: Enhanced hypotensive effect

***Quinidine:** Cardiac toxicity of quinidine increased by hypokalaemia caused by hydrochlorothiazide

Salbutamol: Increased risk of hypokalaemia with high doses of salbutamol

Sodium nitroprusside: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Verapamil: Enhanced hypotensive effect

Hydrocortisone

NOTE. Interactions do not generally apply to hydrocortisone used for topical application

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect

Amiloride: Antagonism of diuretic effect

Amlodipine: Antagonism of hypotensive effect

***Amphotericin B**: Increased risk of hypokalaemia (avoid concomitant use unless hydrocortisone needed to control reactions)

Aspirin: Increased risk of gastrointestinal bleeding and ulceration; hydrocortisone reduces plasmasalicylate concentration

Atenolol: Antagonism of hypotensive effect

Calcium salts: Reduced absorption of calcium salts

***Carbamazepine:** Accelerated metabolism of hydrocortisone (reduced effect)

Contraceptives, Oral: Oral contraceptives containing estrogens increase plasma concentration of hydrocortisone

Digoxin: Increased risk of hypokalaemia

Enalapril: Antagonism of hypotensive effect

Erythromycin: Erythromycin possibly inhibits metabolism of hydrocortisone

Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia

Glibenclamide: Antagonism of hypoglycaemic effect

Glyceryl trinitrate: Antagonism of hypotensive effect

Hydralazine: Antagonism of hypotensive effect

Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia

Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration

Insulins: Antagonism of hypoglycaemic effect

Isosorbide dinitrate: Antagonism of hypotensive effect

Metformin: Antagonism of hypoglycaemic effect

***Methotrexate:** Increased risk of haematological toxicity

Methyldopa: Antagonism of hypotensive effect

Mifepristone: Possibly reduced effects of hydrocortisone for 3–4 days

Nifedipine: Antagonism of hypotensive effect

***Phenobarbital**: Metabolism of hydrocortisone accelerated (reduced effect)

***Phenytoin**: Metabolism of hydrocortisone accelerated (reduced effect)

Propranolol: Antagonism of hypotensive effect

***Rifampicin:** Accelerated metabolism of hydrocortisone (reduced effect)

Ritonavir: Plasma concentration possibly increased by ritonavir

Salbutamol: Increased risk of hypokalaemia if high doses of salbutamol given with hydrocortisone

Sodium nitroprusside: Antagonism of hypotensive effect

Spironolactone: Antagonism of diuretic effect

Vaccine, Influenza: High doses of hydrocortisone impair immune response

***Vaccine, Live:** High doses of hydrocortisone impair immune response; avoid use of live vaccines

Verapamil: Antagonism of hypotensive effect

***Warfarin:** Anticoagulant effect possibly enhanced or reduced (high-dose hydrocortisone enhances anticoagulant effect)

Hydroxocobalamin

Chloramphenicol: Response to hydroxocobalamin reduced

Ibuprofen

Acetazolamide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect

Amiloride: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia

Amlodipine: Antagonism of hypotensive effect

***Aspirin:** Avoid concomitant use (increased adverse effects); antiplatelet effect of acetylsalicylic acid possibly reduced

Atenolol: Antagonism of hypotensive effect

***Ciclosporin:** Increased risk of nephrotoxicity

***Ciprofloxacin**: Possibly increased risk of convulsions

Dexamethasone: Increased risk of gastrointestinal bleeding and ulceration

Digoxin: Possibly exacerbation of heart failure, reduced renal function, and increased plasma-digoxin concentration

Enalapril: Antagonism of hypotensive effect, increased risk of renal impairment

Furosemide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect

***Glibenclamide**: Possibly enhanced effect of glibenclamide
Glyceryl trinitrate: Antagonism of hypotensive effect
Heparin: Possibly increased risk of bleeding
Hydralazine: Antagonism of hypotensive effect
Hydrochlorothiazide: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect
Hydrocortisonel: Increased risk of gastrointestinal bleeding and ulceration
Isosorbide dinitrate: Antagonism of hypotensive effect
***Levofloxacin:** Possibly increased risk of convulsions
***Lithium:** Reduced excretion of lithium (increased risk of toxicity)
***Methotrexate**: Excretion of methotrexate reduced (increased risk of toxicity)
Methyldopa: Antagonism of hypotensive effect
Mifepristone: Avoidance of ibuprofen advised by manufacturer of mifepristone
Nifedipine: Antagonism of hypotensive effect
***Ofloxacin:** Possible increased risk of convulsions
Penicillamine: Possible increased risk of nephrotoxicity
***Phenytoin**: Effect of phenytoin possibly enhanced
Prednisolone: Increased risk of gastrointestinal bleeding and ulceration
Propranolol: Antagonism of hypotensive effect
Ritonavir: Plasma concentration possibly increased by ritonavir
Sodium nitroprusside: Antagonism of hypotensive effect
Spironolactone: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Verapamil: Antagonism of hypotensive effect
***Warfarin:** Anticoagulant effect possibly enhanced
Zidovudine: Increased risk of haematological toxicity

Imipenem + Cilastatin

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Immunoglobulin, Anti-D

***Vaccine, Live:** Avoid use of live virus vaccine during *4 weeks before* or during *3 months after* injection of anti-D immunoglobulin (impairment of immune response) but rubella vaccine (either as MMR or as single antigen rubella vaccine) may be given at the same time as anti-D immunoglobulin

Indinavir

***Artemether +Lumefantrine**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
Carbamazepine: Possibly reduced plasmaindinavir concentration
Dexamethasone: Possibly reduced plasma-indinavir concentration
Efavirenz: Efavirenz reduces plasma concentration of indinavir

Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
Nevirapine: Nevirapine reduces plasma concentration of indinavir
***Phenobarbital**: Plasma concentration of indinavir possibly reduced
Phenytoin: Plasma-indinavir concentration possibly reduced
***Rifampicin:** Metabolism accelerated by rifampicin (plasma-indinavir concentration reduced—avoid concomitant use)
Ritonavir: Ritonavir increases plasma concentration of indinavir
Saquinavir: Indinavir increases plasma concentration of saquinavir

Insulins

Alcohol: Enhanced hypoglycaemic effect
Atenolol: Enhanced hypoglycaemic effect; atenolol may mask warning signs of hypoglycaemia such as tremor
Contraceptives, Oral: Antagonism of hypoglycaemic effect by estrogens and progestogens
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
Levonorgestrel: Antagonism of hypoglycaemic effect
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Nifedipine: Occasionally impaired glucose tolerance
Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Enhanced hypoglycaemic effect; propranalol may mask warning signs of hypoglycaemia such as tremor
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Enhanced hypoglycaemic effect; timolol may mask warning signs of hypoglycaemia such as tremor

Iron: *see* Ferrous salts

Isoniazid

Amitriptyline: Increased plasma concentration of isoniazid
Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of isoniazid
***Carbamazepine:** Increased plasma-carbamazepine concentration (also isoniazid hepatotoxicity possibly increased)
Cycloserine: Increased risk of CNS toxicity
Diazepam: Metabolism of diazepam inhibited
***Ethosuximide:** Metabolism of ethosuximide inhibited (increased plasma-ethosuximide concentration and risk of toxicity)
Halothane: Possible potentiation of isoniazid hepatotoxicity

Ketamine: Possible potentiation of isoniazid hepatotoxicity
Nitrous oxide: Possible potentiation of isoniazid hepatotoxicity
***Phenytoin:** Metabolism of phenytoin inhibited (enhanced effect)
Thiopental: Possible potentiation of isoniazid hepatotoxicity

Isophane insulin: *see* Insulins

Isosorbide dinitrate

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Atropine: Possibly reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Biperiden: Possibly reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Chlorpromazine: Enhanced hypotensive effect
Clomipramine: Reduced effect of sublingual isosorbide dinitrate tablets (failure to dissolve under the tongue owing to dry mouth)
Contraceptives, Oral: Antagonism of hypotensive effect by estrogens
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Ketamine

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
***Chlorpromazine:** Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
***Fluphenazine:** Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
***Haloperidol:** Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
***Verapamil:** Enhanced hypotensive effect and AV delay

Lamivudine

Sulfamethoxazole +Trimethoprim: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose sulfamethoxazole + trimethoprim)

Levamisole

Alcohol: Possibility of disulfiram-like reaction
Phenytoin: Plasma-phenytoin concentration possibly increased
***Warfarin:** Anticoagulant effect possibly enhanced

Levodopa

Acetazolamide Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Atropine: Absorption of levodopa possibly reduced

Biperiden: Absorption of levodopa possibly reduced
Chlorpromazine: Antagonism of effects of levodopa
Diazepam: Possibly antagonism of levodopa effects
Enalapril: Enhanced hypotensive effect
Ferrous salts: Absorption of levodopa may be reduced by oral ferrous salts
Fluphenazine: Antagonism of effects of levodopa
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Haloperidol: Antagonism of effects of levodopa
***Halothane:** Risk of arrhythmias
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect; antagonism of antiparkinsonian effect
Nifedipine: Enhanced hypotensive effect
Phenytoin: Possibly reduced effects of levodopa
Propranolol: Enhanced hypotensive effect
Pyridoxine: Antagonism of levodopa unless carbidopa also given
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Levofloxacin

Antacids: Reduced absorption of levofloxacin
***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ciclosporin:** Increased risk of nephrotoxicity
Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)
Ferrous salts: Absorption of levofloxacin reduced by oral ferrous salts
***Ibuprofen:** Possibly increased risk of convulsions
Warfarin: Possibly enhanced anticoagulant effect
Zinc sulfate: Reduced absorption of levofloxacin

Levonorgestrel: *see also* Contraceptives, Oral

***Carbamazepine:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Ciclosporin:** Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
Glibenclamide: Antagonism of hypoglycaemic effect
***Griseofulvin:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
Insulins: Antagonism of hypoglycaemic effect

Metformin: Antagonism of hypoglycaemic effect
Nelfinavir: Contraceptive effect of levonorgestrel possibly reduced
***Nevirapine:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Phenobarbital:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Phenytoin:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Rifampicin:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Ritonavir:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Warfarin:** Antagonism of anticoagulant effect

Levothyroxine

Amitriptyline: Enhanced effects of amitriptyline
Calcium salts: Reduced absorption of levothyroxine
Carbamazepine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
Clomipramine: Possibly enhanced effects of clomipramine
Ferrous salts: Absorption of levothyroxine reduced by oral ferrous salts (give at least 2 hours apart)
Phenobarbital: Metabolism of levothyroxine accelerated (may increase levothyroxine requirements in hypothyroidism)
Phenytoin: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism); plasma concentration of phenytoin possibly increased
Rifampicin: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)
***Warfarin:** Enhanced anticoagulant effect

Lidocaine

NOTE. Interactions less likely when lidocaine is used topically
***Acetazolamide:** Hypokalaemia caused by acetazolamide antagonises action of lidocaine
***Atenolol:** Increased myocardial depression
Bupivacaine: Increased myocardial depression
***Furosemide:** Action of lidocaine antagonized by hypokalaemia caused by furosemide
***Hydrochlorothiazide:** Action of lidocaine antagonized by hypokalaemia caused by hydrochlorothiazide
Lopinavir: Possibly increased plasma concentration of lidocaine
***Procainamide:** Increased myocardial depression
***Propranolol:** Increased myocardial depression; increased risk of lidocaine toxicity
***Quinidine:** Increased myocardial depression

Suxamethonium: Neuromuscular blockade enhanced and prolonged

***Timolol:** Increased myocardial depression

***Verapamil:** Increased myocardial depression

Lithium

***Acetazolamide:** Excretion of lithium increased

Alcuronium: Enhanced muscle relaxant effect

***Amiloride:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)

Amitriptyline: Risk of toxicity

Carbamazepine: Neurotoxicity may occur without increased plasma-lithium concentration

Chlorpromazine: Increased risk of extrapyramidal effects and possibility of neurotoxicity

Clomipramine: Risk of toxicity

***Enalapril:** Enalapril reduces excretion of lithium (increased plasma-lithium concentration)

Fluphenazine: Increased risk of extrapyramidal effects and possibility of neurotoxicity

***Furosemide**: Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide

Haloperidol: Increased risk of extrapyramidal effects and possibility of neurotoxicity

***Hydrochlorothiazide:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity); furosemide safer than hydrochlorothiazide

***Ibuprofen**: Reduced excretion of lithium (increased risk of toxicity)

***Methyldopa:** Neurotoxicity may occur without increased plasma-lithium concentration

Metronidazole: Increased lithium toxicity reported

Neostigmine: Antagonism of effect of neostigmine

Phenytoin: Neurotoxicity may occur without increased plasma-lithium concentration

Pyridostigmine: Antagonism of effect of pyridostigmine

Sodium hydrogen carbonate: Increased excretion of lithium (reduced plasma-lithium concentration)

***Spironolactone:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)

Suxamethonium: Enhanced muscle relaxant effect

Vecuronium: Enhanced muscle relaxant effect

Verapamil: Neurotoxicity may occur without increased plasma-lithium concentration

Lopinavir

NOTE. In combination with ritonavir *see also* Ritonavir

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

***Carbamazepine:** Possibly reduced plasmalopinavir concentration

Chlorphenamine: Possibly increased plasma concentration of chlorphenamine

***Dexamethasone:** Possibly reduced plasmalopinavir concentration

***Efavirenz:** Plasma concentration of lopinavir reduced

Lidocaine: Possibly increased plasma concentration of lidocaine

Nelfinavir: Plasma concentration of lopinavir reduced; plasma concentration of active metabolite of nelfinavir increased

Nevirapine: Plasma concentration of lopinavir possibly reduced

***Phenobarbital:** Plasma concentration of lopinavir possibly reduced

Phenytoin: Plasma-lopinavir concentration possibly reduced

***Rifampicin:** Reduced plasma concentration of lopinavir (avoid concomitant use)

Saquinavir: Increased plasma concentration of saquinavir

Magnesium hydroxide: *see* Antacids

Magnesium (parenteral)

Alcuronium: Enhanced muscle relaxant effect

***Nifedipine:** Profound hypotension reported with nifedipine and intravenous magnesium ulfate in preeclampsia

Suxamethonium: Enhanced muscle relaxant effect

Vecuronium: Enhanced muscle relaxant effect

Magnesium sulfate: *see* Magnesium (parenteral)

Measles vaccine: *see* Vaccine, live

Mebendazole

Carbamazepine: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

Phenobarbital: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

Phenytoin: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

Medroxyprogesterone

***Carbamazepine:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

***Ciclosporin**: Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)

Glibenclamide: Antagonism of hypoglycaemic effect
***Griseofulvin:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
Insulins: Antagonism of hypoglycaemic effect
Metformin: Antagonism of hypoglycaemic effect
***Nevirapine:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
***Phenobarbital**: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
***Phenytoin:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
***Rifampicin:** Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
***Ritonavir**: Accelerated metabolism of medroxyprogesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
***Warfarin:** Antagonism of anticoagulant effect

Mefloquine

Amlodipine: Possible increased risk of bradycardia
***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
Atenolol: Increased risk of bradycardia
***Carbamazepine:** Antagonism of anticonvulsant effect
***Chloroquine:** Increased risk of convulsions
Digoxin: Possibly increased risk of bradycardia
***Ethosuximide:** Antagonism of anticonvulsant effect
Nifedipine: Possibly increased risk of bradycardia
***Phenytoin:** Antagonism of anticonvulsant effect
Propranolol: Increased risk of bradycardia
***Quinidine:** Increased risk of ventricular arrhythmias
***Quinine:** Increased risk of convulsions, but should not prevent the use of intravenous quinine in severe cases
Timolol: Increased risk of bradycardia
***Valproate:** Antagonism of anticonvulsant effect
Verapamil: Possibly increased risk of bradycardia

Mercaptopurine

***Allopurinol:** Effects of mercaptopurine enhanced and toxicity increased, reduce dose of mercaptopurine
Phenytoin: Possibly reduced absorption of phenytoin
***Sulfamethoxazole +Trimethoprim:** Increased risk of haematological toxicity
Sulfasalazine: Possibly increased risk of leukopenia
***Trimethoprim**: Increased risk of haematological toxicity
Vaccine, Live: Avoid use of live vaccines with mercaptopurine

(impairment of immune response)
***Warfarin:** Anticoagulant effect possibly reduced

Metformin

Alcohol: Enhanced hypoglycaemic effect; increased risk of lactic acidosis
Atenolol: Atenolol may mask warning signs of hypoglycaemia such as tremor
Contraceptives, Oral: Antagonism of hypoglycaemic effect by estrogens and progestogens
Dexamethasone: Antagonism of hypoglycaemic effect
Enalapril: Hypoglycaemic effect possibly enhanced
Furosemide: Antagonism of hypoglycaemic effect
Hydrochlorothiazide: Antagonism of hypoglycaemic effect
Hydrocortisone: Antagonism of hypoglycaemic effect
Levonorgestrel: Antagonism of hypoglycaemic effect
Medroxyprogesterone: Antagonism of hypoglycaemic effect
Norethisterone: Antagonism of hypoglycaemic effect
Prednisolone: Antagonism of hypoglycaemic effect
Propranolol: Propranalol may mask warning signs of hypoglycaemia such as tremor
Testosterone: Hypoglycaemic effect possibly enhanced
Timolol: Timolol may mask warning signs of hypoglycaemia such as tremor

Methadone

Abacavir: Plasma concentration of methadone possibly reduced
Alcohol: Enhanced hypotensive and sedative effects
Amitriptyline: Sedative effects possibly increased
Carbamazepine: Reduced plasma concentration of methadone
Chlorpromazine: Enhanced hypotensive and sedative effects
Clomipramine: Sedative effects possibly increased
Diazepam: Increased sedative effect
Efavirenz: Reduced plasma concentration of methadone
Fluphenazine: Enhanced hypotensive and sedative effects
Haloperidol: Enhanced hypotensive and sedative effects
Metoclopramide: Antagonism of effects of metoclopramide on gastrointestinal activity
Nelfinavir: Reduced plasma concentration of methadone
Nevirapine: Possibly reduced plasma concentration of methadone
Phenytoin: Accelerated metabolism of methadone (reduced effect and risk of withdrawal symptoms)
Rifampicin: Accelerated metabolism of methadone (reduced effect)
Ritonavir: Reduced plasma concentration of methadone
Zidovudine: Possibly increased plasma concentration of zidovudine

Methotrexate

Amoxicillin: Reduced excretion of methotrexate (increased risk of toxicity)

Ampicillin: Reduced excretion of methotrexate (increased risk of toxicity)

***Aspirin:** Reduced excretion of methotrexate (increased toxicity)

Benzylpenicillin: Reduced excretion of methotrexate (increased risk of toxicity)

***Ciclosporin:** Increased toxicity

***Cisplatin:** Risk of toxicity

***Dexamethasone**: Increased risk of haematological toxicity

Doxycycline: Increased risk of methotrexate toxicity

***Hydrocortisone**: Increased risk of haematological toxicity

***Ibuprofen**: Excretion of methotrexate reduced (increased risk of toxicity)

***Nitrous oxide**: Increased antifolate effect (avoid concomitant use)

Phenoxymethylpenicillin: Reduced excretion of methotrexate (increased risk of toxicity)

Phenytoin: Reduced absorption of phenytoin; antifolate effect of methotrexate increased

***Prednisolone:** Increased risk of haematological toxicity

***Pyrimethamine:** Antifolate effect of methotrexate increased

Silver sulfadiazine: Increased risk of methotrexate toxicity

Sulfadiazine: Risk of methotrexate toxicity increased

***Sulfadoxine +Pyrimethamine:** Antifolate effect of methotrexate increased; risk of methotrexate toxicity increased

***Sulfamethoxazole +Trimethoprim:** Antifolate effect of methotrexate increased (avoid concomitant use); risk of methotrexate toxicity increased

***Trimethoprim:** Antifolate effect of methotrexate increased (avoid concomitant use)

Vaccine, Live: Avoid use of live vaccines with methotrexate (impairment of immune response)

Methyldopa

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

Amiloride: Enhanced hypotensive effect

Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

Chlorpromazine: Enhanced hypotensive effect; increased risk of extrapyramidal effects

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

Enalapril: Enhanced hypotensive effect

Ferrous salts: Oral ferrous salts reduce hypotensive effect of methyldopa

Fluphenazine: Enhanced hypotensive effect; increased risk of extrapyramidal effects

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

Haloperidol: Enhanced hypotensive effect; increased risk of extrapyramidal effects

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect; antagonism of antiparkinsonian effect

***Lithium:** Neurotoxicity may occur without increased plasma-lithium concentration

Nifedipine: Enhanced hypotensive effect

Nitrous oxide: Enhanced hypotensive effect

Prednisolone: Antagonism of hypotensive effect

Propranolol: Enhanced hypotensive effect

***Salbutamol:** Acute hypotension reported with salbutamol infusion

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

Timolol: Enhanced hypotensive effect

Verapamil: Enhanced hypotensive effect

Methyl-ergometrine: *see* ergometrine

Metoclopramide

Aspirin: Enhanced effect of acetylsalicylic acid (increased rate of absorption)

Atropine: Antagonism of effects of metoclopramide on gastrointestinal activity

Biperiden: Antagonism of effects of metoclopramide on gastrointestinal activity

Chlorpromazine: Increased risk of extrapyramidal effects

*Ciclosporin: Plasma-ciclosporin concentration increased

Codeine: Antagonism of effect of metoclopramide on gastrointestinal activity

Fluphenazine: Increased risk of extrapyramidal effects

Haloperidol: Increased risk of extrapyramidal effects

Methadone: Antagonism of effects of metoclopramide on gastrointestinal activity

Morphine: Antagonism of effect of metoclopramide on gastrointestinal activity

Paracetamol: Increased absorption of paracetamol

Suxamethonium: Enhanced effects of suxamethonium

Metronidazole

Alcohol: Disulfiram-like reaction

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Fluorouracil: Metabolism of fluorouracil inhibited (increased toxicity)

Lithium: Increased lithium toxicity reported

Phenobarbital: Metabolism of metronidazole accelerated (reduced plasma concentration)

***Phenytoin:** Metabolism of phenytoin inhibited (increased plasmaphenytoin concentration)

***Warfarin:** Enhanced anticoagulant effect

Miconazole

Amphotericin B: Possibly antagonism of effects of amphotericin B

Carbamazepine: Plasma concentration of carbamazepine possibly increased

***Warfarin:** Enhanced anticoagulant effect

Mifepristone

Aspirin: Manufacturer of mifepristone advises avoid concomitant use

Beclomethasone: Possibly reduced effects of beclomethasone for 3–4 days

Dexamethasone: Possibly reduced effects of dexamethasone for 3–4 days

Hydrocortisone: Possibly reduced effects of hydrocortisone for 3–4 days

Ibuprofen: Avoidance of ibuprofen advised by manufacturer of mifepristone

Prednisolone: Possibly reduced effects of prednisolone for 3–4 days

MMR vaccine: *see* Vaccine, live

Morphine

Alcohol: Enhanced sedative and hypotensive effect

Amitriptyline: Possibly increased sedation

Chlorpromazine: Enhanced sedative and hypotensive effect

Ciprofloxacin: Manufacturer of ciprofloxacin advises avoid premedication with morphine (reduced plasma-ciprofloxacin concentration) when ciprofloxacin used for surgical prophylaxis

Clomipramine: Possibly increased sedation

Diazepam: Enhanced sedative effect

Fluphenazine: Enhanced sedative and hypotensive effect

Haloperidol: Enhanced sedative and hypotensive effect

Metoclopramide: Antagonism of effect of metoclopramide on gastrointestinal activity

***Ritonavir:** Ritonavir possibly increases plasma concentration of morphine

Nelfinavir

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Carbamazepine: Possibly reduced plasmanelfinavir concentration

***Ciclosporin:** Possibly increased plasmaciclosporin concentration

***Contraceptives, Oral:** Accelerated metabolism of estrogens (reduced contraceptive effect); nelfinavir possibly reduces contraceptive effect of progestogens

Indinavir: Combination may lead to increased plasma concentration of either drug (or both)

Levonorgestrel: Contraceptive effect of levonorgestrel possibly reduced

Lopinavir: Plasma concentration of lopinavir reduced; plasma concentration of active metabolite of nelfinavir increased

Methadone: Reduced plasma concentration of methadone

***Norethisterone:** Possibly reduced contraceptive effect

***Phenobarbital:** Plasma concentration of nelfinavir possibly reduced

Phenytoin: Reduced plasma-phenytoin concentration

***Quinidine:** Increased risk of ventricular arrhythmias (avoid concomitant use)

***Rifampicin:** Plasma concentration of nelfinavir significantly reduced (avoid concomitant use)

Ritonavir: Combination may lead to increased plasma concentration of either drug (or both)

Saquinavir: Combination may lead to increased plasma concentration of either drug (or both)

Neostigmine

Alcuronium: Antagonism of muscle relaxant effect

***Amikacin:** Antagonism of effects of neostigmine

Atropine: Antagonism of effects of neostigmine

Biperiden: Antagonism of effects of neostigmine

Chloroquine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of neostigmine

Clindamycin: Antagonism of effects of neostigmine

***Gentamicin:** Antagonism of effect of neostigmine

Lithium: Antagonism of effect of neostigmine

Procainamide: Antagonism of effect of neostigmine

Propranolol: Antagonism of effect of neostigmine

Quinidine: Antagonism of effect of neostigmine

***Streptomycin:** Antagonism of effect of neostigmine

Suxamethonium: Effect of suxamethonium enhanced

Vecuronium: Antagonism of muscle relaxant effect

Nevirapine

***Contraceptives, Oral:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Efavirenz: Plasma-efavirenz concentration reduced

***Fluconazole:** Increased plasma concentration of nevirapine

Indinavir: Nevirapine reduces plasma concentration of indinavir

***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Lopinavir: Plasma concentration of lopinavir possibly reduced

***Medroxyprogesterone:** Accelerated metabolism of medroxy-progesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

Methadone: Possibly reduced plasma concentration of methadone

***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)

***Rifampicin:** Reduced plasma concentration of nevirapine (avoid concomitant use)

Saquinavir: Plasma concentration of saquinavir reduced

***Warfarin:** Enhanced or reduced anticoagulant effect

Nifedipine

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

Alcuronium: Enhanced muscle relaxant effect

Amiloride: Enhanced hypotensive effect

***Atenolol:** Enhanced hypotensive effect. Possibly severe hypotension and heart failure

Carbamazepine: Probably reduced effect of nifedipine

Chlorpromazine: Enhanced hypotensive effect

Ciclosporin: Possibly increased plasmanifedipine concentration (increased risk of adverse effects such as gingival hyperplasia)

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

***Digoxin:** Possibly increased plasma concentration of digoxin

Enalapril: Enhanced hypotensive effect

Fluphenazine: Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

Grapefruit juice: Increased plasma-nifedipine concentration

Haloperidol: Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Insulins: Occasionally impaired glucose tolerance

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

***Magnesium (parenteral):** Profound hypotension reported with nifedipine and intravenous magnesium sulfate in preeclampsia

Mefloquine: Possibly increased risk of bradycardia

Methyldopa: Enhanced hypotensive effect

Nitrous oxide: Enhanced hypotensive effect

***Phenobarbital:** Effect of nifedipine probably reduced

***Phenytoin:** Probably reduced effect of nifedipine

Prednisolone: Antagonism of hypotensive effect

***Propranolol**: Enhanced hypotensive effect. Possibly severe hypotension and heart failure

Quinidine: Reduced plasma-quinidine concentration

***Ritonavir:** Plasma concentration possibly increased by ritonavir

***Rifampicin:** Accelerated metabolism of nifedipine (plasma concentration significantly reduced)

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Thiopental: Enhanced hypotensive effect

***Timolol:** Enhanced hypotensive effect.Possibly severe hypotension and heart failure

Vecuronium: Enhanced muscle relaxant effect

Vincristine: Possibly reduced metabolism of vincristine

Nitous oxide

Acetazolamide: Enhanced hypotensive effect

Amiloride: Enhanced hypotensive effect

Amitriptyline: Increased risk of arrhythmias and hypotension

Amlodipine: Enhanced hypotensive effect

Atenolol: Enhanced hypotensive effect

***Chlorpromazine:** Enhanced hypotensive effect

Clomipramine: Increased risk of arrhythmias and hypotension

Diazepam: Enhanced sedative effect

Enalapril: Enhanced hypotensive effect

***Fluphenazine:** Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

***Haloperidol:** Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Isoniazid: Possible potentiation of isoniazid hepatotoxicity

Isosorbide dinitrate: Enhanced hypotensive effect

***Methotrexate**: Increased antifolate effect (avoid concomitant use)
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
***Verapamil:** Enhanced hypotensive effect and AV delay

Norethisterone: *see also* Contraceptives, Oral

***Carbamazepine:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Ciclosporin:** Inhibition of ciclosporin metabolism (increased plasma-ciclosporin concentration)
Glibenclamide: Antagonism of hypoglycaemic effect
***Griseofulvin:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
Insulins: Antagonism of hypoglycaemic effect
Metformin: Antagonism of hypoglycaemic effect
Nelfinavir: Possibly reduced contraceptive effect
***Nevirapine:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Phenobarbital**: Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Phenytoin:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Rifampicin:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Ritonavir:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
***Warfarin:** Antagonism of anticoagulant effect

Ofloxacin

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of ofloxacin
***Artemether +Lumefantrine**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ciclosporin:** Increased risk of nephrotoxicity
Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)
Ferrous salts: Absorption of ofloxacin reduced by oral ferrous salts
***Ibuprofen:** Possible increased risk of convulsions
***Warfarin:** Enhanced anticoagulant effect
Zinc sulfate: Reduced absorption of ofloxacin

Oxygen

***Bleomycin**: Serious pulmonary toxicity in patients exposed to conventional oxygen concentrations during anaesthesia

Oxytocin

Ephedrine: Risk of hypertension due to enhanced vasopressor effect of ephedrine
Epinephrine: Risk of hypertension due to enhanced vasopressor effect of epinephrine
Halothane: Oxytocic effect possibly reduced; enhanced hypotensive effect and risk of arrhythmias

Paracetamol

Metoclopramide: Increased absorption of paracetamol
Warfarin: Prolonged regular use of paracetamol possibly enhances anticoagulant effect

Penicillamine

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of penicillamine
Digoxin: Plasma concentration of digoxin possibly reduced
Ferrous salts: Oral ferrous salts reduce absorption of penicillamine
Ibuprofen: Possible increased risk of nephrotoxicity
Zinc sulfate: Absorption of penicillamine and zinc sulfate reduced

Pentamidine

Amphotericin B: possibly increased risk of nephrotoxicity

Phenobarbital

Abacavir: Plasma concentration of abacavir possibly reduced
Acetazolamide: Increased risk of osteomalacia
Alcohol: Enhanced sedative effect
***Amitriptyline**: Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of amitriptyline possibly accelerated (reduced plasma concentration)
***Amlodipine:** Probably reduced effect of amlodipine
***Carbamazepine:** May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of carbamazepine reduced
***Chloramphenicol:** Metabolism of chloramphenicol accelerated (reduced chloramphenicol concentration)
***Chlorpromazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Ciclosporin**: Metabolism of ciclosporin accelerated (reduced effect)
***Clomipramine:** Antagonism of anticonvulsant effect (convulsive

threshold lowered); metabolism of clomipramine possibly accelerated (reduced plasma concentration)

***Contraceptives, Oral:** Metabolism of estrogens and progestogens accelerated (reduced contraceptive effect)

***Dexamethasone:** Metabolism of dexamethasone accelerated (reduced effect)

Doxycycline: Metabolism of doxycycline accelerated (reduced plasma concentration)

Ergocalciferol: Ergocalciferol requirements possibly increased

Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide possibly reduced

Etoposide: Possibly reduced plasma concentration of etoposide

***Fluphenazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Folic acid and Folinic acid: Plasma concentration of phenobarbital possibly reduced

Griseofulvin: Reduction in absorption of griseofulvin (reduced effect)

***Haloperidol:** Antagonism of anticonvulsant effect (convulsive threshold lowered); metabolism of haloperidol accelerated (reduced plasma concentration)

***Hydrocortisone:** Metabolism of hydrocortisone accelerated (reduced effect)

***Indinavir:** Plasma concentration of indinavir possibly reduced

***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Levothyroxine: Metabolism of levothyroxine accelerated (may increase levothyroxine requirements in hypothyroidism)

***Lopinavir:** Plasma concentration of lopinavir possibly reduced

Mebendazole: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infection)

***Medroxyprogesterone:** Accelerated metabolism of medroxy-progesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

Metronidazole: Metabolism of metronidazole accelerated (reduced plasma concentration)

***Nelfinavir:** Plasma concentration of nelfinavir possibly reduced

***Nifedipine:** Effect of nifedipine probably reduced

***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)

Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of phenobarbital often raised

***Prednisolone:** Metabolism of prednisolone accelerated (reduced effect)

Quinidine: Metabolism of quinidine accelerated (reduced plasma concentration)

***Saquinavir:** Plasma concentration of saquinavir possibly reduced

Valproate: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproate reduced; phenobarbital concentration increased

***Verapamil:** Effect of verapamil probably reduced

***Warfarin:** Metabolism of warfarin accelerated (reduced anticoagulant effect)

Phenoxymethylpenicillin

Contraceptives, Oral: Contraceptive effect of estrogens possibly reduced (risk probably small)

Methotrexate: Reduced excretion of methotrexate (increased risk of toxicity)

Phenytoin

Abacavir: Plasma concentration of abacavir possibly reduced

Acetazolamide: Increased risk of osteomalacia

Acetylsalicylic acid: Enhancement of effect of phenytoin

Alcohol: Plasma-phenytoin concentration reduced with regular large amounts of alcohol

Alcuronium: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)

***Amitriptyline**: Antagonism of anticonvulsant effect (convulsive threshold lowered); possibly reduced plasma-amitriptyline concentration

Amlodipine: Probably reduced effect of amlodipine

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of phenytoin

Azathioprine: Possibly reduced absorption of phenytoin

Bleomycin: Possibly reduced absorption of phenytoin

***Carbamazepine:** May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of carbamazepine often lowered

Chlorambucil: Possibly reduced absorption of phenytoin

***Chloramphenicol:** Plasma-phenytoin concentration increased (increased risk of toxicity)

Chloroquine: Possible increased risk of convulsions

***Chlorpromazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Ciclosporin**: Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

Ciprofloxacin: Plasma-phenytoin concentration can be increased or decreased by ciprofloxacin

Cisplatin: Reduced absorption of phenytoin

***Clomipramine:** Antagonism of anticonvulsant effect (convulsive threshold lowered); possibly reduced plasma-clomipramine concentration

***Contraceptives, Oral:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Cyclophosphamide: Possibly reduced absorption of phenytoin

Cytarabine: Reduced absorption of phenytoin

Dacarbazine: Possibly reduced absorption of phenytoin

Dactinomycin: Possibly reduced absorption of phenytoin

Daunorubicin: Possibly reduced absorption of phenytoin

***Dexamethasone:** Metabolism of dexamethasone accelerated (reduced effect)

Diazepam: Plasma-phenytoin concentration possibly increased or decreased by diazepam

Digoxin: Plasma concentration of digoxin possibly reduced

Doxorubicin: Possibly reduced absorption of phenytoin

Doxycycline: Increased metabolism of doxycycline (reduced plasma concentration)

Ergocalciferol: Ergocalciferol requirements possibly increased

***Ethosuximide:** May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin possibly increased; plasma concentration of ethosuximide possibly reduced

Etoposide: Possibly reduced absorption of phenytoin and possibly reduced plasma concentration of etoposide

***Fluconazole:** Plasma concentration of phenytoin increased (consider reducing dose of phenytoin)

Fluorouracil: Metabolism of phenytoin possibly inhibited (increased risk of toxicity)

***Fluphenazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

Folic acid and Folinic acid: Plasma-phenytoin concentration possibly reduced

***Haloperidol:** Antagonism of anticonvulsant effect (convulsive threshold lowered)

***Hydrocortisone:** Metabolism of hydrocortisone accelerated (reduced effect)

***Ibuprofen:** Effect of phenytoin possibly enhanced

Indinavir: Plasma-indinavir concentration possibly reduced

***Isoniazid:** Metabolism of phenytoin inhibited (enhanced effect)

Levamisole: Plasma-phenytoin concentration possibly increased

Levodopa: Possibly reduced effects of levodopa

***Levonorgestrel**: Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism); plasma concentration of phenytoin possibly increased

Lithium: Neurotoxicity may occur without increased plasma-lithium concentration

Lopinavir: Plasma-lopinavir concentration possibly reduced

Mebendazole: Reduced plasma-mebendazole concentration (possibly increase mebendazole dose for tissue infections)

***Medroxyprogesterone:** Accelerated metabolism of medroxy-progesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

***Mefloquine:** Antagonism of anticonvulsant effect

Mercaptopurine: Possibly reduced absorption of phenytoin

Methadone: Accelerated metabolism of methadone (reduced effect and risk of withdrawal symptoms)

Methotrexate: Reduced absorption of phenytoin; antifolate effect of methotrexate increased

***Metronidazole:** Metabolism of phenytoin inhibited (increased plasma-phenytoin concentration)

Nelfinavir: Reduced plasma-phenytoin concentration

***Nifedipine:** Probably reduced effect of nifedipine

***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)

Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of phenytoin often lowered but may be raised; plasma concentration of phenobarbital often raised

Praziquantel: Plasma-praziquantel concentration reduced

***Prednisolone:** Metabolism of prednisolone accelerated (reduced effect)

Procarbazine: Reduced absorption of phenytoin

***Pyrimethamine**: Antagonism of anticonvulsant effect; increased antifolate effect

***Quinidine**: Accelerated metabolism of quinidine (reduced plasma-quinidine concentration)

***Rifampicin:** Accelerated metabolism of phenytoin (reduced plasma concentration)

Saquinavir: Plasma-saquinavir concentration possibly reduced

Silver sulfadiazine: Possibly increased plasma concentration of phenytoin

Sulfadiazine: Plasma-phenytoin concentration possibly increased

***Sulfadoxine +Pyrimethamine:** Plasma-phenytoin concentration possibly increased; increased antifolate effect

***Sulfamethoxazole +Trimethoprim:** Antifolate effect and plasma-phenytoin concentration increased

***Trimethoprim:** Antifolate effect and plasma-phenytoin concentration increased

Vaccine, Influenza: Enhanced effect of phenytoin

Valproate: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproate reduced; plasma concentration of phenytoin increased or possibly reduced

Vecuronium: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)

Verapamil: Reduced effect of verapamil

Vinblastine: Possibly reduced absorption of phenytoin

Vincristine: Possibly reduced absorption of phenytoin

***Warfarin:** Accelerated metabolism of warfarin (possibility of reduced anticoagulant effect, but enhancement also reported)

Zidovudine: Plasma-phenytoin concentration increased or decreased by zidovudine

Phytomenadione

***Warfarin:** Antagonism of anticoagulant effect by phytomenadione

Pilocarpine

Atenolol: Increased risk of arrhythmias

Atropine: Antagonism of effects of pilocarpine

Biperiden: Antagonism of effects of pilocarpine

Propranolol: Increased risk of arrhythmias

Timolol: Increased risk of arrhythmias

Poliomyelitis, oral vaccine: *see* Vaccine, live

Potassium chloride: *see* Potassium salts

Potassium salts

***Amiloride:** Increased risk of hyperkalaemia

***Ciclosporin:** Increased risk of hyperkalaemia

***Enalapril:** Increased risk of severe hyperkalaemia

***Spironolactone:** Risk of hyperkalaemia

Praziquantel

Albendazole: Increased plasma concentration of active metabolite of albendazole

Carbamazepine: Plasma-praziquantel concentration reduced

Chloroquine: Plasma-praziquantel concentration possibly reduced

Dexamethasone: Plasma-praziquantel concentration reduced

Phenytoin: Plasma-praziquantel concentration reduced

Prednisolone

Acetazolamide: Increased risk of hypokalaemia; antagonism of diuretic effect

Amiloride: Antagonism of diuretic effect

Amlodipine: Antagonism of hypotensive effect

***Amphotericin B:** Increased risk of hypokalaemia (avoid concomitant use unless prednisolone needed to control reactions)

Aspirin: Increased risk of gastrointestinal bleeding and ulceration; prednisolone reduces plasmasalicylate concentration

Atenolol: Antagonism of hypotensive effect

Calcium salts: Reduced absorption of calcium salts

***Carbamazepine:** Accelerated metabolism of prednisolone (reduced effect)

Ciclosporin: Increased plasma concentration of prednisolone

Contraceptives, Oral: Oral contraceptives containing estrogens increase plasma concentration of prednisolone

Digoxin: Increased risk of hypokalaemia

Enalapril: Antagonism of hypotensive effect

Erythromycin: Erythromycin possibly inhibits metabolism of prednisolone

Furosemide: Antagonism of diuretic effect; increased risk of hypokalaemia

Glibenclamide: Antagonism of hypoglycaemic effect

Glyceryl trinitrate: Antagonism of hypotensive effect

Hydralazine: Antagonism of hypotensive effect

Hydrochlorothiazide: Antagonism of diuretic effect; increased risk of hypokalaemia

Ibuprofen: Increased risk of gastrointestinal bleeding and ulceration

Insulins: Antagonism of hypoglycaemic effect

Isosorbide dinitrate: Antagonism of hypotensive effect

Metformin: Antagonism of hypoglycaemic effect

***Methotrexate:** Increased risk of haematological toxicity

Methyldopa: Antagonism of hypotensive effect

Mifepristone: Possibly reduced effects of prednisolone for 3–4 days

Nifedipine: Antagonism of hypotensive effect

***Phenobarbital:** Metabolism of prednisolone accelerated (reduced effect)

***Phenytoin:** Metabolism of prednisolone accelerated (reduced effect)

Propranolol: Antagonism of hypotensive effect

***Rifampicin:** Accelerated metabolism of prednisolone (reduced effect)

Ritonavir: Plasma concentration possibly increased by ritonavir

Salbutamol: Increased risk of hypokalaemia if high doses of salbutamol given with prednisolone

Sodium nitroprusside: Antagonism of hypotensive effect

Spironolactone: Antagonism of diuretic effect

Vaccine, Influenza: High doses of prednisolone impair immune response

***Vaccine, Live:** High doses of prednisolone impair immune response; avoid use of live vaccines

Verapamil: Antagonism of hypotensive effect

***Warfarin:** Anticoagulant effect possibly enhanced or reduced (high-dose prednisolone enhances anticoagulant effect)

Primaquine

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Procainamide

***Alcuronium:** Enhanced muscle relaxant effect

***Amitriptyline:** Increased risk of ventricular arrhythmias

***Artemether +Lumefantrine:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)

***Atenolol:** Increased myocardial depression

Bupivacaine: Increased myocardial depression

***Chlorpromazine:** Increased risk of ventricular arrhythmias

***Clomipramine:** Increased risk of ventricular arrhythmias

***Fluphenazine:** Increased risk of ventricular arrhythmias

***Haloperidol**: Increased risk of ventricular arrhythmias

***Lidocaine:** Increased myocardial depression (interaction less likely when lidocaine used topically)

Neostigmine: Antagonism of effect of neostigmine

***Propranolol:** Increased risk of myocardial depression

Pyridostigmine: Antagonism of effect of pyridostigmine

***Quinidine:** Increased myocardial depression

Sulfamethoxazole +Trimethoprim: Increased plasma-procainamide concentration

***Suxamethonium:** Enhanced muscle relaxant effect

*Timolol: Increased myocardial depression

Trimethoprim: Increased plasma-procainamide concentration

***Vecuronium:** Enhanced muscle relaxant effect

Procaine benzylpenicillin *see* Benzylpenicillin

Procarbazine

Alcohol: Disulfiram-like reaction

Phenytoin: Reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with procarbazine (impairment of immune response)

Proguanil

***Artemether +Lumefantrin:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Pyrimethamine: Increased antifolate effect

Warfarin: Isolated reports of enhanced anticoagulant effect

Promethazine

Alcohol: Increased sedative effect

Amitriptyline: Increased antimuscarinic and sedative effects

Atropine: Increased risk of antimuscarinic adverse effects

Biperiden: Increased risk of antimuscarinic adverse effects

Clomipramine: Increased antimuscarinic and sedative effects

Diazepam: Enhanced sedative effect

Propranolol

Acetazolamide: Enhanced hypotensive effect

Alcohol: Enhanced hypotensive effect

Alcuronium: Enhanced muscle relaxant effect

Amiloride: Enhanced hypotensive effect

Amlodipine: Enhanced hypotensive effect

***Bupivacaine:** Increased risk of bupivacaine toxicity

***Chlorpromazine:** Concomitant administration may increase plasma concentration of both drugs; enhanced hypotensive effect

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

Digoxin: Increased risk of AV block and bradycardia

Enalapril: Enhanced hypotensive effect

***Epinephrine**: Severe hypertension

Fluphenazine: Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glibenclamide: Propranalol may mask warning signs of hypoglycaemia such as tremor

Glyceryl trinitrate: Enhanced hypotensive effect

Halothane: Enhanced hypotensive effect

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Insulins: Enhanced hypoglycaemic effect; propranolol may mask warning signs of hypoglycaemia such as tremor

Isosorbide dinitrate: Enhanced hypotensive effect

Ketamine: Enhanced hypotensive effect

Levodopa: Enhanced hypotensive effect

***Lidocaine:** Increased myocardial depression; increased risk of lidocaine toxicity (interaction less likely when lidocaine used topically)

Mefloquine: Increased risk of bradycardia

Metformin: Propranolol may mask warning signs of hypoglycaemia such as tremor

Methyldopa: Enhanced hypotensive effect

Neostigmine: Antagonism of effect of neostigmine

***Nifedipine:** Enhanced hypotensive effect. Possible severe hypotension and heart failure

Nitrous oxide: Enhanced hypotensive effect

Pilocarpine: Increased risk of arrhythmias

Prednisolone: Antagonism of hypotensive effect

***Procainamide:** Increased myocardial depression

Pyridostigmine: Antagonism of effect of pyridostigmine

***Quinidine**: Increased myocardial depression

Rifampicin: Metabolism of propranolol accelerated (significantly reduced plasma concentration)

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Suxamethonium: Enhanced muscle relaxant effect

Thiopental: Enhanced hypotensive effect

Vecuronium; Enhanced muscle relaxant effect
***Verapamil**: Asystole, severe hypotension and heart failure

Pyridostigmine

Alcuronium: Antagonism of muscle relaxant effect
***Amikacin**: Antagonism of effect of pyridostigmine
Atropine: Antagonism of effect of pyridostigmine
Biperiden: Antagonism of effect of pyridostigmine
Chloroquine: Chloroquine has potential to increase symptoms of myasthenia gravis and thus diminish effect of pyridostigmine
Clindamycin: Antagonism of effects of pyridostigmine
***Gentamicin:** Antagonism of effect of pyridostigmine
Lithium: Antagonism of effect of pyridostigmine
Procainamide: Antagonism of effect of pyridostigmine
Propranolol: Antagonism of effect of pyridostigmine
Quinidine: Antagonism of effect of pyridostigmine
***Streptomycin:** Antagonism of effect of pyridostigmine
Suxamethonium: Effect of suxamethonium enhanced
Vecuronium: Antagonism of muscle relaxant effect

Pyridoxine

Levodopa: Antagonism of levodopa unless carbidopa also given

Pyrimethamine

***Artemether +Lumefantrine**: Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Methotrexate:** Antifolate effect of methotrexate increased
***Phenytoin**: Antagonism of anticonvulsant effect; increased antifolate effect
Proguanil: Increased antifolate effect
***Silver sulfadiazine**: Increased antifolate effect
***Sulfadiazine:** Increased antifolate effect
***Sulfamethoxazole +Trimethoprim:** Increased antifolate effect
***Trimethoprim:** Increased antifolate effect
Zidovudine: Increased antifolate effect

Pyrimethamine +Sulfadoxine: *see* Sulfadoxine + Pyrimethamine

Quinidine

***Acetazolamide:** Cardiac toxicity of quinidine increased if hypokalaemia occurs; acetazolamide possibly reduces excretion of quinidine (increased plasma concentration)
***Alcuronium:** Enhanced muscle relaxant effect
***Amitriptyline**: Increased risk of ventricular arrhythmias

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced quinidine excretion in alkaline urine (plasma-quinidine concentration occasionally increased)
***Artemether +Lumefantrine:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)
***Atenolol:** Increased myocardial depression
Bupivacaine: Increased myocardial depression
Chloroquine: Increased risk of ventricular arrhythmias
***Chlorpromazine:** Increased risk of ventricular arrhythmias
***Clomipramine**: Increased risk of ventricular arrhythmias
***Digoxin:** Plasma concentration of digoxin increased (halve dose of digoxin)
***Erythromycin:** Increased risk of ventricular arrhythmias with parenteral erythromycin
***Fluphenazine:** Increased risk of ventricular arrhythmias
***Furosemide:** Cardiac toxicity of quinidine increased by hypokalaemia caused by furosemide
***Haloperidol:** Increased risk of ventricular arrhythmias
***Hydrochlorothiazide:** Cardiac toxicity of quinidine increased by hypokalaemia caused by hydrochlorothiazide
***Lidocaine:** Increased myocardial depression (interaction less likely when lidocaine used topically)
***Mefloquine:** Increased risk of ventricular arrhythmias
***Nelfinavir:** Increased risk of ventricular arrhythmias (avoid concomitant use)
Neostigmine: Antagonism of effect of neostigmine
Nifedipine: Reduced plasma-quinidine concentration
Phenobarbital: Metabolism of quinidine accelerated (reduced plasma concentration)
***Phenytoin:** Accelerated metabolism of quinidine (reduced plasma-quinidine concentration)
***Procainamide:** Increased myocardial depression
***Propranolol:** Increased myocardial depression
Pyridostigmine: Antagonism of effect of pyridostigmine
***Rifampicin:** Accelerated metabolism of quinidine (reduced plasma-quinidine concentration)
***Ritonavir:** Increased plasma-quinidine concentration (increased risk of ventricular arrhythmias—avoid concomitant use)
***Suxamethonium:** Enhanced muscle relaxant effect
***Timolol:** Increased myocardial depression
***Vecuronium:** Enhanced muscle relaxant effect
***Verapamil:** Increased plasma-quinidine concentration (extreme hypotension may occur)
***Warfarin:** Anticoagulant effect may be enhanced

Quinine

***Artemether +Lumefantrine:** Risk of ventricular arrhythmias (manufacturer of artemether with lumefantrine advises avoid concomitant use)

Chloroquine: Increased risk of ventricular arrhythmias

***Digoxin:** Plasma concentration of digoxin increased

***Mefloquine:** Increased risk of convulsions, but should not prevent the use of intravenous quinine in severe cases

Suxamethonium: Possibly enhanced effects of suxamethonium

Rifampicin

Abacavir: Plasma concentration of abacavir possibly reduced

Amitriptyline: Plasma concentration of amitriptyline possibly reduced

Antacids (Aluminium hydroxide; Magnesium hydroxide): Reduced absorption of rifampicin

Chloramphenicol: Accelerated metabolism of chloramphenicol (reduced plasma-chloramphenicol concentration)

***Ciclosporin:** Accelerated metabolism of ciclosporin (reduced plasma-ciclosporin concentration)

Clomipramine: Plasma concentration of clomipramine possibly reduced

***Contraceptives, Oral:** Accelerated metabolism of estrogens and progestogens (reduced contraceptive effect)

Dapsone: Reduced plasma-dapsone concentration

***Dexamethasone**: Accelerated metabolism of dexamethasone (reduced effect)

Diazepam: Metabolism of diazepam accelerated (reduced plasma concentration)

Digoxin: Plasma concentration of digoxin possibly reduced

Doxycycline: Plasma-doxycycline concentration possibly reduced

Efavirenz: Reduced plasma concentration of efavirenz (increase efavirenz dose)

***Fluconazole:** Accelerated metabolism of fluconazole (reduced plasma concentration)

***Glibenclamide**: Possibly accelerated metabolism (reduced effect) of glibenclamide

***Haloperidol**: Accelerated metabolism of haloperidol (reduced plasma-haloperidol concentration)

***Hydrocortisone:** Accelerated metabolism of hydrocortisone (reduced effect)

***Indinavir:** Metabolism accelerated by rifampicin (plasma-indinavir concentration reduced—avoid concomitant use)

***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)

Levothyroxine: Accelerated metabolism of levothyroxine (may increase levothyroxine requirements in hypothyroidism)

***Lopinavir:** Reduced plasma concentration of lopinavir (avoid concomitant use)

***Medroxyprogesterone:** Accelerated metabolism of medroxy-progesterone (does not apply to injectable medroxyprogesterone acetate for contraception)

Methadone: Accelerated metabolism of methadone (reduced effect)

***Nelfinavir:** Plasma concentration of nelfinavir significantly reduced (avoid concomitant use)

***Nevirapine:** Reduced plasma concentration of nevirapine (avoid concomitant use)

***Nifedipine:** Accelerated metabolism of nifedipine (plasma concentration significantly reduced)

***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)

***Phenytoin:** Accelerated metabolism of phenytoin (reduced plasma concentration)

***Prednisolone:** Accelerated metabolism of prednisolone (reduced effect)

Propranolol: Metabolism of propranolol accelerated (significantly reduced plasma concentration)

***Quinidine:** Accelerated metabolism of quinidine (reduced plasma-quinidine concentration)

***Saquinavir:** Plasma concentration of saquinavir significantly reduced—avoid concomitant use

***Verapamil:** Accelerated metabolism of verapamil (plasma concentration significantly reduced)

***Warfarin:** Accelerated metabolism of warfarin (reduced anticoagulant effect)

Zidovudine: Avoidance of rifampicin advised by manufacturer of zidovudine

Ritonavir

***Amitriptyline**: Plasma concentration possibly increased by ritonavir

***Amlodipine:** Possibly increased plasma concentration of amlodipine

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use

Azithromycin: Plasma concentration of azithromycin possibly increased

***Carbamazepine**: Plasma concentration possibly increased by ritonavir

***Chlorpromazine:** Plasma concentration possibly increased by ritonavir

***Ciclosporin:** Plasma concentration possibly increased by ritonavir

***Clomipramine:** Plasma concentration possibly increased by ritonavir

***Codeine:** Ritonavir possibly increases plasma concentration of codeine

***Contraceptives, Oral:** Accelerated metabolism of estrogens (reduced contraceptive effect)

Dexamethasone: Plasma concentration possibly increased by ritonavir

***Diazepam:** Plasma concentration possibly increased by ritonavir (risk of extreme sedation and respiratory depression—avoid concomitant use)

Efavirenz: Increased risk of toxicity (monitor liver function tests)

Erythromycin: Plasma concentration possibly increased by ritonavir

Fluconazole: Plasma concentration increased by ritonavir
***Fluphenazine:** Plasma concentration possibly increased by ritonavir
***Haloperidol:** Plasma concentration possibly increased by ritonavir
Hydrocortisone: Plasma concentration possibly increased by ritonavir
Ibuprofen: Plasma concentration possibly increased by ritonavir
Indinavir: Ritonavir increases plasma concentration of indinavir
***Levonorgestrel:** Accelerated metabolism of levonorgestrel (reduced contraceptive effect)
***Medroxyprogesterone:** Accelerated metabolism of medroxy-progesterone (does not apply to injectable medroxyprogesterone acetate for contraception)
Methadone: Reduced plasma concentration of methadone
***Morphine:** Ritonavir possibly increases plasma concentration of morphine
Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
***Nifedipine:** Plasma concentration possibly increased by ritonavir
***Norethisterone:** Accelerated metabolism of norethisterone (reduced contraceptive effect)
Prednisolone: Plasma concentration possibly increased by ritonavir
***Quinidine:** Increased plasma-quinidine concentration (increased risk of ventricular arrhythmias—avoid concomitant use)
***Saquinavir:** Ritonavir increases plasma concentration of saquinavir
***Verapamil:** Plasma concentration possibly increased by ritonavir
***Warfarin:** Plasma concentration possibly increased by ritonavir

Rubella vaccine: *see* Vaccine, live

Salbutamol

Acetazolamide: Increased risk of hypokalaemia with high doses of salbutamol
Dexamethasone: Increased risk of hypokalaemia if high doses of salbutamol given with dexamethasone
Digoxin: Possibly reduced plasma concentration of digoxin
Furosemide: Increased risk of hypokalaemia with high doses of salbutamol
Hydrochlorothiazide: Increased risk of hypokalaemia with high doses of salbutamol
Hydrocortisone: Increased risk of hypokalaemia if high doses of salbutamol given with hydrocortisone
***Methyldopa:** Acute hypotension reported with salbutamol infusion
Prednisolone: Increased risk of hypokalaemia if high doses of salbutamol given with prednisolone

Saquinavir

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
Carbamazepine: Possibly reduced plasmasaquinavir concentration
***Ciclosporin:** Plasma concentration of both ciclosporin and saquinavir increased
Dexamethasone: Possibly reduced plasma-saquinavir concentration
Efavirenz: Efavirenz significantly reduces plasma concentration of saquinavir
Fluconazole: Plasma concentration of saquinavir possibly increased
Indinavir: Indinavir increases plasma concentration of saquinavir
Lopinavir: Increased plasma concentration of saquinavir
Nelfinavir: Combination may lead to increased plasma concentration of either drug (or both)
Nevirapine: Plasma concentration of saquinavir reduced
***Phenobarbital:** Plasma concentration of saquinavir possibly reduced
Phenytoin: Plasma-saquinavir concentration possibly reduced
***Rifampicin:** Plasma concentration of saquinavir significantly reduced — avoid concomitant use
***Ritonavir:** Ritonavir increases plasma concentration of saquinavir
Warfarin: Possibly enhanced anticoagulant effect

Silver sulfadiazine

NOTE. Interactions may apply when silver sulfadiazine is used to treat large areas of skin
***Ciclosporin:** Increased risk of nephrotoxicity; possibly reduced plasma concentration of ciclosporin
Glibenclamide: Effects of glibenclamide rarely enhanced
Methotrexate: Increased risk of methotrexate toxicity
Phenytoin: Possibly increased plasma concentration of phenytoin
***Pyrimethamine**: Increased antifolate effect
Thiopental: Enhanced effects of thiopental
***Warfarin:** Enhanced anticoagulant effect
Calcium salts: Reduced absorption of sodium fluoride

Sodium bicarbonate

Lithium: Increased excretion of lithium (reduced plasma-lithium concentration)

Sodium lactate compound solution: *see* Potassium salts; Sodium bicarbonate

Sodium nitroprusside

Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect

Amiloride: Enhanced hypotensive effect
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Contraceptives, Oral: Antagonism of hypotensive effect by estrogens
Dexamethasone: Antagonism of hypotensive effect
Diazepam: Enhanced hypotensive effect
Enalapril: Enhanced hypotensive effect
Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Hydrocortisone: Antagonism of hypotensive effect
Ibuprofen: Antagonism of hypotensive effect
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
Prednisolone: Antagonism of hypotensive effect
Propranolol: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Sodium valproate: *see* Valproate

Soluble insulin: *see* Insulins

Spironolactone

Alcohol: Enhanced hypotensive effect
Amitriptyline: Increased risk of postural hypotension
Amlodipine: Enhanced hypotensive effect
Aspirin: Antagonism of diuretic effect
Atenolol: Enhanced hypotensive effect
Carbamazepine: Increased risk of hyponatraemia
Chlorpromazine: Enhanced hypotensive effect
***Ciclosporin:** Increased risk of hyperkalaemia
Cisplatin: Increased risk of nephrotoxicity and ototoxicity
Clomipramine: Increased risk of postural hypotension

Contraceptives, Oral: Antagonism of diuretic effect by estrogens
Dexamethasone: Antagonism of diuretic effect
Diazepam: Enhanced hypotensive effect
***Digoxin:** Plasma concentration of digoxin increased
***Enalapril:** Enhanced hypotensive effect; increased risk of severe hyperkalaemia (monitor plasma-potassium concentration with low-dose spironolactone in heart failure)
Fluphenazine: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrocortisone: Antagonism of diuretic effect
Ibuprofen: Risk of nephrotoxicity of ibuprofen increased; antagonism of diuretic effect; possibly increased risk of hyperkalaemia
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
***Lithium:** Reduced lithium excretion (increased plasma-lithium concentration and risk of toxicity)
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Nitrous oxide: Enhanced hypotensive effect
*** Potassium salts:** Risk of hyperkalaemia
Prednisolone: Antagonism of diuretic effect
Propranolol: Enhanced hypotensive effect
Sodium nitroprusside: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
Timolol: Enhanced hypotensive effect
Verapamil: Enhanced hypotensive effect

Stavudine

***Didanosine:** Increased risk of adverse effects
Doxorubicin: Doxorubicin may inhibit effect of stavudine
***Zidovudine**: May inhibit effect of stavudine (avoid concomitant use)

Streptomycin

***Alcuronium:** Enhanced muscle relaxant effect
Amphotericin B: Increased risk of nephrotoxicity
Capreomycin: Increased risk of nephrotoxicity and ototoxicity
***Ciclosporin:** Increased risk of nephrotoxicity
***Cisplatin:** Increased risk of nephrotoxicity and possibly of ototoxicity
***Furosemide:** Increased risk of ototoxicity
***Neostigmine**: Antagonism of effect of neostigmine
***Pyridostigmine**: Antagonism of effect of pyridostigmine
***Suxamethonium**: Enhanced muscle relaxant effect

Vancomycin: Increased risk of nephrotoxicity and ototoxicity
***Vecuronium:** Enhanced muscle relaxant effect

Sulfadiazine

***Ciclosporin:** Plasma-ciclosporin concentration possibly reduced; increased risk of nephrotoxicity
Glibenclamide: Effect of glibenclamide rarely enhanced
Methotrexate: Risk of methotrexate toxicity increased
Phenytoin: Plasma-phenytoin concentration possibly increased
***Pyrimethamine**: Increased antifolate effect
***Sulfadoxine +Pyrimethamine**: Increased antifolate effect
Thiopental: Enhanced effects of thiopental
***Warfarin:** Enhanced anticoagulant effect

Sulfadoxine +Pyrimethamine

***Artemether +Lumefantrine:** Manufacturer of artemether with lumefantrine advises avoid concomitant use
***Ciclosporin:** Increased risk of nephrotoxicity
Glibenclamide: Effect of glibenclamide rarely enhanced
***Methotrexate:** Antifolate effect of methotrexate increased; risk of methotrexate toxicity increased
***Phenytoin:** Plasma-phenytoin concentration possibly increased; increased antifolate effect
***Sulfadiazine:** Increased antifolate effect
***Sulfamethoxazole +Trimethoprim:** Increased antifolate effect
Thiopental: Enhanced effects of thiopental
***Trimethoprim:** Increased antifolate effect
***Warfarin:** Enhanced anticoagulant effect

Sulfamethoxazole +Trimethoprim

***Azathioprine**: Increased risk of haematological toxicity
***Ciclosporin:** Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
Dapsone: Plasma concentration of both dapsone and trimethoprim may increase with concomitant use
Digoxin: Plasma concentration of digoxin possibly increased
Glibenclamide: Effect of glibenclamide rarely enhanced
Lamivudine: Plasma concentration of lamivudine increased (avoid concomitant use of high-dose sulfamethoxazole +trimethoprim)
***Mercaptopurine:** Increased risk of haematological toxicity
***Methotrexate:** Antifolate effect of methotrexate increased (avoid concomitant use); risk of methotrexate toxicity increased
***Phenytoin:** Antifolate effect and plasma-phenytoin concentration increased
Procainamide: Increased plasma-procainamide concentration

***Pyrimethamine:** Increased antifolate effect
***Sulfadoxine +Pyrimethamine:** Increased antifolate effect
Thiopental: Enhanced effects of thiopental
***Warfarin:** Enhanced anticoagulant effect

Sulfasalazine

Azathioprine: Possibly increased risk of leukopenia
Digoxin: Absorption of digoxin possibly reduced
Folic acid and Folinic acid: Possibly reduced absorption of folic acid
Mercaptopurine: Possibly increased risk of leukopenia

Suxamethonium

***Amikacin:** Enhanced effects of suxamethonium
***Clindamycin**: Enhanced effects of suxamethonium
Cyclophosphamide: Enhanced effect of suxamethonium
Digoxin: Risk of ventricular arrhythmias
***Gentamicin:** Enhanced muscle relaxant effect
Halothane: Enhanced effects of suxamethonium
Lidocaine: Neuromuscular blockade enhanced and prolonged (interaction less likely when lidocaine used topically)
Lithium: Enhanced muscle relaxant effect
Magnesium (parenteral): Enhanced muscle relaxant effect
Metoclopramide: Enhanced effects of suxamethonium
Neostigmine: Effect of suxamethonium enhanced
***Procainamide:** Enhanced muscle relaxant effect
Propranolol: Enhanced muscle relaxant effect
Pyridostigmine: Effect of suxamethonium enhanced
***Quinidine**: Enhanced muscle relaxant effect
Quinine: Possibly enhanced effects of suxamethonium
***Streptomycin:** Enhanced muscle relaxant effect
***Vancomycin:** Enhanced effects of suxamethonium
Verapamil: Enhanced effects of suxamethonium

Tamoxifen

***Warfarin**: Enhanced anticoagulant effect

Testosterone

Glibenclamide: Hypoglycaemic effect possibly enhanced
Insulins: Hypoglycaemic effect possibly enhanced
Metformin: Hypoglycaemic effect possibly enhanced
***Warfarin:** Enhanced anticoagulant effect

Thiopental

Acetazolamide: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amitriptyline: Increased risk of arrhythmias and hypotension
Amlodipine: Enhanced hypotensive effect
Atenolol: Enhanced hypotensive effect
***Chlorpromazine:** Enhanced hypotensive effect
Clomipramine: Increased risk of arrhythmias and hypotension
Diazepam: Enhanced sedative effect
Enalapril: Enhanced hypotensive effect
***Fluphenazine:** Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glyceryl trinitrate: Enhanced hypotensive effect
***Haloperidol:** Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Isoniazid: Possible potentiation of isoniazid hepatotoxicity
Isosorbide dinitrate: Enhanced hypotensive effect
Methyldopa: Enhanced hypotensive effect
Nifedipine: Enhanced hypotensive effect
Propranolol: Enhanced hypotensive effect
Silver sulfadiazine: Enhanced effects of thiopental
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Sulfadiazine: Enhanced effects of thiopental
Sulfadoxine +Pyrimethamine: Enhanced effects of thiopental
Sulfamethoxazole +Trimethoprim: Enhanced effects of thiopental
Timolol: Enhanced hypotensive effect
Vancomycin: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin
***Verapamil:** Enhanced hypotensive effect and AV delay

Timolol

NOTE. Systemic absorption may follow topical application of timolol to the eye
Acetazolamide: Enhanced hypotensive effect
Alcohol: Enhanced hypotensive effect
Amiloride: Enhanced hypotensive effect
Amlodipine: Enhanced hypotensive effect
Chlorpromazine: Enhanced hypotensive effect
Diazepam: Enhanced hypotensive effect
Digoxin Increased AV block and bradycardia
Enalapril: Enhanced hypotensive effect
***Epinephrine:** Severe hypertension

Fluphenazine: Enhanced hypotensive effect
Furosemide: Enhanced hypotensive effect
Glibenclamide: Timolol may mask warning signs of hypoglycaemia such as tremor
Glyceryl trinitrate: Enhanced hypotensive effect
Halothane: Enhanced hypotensive effect
Hydralazine: Enhanced hypotensive effect
Hydrochlorothiazide: Enhanced hypotensive effect
Insulins: Enhanced hypoglycaemic effect; timolol may mask warning signs of hypoglycaemia such as tremor
Isosorbide dinitrate: Enhanced hypotensive effect
Ketamine: Enhanced hypotensive effect
Levodopa: Enhanced hypotensive effect
***Lidocaine:** Increased myocardial depression (interaction less likely when lidocaine used topically)
Mefloquine: Increased risk of bradycardia
Metformin: Timolol may mask warning signs of hypoglycaemia such as tremor
Methyldopa: Enhanced hypotensive effect
***Nifedipine:** Enhanced hypotensive effect. Possible severe hypotension and heart failure
Nitrous oxide: Enhanced hypotensive effect
Pilocarpine: Increased risk of arrhythmias
***Procainamide**: Increased myocardial depression
***Quinidine:** Increased myocardial depression
Sodium nitroprusside: Enhanced hypotensive effect
Spironolactone: Enhanced hypotensive effect
Thiopental: Enhanced hypotensive effect
***Verapamil:** Asystole, severe hypotension and heart failure

Trimethoprim

***Azathioprine:** Increased risk of haematological toxicity
***Ciclosporin:** Increased risk of nephrotoxicity; plasma-ciclosporin concentration possibly reduced by intravenous trimethoprim
Dapsone: Plasma concentration of both dapsone and trimethoprim may increase with concomitant use
Digoxin: Plasma concentration of digoxin possibly increased
Glibenclamide: Effects of glibenclamide rarely enhanced
***Mercaptopurine:** Increased risk of haematological toxicity
***Methotrexate:** Antifolate effect of methotrexate increased (avoid concomitant use)
***Phenytoin:** Antifolate effect and plasma-phenytoin concentration increased
Procainamide: Increased plasma-procainamide concentration

***Pyrimethamine**: Increased antifolate effect
***Sulfadoxine +Pyrimethamine:** Increased antifolate effect
Warfarin: Possibly enhanced anticoagulant effect

Vaccine, Influenza

Dexamethasone: High doses of dexamethasone impair immune response
Hydrocortisone: High doses of hydrocortisone impair immune response
Phenytoin: Enhanced effect of phenytoin
Prednisolone: High doses of prednisolone impair immune response
Warfarin: Effect of warfarin occasionally enhanced

Vaccine, Live

NOTE. Vaccine, Live includes BCG, Measles, MMR, Poliomyelitis (oral), Rubella, and Yellow fever vaccines

Asparaginase: Avoid use of live vaccines with asparaginase (impairment of immune response)
***Azathioprine:** Avoid use of live vaccines with azathioprine (impairment of immune response)
Bleomycin: Avoid use of live vaccines with bleomycin (impairment of immune response)
Chlorambucil: Avoid use of live vaccines with chlorambucil (impairment of immune response)
Chlormethine: Avoid use of live vaccines with chlormethine (impairment of immune response)
***Ciclosporin:** Avoid use of live vaccines with ciclosporin (impairment of immune response)
Cisplatin: Avoid use of live vaccines with cisplatin (impairment of immune response)
Cyclophosphamide: Avoid use of live vaccines with cyclophosphamide (impairment of immune response)
Cytarabine: Avoid use of live vaccines with cytarabine (impairment of immune response)
Dacarbazine: Avoid use of live vaccines with dacarbazine (impairment of immune response)
Dactinomycin: Avoid use of live vaccines with dactinomycin (impairment of immune response)
Daunorubicin: Avoid use of live vaccines with daunorubicin (impairment of immune response)
***Dexamethasone:** High doses of dexamethasone impair immune response; avoid use of live vaccines
Doxorubicin: Avoid use of live vaccines with doxorubicin (impairment of immune response)
Etoposide: Avoid use of live vaccines with etoposide (impairment of immune response)
Fluorouracil: Avoid use of live vaccines with fluorouracil (impairment of immune response)

***Hydrocortisone:** High doses of hydrocortisone impair immune response; avoid use of live vaccines
***Immunoglobulin, Anti-D:** Avoid use of live virus vaccine during *4 weeks before* or during *3months after* injection of anti-D immunoglobulin (impairment of immune response) but rubella vaccine (either as MMR or single antigen rubella vaccine) may be given at the same time as anti-D immunoglobulin
Mercaptopurine: Avoid use of live vaccines with mercaptopurine (impairment of immune response)
Methotrexate: Avoid use of live vaccines with methotrexate (impairment of immune response)
***Prednisolone:** High doses of prednisolone impair immune response; avoid use of live vaccines
Procarbazine: Avoid use of live vaccines with procarbazine (impairment of immune response)
Vinblastine: Avoid use of live vaccines with vinblastine (impairment of immune response)
Vincristine: Avoid use of live vaccines with vincristine (impairment of immune response)

Valproic acid: *see* Valproate

Valproate

***Amitriptyline:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
Aspirin: Enhancement of effect of valproate
Carbamazepine: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproate reduced; plasma concentration of active metabolite of carbamazepine increased
***Chloroquine:** Possible increased risk of convulsions
***Chlorpromazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Clomipramine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
Erythromycin: Metabolism of valproate possibly inhibited (increased plasma concentration)
Ethosuximide: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of ethosuximide possibly increased
***Fluphenazine:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Haloperidol:** Antagonism of anticonvulsant effect (convulsive threshold lowered)
***Mefloquine:** Antagonism of anticonvulsant effect
Phenobarbital: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproate reduced; Phenobarbital concentration increased

Phenytoin: May be enhanced toxicity without corresponding increase in antiepileptic effect; plasma concentration of valproate reduced; plasma concentration of phenytoin increased or possibly reduced

Warfarin: Anticoagulant effect possibly enhanced

Zidovudine: Plasma concentration of zidovudine possibly increased (risk of toxicity)

Vancomycin

Amikacin: Increased risk of nephrotoxicity and ototoxicity

Amphotericin B: Possibly increased risk of nephrotoxicity

Capreomycin: Increased risk of nephrotoxicity and ototoxicity

***Ciclosporin:** Increased risk of nephrotoxicity

Cisplatin: Increased risk of nephrotoxicity and possibly of ototoxicity

***Furosemide**: Increased risk of ototoxicity

Gentamicin: Increased risk of nephrotoxicity and ototoxicity

Halothane: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Ketamine: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Nitrous oxide: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Streptomycin: Increased risk of nephrotoxicity and ototoxicity

***Suxamethonium:** Enhanced effects of suxamethonium

Thiopental: Hypersensitivity-like reactions can occur with concomitant intravenous vancomycin

Vecuronium

***Amikacin**: Enhanced effects of vecuronium

Carbamazepine: Antagonism of muscle relaxant effect (recovery from neuromuscular blockade accelerated)

***Clindamycin**: Enhanced muscle relaxant effect

***Gentamicin:** Enhanced muscle relaxant effect

Halothane: Enhanced effects of vecuronium

Lithium: Enhanced muscle relaxant effect

Magnesium (parenteral): Enhanced muscle relaxant effect

Neostigmine: Antagonism of muscle relaxant effect

Nifedipine: Enhanced muscle relaxant effect

Phenytoin: Antagonism of muscle relaxant effect (accelerated recovery from neuromuscular blockade)

***Procainamide:** Enhanced muscle relaxant effect

Propranolol: Enhanced muscle relaxant effect

Pyridostigmine: Antagonism of muscle relaxant effect

***Quinidine:** Enhanced muscle relaxant effect

***Streptomycin:** Enhanced muscle relaxant effect

Verapamil: Enhanced muscle relaxant effect

Acetazolamide: Enhanced hypotensive effect

Verapamil

Alcohol: Enhanced hypotensive effect; plasma concentration of alcohol possibly increased by verapamil

Alcuronium: Enhanced muscle relaxant effect

Amiloride: Enhanced hypotensive effect

Amitriptyline: Possibly increased plasma concentration of amitriptyline

***Atenolol:** Asystole, severe hypotension and heart failure

***Carbamazepine:** Enhanced effect of carbamazepine

Chlorpromazine: Enhanced hypotensive effect

***Ciclosporin**: Increased plasma-ciclosporin concentration

Clomipramine: Possibly increased plasma concentration of clomipramine

Contraceptives, Oral: Antagonism of hypotensive effect by estrogens

Dexamethasone: Antagonism of hypotensive effect

Diazepam: Enhanced hypotensive effect

***Digoxin**: Increased plasma concentration of digoxin; increased AV block and bradycardia

Enalapril: Enhanced hypotensive effect

***Erythromycin:** Possible inhibition of metabolism of verapamil (increased risk of toxicity)

Fluphenazine: Enhanced hypotensive effect

Furosemide: Enhanced hypotensive effect

Glyceryl trinitrate: Enhanced hypotensive effect

Grapefruit juice: Increased plasma-verapamil concentration

Haloperidol: Enhanced hypotensive effect

***Halothane:** Enhanced hypotensive effect and AV delay

Hydralazine: Enhanced hypotensive effect

Hydrochlorothiazide: Enhanced hypotensive effect

Hydrocortisone: Antagonism of hypotensive effect

Ibuprofen: Antagonism of hypotensive effect

Isosorbide dinitrate: Enhanced hypotensive effect

***Ketamine:** Enhanced hypotensive effect and AV delay

Levodopa: Enhanced hypotensive effect

***Lidocaine:** Increased risk of myocardial depression (interaction less likely when lidocaine used topically)

Lithium: Neurotoxicity may occur without increased plasma-lithium concentration

Mefloquine: Possibly increased risk of bradycardia

Methyldopa: Enhanced hypotensive effect

***Nitrous oxide:** Enhanced hypotensive effect and AV delay

***Phenobarbital:** Effect of verapamil probably reduced

Phenytoin: Reduced effect of verapamil

Prednisolone: Antagonism of hypotensive effect

***Propranolol:** Asystole, severe hypotension and heart failure

***Quinidine:** Increased plasma-quinidine concentration (extreme hypotension may occur)

***Rifampicin:** Accelerated metabolism of verapamil (plasma concentration significantly reduced)

***Ritonavir**: Plasma concentration possibly increased by ritonavir

Sodium nitroprusside: Enhanced hypotensive effect

Spironolactone: Enhanced hypotensive effect

Suxamethonium: Enhanced effects of suxamethonium

***Thiopental:** Enhanced hypotensive effect and AV delay

***Timolol:** Asystole, severe hypotension and heart failure

Vecuronium: Enhanced muscle relaxant effect

Vinblastine

***Bleomycin:** Increased risk of cardiovascular toxicity

***Erythromycin:** Increased toxicity of vinblastine (avoid concomitant use)

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with vinblastine (impairment of immune response)

Vincristine

Nifedipine: Possibly reduced metabolism of vincristine

Phenytoin: Possibly reduced absorption of phenytoin

Vaccine, Live: Avoid use of live vaccines with vincristine (impairment of immune response)

Vitamin D: *see* Ergocalciferol

Warfarin

NOTE. Major changes in diet (especially involving salads and vegetables) and in alcohol consumption may affect anticoagulant control

***Alcohol**: Enhanced anticoagulant effect with large amounts of alcohol; major changes in alcohol consumption may affect anticoagulant control

Allopurinol: Anticoagulant effect possibly enhanced

***Amitriptyline:** Enhanced or reduced anticoagulant effect

Amoxicillin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of amoxicillin

Ampicillin: Studies have failed to demonstrate an interaction, but common experience in anticoagulant clinics is that INR can be altered by a course of ampicillin

***Aspirin:** Increased risk of bleeding due to antiplatelet effect

***Azathioprine:** Anticoagulant effect possibly reduced

***Azithromycin:** Possibly enhanced anticoagulant effect of warfarin

***Carbamazepine:** Accelerated metabolism of warfarin (reduced anticoagulant effect)

***Cefixime:** Possibly enhanced anticoagulant effect

***Ceftazidime**: Possibly enhanced anticoagulant effect

***Ceftriaxone:** Possibly enhanced anticoagulant effect

***Chloramphenicol:** Enhanced anticoagulant effect

***Ciprofloxacin:** Enhanced anticoagulant effect

***Clomipramine:** Enhanced or reduced anticoagulant effect

***Contraceptives, Oral:** Antagonism of anticoagulant effect by estrogens and progestogens

***Dexamethasone:** Anticoagulant effect possibly enhanced or reduced (high-dose dexamethasone enhances anticoagulant effect)

***Doxycycline:** Anticoagulant effect possibly enhanced

***Erythromycin:** Enhanced anticoagulant effect

***Etoposide:** Possibly enhanced anticoagulant effect

***Fluconazole:** Enhanced anticoagulant effect

***Fluorouracil:** Anticoagulant effect possibly enhanced

***Glibenclamide:** Possibly enhanced hypoglycaemic effects and changes to anticoagulant effect

***Griseofulvin:** Reduced anticoagulant effect

***Hydrocortisone:** Anticoagulant effect possibly enhanced or reduced (high-dose hydrocortisone enhances anticoagulant effect)

***Ibuprofen:** Anticoagulant effect possibly enhanced

***Levamisole:** Anticoagulant effect possibly enhanced

Levofloxacin: Possibly enhanced anticoagulant effect

***Levonorgestrel:** Antagonism of anticoagulant effect

Levothyroxine: Enhanced anticoagulant effect

***Medroxyprogesterone:** Antagonism of anticoagulant effect

***Mercaptopurine:** Anticoagulant effect possibly reduced

***Metronidazole**: Enhanced anticoagulant effect

***Miconazole:** Enhanced anticoagulant effect

***Nevirapine:** Enhanced or reduced anticoagulant effect

***Norethisterone:** Antagonism of anticoagulant effect

***Ofloxacin:** Enhanced anticoagulant effect

Paracetamol: Prolonged regular use of paracetamol possibly enhances anticoagulant effect

***Phenobarbital:** Metabolism of warfarin accelerated (reduced anticoagulant effect)

***Phenytoin:** Accelerated metabolism of warfarin (possibility of reduced anticoagulant effect, but enhancement also reported)

***Phytomenadione:** Antagonism of anticoagulant effect by phytomenadione

***Prednisolone:** Anticoagulant effect enhanced or reduced (high-dose prednisolone enhances anticoagulant effect)

Proguanil: Isolated reports of enhanced anticoagulant effect

***Quinidine:** Anticoagulant effect may be enhanced

***Rifampicin:** Accelerated metabolism of warfarin (reduced anticoagulant effect)

***Ritonavir:** Plasma concentration possibly increased by ritonavir

Saquinavir: Possibly enhanced anticoagulant effect

***Silver sulfadiazine:** Enhanced anticoagulant effect
***Sulfadiazine:** Enhanced anticoagulant effect
***Sulfadoxine +Pyrimethamine:** Enhanced anticoagulant effect
***Sulfamethoxazole +Trimethoprim:** Enhanced anticoagulant effect
***Tamoxifen**: Enhanced anticoagulant effect
***Testosterone:** Enhanced anticoagulant effect
Trimethoprim: Possibly enhanced anticoagulant effect
Vaccine, Influenza: Effect of warfarin occasionally enhanced
Valproate: Anticoagulant effect possibly enhanced

Yellow fever vaccine: *see* Vaccine, live

Zidovudine

NOTE. Increased risk of toxicity with nephrotoxic and myelosuppressive drugs
***Fluconazole:** Increased plasma concentration of zidovudine (increased risk of toxicity)
Ibuprofen: Increased risk of haematological toxicity
Methadone: Possibly increased plasma concentration of zidovudine
Phenytoin: Plasma-phenytoin concentration increased or decreased by zidovudine
Pyrimethamine: Increased antifolate effect
Rifampicin: Avoidance of rifampicin advised by manufacturer of zidovudine
***Stavudine:** May inhibit effect of stavudine (avoid concomitant use)
Valproate: Plasma concentration of zidovudine possibly increased (risk of toxicity)

Zinc sulfate

Calcium salts: Reduced absorption of zinc sulfate
Ciprofloxacin: Reduced absorption of ciprofloxacin
Ferrous salts: Absorption of zinc and of oral ferrous salts reduced
Levofloxacin: Reduced absorption of levofloxacin
Ofloxacin: Reduced absorption of ofloxacin
Penicillamine: Absorption of both drugs reduced

Appendix - II
National List of Essential Medicines
Fourth revision, 2010 (final draft)

	Generic Name	Dosage Form
1.	**Anaesthetics**	
1.1	**General Anaesthetics and Oxygen**	
	Halothane	inhalation
	Isoflurane	inhalation
	Ketamine	injection, 50 mg/ml (as hydrochloride) in 10-ml vial
	Nitrous oxide	inhalation
	Oxygen	inhalation (medicinal gas)
	Thiopental	powder for injection, 0.5g, 1.0g (sodium salt) in ampoule
	Complementary	
	Propofol	injection, 10mg/ml in 20-ml ampoule
1.2	**Local Anaesthetics**	
	Bupivacaine	injection, 0.25%, 0.5% (hydrochloride) in vial
	Lidocaine (lignocaine)	injection, 1%, 2% (hydrochloride) in vial; injection for spinal anaesthesia, 5% (hydrochloride) in 2-ml ampoule to be mixed with 7.5% glucose solution
	Lidocaine (lignocaine) + epinephrine (adrenaline)	injection, lignocaine 2% (hydrochloride) + epinephrine 1:200 000, in vial
	Complementary	
	Ephedrine	injection, 30 mg (hydrochloride)/ml in 1-ml ampoule *(For use in spinal anaesthesia during delivery, to prevent hypotension)*
1.3	**Preoperative Medication and Sedation for Short-term Procedures**	
	Atropine	injection, 1 mg (sulfate) in 1-ml ampoule
	Diazepam	injection, 5mg/ml in 2-ml ampoule
	Morphine	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule

	Generic Name	Dosage Form
2.	**Analgesics, Antipyretics, Non-Steroidal Anti-inflammatory Medicines (NSAIMs), Medicines Used to Treat Gout and Disease-Modifying Agents Used in Rheumatic Disorders (DMARDs)**	
2.1.	**Non-opioid Analgesics & NSAIMs**	
	Ibuprofen	tablet, 200 mg, 400 mg
	Paracetamol	tablet, 500mg; injection, 150 mg/ml; oral liquid, 125 mg/5ml
	Complementary	
	Aspirin	tablet, 300 mg
	Diclofenac sodium	tablet, 50 mg; injection, 25 mg/ml
2.2.	**Opioid Analgesics**	
	Morphine	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule; tablet, 10 mg; prolonged release tablet, 10 mg, 30 mg, 60 mg (sulfate); oral liquid 10 mg/5ml (sulfate)
	Pethidine	injection, 50 mg (hydrochloride) in 1-ml ampoule
2.3	**Medicines Used to Treat Gout**	
	Allopurinol	tablet, 100 mg
	Colchicine	tablet, 500 mcg
2.4	**Disease Modifying Agents Used in Rheumatic Disorders (DMARDs)**	
	Methotrexate	tablet, 2.5 mg (as sodium salt)
3.	**Antiallergics and Medicines Used in Anaphylaxis**	
	Chlorphenamine	tablet, 4 mg (maleate)
	Dexamethasone	injection, 4 mg dexamethasone phosphate (as sodium salt) in 1-ml ampoule
	Epinephrine (adrenaline)	injection, 1mg (as hydrochloride or tartrate) in 1-ml ampoule
	Hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
	Pheniramine	injection, 22.75 mg (maleate) /ml
	Prednisolone	tablet, 5mg
4.	**Antidotes and Other Substances Used in Poisonings**	
4.1	**Non-Specific**	
	Charcoal, activated	powder; oral liquid (sorbitol-base slurry)

	Generic Name	Dosage Form
4.2	**Specific**	
	Atropine	injection, 1 mg (sulfate) in ampoule; powder for injection 50 mg (sulfate) in vial
	Dimercaprol	injection in oil, 50 mg/ml in 2-ml ampoule
	Naloxone	injection, 400 mcg (hydrochloride) in 1-ml ampoule
	Pralidoxime	injection, 500 mg or 1 g (mesilate, chloride or iodide) in ampoule
	Complementary	
	Acetylcysteine	injection, 200 mg/ml in 10-ml ampoule
	Calcium gluconate	injection, 100 mg/ml in 10-ml ampoule
	Deferoxamine	powder for injection, 500 mg (mesilate) in vial
	Methylthioninium chloride (Methylene blue)	injection, 10 mg/ml in 10-ml ampoule
	Potassium ferric hexacyano-ferrate (II).2H2O (Prussian blue)	powder for oral administration
	Sodium calcium edentate	injection, 200 mg/ml in 5-ml ampoule
	Sodium nitrite	injection, 30 mg/ml in 10-ml ampoule
5.	**Antiepileptics / Anticonvulsants**	
	Carbamazepine	tablet, 100 mg, 200 mg
	Diazepam	injection, 5mg/ml in 2-ml ampoule (intravenous or rectal)
	Magnesium sulfate*	injection, 500 mg/ml in 2-ml ampoule. ** For use in eclampsia and severe pre-clampsia and not for other convulsant disorders.*
	Phenobarbital	tablet, 15 mg, 30 mg
	Phenytoin	capsule or tablet, 25 mg, 50 mg, 100 mg (sodium salt); injection, 50 mg /ml (sodium salt) in 5-ml vial
	Valproic acid	tablet (enteric coated), 200 mg (sodium salt)
	Complementary	
	Paraldehyde	injection, 500 mg/ml in 2-ml ampoule
6.	**Anti-infective Medicines**	
6.1	**Anthelmintics**	
6.1.1	**Intestinal Anthelmintics**	
	Albendazole	tablet (chewable), 400 mg
	Complementary	
	Niclosamide	tablet (chewable), 500 mg
	Praziquantel	tablet, 150 mg, 600 mg

	Generic Name	Dosage Form
6.1.2	**Antifilarials**	
	Diethylcarbamazine	tablet, 50 mg, 100 mg (dihydrogen citrate)
6.2	**Antibacterials**	
6.2.1	**Beta-lactam medicines**	
	Amoxicillin	capsule or tablet, 250mg, 500mg (as trihydrate); dispersible tablet 125 mg (as trihydrate)
	Ampicillin	powder for injection, 500 mg (sodium salt)
	Benzathine benzylpenicillin	powder for injection, 600 000 IU, 1200 000 IU, 2400 000 IU in vial
	Benzylpenicillin (Penicillin G)	powder for injection, 300 mg (0.5 million IU), 600 mg (1 million IU) (as sodium or potassium salt) in vial
	Cefixime#	tablet, 400 mg *#Only listed for single-dose treatment of uncomplicated ano-genital gonorrhoea*
	Cloxacillin	capsule, 250 mg, 500 mg; powder for oral liquid, 125 mg / 5ml; powder for injection, 500 mg (as sodium salt) in vial
	Phenoxymethylpenicillin (Penicillin V)	tablet, 250mg (as potassium salt); powder for oral liquid, 250 mg
	Procaine benzylpenicillin	powder for injection, 300,000 IU in vial
	Complementary	
	Amoxicillin	powder for oral liquid, 125 mg/5ml
	Cefazolin*	powder for injection, 1 g (as sodium salt) in vial **For surgical prophylaxis*
	Ceftriaxone	powder for injection, 250 mg (as sodium salt) in vial
6.2.2	**Other Antibacterials**	
	Azithromycin*	capsule or tablet 250 mg, 500 mg; oral liquid, 200 mg /5ml. **Only listed for single-dose treatment of genital Chlamydia trachomatis and of trachoma.*
	Chloramphenicol	capsule, 250 mg, 500 mg; oral liquid, 125 mg / 5ml (as palmitate), powder for injection, 1g (as sodium succinate) in vial
	Ciprofloxacin	tablet, 250 mg, 500 mg (as hydrochloride)
	Doxycycline	capsule, 100mg (as hydrochloride)

	Generic Name	Dosage Form
	Gentamicin	injection, 10 mg, 40 mg / ml (as sulfate) in 2-ml vial
	Metronidazole	tablet, 200 mg, 400 mg; injection, 500 mg in 100-ml vial; oral liquid, 100 mg, 200 mg (as benzoate) / 5ml
	Nitrofurantoin	tablet, 100 mg
	Sulfamethoxazole+Trimethoprim	dispersible tablet, 100mg+20 mg, 200 mg+ 40 mg; tablet 400 mg + 80 mg, 800 mg + 160 mg; oral liquid, 200mg + 40mg /5ml
	Complementary	
	Erythromycin	tablet, 250 mg (stearate); oral liquid, 250 mg / 5ml (stearate)
	Nalidixic acid	tablet, 250 mg, 500 mg
6.2.3	**Antileprosy Medicines**	
	Clofazimine	capsule, 50 mg, 100 mg
	Dapsone	tablet, 50 mg, 100 mg
	Rifampicin	capsule or tablet 150 mg, 300 mg
6.2.4	**Antitubercular Medicines**	
	Ethambutol	tablet, 400 mg (hydrochloride)
	Ethambutol + isoniazid	tablet, 400mg + 150mg
	Ethambutol + rifampicin +isoniazid	tablet, 275 mg + 150 mg+ 75 mg
	Ethambutol + rifampicin +isoniazid+ pyrazinamide	tablet, 275 mg+150 mg+ 75 mg + 400 mg
	Isoniazid	tablet, 100 mg, 300 mg
	Isoniazid + rifampicin	tablet, 30 mg + 60 mg, 75 mg + 150mg
	Isoniazid + rifampicin + pyrazinamide	tablet, 30 mg+ 60 mg+ 150 mg
	Rifampicin	capsule or tablet, 150mg, 300mg
	Streptomycin	powder for injection, 1 g (as sulfate) in vial
	Complementary list:	Second-line medicines for the treatment of multi-drug resistant tuberculosis (MDR-TB) - to be made available only in specialised centres adhering to standard treatment protocol.
	Amoxicillin + clavulanic acid	tablet, 500 + 125 mg
	Capreomycin	powder for injection, 1 g vial
	Clofazimine	capsule, 100 mg
	Cycloserine	tablet, 250 mg

	Generic Name	Dosage Form
	Ethionamide	tablet, 250 mg
	Kanamycin	powder for injection 1 g in vial
	Ofloxacin	tablet, 200 mg
		(Levofloxacin 250 mg & 500 mg tablet and Moxyfloxacin 100 mg capsule may be an alternative based on availability and programme considerations)
	p-aminosalicylic acid (PAS)	
		granules, 4 g in sachet; tablet 500 mg
	Pyrazinamide	tablet, 400mg
6.3	**Antifungal Medicines**	
	Clotrimazole	cream, 1%; pessary 100 mg
	Fluconazole	capsule or tablet, 150 mg
	Nystatin	lozenge, 100 000 IU
6.4	**Antiviral Medicines**	
6.4.1	**Antiherpes Medicines**	
	Aciclovir	powder for injection 250 mg (as sodium salt) in vials, tablet 200 mg
6.4.2	**Antiretrovirals**	
6.4.2.1	**Nucleoside/Nucleotide Reverse Transcriptase Inhibitors**	
	Abacavir (ABC)	tablet, 300 mg (as sulfate); oral liquid, 100 mg (as sulfate)/5ml
	Didanosine (ddI)	enteric coated capsules 250 mg, 400 mg
	Lamivudine (3TC)	tablet, 150 mg; oral liquid 50 mg/5ml
	Stavudine (d4T)	capsule, 15 mg, 20 mg, 30 mg; powder for oral liquid, 5 mg/5 ml
	Tenofovir disoproxil fumarate (TDF)	
		tablet, 300 mg (equivalent to 245 mg tenofovir disoproxil)
	Zidovudine (ZDV or AZT)	
		capsule, 100 mg; tablet 300 mg; oral liquid 50 mg/ 5ml
6.4.2.2	**Non-nucleoside Reverse Transcriptase Inhibitors**	
	Efavirenz (EFV or EFZ)	
		capsule, 200 mg; tablet, 600 mg
	Nevirapine (NVP)	tablet, 200 mg; oral liquid, 50 mg/5ml
6.4.2.3	**Protease Inhibitors**	
	Indinavir (IDV)	capsule, 400 mg (as sulfate)
	Lopinavir + ritonavir (LPV/r)	capsule 200 mg + 50 mg
	Nelfinavir (NFV)	tablet, 250 mg (as mesilate)
	Saquinavir (SQV)+ritonavir	oral dosage form, 1g+100 mg

	Generic Name	Dosage Form
6.4.2.4	**Fixed-dose Combination**	
	Lamivudine + stavudine	tablet, 150 mg + 30 mg
	Stavudine + lamivudine + nevirapine	
		tablet, 30 mg + 150 mg + 200 mg
	Zidovudine + lamivudine	
		tablet, 300 mg + 150 mg
	Zidovudine + lamivudine + nevirapine	
		tablet, 300 mg + 150 mg + 200 mg
6.5	**Antiprotozoal Medicines**	
6.5.1	**Antiamoebic and Antigiardiasis Medicines**	
	Diloxanide	tablet, 500 mg (furoate)
	Metronidazole	tablet, 200mg, 400mg; oral liquid, 200 mg (as benzoate) / 5 ml.
	Complementary	
	Tinidazole	tablet, 500mg
6.5.2	**Antileishmaniasis Medicines**	
	Miltefosine	capsule, 50 mg
	Complementary	
	Amphotericin B	powder for injection, 50 mg in vial
		(as deoxycholate or liposomal)
	Sodium stibogluconate	injection, 100mg/ml
6.5.3	**Antimalarial Medicines**	
	Artemether*	oily injection, 80 mg/ml in 1-ml ampoule.
		** For use in the management of severe malaria.*
	Artemether+lumefantrine#	
		tablet, 20 mg+ 120 mg
		# Not recommended in the first trimester of pregnancy or in children below 5 kg.
	Artesunate	injection, ampoules, containing 60 mg anhydrous artesunic acid with a separate ampoule of 5% sodium bicarbonate solution; tablet 50 mg
	Chloroquine	tablet, 150 mg base (as phosphate or sulfate); oral liquid, 50 mg / 5ml (as phosphate or sulfate); injection, 40mg /ml in 5- ml ampoule (as phosphate, sulfate or hydrochloride)
	Primaquine	tablet, 7.5 mg, 15 mg (as diphosphate)
	Sulfadoxine + Pyrimethamine	
		tablet, 500 mg + 25 mg

	Generic Name	Dosage Form
	Complementary	
	Quinine	tablet, 300 mg (as bisulfate or sulfate) injection, 300mg (as dihydrochloride)/ ml in 2-ml ampoule.
7.	**Antimigraine Medicines**	
7.1	**For Treatment of Acute Attack**	
	Paracetamol	tablet, 500 mg
	Ergotamine	tablet, 1 mg (tartrate)
7.2	**For Prophylaxis**	
	Propranolol	tablet 20 mg, 40mg (hydrochloride)
8.	**Antineoplastic, Immunosuppressives and Medicines Used in Palliative Care**	
8.1	**Immunosuppressive Medicines**	
	Ciclosporin	capsule 25 mg
8.2	**Cytotoxic Medicines**	
	Calcium folinate (Calcium leucovorin)	tablet, 15 mg
	Cisplatin	powder for injection, 10 mg, 50 mg in vial.
	Cyclophosphamide	tablet, 25 mg; powder for injection, 200 mg, 500 mg, 1 g in vial
	Cytarabine	injection 100 mg, 500 mg in vial
	Doxorubicin	powder for injection, 10 mg, 50 mg in vial
	Etoposide	injection 20 mg/ml in 5-ml ampoule
	Fluorouracil	injection 50 mg/ml in 5-ml, 10-ml ampoule
	Hydroxy urea	capsule 500 mg
	Ifosfamide + Mesna	injection, 1g + 200 mg, in vial
	Melphalan	tablet, 2 mg, 5 mg; powder for injection, 50mg in vial
	Mercaptopurine	tablet, 50 mg
	Methotrexate	tablet, 2.5 mg (as sodium salt); powder for injection 15 mg, 50 mg (as sodium salt) in vial
	Mitomycin	powder for injection, 2mg, 10mg, 20mg in vial
	Vincristine	powder for injection, 1 mg (sulfate) in vial
	Complementary	
	Bleomycin	powder for injection, 15mg (as sulfate) in vial
	Carboplatin	injection 150 mg, 450 mg in vial

	Generic Name	Dosage Form
	Chlorambucil	tablet, 2 mg, 5 mg
	Dactinomycin	powder for injection, 500 mcg in vial
	Daunorubicin	powder for injection 20 mg (as hydrochloride) in vial
	Dacarbazine	powder for injection, 100 mg in vial
	Epirubicin	injection, 10 mg, 50 mg (hydrochloride) in vial
	Lomustine	capsule, 40 mg
	Mitoxantrone	injection, 2 mg/ml in 10ml ampoule
	Vinblastine	powder for injection 10 mg (sulfate) in vial
8.3	**Hormones and Antihormones**	
	Hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
	Tamoxifen	tablet, 20mg (as citrate)
	Complementary	
	Bicalitumide	tablet or capsule 50 mg
	Dexamethasone	Dexamethasone phosphate 4 mg /ml (as sodium salt) in 2-ml ampoule
	Prednisolone	tablet, 5 mg, 10 mg, 20 mg
8.4	**Miscellaneous**	
	L-Asparaginase	injection, 5 000 IU, 10 000 IU in vial
	Granulocyte Colony Stimulating Factor (GCSF)	injection, 30 million unit in vial
	Interferon	injection, 5 million units/ml in vial
	Ondansetron	injection, 2 mg/ml (as hydrochloride) in 2-ml, 4-ml vial; tablet 2mg, 4mg (as hydrochloride)
9.	**Antiparkinsonism Medicines**	
	Levodopa + Carbidopa	tablet, 100 mg + 10 mg, 250 mg + 25 mg
	Trihexyphenidyl (benzhexol)	tablet, 2 mg (hydrochloride)
10.	**Medicines Affecting the Blood**	
10.1	**Antianaemia Medicines**	
	Ferrous sulfate*	tablet, equivalent to 60 mg iron; oral liquid, equivalent to 25 mg iron/ ml
	Ferrous sulfate*+Folic acid	tablet, equivalent to 60 mg Iron+ 400 mcg Folic acid.
	Folic acid	tablet, 5mg
		**Ferrous fumarate may be used*

	Generic Name	Dosage Form
	Complementay	
	Iron Dextran	injection, equivalent to 50 mg iron/ml in 2-ml ampoule
10.2	**Medicines Affecting Coagulation**	
	Heparin sodium	injection, 1000 IU / ml, 5000 IU / ml, 20000 IU / ml in 1-ml ampoule
	Phytomenadione	injection, 10mg / ml in 5-ml ampoule; tablet 10 mg
	Protamine sulfate	injection, 10mg/ml in 5-ml ampoule
	Warfarin	tablet, 5 mg (sodium salt)
	Complementary	
	Acenocoumarol	tablet, 1mg
11.	**Blood Products and Plasma Substitutes**	
11.1	**Plasma Substitutes**	
	Albumin, human	injectable solution, 20 or 25%
	Polygeline	injectable solution, 3.5%
11.2	**Plasma Fractions For Specific Use**	
	Factor VIII Concentrate	dried concentrate
	Factor IX complex	dried concentrate
12.	**Cardiovascular Medicines**	
12.1	**Antianginal Medicines**	
	Atenolol	tablet, 50 mg, 100 mg
	Glyceryl trinitrate	tablet (sublingual), 500 mcg
	Isosorbide dinitrate	tablet (sublingual), 5 mg, 10 mg
	Verapamil	tablet, 40 mg, 80 mg (hydrochloride); injection, 2.5 mg / ml in 2-ml ampoule
12.2	**Antiarrhythmic Medicines**	
	Atenolol	tablet 25 mg, 50 mg, 100 mg
	Digoxin	tablet, 62.5mcg, 250mcg; oral liquid, 50 mcg / ml; injection, 250 mcg / ml in 2-ml ampoule
	Epinephrine (Adrenaline)	100 mcg/ml (as acid tartrate or hydrochloride) in 10 ml ampoule
	Isoprenaline	injection, 1 mg (hydrochloride)/ml in vial
	Complementary	
	Disopyramide	capsule, 100 mg, 150 mg
	Procainamide	tablet, 250mg (hydrochloride); injection, 100 mg /ml in 10-ml ampoule

	Generic Name	Dosage Form
12.3	**Antihypertensive Medicines**	
	Atenolol	tablet, 50 mg, 100 mg
	Enalapril	tablet, 5 mg, 10 mg, 20 mg
	Hydrochlorothiazide	tablet, 25 mg, 50 mg
	Complementary	
	Nifedipine	capsule or tablet, 10 mg, 20 mg
	Prazosin	tablet 500 mcg, 1mg (mesilate)
	Sodium nitroprusside	powder for infusion, 50 mg in ampoule
12.4	**Medicines Used in Heart Failure**	
	Digoxin	tablet, 62.5 mcg, 250 mcg; oral solution, 50 mcg / ml; injection, 250 mcg / ml in 2-ml ampoule
	Enalapril	tablet, 5 mg, 10 mg, 20 mg
	Complemenary	
	Dobutamine	injection, 12.5 mg/ml (as hydrochloride) in 20ml ampoule
	Dopamine	40 mg/ml (hydrochloride) in 5 ml vial
12.5	**Antithrombotic Medicines**	
	Aspirin	tablet, 50mg, 75 mg, 100mg
	Streptokinase	injection 750 000 IU, 1500 000 IU in vial
12.6	**Lipid Lowering Agent**	
	Atorvastatin	tablet, 10 mg, 20 mg (as calcium trihydrate)
13.	**Dermatological Medicines**	
13.1	**Antifungal Medicines**	
	Benzoic acid + Salicylic acid	ointment or cream, 6% + 3%
	Clotrimazole	cream, 1%
	Complementary	
	Selenium sulfide	detergent-based suspension, 2%
13.2	**Anti-infective Medicines**	
	Povidone iodine	solution, 5%
	Silver sulfadiazine	cream, 0.2%
	Complementary	
	Gentian violet (Methylrosanilinium chloride)	aqueous solution 1%

	Generic Name	Dosage Form
13.3	**Anti-inflammatory and Antipruritic Medicines**	
	Betamethasone	ointment or cream, 0.1% (as valerate)
	Calamine lotion	lotion, 15%
	Hydrocortisone	ointment or cream, 1% (acetate)
13.4	**Medicines Affecting Skin Differentiation and Proliferation**	
	Benzoyl peroxide	cream or lotion, 5%
	Coal tar	solution, topical 5%
13.5	**Scabicides and Pediculicides**	
	Lindane (Gamma benzene hexachloride)	cream or lotion, 1%
	Complementary	
	Permethrin	lotion 1%, cream 5%
14.	**Diagnostic Agents**	
14.1	**Ophthalmic Medicines**	
	Fluorescein	eye drops, 1%, 2% (sodium salt); injection, 10%, 20% (sodium salt) in 5-ml ampoule
14.2	**Radiocontrast Media**	
	Amidotrizoate	injection, 140-420 mg iodine/ml (as sodium or meglumine salt) in 20ml ampoule
	Barium sulfate	aqueous suspension
	Iohexol	injection, 140-350 mg iodine/ml in 5-ml, 10-ml ampoule
	Complementary	
	Meglumine iotroxate	solution, 5-8 g iodine in 100-250 ml
15.	**Disinfectants and Antiseptics**	
15.1	**Antiseptics**	
	Chlorhexidine	solution, 5% (digluconate) for dilution
	Gentian violet (Methylrosanilinium chloride)	aqueous solution 1%
	Povidone iodine	solution, 5%
	Rectified spirit	liquid
15.2	**Disinfectants**	
	Chlorine based compound	powder, (0.1% available chlorine) for solution
	Formaldehyde	solution, 3%

	Generic Name	Dosage Form
	Glutaraldehyde	solution, 2%
	Cetrimide	solution, 20% for dilution
16.	**Diuretics**	
	Furosemide	tablet, 40 mg; injection, 10 mg/ml in 2-ml ampoule
	Hydrochlorothiazide	tablet, 25mg, 50mg
	Mannitol	injectable solution, 10%, 20%
	Spironolactone	tablet, 25mg, 100mg
	Triamterene	tablet, 50mg
17.	**Gastrointestinal Medicines**	
17.1	**Antacids and Other Anti-ulcer Medicines**	
	Dried aluminium hydroxide gel + Magnesium hydroxide	tablet, 250mg + 250 mg
	Ranitidine	tablet, 150 mg, 300 mg (as hydrochloride); injection 25 mg/ml in 2-ml ampoule
	Complementary	
	Omeprazole	tablet, 20 mg
17.2	**Antiemetic Medicines**	
	Metoclopramide	tablet, 10 mg (hydrochloride); injection, 5mg (hydrochloride)/ml in 2-ml ampoule
	Promethazine	tablet, 25 mg (theoclate); oral liquid, 5 mg (hydrochloride)/ 5ml; injection, 25 mg (hydrochloride) / ml in 2-ml ampoule
17.3	**Anti-inflammatory Medicines**	
	Sulfasalazine	tablet, 500 mg
17.4	**Laxatives**	
	Magnesium sulfate	powder, 500 g
	Lactulose	solution, 3.35 mg / 5ml
	Complementary	
	Bisacodyl	tablet, 10 mg
17.5	**Medicines Used in Diarrhoea**	
17.5.1	**Oral Rehydration**	
	Oral rehydration salts*	sachet containing: Dextrose, anhydrous 13.5 g, Sodium chloride 2.6 g, Potassium chloride 1.5 g, Trisodium citrate dihydrate 2.9 g, appropriate flavour q.s. Dissolved to produce 1 litre, provides dextrose 75

	Generic Name	Dosage Form
		mEq, sodium 75 mEq or mmol/l, chloride 65 mEq or mmol/l, potasium 20 mEq or mmol/l, citrate 10 mmol/l and osmolarity 245 mOsm/l
		** In case of cholera a higher concentration of sodium may be required.*
17.5.2	**Medicine for Diarrhoea in Children**	
	Zinc sulfate*	dispersible tablet, equivalent to Zinc 10 mg, 20 mg (scored)
		** In acute diarrhoea, zinc sulfate should be used as an adjunct to oral rehydration salts*
17.6	**Antispasmodic Medicines**	
	Hyoscine butylbromide	
		tablet, 10 mg, 20 mg; injection, 20mg/ml in 1-ml ampoule
18.	**Hormones, Other Endocrine Medicines and Contraceptives**	
18.1	**Adrenal Hormones and Synthetic Substitutes**	
	Dexamethasone	tablet, 500 mcg; injection, 4 mg/ml dexamethasone phosphate (as sodium phosphate) in 1-ml ampoule
	Hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial; tablet, 10 mg, 20 mg
	Prednisolone	tablet, 5 mg, 10 mg
	Complementry	
	Fludrocortisone	tablet, 100 mcg (acetate)
18.2	**Androgens**	
	Testosterone	injection, 200 mg in 1-ml ampoule
18.3	**Contraceptives**	
18.3.1	**Oral Harmonal Contraceptives**	
	Ethinylestradiol + Levonorgestrel	
		tablet, 30 mcg +150 mcg
	Ethinylestradiol + Norethisterone	
		tablet, 35 mcg + 1.0 mg
	Levonorgestrel	tablet, 750 mcg (pack of two), 1.5 mg
18.3.2	**Injectable Hormonal Contraceptive**	
	Medroxyprogesterone acetate	
		depot injection, 150 mg / ml in 1-ml vial
18.3.3	**Intrauterine Devices**	
	Copper-containing devices	

	Generic Name	Dosage Form
18.3.4	**Barrier Methods**	
	Condoms	
18.3.5	**Implantable Contraceptives**	
	Levonorgestrel-releasing implant	
		Two-rod levonorgeatrel-releasing implant, each rod containing 75 mg of levonorgestrel (150 mg total)
18.3.6	**Miscellaneous**	
	Ring pessary	
18.4	**Estrogens**	
	Ethinylestradiol	tablet, 50 mcg
18.5	**Insulins and Other Antidiabetic Agents**	
	Glibenclamide	tablet, 2.5mg, 5 mg
	Insulin (soluble)	injection, 40 IU / ml in 10- ml vial
	Intermediate acting insulin	
		injection, 40 IU / ml in 10- ml vial (as compound insulin zinc suspension or isophane insulin)
	Metformin	tablet, 500mg (hydrochloride)
	Complementary	
	Glipizide	tablet, 2.5 mg, 5 mg
18.6	**Ovulation Inducers**	
	Clomifene	tablet, 50 mg (citrate)
18.7	**Progestogens**	
	Norethisterone	tablet, 5 mg
	Medroxyprogesterone acetate	
		tablet, 5 mg
18.8	**Thyroid Hormones and Antithyroid Medicines**	
	Carbimazole	tablet, 5 mg
	Levothyroxine	tablet, 100 mcg (sodium salt)
	Lugol's Iodine	oral solution (Iodine 5%+Potassium iodide 10%)
18.9	**Posterior Pituitary Hormone**	
	Desmopressin	injection, 4 mcg/ml; nasal spray 10 mcg / metered spray
19.	**Immunologicals**	
19.1	**Diagnostic Agents**	
	Tuberculin, purified protein derivative (PPD)	injection

	Generic Name	Dosage Form
19.2	**Sera and Immunoglobulins**	
	Anti-D immunoglobulin (human)	injection, 250 mcg in single dose vial
	Antirabies hyperimmune serum	injection, 1000 IU in 5-ml ampoule
	Polyvenum antisnake serum	injection in vial
	Tetanus antitoxin	injection, 1 000 IU/ml, 3 000 IU/ml in vial
	Tetanus immunoglobulin (human)	injection, 500 IU in vial
19.3	**Vaccines**	
19.3.1	**For Universal Immunization**	
	BCG	vaccine
	Diphtheria, Tetanus, Pertussis, Hepatitis B vaccine	
	Diphtheria, Tetanus, Pertussis, Hepatitis B, *Haemophilus influenzae* type b vaccine	
	Measles	vaccine (live attenuated)
	Poliomyelitis (oral)	vaccine
	Tetanus toxoid	vaccine
19.3.2	**For Specific Groups of Individuals**	
	Hepatitis A	vaccine
	Hepatitis B	vaccine
	Influenza	vaccine
	Japanese Encephalitis	SA 14-14-2 strain live attenuated vaccine
	Meningococcal meningitis vaccine	
	Mumps	vaccine
	Rabies vaccine, freeze-dried vaccine	
	Rubella	vaccine
	Typhoid	vaccine
	Yellow fever vaccine	vaccine
20.	**Muscle Relaxants (Peripherally Acting) and Cholinesterase Inhibitors**	
	Neostigmine	tablet, 15 mg (bromide); injection 500 mcg, 2.5 mg (metilsulfate) in 1-ml ampoule
	Pancuronium bromide	injection, 2 mg / ml in 2-ml ampoule
	Suxamethonium chloride	injection, 50mg /ml in 2- ml ampoule
	Vecuronium bromide	powder for injection 10 mg in vial

	Generic Name	Dosage Form
21.	**Ophthalmological, Ear, Nose and Throat Preparations**	
21.1	**Ophthalmological Preparations**	
21.1.1	**Anti-infective Agents**	
	Aciclovir	ointment, 3%w/w
	Gentamicin	solution (eye drops), 0.3% (sulfate)
	Complementary	
	Chloramphenicol	applicap, 1%
	Ciprofloxacin	eye/ear drops, 0.3% (as hydrochloride); eye ointment, 0.3%
	Tetracycline	eye ointment, 1% (hydrochloride)
21.1.2	**Anti-inflammatory agents**	
	Prednisolone	solution (eye drops), 0.5%
21.1.3	**Local Anaesthetics**	
	Lignocaine (Lidocaine)	injection, 2%, 4% (topical)
	Complementary	
	Tetracaine	solution (eye drops), 0.5%
21.1.4	**Miotics and antiglaucoma medicines**	
	Acetazolamide	tablet, 250 mg
	Pilocarpine	solution (eye drops), 2%, 4% (hydrochloride)
	Timolol	solution (eye drops), 0.5 % (maleate)
21.1.5	**Mydriatics**	
	Atropine	solution (eye drops), 1% (sulfate)
	Tropicamide	solution (eye drop), 0.5%
21.2.	**Ear, Nose and Throat Preparations**	
	Lignocaine (Lidocaine)	topical (viscous), 2%, 4%
	Bismuth Iodoform Paraffin	solution, 70%
	Chloramphenicol	ear drops, 5%
	Ichthammol + Glycerine	ear drop, 10%+5%
	Oxymetazoline	solution (nasal drops), 0.025%, 0.05%
	Sodium bicarbonate + Glycerin	ear drops, 1%+5%
21.3	**Dental**	
	Clove oil	oil
	Chlorhexidine	solution, 0.2% (gluconate)
	Zinc oxide	powder

Generic Name	Dosage Form
22. Oxytocics and Antioxytocics	
22.1 Oxytocics	
Methylergometrine	injection, 200mcg (maleate) /ml in ampoule
Oxytocin	injection, 5 IU/ml in1-ml ampoule
Complementary	
Misoprostol	tablet, 200 mcg
Mifepristone*-misoprostol	tablet, 200mg- 200 mcg
**Combi-pack, containing 1 tablet of mifepristone and 4-tablet of misoprostol. Requires close medical supervision. Approved for abortion services only in listed sites.*	
22.2 Anti-oxytocics	
Isoxsuprine hydrochloride	injection, 5mg/ml
23. Peritoneal Dialysis Solution	
Intraperitoneal dialysis solution	parenteral solution of appropriate composition
24. Psychotherapeutic Medicines	
24.1 Medicines Used in Psychotic Disorders	
Chlorpromazine	tablet, 50 mg, 100mg (hydrochloride); oral liquid, 25 mg (hydrochloride) / 5ml; injection, 25 mg (hydrochloride) /ml in 2-ml ampoule
Fluphenazine	injection, 25 mg (decanoate or enantate) in 1-ml ampoule
Haloperidol	tablet 2 mg, 5 mg; injection, 5 mg in 1-ml ampoule
Complementary	
Thioridazine	tablet, 10mg, 25mg, 100mg
24.2 Medicines Used in Mood Disorders	
24.2.1 Medicines used in depressive disorders	
Amitriptyline	tablet, 10 mg, 25 mg, 75mg (hydrochloride)
Fluoxetine	capsule or tablet, 20 mg (as hydrochloride)
24.2.2 Medicines Used in Bipolar Disorders	
Lithium carbonate	capsule or tablet, 300mg

Generic Name	Dosage Form
24.3 Medicines Used in Generalised Anxiety and Sleep Disorders	
Alprazolam	tablet, 0.25 mg, 0.5 mg, 1 mg
Chlordiazepoxide	tablet, 10 mg, 25 mg
Diazepam	tablet 2 mg, 5 mg
24.4 Medicines Used for Obsessive Compulsive Disorders and Panic Attacks	
Clomipramine	capsules, 10 mg, 25 mg (hydrochloride)
24.5 Medicines Used in Substance Dependence Programmes	
Methadone*	concentrate for oral liquid, 5 mg/ml, 10 mg/ml (hydrochloride), oral liquid, 5 mg/5ml, 10 mg/5 ml
	**The medicines should only be used within an established support programme.*
25. Medicines Acting on the Respiratory Tract	
25.1 Antiasthmatic and Medicines for Chronic Obstructive Pulmonary Disease	
Aminophylline	Injection, 25 mg/ml
Chromoglicic acid	inhalation (aerosol), 5 mg, 20 mg (sodium salt) per dose
Epinephrine (Adrenaline)	injection, 1 mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule.
Hydrocortisone	injection (sodium succinate) 100 mg, 200 mg in vial; tablet, 10 mg
Ipratropium bromide	inhalation, 20 mcg/ dose
Salbutamol	tablet, 2 mg, 4 mg (as sulfate); rotacap 200 mcg (as sulfate) per dose; oral liquid, 2mg (as sulfate)/5ml; injection 50mcg /ml in 5-ml ampoule
Complementary	
Beclomethasone	inhalation (aerosol), 50mcg (as dipropionate) per dose
Theophylline	tablet, 300 mg
26. Solution Correcting Water, Electrolyte and Acid Base Disturbances	
26.1 Oral	
Oral rehydration salts*	sachet containing: Dextrose, anhydrous 13.5 g, Sodium chloride 2.6 g, Potassium chloride 1.5 g, Trisodium citrate

	Generic Name	Dosage Form
		dihydrate 2.9 g, appropriate flavour q.s. Dissolved to produce 1 litre, provides Dextrose 75 mEq, sodium 75 mEq or mmol/l, chloride 65 mEq or mmol/l, potasium 20 mEq o mmol/l, citrate 10 mmol/l and osmolarity 245 mOsm/l
26.2	**Parenteral**	
	Compound solution of Sodium lactate (Ringer's Lactate)	injectable solution
	Glucose	injectable solution, 5% isotonic, 50% hypertonic
	Glucose with Sodium chloride	injectable solution, 5% glucose, 0.9% sodium chloride
	Potassium chloride	injection, 15% in 20ml ampoule
	Sodium chloride	injectable solution, 0.9% isotonic
	Sodium bi-carbonate	injectable solution 1.4%, 8.4% solution in 10-ml ampoule
26.3	**Miscellaneous**	
	Water for injection	5-ml, 10-ml ampoule
	Ethyl alcohol	injection
	Complementary	
	Disulfiram	tablet, 200 mg
27.	**Vitamins and Minerals**	
	Ascorbic acid	tablet, 50mg
	Calcium gluconate	injection, 100 mg / ml in 10-ml ampoule
	Ergocalciferol	capsule or tablet, 1.25 mg (50 000 IU) oral solution, 250 mcg/ ml) (10000 IU / ml)
	Pyridoxine	tablet, 25mg (hydrochloride)
	Retinol	tablet (sugar coated), 10000 IU; capsule, 20000 IU (as palmitate); oral oily solution, 100 000 IU/ ml in multi-dose dispenser; water miscible injection, 100 000 IU (as palmitate) in 2-ml ampoule
	Retinol +DL-alpha-tocopherol	Retinol (as palmitate)+DL-alpha-tocopherol or tocopheryl acetate, soft gel capsule, 200 000 IU+ 40 IU, 100 000 IU+ 20 IU, 50 000 IU+ 20 IU
	Riboflavin	tablet, 5 mg
	Vitamin B complex	tablet containing: thiamine mononitrate 5 mg, riboflavin 5 mg, pyridoxine hydrochloride 1.5 mg, nicotinamide 50 mg, calcium pantothenate 25 mg.

Appendix - III

Adverse Drug Reaction Reporting

National Focal Point (National Centre)

Department of Drug Administration

Madan Bhandari Path – 4, Bijuli Bazar, New Baneshwor, Kathmandu
Phone: 01-4780227, 4780432 Fax. 01-4780572
e-mail: druginfo@dda.gov.np; dda@healthnet.org.np

Branch Offices

National Medicines Laboratory

Madan Bhandari Path, Bijulibazar, New Baneshwor, Kathmandu
Phone 01-4781269; Fax 01-4780064
e-mail: nml@dda.gov.np; rdrl@healthnet.org.np

Biratnagar Branch Office

Kanchanbari, Biratnagar, Sunsari
Phone/Fax 021-420849

Birgunj Branch Office

Murali Bagaicha, Birganj, Parsa
Phone/Fax 051-527753

Nepalganj Branch Office

Surkhet Road, Nepalgunj, Banke
Phone/Fax: 081-522074

Regional Centres

B.P. Koirala Institute of Health Sciences, Dharan, Sunsari

Phone: 025-521017 extn 2483
e-mail:gprauniar@hotmail.com

KIST Medical College, Imadol, Lalitpur

Phone: 01-5201680
e-mail:ravi.dr.shankar@gmail.com

Manipal Teaching Hospital (MTH), Pokhara, Kaski

Phone: 061-526420 or 526416-19 (extn: 221)
e-mail: dicmth@fewanet.com.np

Nepal Medical College Hospital (NMCH), Attarkhel, Kathmandu

e-mail: vkkul40@yahoo.com

Tribhuvan University Teaching Hospital (TUTH), Maharajgunj, Kathmandu

Phone: 01-4412404 extn: 1093
e-mail: diu@iom.edu.np

Government of Nepal

Ministry of Health and Population

Department of Drug Administration

Adverse Drug Reactions Reporting Form

Hospital record No. or chart No. or patient ID No. _____

Patient's Name: _____ **Sex: F/ M** **Age** _____

Description of the adverse reaction/s: **Onset date of reaction:** _____

_____

_____

_____

_____

Information on Suspected Medicine				
Medicines (Brand & Generic Name, Manufacturer, Batch No., Dosage Form)	**Daily dosage**	**Date started**	**Date stopped**	**Reason for use**

Additional relevant information (eg. medical history, test result, known allergies, drug interactions)

_____

_____

_____

_____

Reported by: Name:_____ Hospital / Department: _____

Date: _____ Signature: _____

Please return this form to your local Drug Information Unit or Hospital Pharmacy. Thank you for taking the time to fill in this report!

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