Zambia National Formulary

ZNF 04

2017
Foreword

The Zambia National Formulary (ZNF) is an integral component of the Zambia National Medicines Policy that is aimed at making available and accessible essential medicines of proven efficacy, safety and quality at affordable cost. The ZNF is a major strategy in promotion of rational use of medicines.

This edition of the ZNF has maintained the basic objectives and organization of the previous edition. This edition emphasizes the need for evidence based treatments as derived from the Standard Treatment Guidelines (STDs). The development of this document is consultative and participatory. The ZNF is a very dynamic document that needs regular review and update to make it truly relevant in meeting health needs of our communities.

The Zambia national Formulary Committee (ZNFC) responsible for development and dissemination of this document welcomes the active participation of all stakeholders to achieve our goal of promoting rational use of medicines in the delivery of quality health care.

Dr. Jabbin Mulwanda
Permanent Secretary - Health Services
MINISTRY OF HEALTH
Preface

The publication of Zambia National Formulary (ZNF) is yet another milestone of Zambia National Formulary committee activities. The ZNF is authentic publication that reflects the priorities of the Zambia National Medicines Policy and is accepted as a reliable guide by health workers for the purpose of prescription of medicines.

The ZNF is accepted by government as a standard reference document and as an authority as far as the formulary is concerned.

The formulary contains information about essential and rational medicines available on the Zambia Essential Medicines List (ZEML). The indications, contraindications, drug interactions, side effects and dosages are provided.

It is hoped that this publication will equip the health worker both in public and private sectors with enough information for rational prescribing, help to keep cost of medication reasonable and affordable and reduce adverse effects.

The Ministry of Health will update this document on biennially basis to keep it relevant for practice.

Dr. Mzaza Nthele
Director, Clinical Care & Diagnostics Services
Acknowledgement

The Zambia National Formulary Committee is grateful to the Ministry of Health for the support given to the Committee during the preparation of this edition of the Formulary. The Committee would also like to thank WHO, MSH – RPM Plus and Clinton Foundation for financial and technical support towards the preparation of the Formulary.

Some advice and contributions were also received from various health professionals from various institutions.

The Committee would also like to thank Mr. Boyd Mwanashimbala, Mr Chikuta Mbewe, Mrs Bernice Mwale, Mr Luke Alutuli, Mr George Kadimba, Mr Maxwell Kasonde, Ellis Mwanza from ZNFC Secretariat for their support and facilitating review of this document.

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Introduction

The fifth edition of the Zambia National Formulary seeks to provide a list of drugs suitable for use in Zambia together with essential information about their use.

The drug selection has been based on the proven efficacy and potential availability.

Arrangement of Information

The main text consists of classified notes and preparations. These have been divided into chapters according to a particular system of the body or an aspect of medical care.

Chapters are further divided into sections which were necessary, have introductory notes for health care providers who include doctors, pharmacists, nurses and other health professionals. This information is intended to facilitate the selection of appropriate treatment.

Drug monographs and details of relevant preparations follow the notes.

Guidance an Prescribing and Prescription Writing

This part of the formulary contains information on prescription writing, prescribing for children and the elderly, advice on promoting compliance, drug stability, storage conditions and the VEN classification system for setting procurement and stocking priorities.

Drug Name – Appears under approved name or non-proprietary title on the International Non-proprietary name (INN)

Presentation Indicates the dosage form in which the drug is prescribed.

Indications Gives details of the indications for the use of the drug

Caution Highlights precaution required. May include counselling of patient on how to take the medication.

Contra –Indications Any contra indications to the use of the drug are specified.

Side Effects Gives details of common and more serious side effects.

General Treatment of Poisoning

This chapter deals with the management of all cases of poisoning or suspected poisoning when first seen in the home through referral to a health facility.

Appendixes And Indexes

The appendixes include information on immunisation schedules, drug interactions, haematological and clinical chemistry reference values for children, adults and during pregnancy, thyroid and reproductive hormones reference levels, additives to intravenous (I.V.) fluids and drugs in pregnancy.

A special section on patients leaflets and instructions give information on how to administer and use nasal drops, aerosols vaginal creams, ointments and gels, pessaries, suppositories, ear drops, eye drops and ointments. This section follows the appendixes.

The indexes lists the drugs in alphabetical order by approved name or INN.

Prescriber Control and Drug Availability

Prescriber categories are not indicated in the text because it is expected that the drug availability will be controlled by:

i. Drugs and therapeutic committees actively defining policies for prescribing within an institution or District.

ii. The range of availability of drugs in any institution being restricted according to the level of institution and to the categories of staff prescribing.

Prescribers are advised to follow rational prescribing habits which emphasise the priority use of essential and economic treatment regimes.

Price of Drugs

Because of constant price fluctuations it is impossible to include specific prices for drugs. However, your pharmacy staff will be able to give up to date information for your guidance.

Revision of Formulary Contents

The Zambia National Formulary Committee recognises the fact that the field of drugs is a continuously changing one, thus revision of the formulary contents will be continuous. Contributions can be submitted for consideration by the Committee to Secretariat at Ministry of Health

PROFESSOR C. CHINTU, MD, FRCPC, FRCP
(Lo)
Chairman,
Zambia National Formulary Committee
General Practice Prescriptions
A well-written prescription should contain the following information:

1. Name and address of the patient and the age if for a child
2. Name, dosage form and strength of the preparation
3. The dosage and frequency together with the duration of treatment
4. PRN prescriptions should clearly state a time limit for treatment
5. The directions for use
6. The prescriber’s name, initials in block letters and practicing license number
7. The signature of the prescriber
8. Name and address of hospital or clinic
9. Date.

Hospital prescriptions
There should be prescription sheets on which only prescriptions and a record of dispensing and administration are written.

At any one time use only one prescription sheet per patient.

Frequency of administration for “as required” medicines should be indicated by clear and definitely stated intervals or indications.

The route of administration should be clearly indicated.

The prescription sheet should show signed and dated cancellation of any prescriptions no longer current.

Quantities and strengths on a Prescription
1. For solids, quantities less than 1 gram should be written in milligrams, e.g. 500mg, not 0.5g; quantities less than 1mg should be written in micrograms, e.g. 100micrograms, not 0.1mg.
2. Use the term millilitre (ml) for fluid measurements.
3. For liquid preparations suitable quantities of the preparations should be used viz: Elixirs, Linctuses and pediatric mixtures (usually 5ml dose) 50ml, 100ml or 150 ml. Adult mixtures (10ml dose) 200ml.
4. Injections should be limited to cases where they are absolutely necessary.

Abbreviations
Routes of Administration

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Po</td>
<td>Oral</td>
</tr>
<tr>
<td>i.m</td>
<td>Intramuscular</td>
</tr>
<tr>
<td>i.v</td>
<td>Intravenous</td>
</tr>
<tr>
<td>p.r</td>
<td>Per rectal</td>
</tr>
<tr>
<td>p.v</td>
<td>Per vaginal</td>
</tr>
<tr>
<td>s.c</td>
<td>Subcutaneous</td>
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</tbody>
</table>

Dosage Forms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tabs</td>
<td>Tablets</td>
</tr>
<tr>
<td>Caps</td>
<td>Capsules</td>
</tr>
<tr>
<td>Susp</td>
<td>Suspension</td>
</tr>
<tr>
<td>Syr</td>
<td>Syrup</td>
</tr>
<tr>
<td>Inj</td>
<td>Injection</td>
</tr>
<tr>
<td>Amp</td>
<td>Ampoule</td>
</tr>
<tr>
<td>Oint</td>
<td>Ointment</td>
</tr>
<tr>
<td>Soln</td>
<td>Solution</td>
</tr>
<tr>
<td>Lot.</td>
<td>Lotion</td>
</tr>
<tr>
<td>Mixt.</td>
<td>Mixture</td>
</tr>
<tr>
<td>Suppos.</td>
<td>Suppositories</td>
</tr>
<tr>
<td>Lin.</td>
<td>Liniment</td>
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<tr>
<td>Applic.</td>
<td>Application</td>
</tr>
<tr>
<td>Linct.</td>
<td>Linctus</td>
</tr>
<tr>
<td>Pess</td>
<td>Pessary</td>
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</table>

Frequency

<table>
<thead>
<tr>
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<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocte</td>
<td>at night</td>
</tr>
<tr>
<td>on</td>
<td>at night</td>
</tr>
<tr>
<td>om</td>
<td>in the morning</td>
</tr>
<tr>
<td>od</td>
<td>once a day</td>
</tr>
<tr>
<td>bd</td>
<td>twice a day</td>
</tr>
<tr>
<td>tds</td>
<td>three times a day</td>
</tr>
<tr>
<td>qds</td>
<td>Four times a day</td>
</tr>
<tr>
<td>qid</td>
<td>every 6 hours</td>
</tr>
<tr>
<td>prn</td>
<td>When required</td>
</tr>
<tr>
<td>sos</td>
<td>When necessary</td>
</tr>
<tr>
<td>ac</td>
<td>before food</td>
</tr>
<tr>
<td>cc</td>
<td>with food</td>
</tr>
<tr>
<td>pc</td>
<td>after food</td>
</tr>
<tr>
<td>stat</td>
<td>at once</td>
</tr>
<tr>
<td>ic</td>
<td>in between meals</td>
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</table>

Units

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>mg</td>
<td>milligram</td>
</tr>
<tr>
<td>mcg</td>
<td>microgram</td>
</tr>
<tr>
<td>kg</td>
<td>kilogram</td>
</tr>
<tr>
<td>l</td>
<td>litre</td>
</tr>
<tr>
<td>ml</td>
<td>millilitre</td>
</tr>
<tr>
<td>iu</td>
<td>international units</td>
</tr>
<tr>
<td>Mmol</td>
<td>millimoles</td>
</tr>
</tbody>
</table>
Prescribing for Children

In children the risk of toxicity is increased by inefficient renal filtration, relative enzyme deficiencies, differing target organ sensitivity and inadequate detoxifying systems causing delayed excretion.

In the neonatal period (first 28 days of life) and in childhood, dosage is usually calculated according to body weight (until 50kg or puberty is reached) and a set of scales should be available in all clinics where children are treated.

Approximate doses can be calculated from adult doses using the following age ranges and corresponding fractions:
- first month (neonate) – 1/8
- up to 12 months (infant) – ¼
- 1 – 5 years – 1/3
- 6 – 12 years – ½

The manufacturer’s recommended dose should be checked.

Body-surface area (BSA) estimates are more accurate for calculation of paediatric doses than body-weight since many physical phenomena are more closely related to body-surface area. The average body-surface area of a 70-kilogram human is about 1.8m². Thus, to calculate the dose for a child the following formula may be used:

\[
\text{Approximate dose for patient} = \text{surface area of patient (m}^2\text{)} \times \text{adult dose}
\]

The percentage method below may be used to calculate paediatric doses of commonly used drugs. In general, the use of oral medication is preferred by children and injection should be limited to when it is absolutely necessary.

Prescribing for the Elderly

Elderly patients are usually at a greater risk of adverse reactions to drugs and interactions because of multiple drug therapy for their multiple diseases.

Manifestations of normal ageing in the very old patients are sometimes mistaken for disease and lead to inappropriate prescribing. For example, drugs such as prochlorperazine are commonly misprescribed for giddiness due to age-related loss of postural stability.

Self medication with drugs prescribed for a previous illness or even for another person maybe an added complication. The ageing nervous system shows increased susceptibility to many commonly used drugs such as benzodiazepines and opioid analgesics. These should be used with caution.

Before prescribing one should always pose the question whether a drug is indicated at all. It is also sensible to prescribe from a limited range of drugs and to be thoroughly familiar with their effects in the elderly.

Compliance

Patients often do not take their medicines correctly. Surveys show that many patients are not told what is wrong with them and how to take their medicines. Others start taking their medication for a while, they then stop or forget when they start feeling better, or suffer side effects.

Patient compliance is a measure of the extent to which a patient follows instructions on the use of a drug. These instructions should be given by both the prescriber and the dispenser. The result of the use of the medicine will be better when compliance is high. Prescribers and dispensers should always aim at high patient compliance.

If patients do not take their medicines properly, they are unlikely to improve and they may return to the health facility for further treatment. Spending a small amount of time in improving patient compliance is a worthwhile investment in terms of saving time and money.

Do not give too many drugs

The more drugs a patient has the less likely they are to take any of them properly! Giving the most important drugs and ensuring that they are taken properly is much better than giving a lot of drugs which may not be taken properly.

Reduce the number of medication times

Compliance is improved by keeping the types and number of medications, the frequency at which each medication is to be taken and the number of times which medication is taken as few as possible, e.g. 3 times a day dosages are better than 4 times a day dosage.
Different medication with one being taken 3 times a day and another taken 4 times a day are bound to be taken wrongly.

Check compliance with chronic patients
Patients having medication for chronic conditions are most prone to non-compliance, especially those illnesses requiring long term medications for suppression or prophylaxis during which time the patient has few, if any symptoms.

The attitude of the prescriber should be positive and helpful all the time.

**DRUGS STABILITY**

Drugs deteriorate with time, this is worsened if they are not stored or handled properly. When drugs deteriorate they may become useless or even harmful.

Usually drugs carry expiry dates. This means that they should not be used after that date.

This date relies on the drugs being stored under suitable storage conditions.

Drugs are susceptible to heat, light and moisture and dirt. Exposure to one or all of these will affect the stability of the drug. Storage should be such as to minimise exposure to heat, light and moisture. Signs that could indicate that deterioration has occurred include:

- Bad smell
- Bad taste
- Change in colour
- Development of bubbles in liquids
- Growth of bacteria or fungus often appearing as brown spots
- Melting, sticking or cracking of tablets
- Liquid has separated out from creams
- Development of turbidity or crystallization in liquids

Certain drugs however, may not show visible signs of deterioration after the expiry date or when affected by adverse storage conditions.

Patients need education on how to store drugs. It is best to advise patients to use and finish the drug within the prescribed period.

**Moisture**
When containers for medicaments are not properly closed, moisture can easily get in and destroy the contents. Tablets may get wet and eventually break or stick to one another. Certain drugs like aspirin deteriorate in the presence of moisture emitting an acidic smell like vinegar.

Drugs should be stored in a dry place with good ventilation. Containers should be tightly closed and should not be left open. Only open containers when necessary and close them immediately after use. Do not remove desiccant put in the containers by the manufacturer.

**Light**
Chemical breakdown can be caused by exposure of drugs to sunlight.

**Drugs should be kept out of direct sunlight.**

**Heat**
Heat affects many drugs. Drugs stored in cool conditions will remain effective for a longer period of time. Some drugs may require refrigeration during transportation and storage, e.g. insulin and vaccines. Always check for and follow the manufacturer’s recommended storage conditions.

**Dirt**
Drugs should be protected from dirt. The dispensary and store should be cleaned often and this should be done in such a way to prevent the dust created from covering the products.
## Drug Storage Information

Below are storage conditions and signs of deterioration for some common drugs.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>STORAGE TEMPERATURE °C</th>
<th>PROTECT FROM</th>
<th>SIGNS OF DETERIORATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>15-30</td>
<td>Moisture, heat</td>
<td>Vinegar smell</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>15-30</td>
<td>Moisture, heat</td>
<td></td>
</tr>
<tr>
<td>Amoxycillin Syrup</td>
<td>Room temperature</td>
<td>Heat, extreme cold</td>
<td></td>
</tr>
<tr>
<td>Benzylpenicillin Injection</td>
<td>Refrigerated; As powder 14 days &lt;30°C As liquid: room temp. 24hrs. refrigerated: 14 days</td>
<td>Heat, freezing</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol Injection</td>
<td>As liquid, &lt;30°C, 30 days</td>
<td>Moisture, heat</td>
<td>Cloudy (should be clear)</td>
</tr>
<tr>
<td>Coartem Tablets</td>
<td>15-30°C</td>
<td>Moisture, heat</td>
<td></td>
</tr>
<tr>
<td>Co-trimoxazole Tablets</td>
<td>1-30</td>
<td>Moisture, Direct light, extreme cold</td>
<td></td>
</tr>
<tr>
<td>Co-trimoxazole Syrup</td>
<td>15-30</td>
<td>Direct light, extreme cold</td>
<td></td>
</tr>
<tr>
<td>Erythromycin tablets</td>
<td>15-30</td>
<td>Moisture, heat direct light,</td>
<td></td>
</tr>
<tr>
<td>Gentian violet</td>
<td>15-30</td>
<td>Moisture, freezing</td>
<td></td>
</tr>
<tr>
<td>Iron/folate tablet</td>
<td>15-30</td>
<td>Moisture, light</td>
<td></td>
</tr>
<tr>
<td>Gentamycin injection</td>
<td>15-30</td>
<td>Freezing</td>
<td></td>
</tr>
<tr>
<td>Mebendazole tablet</td>
<td>15-30</td>
<td>Moisture</td>
<td></td>
</tr>
<tr>
<td>Nalidixic acid tablet</td>
<td>15-30</td>
<td>Moisture</td>
<td></td>
</tr>
<tr>
<td>ORS</td>
<td>15-30</td>
<td>Moisture</td>
<td></td>
</tr>
<tr>
<td>Paracetamol tablets</td>
<td>&lt;40</td>
<td>Moisture, direct light, heat</td>
<td></td>
</tr>
<tr>
<td>Quinine injection</td>
<td>&lt;40</td>
<td>Light, heat</td>
<td></td>
</tr>
<tr>
<td>Sulphadoxine + Pyrimethamine</td>
<td>15-30</td>
<td>Moisture, light</td>
<td></td>
</tr>
<tr>
<td>Tetracycline eye ointment</td>
<td>15-30</td>
<td>Moisture, light, freezing</td>
<td></td>
</tr>
<tr>
<td>Tetracycline tablet</td>
<td>15-30</td>
<td>Moisture, light</td>
<td></td>
</tr>
<tr>
<td>Vitamin A tablets</td>
<td>15-30</td>
<td>Moisture, light, heat</td>
<td></td>
</tr>
</tbody>
</table>
One way to maximize the effectiveness of health care when funds are limited is to set procurement and stock-keeping priorities according to the potential health impact of individual medical supplies. A method of doing this is the VEN system, in which all of the items on the supply list are placed into one of the following three categories.

**VITAL** items are potentially life saving, which have significant withdrawal side effects.

**ESSENTIAL** items: are effective against less severe, but nevertheless significant forms of illness.

**NON ESSENTIAL** items for minor - or self limited illness, items which are of questionable efficacy, and items with a high cost for marginal therapeutic advantage.

**Guiding purchases with the VEN system**

Often requirements exceed available resources. Under these constraints, requests need to be revised, but the process for doing so is frequently haphazard.

Purchase quantities should be reduced in proportion to the quantities requested. Items, which are unfamiliar to the person making the adjustment, may be omitted despite their medical importance.

The VEN system helps to minimise these and other distortions in the procurement process, and thus maximize the health impact of available funds.

Once medical personnel have established the VEN - categories, adjustments in purchases can quickly and easily be done, even by non medical staff.
Drugs used in anaesthesia

1. Drugs used in general anaesthesia
   1.1 Intravenous and intramuscular anaesthetics
   1.2 Inhalational anaesthetics
   1.3 Muscle relaxants
   1.4 Anticholinesterases used in surgery.

These should only be used by experienced personnel and in premises where adequate resuscitation equipment is available.

1.1 Intravenous and Intramuscular Anaesthetics

**KETAMINE**

Presentation: Injection containing 50mg/ml, 100mg/ml ketamine hydrochloride.

Indications: Induction and maintenance of anaesthesia for operations of short duration. May also be used for operations of longer duration if given by continuous intravenous infusion.

Administration: By slow intravenous injection 1 - 2mg/kg over 60 seconds, repeated according to patient’s response. By deep intramuscular injection 4 - 10mg/kg repeated according to patient’s response.

Side effects: Recovery reactions include hallucinations, vomiting, transient rise in blood pressure and heart rate. N.B. Diazepam can reduce hallucinations.

Caution: Maintain full anaesthetic vigilance and avoid patient stimulation during recovery.

Contraindications: Hypertension, history of mental illness.

**THIOPENTONE SODIUM**

Presentation: Powder for reconstitution containing thiopentone sodium in 1g and 5g vials.

Indications: Induction of anaesthesia in operations of short duration.

Dose: By intravenous injection 100 - 150mg as 2.5% solution) repeated if necessary according to patient’s response or up to 4mg/kg. Child; induction, 2 - 7mg/kg

Side effects: Coughing, sneezing, laryngeal and bronchial spasm during induction, thrombophlebitis, sensitivity reactions, depression of respiration, depression of cardiac output and initially, fall in blood pressure.

Caution: Avoid injections outside a vein.

Contraindications: Shock, dehydration and severe anaemia, porphyria.

1.1.2 Inhalational Anaesthetics

Inhalational anaesthetics may be gases or volatile liquids. They can be used both for induction and maintenance of anaesthetics. Gaseous agents must be given with adequate concentration of oxygen to prevent hypoxia.

**HALOTHANE**

Presentation: Volatile liquid

Indications: All purpose anaesthesia

Administration: Using a suitable vaporizer:

Adult: Induction, increased gradually to 2% - 4% in oxygen or nitrous oxide/oxygen. Child; 1.5% - 2%.

Side effects: May produce hypotension or arrhythmia, shivering and jaundice.

Contraindications: A history of unexplained jaundice or fever in a patient following exposure to halothane is an absolute contraindication.

Caution: Adrenaline infiltrations should be avoided in patients anaesthetised with halothane as ventricular arrhythmias may result.

**NITROUS OXIDE**

Presentation: Compressed gas

Indications: Induction and maintenance of anaesthesia. Analgesic in sub-anaesthetic concentrations.

Administration: Anaesthetic; Induction, 80% nitrous oxide with 20% oxygen and maintained at 70% nitrous oxide with 30% oxygen. Analgesic; 50% nitrous oxide with 50% oxygen as required.

Side effects: Convulsions

Caution: Risk of addiction and megaloblastic anaemia. Always administer with oxygen. Care is needed in patients with pneumothorax

Contraindications: Jaundice
1.1.3  Muscle Relaxants

These drugs are mainly used as an adjuvant to anaesthesia to enable muscle relaxation to be achieved using a minimal dose of anaesthetic.

Caution: Administration of these drugs may conceal signs of returning consciousness.

1.1.3  Anticholinesterases Used in Surgery

NEOSTIGMINE METHYLSULPHATE

Presentation: Injection containing 2.5mg/ml neostigmine methylsulphate.

Indication and dose: Reversal of muscular relaxation produced by non-depolarising muscle relaxants e.g. pancuronium. Adult; 2.5 – 5mg with atropine sulphate by slow intravenous injection over 60 seconds. Child; 80mcg/kg with 20mcg/kg atropine.

Diagnosis of myasthenia gravis; 1.5mg intramuscularly with 600mcg atropine sulphate.

Treatment of myasthenia gravis; 1.0mg - 3.5mg subcutaneously, intramuscularly or intravenously several times a day according to the severity of the condition.

1.2  Drugs used in local anaesthesia

LIGNOCAINE HYDROCHLORIDE

Presentation: 0.5% injection containing 5mg/ml lignocaine in vials. 1% injection containing 10mg/ml lignocaine hydrochloride solution in vials. 2% injection containing 20mg/ml lignocaine hydrochloride in vials.

Indications: Local anaesthesia, infiltration anaesthesia.

Dose: Local infiltration and peripheral nerve block using 0.5% solution adult up to 250mg (up to 50ml); using 1% solution, adult up to 250mg (up to 25ml)

Side effects: Bradycardia, hypotension, cardiac arrhythmias, cardiac arrest, anxiety, restlessness, tremor, dizziness, respiratory arrest, hypersensitivity reactions manifested by oedema, status asthmaticus or anaphylactic reaction.

Caution: It should be used with caution in severely debilitated patients and in those with liver disease.

Contraindications: In patients with known hypersensitivity to the drug.

LIGNOCAINE + DRENALINE

Presentation: 1% injection containing 10mg/ml lignocaine hydrochloride and adrenaline 1 in 200, 000 (5mcg/ml). 2% injection containing 20mg/ml lignocaine hydrochloride and adrenaline 1 in 200,000 (5mcg/ml)

Indications: Local anaesthesia

Dose: Adjusted according to site of operation and response of patient. Maximum dose 200mg or 500mg with solution which also contains adrenaline.
Local infiltration and peripheral nerve block; using 1% solution with adrenaline, adult up to 400mg (up to 40ml). Using 2% solution (dental anaesthesia) with adrenaline, adult 20 - 100mg (1 - 5ml).

Side effects: See lignocaine
Caution: See under lignocaine
Contraindications: Patients with known hypersensitivity to the particular drug.

1.3 Drugs used in spinal anaesthesia

These require great care and should be used by people with experience.

BUPIVACAINE HYDROCHLORIDE

Presentation: Injection containing bupivacaine hydrochloride 5mg.
Indications: Infiltration anaesthesia, peripheral nerve block, epidural block.
Dose: Adjusted according to the site of operation and response of the patient;
Local infiltration; 0.24% (maximum 60ml).
Epidural block, surgery, lumbar; 0.5 - 0.75% (maximum 20ml)

Side effects: See under lignocaine hydrochloride
Caution: See under lignocaine hydrochloride
Contraindications: As for lignocaine hydrochloride. Note: 0.75% is contraindicated for epidural use in obstetrics.
2 Drugs Acting on the Gastro-Intestinal System

2.1 Antacids

Neutralization of gastric acid relieves the pain caused by hyperacidity in case of peptic ulcer disease. Non absorbable antacids are preferable. These include aluminium and magnesium hydroxide and magnesium trisilicate. They are best given when symptoms occur or are expected, usually between meals and at bedtime, four or more times daily. Additional doses may be required up to once an hour to reduce gastric acidity throughout the day. Antacids should not be given at the same time as other drugs like tetracycline, Chloroquine, rifampicin, ACE inhibitors, antifungals, and other drugs. For elaborate list of these other drugs see appendix 2. The reason being that absorption of these drugs may be impaired when given together with antacids. Furthermore, they should not be given together with enteric-coated tablets.

**ALUMINIUM HYDROXIDE**

**Presentation:** Gel containing 4% of hydrated aluminium hydroxide. Tablets containing 500mg dried aluminium hydroxide. Oral suspension containing 4% aluminium hydroxide in water. **Indications:** Hyperacidity, peptic ulcer disease, hyperphosphataemia **Dose:** Gel, adult; 7.5 - 15ml repeat as required. As an intragastric drip diluted with 2 - 3 parts of water, the rate of flow being 15 - 20 drops a minute throughout the day. Tablets; 1 - 4 tablets chewed in between meals and at bedtime when required. Oral suspension, adult; 5 - 10ml 4 times daily between meals and at bedtime as required. Child 6 - 12 years; up to 5ml 3 times daily **Side effects:** Constipation **Caution:** Impaired renal function

**MAGNESIUM TRISILICATE**

**Presentation:** Magnesium trisilicate tablet compound containing magnesium trisilicate 250mg, dried aluminium hydroxide 120mg. Mixture, each 10ml containing magnesium trisilicate 500mg, light magnesium carbonate 500mg, sodium bicarbonate 500mg, concentrated peppermint emulsion 0.25ml, double strength chloroform water 5ml. **Indications:** Hyperacidity, peptic ulcer disease, hyperphosphataemia **Dose:** Tablets; 1 - 2 tablets to be chewed 3 - 4 times daily in between meals and at bedtime when required. Mixture; 10 - 20ml 3 - 4 times daily in between meals and at bedtime when required. **Side effects:** Diarrhoea **Caution:** impaired renal function

2.2 Antispasmodics

These are antimuscarinic drugs which reduce gastro-intestinal motility. They reduce spasm, delaying gastric emptying time and thus prolonging the action of antacids. They are useful for all colics but may cause blurring of vision and dry mouth.

**HYOSCINE BUTYLBROMIDE**

**Presentation:** Tablets (coated) containing 10mg hyoscine butylibromide. Injection containing 20mg/ml hyoscine butylibromide. **Indications:** Adjunct in gastro-intestinal disorders characterized by smooth muscle spasm, irritable bowel syndrome **Dose:** Adult; 20mg 3 - 4 times daily. Child, 6 - 12 years; 10mg 3 times daily. Irritable bowel syndrome; 10mg 3 times daily increased if necessary to 20mg, 4 times daily. Intramuscular or intravenous injection for acute spasm and spasm in diagnostic procedures; 20mg repeated after 30 minutes if necessary. **Side effects:** Dry mouth, tachycardia, difficulty in micturition, dilatation of pupils, constipation and hyperpyrexia. **Caution:** Patients with prostatic enlargement and cardiac disease **Contraindications:** Glaucoma

**PROPANTHELIN BROMIDE**

**Presentation:** Tablets (sugar coated) containing 15mg propanthelin bromide. **Indications:** Adjunct in gastro-intestinal disorders characterized by smooth muscle spasm, urinary frequency. **Dose:** 15mg 3 times daily 1 hour before meals and 30mg at bedtime. Maximum 120mg daily. Not recommended in children. **Side effects:** Dry mouth, dilatation of pupils,
Drugs Acting on the Gastro-Intestinal System

constipation and hyperpyrexia.
Caution: In patients with prostatic enlargement and cardiac disease
Contraindications: Glaucoma.

2.3 Ulcer healing Drugs

-H₂-receptor antagonists
-Complexes
-Proton pump inhibitors
-Prostaglandin analogues

Pepitic ulceration often involves the stomach, duodenum and lower oesophagus. Healing can be promoted by general measures such as stopping smoking, taking antacids and by antisecretory treatment. Nearly all duodenal ulcers and most gastric ulcers not caused by NSAIDs are caused by Helicobacter pylori.

The management of Helicobacter pylori and NSAID associated ulcer is discussed below. The recommended treatment is acid inhibition combined with antibacterial treatment. One week triple therapy regimens that comprising a proton pump inhibitor, amoxicillin and metronidazole (see dosage table below) are indicated.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esomeprazole</td>
<td>20mg twice daily</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>1g twice daily</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>400mg twice daily</td>
</tr>
<tr>
<td>Omeprazole</td>
<td>20mg twice daily</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>1g twice daily</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>400mg 3 times daily</td>
</tr>
<tr>
<td>Ranitidine bismuth citrate</td>
<td>400mg twice daily</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>1g twice daily</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>400mg twice daily</td>
</tr>
</tbody>
</table>

2.3.1 H₂ - receptor antagonists

These drugs heal ulcers by reducing gastric acid output as a result of H₂ – receptor blockade. They also help relieve peptic oesophagitis.

Maintenance treatment with low doses reduces the rate of ulcer relapse. They will not modify the natural course of the disease when treatment is stopped and Helicobacter pylori (H. pylori) eradication should be considered in such cases. Maintenance treatment may occasionally be used in frequent severe recurrences and in the elderly to prevent complications from peptic ulcer diseases.

These drugs are also used in healing ulcers associated with NSAIDs but cannot prevent complications from these ulcers.

CIMETIDINE

Presentation: Tablets containing 200mg, 400mg, 800mg cimetidine. Syrup/suspension containing 200mg/5ml cimetidine. Injection containing 100mg/ml cimetidine.

Indications: Benign gastric and duodenal ulceration, stomal ulcer, zollinger-ellison syndrome and other conditions where gastric acid reduction is beneficial.

Dose: Oral; tablets 400mg twice daily (with breakfast and at night) or 800mg at night (benign gastric and duodenal ulceration) for at least 4 weeks (at least 6 weeks in gastric ulceration and 8 weeks in NSAID associated ulceration). When necessary dosage maybe increased to 400mg 4 times daily or rarely (e.g. stress ulceration) increased to a maximum of 2.4g daily in divided doses. Infants under 1 year 20mg/kg daily in divided doses. Child over 1 year; 25-30mg/kg daily in divided doses. Maintenance; 400mg at night or 400mg in the morning and at night. Reflux oesophagitis; 400mg 4 times daily for 4 - 8 weeks. Zollinger-ellison syndrome; 400mg 4 times daily or occasionally more.

Gastric acid reduction (prophylaxis of acid aspiration), obstetrics 400mg start of labour, then up to 400mg every 4 hours. Short bowel syndrome; 400mg twice daily with breakfast and at bedtime. Intramuscularly 200mg 4 - 6 hourly, maximum 2.4g. Intravenously 200mg may be repeated every 4 - 6 hours. Infants; slow intravenous injection or intramuscular injection 20mg/kg daily in divided doses. Child over 1 year; 25 - 30mg/kg daily in divided doses.

Caution: Renal and hepatic impairment, pregnancy, breast-feeding. Cardiovascular impairment.

RANITIDINE

Presentation: Tablet containing 150mg, 300mg ranitidine hydrochloride. Oral solution containing 75mg/ml ranitidine hydrochloride. Effervescent tablets containing 150mg, 300mg ranitidine hydrochloride. Injection containing 25mg/ml ranitidine hydrochloride.

Indications: See under cimetidine

Dose: Oral, adult; 150mg twice daily or 300mg at night for 4 - 8 weeks. Child; 2 - 4mg/kg twice daily, maximum 300mg daily. Maintenance 150mg at night.

Prophylaxis of NSAID induced duodenal ulceration; 150mg twice daily for 8 weeks. Reflux oesophagitis; 150mg twice daily or 300mg daily for up to 8 - 12 weeks. Long term treatment of healed oesophagitis; 150mg twice daily. Zollinger-ellison syndrome; 150mg 3 times daily up
to maximum 6g in divided doses. Gastric acid reduction; 150mg on onset of labour then every 6 hours. Surgical procedures by intramuscular or intravenous injection 50mg, 45 - 60 minutes before anaesthesia. By intramuscular injection; 50mg every 6 - 8 hours. By intravenous injection 50mg diluted to 20ml and given over at least 2 minutes, maybe repeated every 6 - 8 hours. 

**Side effects:** See under cimetidine 

**Caution:** See under cimetidine. Avoid in porphyria

### SUCRALFATE

Sucralfate acts by protecting the mucosa from acid-pepsin attack on gastric and duodenal ulcers. It is a complex of aluminium hydroxide and sulfated sucrose.

**Presentation:** Tablets containing sucralfate 1g. Suspension containing sucralfate 1g/ml.

**Indications:** Benign gastric and duodenal ulceration, chronic gastritis, prophylaxis of stress ulceration.

**Dose:** Benign gastric & duodenal ulceration, chronic gastritis, 2g twice daily (on rising and at bedtime) or 1g 4 times daily before meals and at bedtime for 4 - 6 weeks up to 12 weeks, maximum. Prophylaxis of stress ulceration; (suspension) 1g 6 times daily (maximum 8g daily). Not recommended in children.

**Side effects:** Constipation, diarrhoea, nausea, indigestion, gastric discomfort, dry mouth, rash, hypersensitivity reactions, back pain, dizziness, headache, vertigo and drowsiness.

#### 2.5 Proton Pump Inhibitors

These inhibit gastric acid production by blocking the hydrogen-potassium adenosine triphosphate enzyme system (the “proton pump”). They are also used in combination with antibacterials for the eradication of *Helicobacter pylori*.

### OMEPRAZOLE

**Presentation:** Capsules containing 10mg, 20mg, 40mg omeprazole enteric coated granules. Tablets containing 10mg, 20mg, 40mg enteric coated omeprazole. Intravenous infusion containing 40mg omeprazole. Intramuscular injection containing 40mg omeprazole.

**Indications:** Benign gastric or duodenal ulcers, NSAID associated gastric or duodenal ulcers, duodenal erosions, prophylaxis in patients with history of above.

**Dose:** Oral, Benign gastric and duodenal ulcers; 20mg once daily for 4 weeks in duodenal ulceration or 8 weeks in gastric ulceration; in severe or recurrent cases increase to 40mg daily; Maintenance for recurrent duodenal ulcers, 20mg once daily; Prevention of relapse in duodenal ulcer; 10mg daily increasing to 20mg once daily if symptoms return. NSAID associated gastric or duodenal ulceration and gastroduodenal erosions 20mg once daily for 4 weeks; followed by a further 4 weeks if not fully healed; Prophylaxis in patients with a history of NSAID associated gastric or duodenal ulceration, gastroduodenal lesions, or dyspeptic symptoms who require continued NSAID treatment, 20mg once daily.

Duodenal ulcer associated with *Helicobacter pylori* see table in 2.3 above. Benign gastric ulcer associated with *Helicobacter pylori*, Omeprazole 40mg daily in 1 - 2 divided doses (plus amoxycillin 0.75 - 1g twice daily) for 2 weeks. Zollinger-Ellison syndrome; initially 60mg once daily; usual range 20 - 120mg daily (above 80mg in 2 divided doses). Prophylaxis of acid aspiration, 40mg on the preceding evening then 40mg 2 - 6 hours before surgery. Gastro-oesophageal reflux disease, 20mg once daily for 4 weeks, followed by a further 4 - 8 weeks if not fully healed; 40 mg once daily has been given for 8 weeks - gastro oesophageal reflux
disease refractory to other treatment. Acid reflux disease (long term management), 10mg daily increasing to 20mg once daily if symptoms return. Acid related dyspepsia 10 - 20mg once daily for 2 - 4 weeks according to response. Child over 2 years; severe ulcerating reflux oesophagitis, 0.7 - 1.4mg/kg daily for 4 - 12 weeks' maximum 40mg daily (to be initiated by hospital paediatrician).

By intravenous injection over 5 minutes or by intravenous infusion, gastric acid reduction during anaesthesia (prophylaxis of acid aspiration), 40mg completed 1 hour before surgery. Benign gastric or duodenal ulceration and gastro-oesophageal reflux; 40mg once daily until oral administration possible. Not recommended in children.

**Counselling:** Swallow capsule whole or dispense tablets in water or mix capsule contents or tablets with fruit juice or yoghurt.

**Side effects:** Gastro-intestinal disturbances, headache, hypersensitivity reactions, pruritis, dizziness, peripheral oedema, muscle and joint pain, malaise, blurred vision, depression and dry mouth. Proton pump inhibitors decrease gastric acidity and may increase risk of gastro-intestinal infection.

**Caution:** Proton pump inhibitors should be used with caution in patients with liver disease, in pregnancy and in breast feeding. They may also mask symptoms of gastric cancer; particular care should be given in those whose symptoms change and those over 45 years of age. The presence of gastric malignancy should be excluded before treatment.

### ESOMEPRAZOLE

**Presentation:** Tablets containing 20mg, 40mg esomeprazole magnesium trihydrate

**Indications:** Duodenal ulceration associated with *Helicobacter pylori*, gastro-oesophageal reflux disease.

**Dose:** Duodenal ulceration associated with *Helicobacter pylori*; 20mg twice daily. gastro-oesophageal reflux disease; 40mg once daily for 4 weeks followed by further 4 weeks if symptoms persist. Maintainance; 20mg daily. Symptomatic treatment in the absence of oesophagitis 20mg daily for up to 4 weeks followed by 20mg daily when required. Not recommended in children.

**Counselling:** Swallow tablet whole or disperse in water.

### 2.5 Prostaglandin analogues

#### MISOPROSTOL

This is a synthetic prostaglandin analogue with antisecretory and protective properties promoting gastric and duodenal ulcer treating. This drug is mostly recommended for the elderly or frail maintained on NSAIDs

**Presentation:** Tablets containing 200mcg misoprostol

**Indications:** Prevention of NSAID associated ulceration in the elderly and the frail. Healing of gastric and duodenal ulcers.

**Dose:** Benign gastric or duodenal ulcer 800mcg (in 2 - 4 divided doses) with breakfast (or main meals) and at bedtime. Treatment should be continued for at least 4 weeks. Treatment can go up to 8 weeks. Prophylaxis of NSAID associated ulcer 200mcg 2 - 4 times daily taken with the NSAID. Not recommended in children.

### CODEINE PHOSPHATE

**Presentation:** Tablets containing 15mg, 30mg, 60mg codeine phosphate

**Indications:** Diarrhoea, relief of nerve, muscular and abdominal pain

**Dose:** Adult; 10 - 60mg. Maximum 300mg in 24 hours.

**Side effects:** Constipation, nausea, vomiting and drowsiness

**Caution:** In children, in the elderly and in severe respiratory depression. Dependence may occur with prolonged use. Not recommended in children.

### LOPERAMIDE

**Presentation:** Capsules containing 2mg loperamide hydrochloride. Syrup containing 1mg/ml loperamide hydrochloride.

### 2.6 Drugs used for the treatment of diarrhoea

Dehydration resulting from acute diarrhoea is the main cause of death in children and the elderly. The first line treatment, regardless of the cause of diarrhoea, must be the replacement of fluids and electrolytes. The use of oral rehydration salts (ORS) is the preferred method in mild and moderate dehydration but in severe dehydration intravenous fluids need to be used.

There are a variety of pathogens (bacterial, viral, parasitic) that can cause diarrhoea but very few can be specifically treated. Antibiotics and sulphonamides are not indicated for routine treatment of acute diarrhoea.

When rehydration has been achieved; consideration can be given to the treatment of the cause of diarrhoea particularly if parasitic. Many acute diarrhoeas are self limiting and oral rehydration therapy alone is sufficient. In watery stool with vomiting, criteria for the treatment is decided upon by the degree of dehydration.
Indications: AIDS related diarrhoea
Dose: Adult, chronic diarrhoea; initially 4 - 8mg daily in divided doses, subsequently adjusted according to response. Maintenance 2 divided doses.
Side effects: Dizziness, abdominal pains, drowsiness, skin reactions including urticaria, paralytic ileus and abdominal bloating.
Caution: Prolonged use could aggravate irritable bowel syndrome.

ORAL REHYDRATION SALTS (ORS)

Presentation: The oral fluids can be made with chemicals as follows (WHO recommendations); Sodium chloride 3.5g, potassium chloride 1.5g, Sodium citrate 2.9g, anhydrous glucose 20g. The salts are dissolved in water up to 1 litre of solution. Recommended treatment of dehydration is shown in rehydration tables (see page 21)

Zinc Sulphate

Zinc sulphate is a salt used for the treatment of zinc deficiency. Zinc sulphate contains 23 percentage of elemental zinc. Zinc sulphate is absorbed over a wide range of pH and may cause GI irritation. Zinc is an essential element of nutrition and traces are present in a wide range of foods. It is a constituent of many enzyme systems and it is present in all the tissues. Normal growth and tissue depend upon adequate zinc. Zinc acts as an integral part of several enzymes important to protein and carbohydrate metabolism. Features of zinc deficiency include growth retardation and defects of rapidly dividing tissues such as skin and the intestinal mucosa. Zinc facilitates wound healing and helps maintain normal growth rates, normal skin hydration and senses of taste and smell. Zinc improves absorption of water electrolytes. Zinc supplements prevent subsequent episodes of diarrhea (in the ensuing 2-3 months after treatment). Zinc deficiency in humans alters aspects of immune function. Immune defects associated with zinc deficiency include impaired function of lymphocytes, natural killer cells and neutrophils. Zinc deficiency has also been hypothesized to exacerbate malaria and other diseases (infection with human immunodeficiency virus and tuberculosis) that rely on macrophage killing of infected cells. An adequate intake of zinc shortens the duration of respiratory tract infections including common cold.

ZINC SULPHATE DISPERSIBLE TABLETS

Presentation: Dispersible tablets, zinc sulphate monohydrate USP 54.9mg equivalent to elemental Zinc 20mg
Indications: Used in acute and persistent diarrhoea in children, along with oral rehydration salts (ORS), respiratory tract infections, common cold, malaria, acrodermatitis enteropathica sickle cell anaemia and Wilson's disease.
Dose Acute diarrhoea: Children below 6 months: 10mg elemental Zinc daily for 10-14 days. For children above six months: 20mg elemental Zinc daily for 10-14 days.
Wilson's disease: 25 – 50mg elemental Zinc two to three times daily.
Sickle cell anaemia: 10-15mg elemental zinc daily.
Acrodermatitis enteropathica: 1-2 mg elemental zinc per kg of body weight.
Zinc sulphate tablets should be taken between meals.
Side effects: It may cause copper deficiency if excessive doses are taken. Nausea and vomiting may occur. If GIT symptoms occur, Zinc sulphate tablets can taken with food, but food high in calcium, phosphorus and phytates must be avoided. Caution: No problems have been observed in human beings especially pediatrics when taken in normal daily recommended doses.
Contraindication: Concomitant administration with penicillamine, sodium valproate and ethambutal which inhibit zinc absorption. It is contraindicated to patients with hypersensitivity to the active substance or to any of the excipients.
Mode of administration: Place the tablet in a teaspoon/tablespoon. Add 5mL water or breast milk. Allow tablet to disperse (about 45 seconds). Give the entire spoonful to child.
**REHYDRATION TABLES**

### MODERATE DEHYDRATION

**Amount of ORS solution to give in first 4 to 6 hours**

<table>
<thead>
<tr>
<th>Patient’s age</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
<th>12</th>
<th>18</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>15</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s weight in kilogrammes</td>
<td>3</td>
<td>5</td>
<td>7</td>
<td>9</td>
<td>11</td>
<td>13</td>
<td>15</td>
<td>20</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Give this Much Solution For 4 -6 Hours</td>
<td>200 - 400</td>
<td>400 - 600</td>
<td>600 - 800</td>
<td>800 - 1000</td>
<td>1000-2000</td>
<td>2000-4000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Use the patient age if you do not know the weight. If the patient wants more ORS give more.

### SEVERE DEHYDRATION OR WHERE PATIENT UNABLE TO DRINK

**GUIDELINES FOR REHYDRATION THERAPY**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Type of fluid</th>
<th>Amount of fluid (kg) body weight</th>
<th>Time of Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (under 12 months)</td>
<td>i.v. Ringers lactate or half strength Darrows</td>
<td>30ml/kg</td>
<td>Within 1 hour</td>
</tr>
<tr>
<td></td>
<td>i.v. Ringers lactate or half strength Darrows</td>
<td>Followed by 40ml/kg</td>
<td>Within next 2 hours</td>
</tr>
<tr>
<td></td>
<td>ORS Solution</td>
<td>Followed by (if appropriate) 40ml/kg</td>
<td>Within next 3 hours</td>
</tr>
<tr>
<td>Older children and adults</td>
<td>i.v. Ringer's lactate</td>
<td>100ml/kg</td>
<td>Within three hours; initially as fast as possible until radial pulse is easily felt</td>
</tr>
</tbody>
</table>

### 2.8 Laxatives

#### 2.8.1 Bulk forming laxatives

These help relieve constipation by increasing faecal mass which stimulates peristalsis; the full effect may take some days to develop and patients should be told this. A balanced diet with plenty of water and fibre is important in preventing constipation.

### ISPAGHULA HUSK

**Presentation:** Granules or powder containing ispaghula husk

### SENNA

**Presentation:** Tablets containing 7.5mg sennocides.

**Indications:** Constipation

**Dose:** 1 sachet or 2 level 5ml spoonfuls in a glass of water twice daily, preferably after meals. Child 6-12 years ½ - 1 level 5ml spoonful in a glass of water.

**Side effects:** Abdominal colic and flatulence. Contraindications: Should not be given to patients with abdominal pain of unknown cause.
**BISACODYL**

**Presentation:** Tablet containing 5mg bisacodyl, Suppositories containing 10mg. Paediatric suppositories containing 5mg bisacodyl.

**Indications:** Constipation

1.1.2 Stimulant laxatives

**GLYCEROL SUPPOSITORIES**

**Presentation:** Adult size (4g) containing 2.8g glycerol. Child size (3g) containing 2.1g glycerol. Infant size (1g) containing 700mg glycerol.

**Indications:** Constipation especially when the stool is very hard

**Dose:** Oral, 5 - 10mg at night occasionally maybe increased to 15 - 20mg. Child, under 10 years 5mg. By rectum in suppositories for constipation, 10mg in the morning. Child, under 10 years 5mg. Before radiological procedures and surgery, 10mg orally at bedtime for 2 days before examination and, if necessary a 10mg suppository 1 hour before examination. Child; half the adult dose.

**Side effects:** Gripping, local irritation for suppositories, hypokalaemia and atonic non functioning colon in prolonged use.

**Caution:** intestinal obstruction.

2.8.3 Faecal softeners

**ARACHIS OIL**

**Presentation:** Enema containing arachis oil (peanut) in 130ml single dose disposable packs.

**Indications:** Constipation

**Dose:** To soften impacted stool, 130ml. The enema should be warmed before use. It is not recommended for children below 3 years. Children above 3 years reduce adult dose in proportion to body weight.

**Fleet phospho-soda**

**Presentation:** Oral solution containing sugar free sodium dihydrogen phosphate dihydrate 24.4g, disodium phosphate dodecahydrate10.8g/45ml

**Indications:** See under citramag

**Dose:** 45ml diluted with half a glass (120ml) of cool water, followed by one full glass (240ml) of cool water. Timing of doses is dependent on the time of the procedure; For morning procedure, first dose should be taken at 7.00 am and the second at 7.00 PM on the day before the procedure. For afternoon procedure, first dose should be taken at 7.00 PM on the day before and the second dose at 7.00AM on the day of the procedure. Solid food must not be taken during dosing period; clear liquids or water should be substituted for meals. Child and adolescent; Not recommended for children under 15 years old. The patient information leaflet provides more information on the usage of individual products.

**Side effects:** see under citramag

**Caution:** see under citramag

**Contraindications:** see under citramag.

**CITRAMAG**

**Presentation:** Citramag prep oral effervescent powder containing magnesium carbonate 11.57g, anhydrous citric acid 17.79g/sachet.

**Indications:** Colonic surgery, colonoscopy or radiological examination to ensure the bowel is free of solid contents.

**Dose:** Bowel evacuation for surgery or radiological examination on day before the procedure; 1 sachet between 2 - 4 PM. Child, 5 - 9 years 1/3 adult dose; over 10years and frail elderly 1/2 the adult dose.

**Side effects:** Nausea and bloating; less frequently abdominal cramps (usually transient, this can be removed by taking the drug more slowly), vomiting.

**Caution:** Pregnancy, renal impairment, heart disease, ulcerative colitis, diabetes mellitus, reflux oesophagitis, impaired gag reflex, unconscious or semiconscious or possibility of regurgitation or aspiration.

**Contraindications:** Gastrointestinal obstruction, gastric retention, gastrointestinal ulceration, perforated bowel, congestive cardiac failure, toxic colitis, toxic megacolon or ileus.

Bowel cleansing solutions

These are used before colonic surgery, colonoscopy or radiological examination to ensure the bowel is free of solid contents. They are not treatments for constipation.
Drugs acting on the central nervous system

3.1 Antipsychotic drugs

The term “antipsychotic” refers to several classes of drugs (see Table I) which includes conventional antipsychotic drugs (often referred to as “neuroleptics”) and “atypical antipsychotics”). Anti-psychotics vary in potency and propensity to induce side effects. The conventional antipsychotics are usually classified into 3 groups according to their antipsychotic potency.

The high-potency agents include haloperidol and fluphenazine, the intermediate-potency include loxapine and perphenazine and the low-potency include chlorpromazine and thioridazine. Side effects: Antipsychotic medications can cause a broad spectrum of side effects. Many are the result of pharmacological effects on the neurotransmitter systems in other regimes than the target site for the intended therapeutic effects. Common side effects include sedation, dry mouth, blurred vision, constipation, tachycardia and urinary retention, postural hypotension and tachycardia. Neurological (Extrapyramidal) side effects including medication induced parkinsonism characterised by rigidity, tremor, akinesia and bradykinesia. These symptoms arise in the early days of antipsychotic medication and are drug dependent. Dystonia characterised by the spastic contractions of discrete muscle groups.

Akathisia (characterised by somatic restlessness that is manifested subjectively and objectively. Patients complain of inner sensation of restlessness and irresistible urge to move various parts of their bodies. Objectively this is seen as increased motor activity. The most common form involves pacing and inability to sit still.

Neuroleptic Malignant Syndrome characterised by a triad of rigidity, hypothermia and autonomic instability (including hypertension and tachycardia). Tardive dyskinesia is a hyperkinetic abnormal involuntary movement disorder caused by sustained exposure to antipsychotic drugs that can affect neuromuscular function in any body region but is most commonly seen in the ‘oro-facial region’.

Other side effects include seizures, endocrine -galactorrhea, amenorrhoea, reduced fertility, impotence, metabolic- weight gain, haematological- bone marrow depression and allergic-cholestatic jaundice.

IMPLEMENTATION

Antipsychotic drugs have a wide therapeutic index. Thus, overdose is rarely fatal unless they are complicated by pre-existing medical problems or concurrent ingestion of alcohol or other medication. Clinical features of overdose are generally characterised by exaggerations of the adverse effects with respiratory depression and hypotension presenting the greatest danger.

ROUTE OF ADMINISTRATION

Administration of antipsychotic drugs can be in form of oral, short acting intramuscular injections or as long acting depot drugs. Depot drugs are helpful in the maintenance phase.

DRUG CHOICE

Different drugs differ in predominant actions and side effects. Selection is therefore influenced by the degree of sedation required and the patients susceptibility to extrapyramidal side effects. However, the differences between psychotic drugs are less important than the great variability in patients response. Moreover, tolerance to adverse effects usually develops.

DOSAGE

After an initial period of stabilisation, in most patients, the long half life of antipsychotic drugs allows the total daily dose to be given as a single dose.

WITHDRAWAL

Withdrawal of antipsychotic drugs after long-term therapy should always be gradual and monitored to avoid the risk of withdrawal syndrome or rapid relapse.
**IMPORTANT**

(1) Prescribing of more than one antipsychotic drug is not recommended.
(2) Consider potential drug interaction.
(3) Carry out ECG periodically to exclude abnormalities such as prolonged QT interval.
(4) Carry out regular pulse rate, blood pressure, temperature, ensure that the patient maintains adequate fluid balance.
(5) Increase the dose slowly and not more than once a week.
(6) Consider high dose therapy to be for limited period and review regularly. Abandon if no improvement after 3 months (return to standard dosage).

### 3.1.1 Chlorpromazine Hydrochloride

**Presentation:** Tablets containing 10mg, 25mg, 50mg, 100mg chlorpromazine hydrochloride. Syrup containing 25mg/5ml chlorpromazine hydrochloride. Injection containing 25mg/1ml chlorpromazine hydrochloride.

**Indications:** Psychosis, autism, hiccup

**Dose:** Oral, Short term adjunctive management of severe anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behaviour; 25mg 3 times a day or (75mg at night) adjusted according to response to usual maintenance dose of 75-300mg (but up to 2g may be required in psychosis). *Elderly* (or debilitated) \( \frac{1}{2} \) to \( \frac{1}{3} \) adult dose. *Child* (childhood schizophrenia and autism) 1-5 years; 5mg/kg per day every 4-6 hours (maximum dose 40mg daily). 6-12 years; \( \frac{1}{2} \) to \( \frac{1}{3} \) adult dose (maximum dose 75mg daily).

**By injection:** For relief of acute symptoms (note Caution and side effects); 25-50mg 6-8 hourly daily. Intratracic hiccup 25-50mg 3-4 times a day.

**Side effects:** Sedation, drowsiness, apathy, constipation, urine retention, tachycardia, hypotension, arrhythmia, parkinsonism, dystonia, akathisia, neuroleptic, malignant syndrome, amenorrhoea, infertility, impotence, galactorrhoea, gynaecomastia, cholestatic jaundice, pigmentary retinopathy after prolonged use, convulsions, leucopenia, weight gain and respiratory depression.

**Caution:** Parkinsonism, epilepsy, acute infections, pregnancy and breast feeding, renal and hepatic impairment, history of jaundice, leucopenia, cardiovascular, cerebrovascular and respiratory diseases, hypothyroidism, myasthenia gravis, prostatic enlargement, closed angle glaucoma, the elderly.

**Contra-indications:** Coma caused by Central Nervous System depression, bone marrow depression, phaeochromocytoma.

### THIORIDAZINE HYDROCHLORIDE

**Presentation:** Tablet containing 10mg, 25mg, 50mg thioridazine hydrochloride. Syrup containing 25mg/5ml thioridazine hydrochloride.

**Indications:** See under 3.1.1.

**Dose:** adult: 150-600mg daily (initially in divided doses) maximum dose 800mg daily for up to 4 weeks. Short term adjunctive management of psychomotor agitation, excitement, violent or dangerously impulsive behaviour 75-200mg daily. Short-term adjunctive management of severe anxiety and restlessness in the elderly 30-100mg daily.

**Side effects:** It has less extrapyramidal and sedative side effects. It is more likely to induce hypotension with increased risk of cardiotoxicity. It has marked cholinergic side effects with sexual dysfunction (retrograde ejaculation), prolonged use leads to pigmentary retinopathy.

**child:** Severe mental disorders only 1-5 years; 1mg/kg daily. 5-12 years; 75-150mg/day and in severe cases up to 300mg/day.

**Caution:** See under 3.1.1. **Contra-indications:** See under 3.1.1

### TRIFLUOPERAZINE

**Presentation:** Tablets containing 1mg, 2mg, 5mg trifluoperazine. Syrup containing 1mg/5ml trifluoperazine.

**Indications:** See 3.1.1.

**Dose:** Schizophrenia and other psychoses, short term adjunctive management of psychomotor agitation, excitement and violent or dangerous impulsive behaviour; *Adult,* initially 5mg twice daily or 10mg in modified release form, increase by 5mg after 1 week, then at intervals of 3 days according to response.

**Adult; Child:** up to 12 years; initially up to 5mg daily in divided doses and adjusted according to response, age and body weight.

Short term adjunctive management of severe anxiety 2-4mg/daily in divided doses or 2-4mg in modified release form. Increase if necessary to 6mg/daily. *Child* 3-5 years; up to 1mg/day 6-12 years to 4mg/day.

**Side effects:** It has less sedative, hypotensive, hypothermic and muscarinic side effects. Expyramidal side effects notably dystonia and akathisia are more frequent (particularly in large doses exceeding 6mg), caution in children.

**Caution:** See 3.1.1., *Children* **Contra-indications:** See 3.1.1

### HALOPERIDOL

**Presentations:** Capsule containing 500mcg haloperidol. Tablets containing 1.5mg, 5mg, 10mg haloperidol. Syrup containing 2mg/ml haloperidol. Injection containing 10mg/ml haloperidol.

**Indications:** See 3.1.1., acute mania.

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**Drugs acting on the central nervous system**
Drugs acting on the central nervous system

Dose: Oral, Adult; short term management of psychomotor agitation, excitement, violent or dangerously impulsive behaviour. Initially 3-5mg 2-3 times a day. In resistant schizophrenia up to 100mg daily adjusted according to clinical response, to a lowest effective maintenance dose of 5-10mg daily. Elderly or debilitated; initially ½ the adult dose. Child; 50mcg/kg daily in divided doses to a maximum of 10mg daily. Short term adjunctive management of severe anxiety adults 500mcg twice a day. Not recommended in children.

Injection intramuscularly 2-10mg, subsequent doses being given every 4-8 hours according to response (up to every hour if necessary) to maximum 60mg daily. Severely disturbed patients may require an initial dose of up to 30mg (not recommended in children).

Nausea and vomiting 1-2mg/day.

Side effects: See 3.1.1. The relative sedative antimuscarinic and adrenergic and extrapyramidal side effects (see Table I) such as akathisia and dystonic reactions are more frequent in thyrotoxicosis.

Contra-indications: See 3.1.1. Avoid in basal ganglia disease.

Antipsychotic Depot Injections

For maintenance therapy, long acting, depot injections of antipsychotic drugs are used because they are more convenient than oral preparations. They ensure better patient compliance. However, they may give rise to higher incidence of extrapyramidal reactions than oral preparations. Depot antipsychotics are administered by deep intramuscular injections at intervals of 1-4 weeks. Patients should first be given a test dose as undesirable side effects are prolonged. Treatment requires careful monitoring for optimum effects. Extrapyramidal side effects occur frequently. When transferring from oral to depot therapy, dosage by mouth should be gradually phased out. Not recommended in children.

Fluphenazine Decanoate

Presentation: Injection containing 25mg/ml, 100mg/ml fluphenazine decanoate

Indications: Maintenance in Schizophrenia and other psychosis

Dose: By deep intramuscular injection in the gluteal muscle test dose 12.5mg (6.5mg in the elderly) then after 4-7 days 12.5-100mg repeated at the interval of 4-35 days adjusted according to the response.

Side effects: See notes above. Extrapyramidal side effects usually appear few hours after the dose has been administered and continue for 2 days but they may be delayed. Contra-indicated in severely depressed states.
3.2 Drugs used in parkinsonism and related disorders

3.2.1 Antimuscarinic Drugs

Antimuscarinic drugs exert their antiparkinsonism effect by correcting the relative central cholinergic excess thought to occur in parkinsonism as a result of dopamine deficiency. These drugs also reduce the symptoms of drug induced parkinsonism as seen for example with antipsychotic drugs. There is no justification for giving them simultaneously with antipsychotic drugs unless parkinsonism side effects occur. Tardive dyskinesia is not improved with antimuscarinic drugs and may be made worse. No important differences exist between the many synthetic antimuscarinic drugs available but some patients tend to tolerate one better than the other. The most commonly used are benzhexol and procyclidine. Procyclidine may be given parenterally and is effective emergency treatment of acute drug dystonic reactions which may be severe.

BENZTROPINE MESYLATE

**Presentation:** Tablet containing 2mg benztpine mesylate. Injection containing 1mg/ml benztpine mesylate

**Indications:** See 3.2.1.

**Dose:** Oral; 0.5-1mg daily usually at bed time, gradually increasing to a maximum of 6mg daily. Maintenance dose; 1-4mg daily in a single dose or in divided doses. Elderly; preferably lower end of the dosage range.

**Injection:** 1-2mg intramuscularly or intravenously repeat if symptoms reappear. Elderly; preferably lower end of the dosage range

**Side effects:** See 3.2.1. causes sedation rather than

**Caution:** See 3.2.1.

**Contra-indications:** See 3.2.1.

ORPHENADRINE HYDROCHLORIDE

**Presentation:** Tablets containing 50mg orphanadrine hydrochlorideSyrup containing 50mg/5ml orphanadrine hydrochloride

**Indications:** See under benzhexol hydrochloride

**Dose:** Oral; 150mg daily in divided doses, gradually increasing to a maximum of 400mg. Elderly; preferably in lower end of dosage range.

**Side effects:** See 3.2.1., but more euphoric, may cause insomnia and porphyria

**Caution:** See 3.2.1.

**Contra-indications:** See 3.2.1.

3.3 Antidepressants

Antidepressants are used to treat depression and manic-depressive disorders. Other methods of treatment include psychotherapy, which may be all that is required for the milder forms of depression, and electroconvulsive therapy (ECT) which is used in severe depression or where antidepressants have failed.

**Classification**

The two traditional categories of tricyclic antidepressants (typified by amitriptyline) and monoamine oxidase inhibiting antidepressants (MAOIs) (typified by phenelzine) continue to be widely used.

Of late there is recent generation of antidepressants called selective serotonin re-uptake inhibitors (SSRIs) typified by fluoxetine which have come into use. Imipramine and amitriptyline despite having marked antimuscarinic or cardiac side effects than
compounds such as the SSRIs and MAOIs, are well established and relatively safe and effective to treat depression.

### Choice

There is a relatively widespread view that certain types of depression respond preferentially to certain classes of antidepressants. Tricyclic and related antidepressants are usually considered to be more effective than monoamine oxidase inhibitors in major depression or endogenous depression, whereas the converse may be true in atypical depression or reactive depression. Choice of an antidepressant within a given class lies therefore, not primarily in supposed efficacy, but in the ability to select or avoid an agent possessing known pharmacological properties unrelated to antidepressant action. For example, some tricyclics possess marked sedative properties and if given at night this effect may be of particular advantage in patients with insomnia, whereas drugs with less of a sedative action or those with a stimulant action may be preferred in apathetic or hypersonniac patients. Additionally, some antidepressants appear to have less of an antimuscarinic action or exhibit reduced cardiotoxicity or epileptogenic potential, factors which may be of importance in individual patients.

### Withdrawal

All antidepressants should generally be withdrawn gradually in order to prevent withdrawal symptoms. It should be remembered that a characteristic feature of several types of depression is that remissions and relapses are likely to occur and that re-introduction of therapy may become necessary.

#### AMITRIPTYLINE HYDROCHLORIDE

**Presentation:** Tablets containing 10mg, 25mg, 50mg amitriptyline hydrochloride. Syrup containing 25mg/5ml amitriptyline hydrochloride. Injection containing 10mg/ml amitriptyline hydrochloride.

**Indications:** Depression (especially where sedation is needed), nocturnal enuresis.

**Dose:** Oral, Depression initially 75mg daily (adolescents and elderly 30-75mg daily) in divided or single doses at bedtime to a maximum dose of 150mg daily. Maintenance dose 50-100mg daily. Not recommended in children under 16 years. Nocturnal enuresis, Child; 7-10 years 10-20mg daily, 11-16 years 25-50mg daily at night (maximum period of treatment including gradual withdrawal is 3 months).

**Injection,** depression; 10-20mg 4 times daily (not recommended in children under 16 years)

**Side effects:** Sedation, dry mouth, blurred vision, nausea, constipation, difficulty in micturition, arrhythmias, postural hypotension, tachycardia, sweating, syncope, (in high doses), urticaria, hypomania/mania, confusion (in elderly).

Increased appetite and weight gain, testicular enlargement, fever.

**Caution:** History of epilepsy, hepatic disease (avoid if severe) thyroid disease, phaeochromocytoma, mania and psychosis (may aggravate psychosis), urine retention, concurrent electroconvulsive therapy (ECT), anaesthesia (increase the risk of arrhythmia and hypotension), cardiac arrhythmias and porphyria, caution in elderly. Avoid abrupt withdrawal.

**Contra-indications:** Severe liver disease; manic phase; cardiac arrhythmias especially heart block, recent myocardial infarction

#### IMIPRAMINE HYDROCHLORIDE

**Presentation:** Tablet containing 10mg, 25mg imipramine hydrochloride. Syrup containing 25mg/5ml imipramine hydrochloride

**Indications:** See 3.3.1.

**Dose:** Depression initially up to 75mg daily in divided doses increasing gradually to 150-200mg daily (up to 150mg may be given as a single dose at bedtime). Maintenance dose; 50-100mg daily. Elderly; initially 10mg/day increasing gradually to 30-50mg daily. Child: not recommended for depression. Nocturnal enuresis, 7 years; 25mg daily. 8-11 years; 25-50mg daily. Over 11 years 50-75mg daily at bedtime. Maximum period of treatment (including gradual withdrawal) is 3 months.

**Caution:** See 3.3.1

**Contra-indications:** See 3.3.1. Less sedating than amitriptyline.

#### LITHIUM CARBONATE

**Presentation:** See under dose

**Indications:** Treatment and prophylaxis of mania, manic depressive illness and recurrent depression.

**Dose:** (Camcolit, Tablet: 250mg and 400mg) It must be adjusted to attain a plasma concentration of 0.4-1.0mmol Li+ / L. 12 hours after the preceding dose, on the 4th and 7th day of treatment, then weekly until dosage has remained constant for 4 weeks and every 3 months thereafter. Initially, the doses are in divided doses but after a stable plasma concentration, single dose per day is preferable. Initially 1.5 - 2g per day (Elderly 0.5-3g per day). Prophylaxis; 0.5 - 1.2g per day (Elderly 0.5 – lg per day)

Not recommended in children. Camcolit 250mg should be given in divided doses, whereas Camcolit 400 may be given either in single or divided doses.

**Side effects:**

1. Common (relatively harmless)
   - Nausea, vomiting, mild diarrhoea, fine tremors, weight gain and oedema (may respond to dose reduction).
2. **Acute (Suggestive of Lithium Toxicity)**
   - (i) > 1.5mmol Li+ /L severe nausea, vomiting, anorexia and diarrhoea, coarse tremor, drowsiness, vertigo, dysartria, cardiac arrhythmias, blurred
vision, sluggishness to giddiness, ataxia and lack of co-ordination.

(ii) > 2mmol Li⁺/L: hyperreflexia, hyperextension of limbs, convulsions, toxic psychoses, syncope, circulatory failure and occasionally death (withdraw the drug).

(3) Chronic (Long term effects of gradual onset) hypothyroidism, diabetes insipidus, hyperuricaemia and non toxic goitre. Caution: Lithium has a narrow therapeutic/toxic index therefore; it must be administered where facilities to monitor plasma concentration are available. The normal Lithium plasma concentration range is 0.4 - 1.0 mmol L⁻¹/1. Once stable regime has been attained, measurement of Lithium plasma concentration must be done regularly (3 monthly). Thyroid, renal and cardiac function tests must be done before starting treatment and thereafter annually. Lithium should only be used in low doses, and under frequent supervision in patients who have thyroid, renal and cardiac impairment. A positive fluid and electrolyte balance must be maintained particularly sodium. Thus use with caution in diabetes insipidus, Addison's disease and patients on diuretics.

Lithium used in the 1st trimester of pregnancy is said to be teratogenic but is safe after this period. Use with caution in breast feeding and myasthenia gravis (reduce the dose).

### 3.4 Antimanic drugs

- **Chlorpromazine**: See 3.1.1
- **Haloperidol**: See 3.1.4
- **Lithium Carbonate**: See 3.3.3
- **Carbamazepine**: See 3.5.1

### Carbamazepine

**Presentation:** Tablet containing 100mg, 200mg and 400mg carbamazepine. Liquid, sugar free containing 100mg/5ml carbamazepine. Suppositories containing 125mg carbamazepine.

**Indications:** Partial and generalised tonic-clonic seizures, temporal lobe epilepsy, idiopathic trigeminal neuralgia. Prophylaxis of manic depressive illness unresponsive to lithium.

**Dose:** Oral, epilepsy; initially 100 - 200mg 1 - 2 times daily, increased slowly to usual dose of 0.8 - 1.2g daily in divided doses. In some cases 1.6 - 2g daily may be needed. Elderly; reduce initial dose. Child; daily in divided doses, up to 1 year 100-200mg, 1 - 5 years 200 - 400mg, 5 - 10 years 400 - 600mg, 10 - 15 years 0.6 - 1g.

Trigeminal neuralgia, initially 100mg 1 - 2 times daily (some patients may require higher initial dose), increased gradually according to response; usual dose 200mg 3 - 4 times daily, up to 1.6g daily in some patients.

Prophylaxis of bipolar disorder, unresponsive to lithium, initially 400mg daily in divided doses increased until symptoms are controlled, usual range 400 - 600mg daily, maximum 1.6g daily.

**Side effects:** Nausea, vomiting, dizziness, bone marrow depression, Steven Johnson's syndrome, impotence.

**Caution:** Hepatic, renal and cardiac diseases and glaucoma

**Contra-indications:** History of bone marrow depression, porphyria, AV conduction abnormalities.

### ETHOSUXIMIDE

**Presentation:** Capsule containing 250mg ethosuximide. Syrup containing 250mg/5ml ethosuximide

**Indications:** Absence seizures

**Dose:** Adult and child over 6 years initially, 500mg, increased by 250mg at intervals of 4 - 7 days to usual dose of 1 - 1.5g daily; occasionally up to 2g daily maybe needed. Child up to 6 years initially 250mg daily increased gradually to usual dose of 20mg/kg daily.

NOTE: Plasma concentration for optimum response 40 - 100mg/litre (500 - 700micromol/litre)

**Side effects:** Anorexia; nausea, vomiting, agitation, drowsiness, headache, lethargy, parkinsonism and psychosis, Steven John syndrome, …..disorders

**Caution:** Renal and hepatic impairment

### PHENOBARBITONE

**Presentation:** Tablet containing 15mg, 30mg phenobarbitone. Syrup containing 15mg/5ml phenobarbitone. Injection containing 200mg/1ml

**Indications:** All forms of epilepsyexcept absence
seizures; status epilepticus.

**Dose:** Oral, 60 - 180mg at night. Child; 5.8mg/kg daily. Intramuscular injection, 200mg repeated after 6 hours if necessary; Child, 15mg/kg. Status epilepticus, (dilute injection in 10 with water for injection) 10mg/kg at a rate of not more than 10mg/minute, maximum 1g.

**Side effects:** Fatigue, listlessness, tiredness, depression, Restlessness, insomnia, distractability, aggression, poor memory, decreased libido, impotence, folate deficiency, neonatal haemorrhage, hypocalcaemia and osteomalacia.

**Caution:** Elderly, debilitated, avoid long term usage in children, renal and hepatic impairment, respiratory depression, pregnancy and breast feeding.

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**PHENYTOIN SODIUM**

**Presentation:** Tablet containing 50mg phenytoin sodium. Capsule containing 25mg, 50mg, 100mg phenytoin sodium. Syrup containing 30mg/5ml phenytoin sodium. Injection containing 50mg/ml phenytoin sodium in 5ml ampoule.

**Indications:** All forms of epilepsy except absence seizures, trigeminal neuralgia, status epilepticus.

**Dose:** Orally, Seizures; initially 3 - 4mg/kg daily or 150 - 300mg daily (as a single dose or in two divided doses) increased gradually as necessary; usual dose 200 - 500mg daily (exceptionally higher doses may be used ). Child; initially 5mg/kg daily in 2 divided doses, usual dose range 4 - 8mg/kg daily (maximum 300mg).

Status epilepticus, by intravenous infusion 15 - 18mg/kg at a rate not exceeding 50mg/minute as a loading dose. Maintenance dose 100mg every 6 - 8 hours, monitored by measurement of plasma concentration. Child; 15mg/kg as a loading dose (neonates 15 20mg/kg at a rate of 1 - 3mg/minute).

**NOTE:** Plasma concentration for optimum response 10 -20mg/litre (40 - 80micrpmpl/litre).

**Counselling:** Preferably take with or after food.

**Side effects:** Anorexia, dyspepsia, nausea, vomiting, aggression, ataxia, cognitive impairment, depression, drowsiness, headache, nystagmus, paradoxical seizures, gum hypertrophy, coarse facies, hirsutism, megaloblastic anaemia, hypoglycaemia, osteomalacia, neonatal haemorrhage, Steven Johnson syndrome, aplastic anaemia, thrombocytopenia, agranulocytosis, peripheral neuropathy, cardiovascular depression.

**Caution:** Hepatic impairment

**Contraindications:** Active liver disease, family history of severe hepatic dysfunction.

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**SODIUM VALPROATE**

**Presentation:** Tablet containing 200mg sodium valproate. Syrup containing 200mg/5ml sodium valproate.

**Indications:** Primary generalised epilepsies, Dose: orally, initially 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg/day at 3 day intervals to a maximum of 2.5g daily in divided doses, usual maintenance 1 - 2g daily (20 - 30mg/kg daily). Child, up to 20kg initially 20mg/kg daily in divided doses, maybe increased provided plasma concentrations are monitored partial seizures, prophylaxis of febrile convulsions. (above 40mg/kg also monitor clinical chemistry and haematological parameters). Over 20kg, initially 400mg daily in divided doses increased until control (usually 20 - 30mg/kg daily) maximum 35mg/kg daily.

By intravenous injection (when oral valproate is not possible) over 3 - 5 minutes 400 - 800mg (up to 10mg/kg) followed by intravenous infusion up to maximum 2.5g daily. Child; usually 20 - 30mg/kg daily.

**Side effects:** Anorexia, dyspepsia, nausea, vomiting, hair loss, rash, peripheral oedema, drowsiness and tremors.

**Contraindications:** All active liver diseases and family history of severe hepatic dysfunction, first trimester of pregnancy.

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**CLONAZEPAM**

**Presentation:** Tablet containing 500mg clonazepam. Injection containing 1mg/1ml clonazepam

**Indications:** Myoclonic and generalised tonic-clonic seizures, status epilepticus.

**Dose:** 1mg (elderly 500mcg) initially at night for 4 nights, increased over 2 - 4 weeks to a usual maintenance dose of 4 - 8mg daily in divided doses. Child, up to 1 year 250mcg increased as above to 0.5 1mg, 1 - 5 years 250mcg increased to 1 - 3mg, 5 - 12 years 500mcg increased to 3 - 6mg.

**Side effects:** Fatigue, dizziness, drowsiness, ataxia, irritability, aggression, hyperkinesia, hypersalivation, weight gain, muscle hypotonia.

**NOTE:** drowsiness may affect performance of skilled tasks such as driving.

**Caution:** Renal, hepatic and respiratory disease, pregnancy and breast feeding, elderly and debilitated, porphyria, avoid sudden withdrawal.

**Contraindications:** Respiratory depression and acute pulmonary insufficiency.

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### 3.6.1 Hypnotics and anxiolytics

Prescribing of hypnotics and anxiolytics is widespread but dependence (physiological and psychological) and tolerance occurs. This may lead to difficulty in withdrawing the drug after the patient has been taking it for a few weeks. Hypnotics and anxiolytics should not be prescribed indiscriminately and should never be used for long term treatment. They should be restricted to short courses to alleviate acute conditions after causal factors have been established. Benzodiazepines are the most commonly used anxiolytics and hypnotics.
**PARADOXICAL EFFECTS**

An increase in hostility and aggression may be observed in patients taking benzodiazepines. The effects will range from talkativeness and excitement to aggressive and antisocial acts. Adjustment of dose either upwards or downwards usually effectively controls these acts.

Hypnotics and anxiolytics impair judgement. This affects the ability to drive or perform skills requiring concentration. Withdrawal of these drugs should be gradual as abrupt withdrawal may cause withdrawal effects such as confusion, toxic psychosis or delirium.

**3.6.1.1 Hypnotics**

Before prescribing a hypnotic, the cause of insomnia should be established and the causative factors should be attended to appropriately. Hypnotics should not be prescribed for more than 3 weeks (preferably 1 week) in short term insomnia while one or two doses are adequate in transient insomnia.

Hypnotics should never be prescribed in children except in cases such as in night terrors and sleepwalking. They should also be avoided in the elderly, as they are more at risk of ataxia and confusion.

**CHLORMETHIAZOLE**

**Presentation:** Capsule containing 192mg chlormethiazole base. Syrup containing 250mg/5ml chlormethiazole edisylate (1 capsule = 5ml syrup). Intravenous infusion containing 8mg/ml chlormethiazole edisylate.

**Indications:** Hypnosis (especially useful in the elderly as it does not give hangover). It is also used in status epilepticus and sedation during regional anaesthesia.

**Dose:** Oral, severe insomnia in the elderly; 1 – 2 capsules or 5 – 10ml syrup at bedtime.

**Side effects:** Nasal congestion and irritation, conjunctival irritation, headache, rarely paradoxical excitement, confusion, dependence, gastro-intestinal disturbances, rash.

**Caution:** Cardiac and respiratory disease, Contrerenal and hepatic insufficiency, history of drug abuse, marked personality disorders.

**Contra-indications:** Acute pulmonary insufficiency, alcohol dependent patients who are still continuing with alcohol drinking.

**LORAZEPAM**

**Presentation:** Tablets, lorazepam 1 mg. Injection, lorazepam 4 mg/mL

**Indications** short-term use in anxiety or insomnia; status epilepticus; peri-operative

**Cautions:** see under Diazepam; short acting; when given parenterally, facilities for managing respiratory depression with mechanical ventilation must be at hand

**Contra-indications** see under Diazepam

**Dose:** By mouth, anxiety, 1–4 mg daily in divided doses;

**ELDERLY** (or debilitated) half adult dose

**Insomnia** associated with anxiety, 1–2 mg at bedtime;

**CHILD** not recommended

**Note:** Only use intramuscular route when oral and intravenous routes not possible.

**NITRAZEPAM**

**Presentation:** Tablet containing 5mg nitrazepam. Oral suspension containing 2.5mg/5ml nitrazepam.

**Indications:** Insomnia (short term)

**Dose:**

- **Adult;** 5 – 10mg taken 30 minutes before bedtime. Elderly or debilitated; 2.5 – 5mg. Not recommended in children.

**Side effects:** Drowsiness, light-headedness the following day, confusion and ataxia (particularly in the elderly),

**Caution:** Should never be used for long term treatment, respiratory disease, muscle weakness, history of drug abuse, pregnancy, breast feeding, personality disorders, hepatic and renal impairment, porphyria. Drowsiness may persist the following day and hence affect performance of skilled tasks such as driving etc.

**Contra-indications:** Respiratory depression, pulmonary insufficiency, myasthenia gravis, severe hepatic impairment.

**ANXIOLYTICS**

Anxiolytics are widely prescribed and are useful in alleviating anxiety states. However their use in most of these instances is unjustified. They should not be used to treat depression or chronic psychosis. Treatment should be limited to the lowest possible dose and for the shortest possible
Drugs acting on the central nervous system

3.7 Drugs used in alcohol dependence and abuse

Sedatives are used to reduce symptoms of alcohol withdrawal and if administered promptly can prevent further development of more serious symptoms, like seizures and delirium tremens. Benzodiazepines and chlormethiazole are the most widely used. To prevent dependence these drugs should only be used for short periods.

Once the initial acute withdrawal symptoms have been treated, long-term abstinence has to be maintained. Disulfiram can be used as an adjunct to treat alcohol dependence. A patient who takes alcohol after taking adequate doses of disulfiram will experience severe and unpleasant reactions, which it is hoped, will deter the patient from further ingesting alcohol. These include flushing of the face, palpitations, tachycardia, throbbing headache, nausea and vomiting. With large doses of alcohol the following will also occur arrhythmias, hypotension and collapse. It must be noted that even small amounts of alcohol contained in some medications may be enough to precipitate a reaction.
achieve the lowest possible rate to maintain shallow sleep and adequate spontaneous respiration. Urgent deep sedation (this should only be administered under direct medical supervision); 40 – 100ml (320 – 800mg) over 3 – 5 minutes then reduced to maintenance as indicated above. (See caution on intravenous administration below).

**Side effects:** Nasal congestion and irritation, conjunctival irritation, headache, rarely paradoxical excitement, confusion, dependence, gastro-intestinal disturbances, rash.

**Caution:** Cardiac and respiratory disease, renal and hepatic insufficiency, history of drug abuse, marked personality disorders, pregnancy and breast feeding, elderly, renal impairment, avoid prolonged use and abrupt withdrawal thereafter.

**Special caution in intravenous infusion:** Resuscitation facilities must be available. Rapid infusion should only be given under direct medical supervision. During continuous infusion induced sleep may lapse into unconsciousness and patient must be kept under constant observation.

**Contra-indications:** Acute pulmonary insufficiency, alcohol dependent patients who are still continuing with alcohol drinking.

### DIAZEPAM

**Presentations:** See 3.5.1.1.

**Indications:** Acute alcohol withdrawal symptoms. For other indications see 3.5.1.1.

**Dose:** 10mg repeated if necessary after not less than 4 hours

**Side effects:** See 3.5.1.1.

**Caution:** See 3.5.1.1.

**Contra-indications:** See 3.5.1.1

### DISULFIRAM

**Presentations:** Tablet containing 200mg disulfiram maleate. Syrup containing 5mg/5ml disulfiram maleate.

**Indications:** Adjunct in the treatment of chronic alcohol dependence

**Dose:** (under specialist supervision) 800mg as a single dose on first day, reducing over 5 days to 100 – 200mg daily. It should not be continued for more than 6 months without review.

**Side effects:** Initially drowsiness and fatigue, nausea, vomiting, halitosis, reduced libido, rarely psychotic reactions, allergic dermatitis, peripheral neuritis, hepatic cell damage.

**Caution:** Alcohol should not be consumed at least 24 hours before giving disulfiram. Hepatic or renal impairment, respiratory disease, diabetes mellitus, epilepsy. Patients must be warned of unpredictable or severe alcohol/disulfiram reactions. These reactions can occur from 10 minutes after administration and last for several hours. Patients must be warned not take any alcohol at all. They should also be warned of the presence of alcohol in certain foods and remedies and toiletries. Alcohol should not be consumed for 1 week after taking treatment.

**Contra-indications:** Cardiac failure, coronary artery disease, history of cerebrovascular accident, psychosis, hypertension, severe personality disorders, pregnancy, breast feeding.

### THIAMINE (B1) See 11. 1.8 (page 103)

### 3.8 Drugs used for the treatment of nausea and vomiting

Anti-emetics should only be prescribed when the cause of the vomiting is established. This is particularly important in children as the symptomatic relief may affect accurate diagnosis. They may not be necessary and may be harmful in cases where the cause of emesis can be treated. If nausea treatment is indicated the choice of the drug will depend on the aetiology of the illness.

Nausea in the first trimester of pregnancy does not require drug treatment. Occasionally when vomiting becomes severe an antihistamine may be required. If symptoms do not subside in 48 hours then specialist opinion must be sought.

### DOMPERIDONE

**Presentations:** Tablet containing 10mg domperidone maleate. Syrup containing 5mg/5ml domperidone maleate.

**Indications:** Nausea and vomiting in gastro-intestinal disorders and during treatment with cytotoxic drugs.

**Dose:** Nausea and vomiting, oral; 10 – 20mg every 4 – 8 hours. Maximum period of treatment 2 weeks. Child, nausea and vomiting following cytotoxic therapy or radiotherapy; 200 – 400mcg/kg body weight every 4 - 8 hours.

**Side effects:** Increased prolactin concentrations, reduced libido, rashes and other allergic reactions, acute dystonic reactions.

**Caution:** Renal impairment, pregnancy and breast feeding.

**Contra-indications:** Routine prophylaxis of postoperative vomiting or chronic administration.

### ONDANSETRON

**Presentation:** tablet, ondansetron (as hydrochloride) 4 mg, Injection, ondansetron (as hydrochloride) 2 mg/mL, Syrup, sugar-free, strawberry-flavoured, ondansetron (as hydrochloride) 4 mg/5 mL

**Suppositories,** ondansetron 16 mg,

**Indications** see under Dose

**Dose** Moderately emetogenic chemotherapy or radiotherapy, by mouth, 8 mg 1–2 hours before treatment or by rectum, 16 mg 1–2 hours before
Drugs acting on the central nervous system

3

**METOCLOPRAMIDE**

**Presentation:** Tablet containing 10mg metoclopramide hydrochloride. Oral solution containing 5mg/5ml metoclopramide hydrochloride. Injection containing 5mg/ml metoclopramide hydrochloride.

**Indications:** Nausea and vomiting particularly in gastro-intestinal disorders and in treatment with cytoxotics or radiotherapy.

**Dose:** Oral or by intramuscular or intravenous injection, *adults:* 10mg (5mg in those below 60kg) 3 times daily. *Child,* up to 1 year; 1mg twice daily. 1 – 3 years; 1mg 2 – 3 times daily. 3 – 5 years; 2mg 2 – 3 times daily. 5 – 9 years; 2.5mg 3 times daily. 9 – 14 years; 5mg 3 times daily.

**Side effects:** Diarrhea, drowsiness, extra-pyramidal effects especially in children and young adults.

**Caution:** Renal and hepatic impairment, elderly, children and young adults, pregnancy and breast feeding, porphyria.

**Contra-indications:** Undiagnosed nausea and vomiting especially in children and young adults.

**PROCHLORPERAZINE**

**Presentation:** Tablet containing 5mg, 25mg prochlorperazine maleate.

**Indications:** Severe nausea, vomiting, vertigo.

**Dose:** *Adults:* 20mg initially, then 10mg after 2 hours. Prevention; 5 – 10mg 2 – 3 times daily. *Child* (over 10kg only); 250mcg/kg body weight 2 – 3 times daily.

**Side effects:** Dry mouth, drowsiness, extrapyramidal effects may occur in children, young adults and in the elderly.

**Caution:** liver dysfunction, cardiac insufficiency, epilepsy, pregnancy.

**Contra-indications:** Children less than 10kg, depression, coma caused by Central Nervous System depressants.

**PROMETHAZINE**

**Presentation:** Tablet containing 10mg, 25mg promethazine hydrochloride. Syrup containing 5mg/5ml promethazine hydrochloride. Injection containing 25mg/ml promethazine hydrochloride.

**Indications:** Nausea, vomiting, vertigo, allergies, pre-operative medication.

**Dose:** *Adults:* 20 – 50mg daily. *Child* up to 2 years; not recommended. 2 – 5 years; 5 – 15mg daily. 5 – 10 years; 10 – 25mg daily.

**Side effects:** Drowsiness

**Caution:** Epilepsy, hepatic disease, glaucoma

**Contra-indications:** Porphyria, severe hepatic disease

**TRIFLUOPERAZINE**

**Presentation:** Tablet containing 1mg, 5mg trifluoperazine hydrochloride. Oral solution containing 5mg/5ml trifluoperazine hydrochloride.

**Indications:** Severe nausea and vomiting.

**Dose:** *Oral:* 2 – 4mg daily in divide doses, maximum 6mg daily. *Child;* 3 – 5 years; up to 1mg daily. 6 – 12 years; up to 4mg daily.

**Side effects:** Extrapyramidal symptoms, drowsiness.

**Caution:** Cardiovascular and cerebrovascular disease, parkinsonism, epilepsy, respiratory disease, acute infections, pregnancy and breast feeding, renal and hepatic impairment (avoid if severe), myasthenia gravis, elderly, children, avoid...
abrupt withdrawal.

**Contra-indications:** Bone marrow depression, coma caused by CNS depressants.

### 3.9 Analgesics

#### 3.1.1 Non opioid analgesics

The non opioid drugs e.g. Acetyl salicylic acid and paracetamol are more suitable for pain in musculoskeletal conditions whereas opioid analgesics are more suitable for severe visceral pain. Acetyl salicylic acid has anti-inflammatory properties and is an anti-pyretic. Gastric irritation may be a problem and this is minimised by taking it after food. Acetyl salicylic acid interacts with a number of other drugs such as other analgesics (NSAIDs), antacids, adsorbents, cytotoxics, diuretics, antiepileptics and antiocoagulants (particularly its hazardous interaction with warfarin).

Paracetamol is similar in efficacy to acetyl salicylic acid but has weak anti-inflammatory activity. Overdose with paracetamol is of particular danger as it may cause hepatic damage, which may not be apparent for 4 to 6 days.

Anti-inflammatory analgesics are particularly useful in chronic disease accompanied by pain and inflammation. Other uses include dysmenorrhoea and pain caused by secondary tumours.

**Acetyl Salicylic Acid (Aspirin)**

**Presentation:** Tablet containing 75mg, 300mg acetyl salicylic acid.

**Indications:** Mild to moderate pain, pyrexia, prophylaxis of cerebrovascular disease or myocardial infarction (secondary prevention of thrombotic cerebrovascular or cardiovascular disease), inflammatory conditions.

**Dose:** Anti-inflammatory/analgesic; **Adults:** 300 – 900mg every 4 – 6 hours when necessary, maximum: 4g daily. For secondary prevention of thrombotic cerebrovascular or cardiovascular disease; 75 – 300mg daily. After myocardial infarction; 150mg daily. Following bypass surgery; 75mg or 100mg daily (low dose).

**Side effects:** Generally mild and infrequent but high incidence of gastro-intestinal irritation, easy bleeding, bronchospasm and skin reaction in hypersensitive patients.

**Caution:** Asthma, allergic disease, impaired renal or hepatic function, dehydration and pregnancy.

**Contra-indications:** Gastro-intestinal ulceration, children under 12 years (except for juvenile arthritis) due to association with Reye’s syndrome, breastfeeding, haemophilia and other bleeding disorders, history of hypersensitivity to aspirin and other NSAIDS includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or other NSAIDS, concurrent anticoagulant therapy.

**PARACETAMOL**

**Presentation:** Tablet containing 500mg paracetamol, syrup (paediatric) containing 120mg/5ml paracetamol.

**Indications:** Mild to moderate pain, pyrexia. Alternative for patients who are sensitive to acetyl salicylic acid.

**Dose:** **Adult:** 500mg to 1g every 4 – 6 hours., maximum 4g daily. **Child:** under 3 months (on doctor’s advise only) 10mg/kg body weight. 3 months to 1 year; 60 – 120mg. 1 – 5 years; 120 – 250mg. 6 – 12 years; 250 – 500mg. These doses are repeated every 4 – 6 hours (maximum 4 doses in 24 hours).

**Side effects:** Liver damage on prolonged use or overdose. (See section 16)

**Caution:** Impaired kidney or liver function, alcoholism.

**IBUPROFEN**

**Presentation:** Tablet containing 200mg, 400mg Ibuprofen, syrup containing 100mg/5ml Ibuprofen.

**Indications:** Fever and pain in children, mild to moderate pain including dysmenorrhoea, postoperative analgesia. (see also section 14)

**Dose:** **Adult:** initially 1.2 – 1.8g daily in 3 – 4 divided doses preferably after food; increased if necessary to maximum 2.4g daily. Maintenance dose of 0.6 – 1.2g daily may be adequate. see Not recommended for children under 7kg.

**Side effects:** see notes above (section 3.9.1.)

**Caution:** see notes above (section 3.9.1.)

**Contra-indications:** History of hypersensitivity to acetyl salicylic acid or any other NSAID.

#### 3.1.2 Opioid analgesics

Opioid analgesics are used to relieve moderate to severe pain particularly of visceral origin.

**Caution:** Drugs in this group should not be administered repeatedly when used for acute pain as dependence and tolerance occurs.

**Side effects:** Most common are nausea, vomiting, constipation and drowsiness. Larger doses produce respiratory depression and hypotension. Opioid analgesics interact with a number of drugs notably anti-depressants, anti-epileptics,
Drugs acting on the central nervous system

3.1.3 Antimigraine drugs

Most migraine headaches respond to non opioid analgesics such as acetylsalicylic acid or paracetamol. Ergotamine is used in patients who do not respond to non opioid analgesics. It relieves migraine by constricting cranial arteries but visual and other prodromal symptoms are not affected by the prescriber.

**Indications:** Relief of severe persistent pain, acute pulmonary oedema, pre-operative analgesia.

**Dose:** Subcutaneous or intramuscular injection; *Adult:* 5 to 20mg as required every 4 hours. *Child:* up to 1 month; 0.15mg/kg body weight. 1 – 12 months; 0.2mg/kg body weight. 1 – 5 years; 2.5 – 5mg/kg body weight. 6 – 12 years; 5 – 10mg/kg body weight. By slow intravenous injection; quarter to half corresponding intramuscular dose.

**Myocardial infarction:** by slow intravenous injection (2mg/minute), 10mg followed by a further 5 – 10mg if necessary. Acute pulmonary oedema; by slow intravenous injection (2mg/minute), 5 – 10mg. *Oral:* Approximately double corresponding intramuscular dose.

**Side effects:** see notes above, cough suppression, urinary retention, dry mouth, sweating, facial flushing, tolerance, vertigo, bradycardia, palpitations, postural hypotension, hypothermia, hallucinations, mood changes, dependence, miosis, urticaria and pruritis.

**Caution:** see notes above, patients taking MAOIs, pregnancy and breast feeding. Drug dependence occurs easily.

**Contra-indications:** Concomitant use with tranquilisers.

**MORPHEINE**

**Presentation:** Tablet containing 15mg morphine hydrochloride in 5ml of chloroform water. Tablet containing 10mg, 20mg morphine sulphate. Suppository containing 15mg morphine sulphate or hydrochloride. Injection containing 10mg/ml morphine sulphate.

*Note:* Both the strength of the suppositories and the morphine salt contained in them must be specified by the prescriber.

**Indications:** Relief of severe persistent pain, acute pulmonary oedema, pre-operative analgesia.

**Dose:** Subcutaneous or intramuscular injection; *Adult:* 5 to 20mg as required every 4 hours. *Child:* up to 1 month; 0.15mg/kg body weight. 1 – 12 months; 0.2mg/kg body weight. 1 – 5 years; 2.5 – 5mg/kg body weight. 6 – 12 years; 5 – 10mg/kg body weight. By slow intravenous injection; quarter to half corresponding intramuscular dose.

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**Caution:** see notes above, patients taking MAOIs, pregnancy and breast feeding. Drug dependence occurs easily.

**Contra-indications:** Concomitant use with tranquilisers.

**PETRIDINE**

**Presentation:** Tablet containing 25mg, 50mg pethidine hydrochloride. Injection containing 50mg/ml pethidine hydrochloride.

**Indications:** Moderate to severe pain, obstetric analgesia and operative analgesia. Not suitable for severe continuing pain.

**Dose:** *Oral;* *Adult:* 50 – 150mg every 4 hours. *Child;* 0.5 – 2mg/kg body weight. 0.5 – 2mg/kg body weight. 1 – 12 months; 0.5 – 2mg/kg body weight. 1 – 12 months; 0.5 – 2mg/kg body weight. Maximum 400mg in 24 hours.

**Side effects:** see notes above.convulsions reported in overdosage. Avoid in acute abdomen, paralytic ileus, head injury, raised intracranial pressure (affected papillary response). Less constipating than morphine.

**Caution:** see notes above

**Contra-indications:** Renal impairment.

**DIHYDROCODEINE**

**Presentation:** Tablet containing 30mg dihydrocodeine tartrate. Syrup containing 10mg/ml dihydrocodeine tartrate. Injection containing 50mg/ml dihydrocodeine tartrate.

**Indications:** Moderate to severe pain

**Dose:** *Oral;* *Adult;* 30 – 60mg every 4 hours when necessary to a maximum of 240mg daily. *Child,* 1 – 12 years, 3mg/kg body weight daily in divided doses.

**Side effects:** caution, and contra-indications: see notes above. Use of cough suppressants containing codeine or other similar opioid analgesics is generally not recommended in children and should be avoided altogether in those under 1 year.

**CODEINE**

**Presentation:** Tablet containing 15mg codeine phosphate. Syrup containing 25mg/5ml codeine phosphate.

**Indications:** Mild to moderate pain.

**Dose:** *Adult;* 30 – 60mg every 4 hours when necessary to a maximum of 240mg daily. *Child,* 1 – 12 years , 3mg/kg body weight daily in divided doses.

**Side effects:** caution, and contra-indications: see notes above. Use of cough suppressants containing codeine or other similar opioid analgesics is generally not recommended in children and should be avoided altogether in those under 1 year.

**Morphine**

Morphine is the most valuable for severe pain although it causes nausea and vomiting when used frequently. It also gives a state of euphoria and mental detachment. It is the treatment of choice for oral treatment of severe pain in terminal care.

Codeine is effective in relieving mild to moderate pain but is too constipating for long term use. Dihydrocodeine has analgesic efficacy similar to codeine.

Pethidine produces prompt but short lasting analgesia. It has less constipating effect than morphine but is less potent. It is not suitable for severe continuing pain but is useful in labour and in neonates.

**anxiolytics, alcohol (see appendix 2).**

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Codeine is effective in relieving mild to moderate pain but is too constipating for long term use. Dihydrocodeine has analgesic efficacy similar to codeine.

Pethidine produces prompt but short lasting analgesia. It has less constipating effect than morphine but is less potent. It is not suitable for severe continuing pain but is useful in labour and in neonates.
and vomiting may be made worse. Repeated administration may cause habituation. Headache may be provoked by either chronic overdosage or rapid withdrawal of the drug.

### ERGOTAMINE

**Presentation:** Tablet containing 1mg, 2mg ergotamine tartrate.

**Indications:** Acute attacks of migraine unresponsive to analgesics.

**Dose:** 1 – 2mg at onset repeated after 30 minutes if necessary. Maximum 8mg in 24 hours at intervals of not less than 4 days. Maximum 10 tablets per week.

**Side effects:** Parasthesia of fingers and toes, nausea, vomiting, abdominal pain, and muscular cramps.

**Caution:** Withdraw treatment immediately if numbness or tingling of extremities develops, should not be used for migraine prophylaxis, if vomiting worsens, may add an anti-emetic.

**Contra-indications:** Pregnancy and peripheral vascular disease.

### METHYLPHENIDATE

**Presentation:** Tablet (scored) containing 5mg, 10mg, 20mg methylphenidate hydrochloride.

**Indications:** Attention deficit hyperactivity disorder when remedial measures alone prove insufficient.

**Dose:** Child, under 6 years; not recommended; over 6 years, initially 5mg 1 - 2 times daily increased if necessary at weekly intervals by 5 - 10mg daily to maximum 60mg daily in divided doses. Discontinue if there is no response after 1 month, also suspend periodically to assess child's condition (usually final discontinuation is during or after puberty).

**Side effects:** see under 3.10.1, also sleep disturbances, pruritis, urticaria, fever, arthralgia, alopecia, exfoliative dermatitis, erythema multiforme, thrombocytopenic purpura, thrombocytopenia, leucopenia, urinary disorders, and very rarely liver damage.

### DEXAMPHETAMINE

**Presentation:** Tablet containing 5mg dexamphetamine sulphate

**Indications:** Narcolepsy, as an adjunct in the management of refractory hyperkinetic states in children.

**Dose:** Narcolepsy; 10mg (elderly 5mg) daily in divided doses increased by 10mg (elderly 5mg) daily at intervals of 1 week to a maximum of 60mg daily.

Hyperkinesia; child; under 6 years not recommended, over 6 years 5 - 10mg daily increased if necessary by 5mg at intervals of 1 week to usual maximum dose of 20mg daily (older children have received maximum 40mg daily).

**Side effects:** Insomnia, restlessness, irritability and excitability, nervousness, night terrors, euphoria, tremour, dizziness, headache, convulsions (see Caution), dependance and tolerance, sometimes psychosis, anorexia, gastrointestinal symptoms, growth retardation in children (see under Caution), dry mouth, sweating, tachycardia and anginal pain, palpitations, increased blood pressure, visual disturbances, cardiomypathy reported with chronic use, central stimulants have provoked choreoathetoid movements, tics and Tourette in predisposed individuals (see Caution)

**Caution:** Mild hypertension, history of epilepsy, monitor growth in children, avoid abrupt withdrawal, porphyria. Treatment to be given strictly under specialist supervision.

**Contra-indications:** Cardiovascular disease including moderate to severe hypertension, history of drug or alcohol abuse, Glaucoma, pregnancy and breastfeeding, hyperthyroidism, hyperexcitability and or agitated states.
4 Drugs used in the treatment of infections

4.1 Antibacterial drugs

4.1.1 Penicillins
4.1.2 Aminoglycosides
4.1.3 Aminocyclitol
4.1.4 Sulphonamides and trimethoprim
4.1.5 Quinolones
4.1.6 Nitrofuran drugs
4.1.7 Macrolides
4.1.8 Chloramphenicol
4.1.9 Cephalosporins and cephamycins
4.1.10 Tetracyclines
4.1.11 5-nitro imidazoles

Antibacterial agents are those drugs that are used for the treatment of bacterial infections. Antibacterial agents should not be prescribed unless there are definite indications. Before selecting an antibacterial agent, the clinician must consider three factors: The patient and the known or likely causative microorganism and sensitivity of the organism. Factors related to the patient which must be considered include history of allergy, renal and hepatic function, resistance to infection, age and weight of the patient; if female whether pregnant and the stage of pregnancy; breast feeding and concurrent medications. It may be necessary in some situations to prescribe therapy before laboratory results are available but it is essential that appropriate specimens are taken before therapy is initiated (where laboratory facilities exist).

The duration of the therapy depends on the nature of the infection, the severity and the response to treatment. Unless otherwise stated, the minimum duration of treatment should be five days.

4.1.1 Natural penicillins

The first group of penicillins to be obtained by fermentation. They remain an important and useful group of antibiotics but they are inactivated by bacterial penicillinases (Beta lactamases). They are the drug of choice for streptococcal, pneumococcal, gonococcal, and meningococcal infections and also for anthrax, diphtheria, gas – gangrene, leptospirosis, syphils, tetanus and yaws. Most natural penicillins are inactivated by gastric acids and the absorption from the gut is low except for Phenoxy methyl Penicillin.

4.1.1.1 Penicillins

4.1.1.1.1 Natural penicillins
4.1.1.1.2 Amino penicillins
4.1.1.1.3 Penicillinase resistant penicillins

These belong to the group of antibiotics called the Beta-lactam antibiotics. They are bactericidal in nature and act by interfering with the synthesis of the bacterial cell wall. They diffuse well into body tissues and fluids but penetration into the cerebrospinal fluid is poor except when the meninges are inflamed. They are excreted in urine in therapeutic concentrations. Probenecid blocks the renal tubular excretion of penicillins producing higher and more prolonged plasma concentrations. They are generally active against most gram positive microorganisms and some gram negative cocci bacteria. The most common side effects associated with their use is hypersensitivity reactions which manifest as rashes and occasionally anaphylaxis reaction which maybe fatal. Diarrhoea frequently occurs during oral penicillin therapy.

Benzathine Penicillin

Presentation: Injection containing 2.4MU benzathine penicillin equivalent to 1.4g of benzyl penicillin powder for reconstitution. For intramuscular injection. Not to be administered by i.v. injection or infusion.

Indications: Penicillin sensitive infections particularly syphils, bejel, yaws.

Dose: Primary syphilis, adult; 2.4MU stat. Secondary syphilis, adult; 2.4MU intramuscularly once weekly for three weeks. Bejel & yaws, 5 years and above; 1.2MU stat. Less than 5 years; 0.6MU stat.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angiodema, anaphylactic shock.

Caution: Penicillin allergy, renal impairment.

Contra-indications: History of hypersensitivity to penicillin.

Benzyl Penicillin

Presentation: Injection containing 300mg, 600mg benzyl penicillin powder for reconstitution.
**Penicillin.**

**Contra-indications:**
Caution: Penicillin allergy, renal impairment.

**Side effects:** Sensitivity reactions including urticaria, fever, joint pains, angiodema, anaphylactic shock.

**Caution:** Penicillin allergy, renal impairment.

**Contra-indications:** History of hypersensitivity to penicillin.

### 4.1.1.2 Amino penicillins

They are synthetic derivatives of 6- amino penicillinoic acid and have a free amino group attached to the penicillin nucleus. Because of their enhanced polarity, they have enhanced activity against gram negative bacteria compared to natural penicillins. They are active against gram positive and gram negative organisms but they are inactivated by penicillinases produced by *Staphylococcus aureus*. They are well excreted in the urine and bile. They are principally indicated in the treatment of exacerbation of chronic bronchitis and middle ear infections due to sensitive microorganisms.

#### AMOXICILLIN

**Presentation:** Capsule containing 250mg, 500mg amoxicillin trihydrate. Suspension containing 125mg/5ml amoxicillin trihydrate. Injection containing 250mg, 500mg amoxicillin sodium.

**Indications:** Urinary tract infections, otitis media, sinusitis, chronic bronchitis, invasive salmonellosis, prophylaxis adjunct in listerial meningitis.

**Dose:** Oral, *Adult*: 250mg every 8 hours. Maximum dose 6g daily in divided doses. *Child*, up to 10 years; 125mg every 8 hours doubled in severe infections. Severe or recurrent purulent respiratory infections 3g every 12 hours. *Child*, 2 – 5 years; 750mg every 12 hours. 5 – 10 years; 1.5g every 12 hours. By intramuscular injection, *adult*: 250 - 500mg every 8 hours. *Child*: 50 – 100mg/kg body weight daily in divided doses. By intravenous injection or by infusion, *adult*: 250 - 500mg every 8 hours increased to 1g every 6 hours in severe infections. *Child*: 50 – 100mg/kg body weight daily in divided doses.

**Side effects:** Nausea, diarrhoea, rashes (discontinue treatment), pseudomembranous colitis (rarely), on prolonged use leucopenia and thrombocytopenia may occur.

**Caution:** History of allergy, renal impairment, erythematous rashes common in glandular fever, chronic lymphatic leukaemia and HIV infection.

**Contra-indications:** Penicillin hypersensitivity.
Indications: Urinary tract infection, otitis media, sinusitis, chronic bronchitis, invasive salmonellosis.

Dose: Oral, adult; 0.25 – 1g every 6 hours at least 30 minutes before food depending on the severity of the infection. Urinary tract infection; 500mg every 8 hours orally or by i.m. injection.

Meningitis; i.v. or by infusion, 500mg every 4 – 6 hours, higher doses maybe required depending on severity of infection. Child, 6 - 10 years; any route, half the adult dose. New born – 5 years; 100mg/kg body weight daily in divided doses.

Side effects: Nausea, diarrhoea, rashes (discontinue treatment), pseudomembranous colitis (rarely), on prolonged use, leucopenia and thrombocytopenia may occur.

Caution: History of allergy, renal impairment, erythematous rashes common in glandular fever and chronic lymphatic leukaemia.

Contra-indications: History of allergy, renal impairment.

Contra-indications: Penicillin hypersensitivity.

4.1.1.3 Penicillinase Resistant Penicillins

They are semi-synthetic derivatives of 6 amino penicillinoic acid. They are stable against hydrolysis by most Staphylococcal penicillinases. They are effective in infections caused by penicillin resistant staphylococi. Since they are acid stable, they can be given by mouth as well as by injection.

AMOXYCILLIN + CLAVULANIC ACID

Presentation: Tablet containing 250mg amoxycillin trihydrate and 125mg clavulanic acid. Suspension containing 125mg amoxycillin trihydrate and 31mg clavulanic acid per 5ml. Injection containing 500mg amoxycillin sodium and 100mg clavulanic acid, 1g amoxycillin and 200mg clavulanic acid powder.

Indications: As for amoxycillin and the treatment of staphylococcal infections.

Dose: Expressed as amoxyxillin, Oral, adult; 250mg every 8 hours, doubled in severe infections. Child, under 1 year; 0.8ml/kg body weight daily in 3 divided doses. 1 – 6 years (10 – 18 kg); 125mg every 8 hours, doubled in severe infections. 6 – 12 years; 250mg every 8 hours, doubled in severe infections.

By intravenous injection (Over 3 minutes) or by infusion; 1g every 8 hours increased to 1g every 6 hours in more serious infections. Infants up to 3 months; 25mg/kg body weight every 8 hours (every 12 hours in premature infants). 3 months – 12 years; 25mg/kg body weight every 8 hours increased to every 6 hours in more serious infection. Surgical prophylaxis; 1g as induction, may be increased to 2 – 3 doses every 8 hours in the first 24 hours. (longer in high risk of infection)

Side effects: See under 4.1.1.2.1.

Caution: See under 4.1.1.2.1., Severe hepatic impairment, pregnancy and breast feeding, hepatitis, cholestatic jaundice and erythema multiform. Treatment not to exceed 14 days without review.

Contra-indications: Penicillin hypersensitivity.

CLOXACILLIN

Presentation: Capsule containing 250mg, 500mg cloxacinol sodium. Injection containing 250mg, 500mg cloxacinol sodium powder for reconstitution.

Indications: Infections due to penicillinase producing staphylococci including otitis externa, adjunct in the treatment of pneumonia, impetigo, cellulitis and staphylococcal endocarditis.

Dose: Oral, adult; 500mg every 6 hours at least 30 minutes before food. I.m. injection, 250mg every 4 – 6 hours. By slow i.v. injection or by infusion 500mg every 4 – 6 hours. Child; any route under 2 years, quarter adult dose. 2 – 10 years, half adult dose.

Side effects: Sensitivity reactions including urticaria, fever, joint pains, angiodemia, anaphylactic shock.

Caution: History of allergy, renal impairment.

Contra-indications: Penicillin hypersensitivity.

Antipseudomonal Penicillins

PIPERACILLIN

Presentation: Injection 2.25g powder for reconstitution containing 2g piperacillin (as sodium salt) and tazobactam 250mg (as sodium salt). Injection 4.5g powder for reconstitution containing 4g piperacillin (as sodium salt) and tazobactam 500mg (as sodium salt). Infusion containing 4.5g piperacillin.

Indications: Lower respiratory tract, urinary tract, intra-abdominal and skin infections. Also septicaemia.

Dose: Adult and child over 12 years; by intravenous injection over 3 - 5 minutes or by intravenous infusion 2.25 - 4.5g every 6 - 8 hours, usually 4.5g every 8 hours.

Complicated appendicitis, by intravenous injection over 3 - 5 minutes or by intravenous infusion 2.25 - 4.5g every 6 - 8 hours (maximum 4.5g every 8 hours) for 5 - 14 days. Child under 2 years; not recommended.

Infections in neutropenic patients (in combination with an aminoglycoside), by intravenous injection over 3 - 5 minutes or by intravenous infusion, adult and child over 50kg, 4.5g every 6 hours. Child less than 50kg 90mg/kg every 6 hours.

Side effects: Nausea and vomiting rarely stomatitis, constipation, dry mouth, hepatitis, cholestatic jaundice, oedema, hypotension, fatigue, myalgia, erythema multiforme, hypokalaemia, injection site injection. See also 4.1.1.1.2.
Caution: Renal impairment, history of allergy
Contraindications: Penicillin hypersensitivity

### FLUCLOXACILLIN

**Presentation:** Capsules containing 250mg, 500mg flucloxacillin sodium. Oral solution (elixir or syrup) containing 125mg/5ml flucloxacillin magnesium. Injection containing 250mg, 500mg flucloxacillin sodium powder for reconstitution.

**Indications:** Infections due to penicillinase producing *Staphylococci* including otitis externa, adjunct in the treatment of pneumonia, impetigo, cellulitis and staphylococcal endocarditis.

**Dose:** Oral, adult; 250mg every 6 hours at least 30 minutes before food. by i.m. injection, 250mg every 6 hours. By slow i.v. injection or by infusion, 0.25 – 1g every 6 hours. The above doses can be doubled in severe infection. Child; under 2 years, any route, quarter the adult dose. 2 – 10 years, half the adult dose.

**Side effects:** Sensitivity reactions including urticaria, fever, joint pains, angioedema, anaphylactic shock, and on prolonged use in old age it will cause thrombocytopenia, leucopenia, hepatitis and cholestatic jaundice

**Caution:** History of allergy, renal impairment and porphyria.

**Contra-indications:** Penicillin hypersensitivity.

### 4.1.2 Aminoglycosides

These are bactericidal antibiotics used primarily in the treatment of gram-negative infections. They bind irreversibly to 30 s ribosomal sub unit blocking the recognition step in protein synthesis and causing misreading of the genetic code. They are very poorly absorbed from the gastro intestinal tract and are thus administered parenterally. They are excreted principally via the kidneys and accumulation occurs in renal impairment. The major side effects are nephrotoxicity and ototoxicity and they may also impair neuromuscular transmission.

### GENTAMICIN

**Presentation:** Injection containing 40mg/ml gentamicin sulphate.

**Indications:** Septicaemia and neonatal sepsis, biliary tract infections, acute pyelonephritis, or prostatitis endocarditis caused by *Streptococcus viridans*, *Streptococcus faecalis*, pneumonia in hospital patients, adjunct in the treatment of listerial meningitis.

**Dose:** Adults; by i.m. or slow i.v. injection over at least 3 minutes or by infusion 2 – 5mg/kg body weight daily every 8 hours. Dosage should be reduced in patients with renal impairment. Gonorrhoea; 240mg intramuscularly stat. Child, up to 2 weeks; 3mg/kg body weight every 12 hours. 2 weeks – 12 years; 2mg/kg body weight every 8 hours.

By *intrathecal injection,* 1mg daily (increased if necessary to 5mg daily).

**Side effects:** Vestibular and auditory damage, nephrotoxicity, rarely hypomagnesaemia on prolonged therapy.

**Caution:** Pregnancy, renal impairment, in infants and the elderly, in patients with hearing and vestibular problems or disturbances. Creatinine levels should be monitored

**Contra-indications:** Myasthenia gravis, dehydrated patients.

### KANAMYCIN

**Presentation:** Injection containing 1g kanamycin sulphate powder for reconstitution.

**Indications:** Similar to those of gentamicin but it is more toxic and resistance develops more rapidly. It is used primarily in the treatment of systemic and urinary tract infections caused by micro organisms which are sensitive to gentamicin, Gonorrhoea.

**Dose:** By i.m. injection; 250mg every 6 hours or 500mg every 12 hours. By infusion; 15 – 30mg/kg body weight daily in divided doses every 8 – 12 hours. Gonorrhoea; 2g stat.

**Side effects:** Same as for gentamicin but kanamycin has a lower therapeutic index. The major effect is damage to the eighth cranial nerve resulting in vertigo and deafness. Also skin eruptions, nausea and vomiting may occur.

**Caution:** Same as for gentamicin

**Contra-indications:** Same as for gentamicin.

### AMIKACIN

**Presentation:** Injection containing 250mg/ml amikacin sulphate. Paediatric injection containing 50mg/ml amikacin sulphate.

**Indications:** Serious gram-negative infections resistant to gentamicin.

**Dose:** By i.m. or slow i.v. injection or by infusion 15mg/kg body weight daily in 2 divided doses.

**Note:** one hour peak concentration should not exceed 30mg/litre.

**Side effects:** see under gentamicin

**Caution:** see under gentamicin

**Contra-indications:** see under gentamicin

### SPECTINOMYCIN

**Presentation:** Injection containing 2g spectinomycin hydrochloride powder.

**Indications:** Acute gonococcal urethritis, proctitis and acute gonococcal cervicitis to susceptible strains of *N gonorrhoeae*. It is only indicated in
Drugs used in the treatment of infections

4.1.4 Sulphonamides and trimethoprim

Sulphonamides are derivatives of para-aminobenzoic acid. They act by inhibiting the enzyme dihydropterate synthetase which is involved in incorporating para-aminobenzoic acid into pteridine in the formation of folic acid.

Trimethoprim is a 2,4 diaminopyrimidine derivative similar to pyrimethamine. It acts by blocking the enzyme dihydrofolate reductase which is involved in the reduction of folic acid to folinic acid.

The combination of sulphonamides and trimethoprim will provide a sequential blockage of the formation of folic acid which is essential for DNA synthesis. The net effect is bactericidal action. The combination of sulphonamethoxazole and trimethoprim is called Co-trimoxazole. The ratio of the combination is sulphamethoxazole 5: trimethoprim 1. The use of sulphonamides alone has decreased because of increasing bacterial resistance. The sulphonamides are bacteriostatic in action and are active against a wide range of gram positive and gram-negative bacteria such as Staphylococci, Streptococci, Enterobacter, E.coli, Klebsiella, Proteus mirabilis, Salmonella and Shigella. They are also active against some strains of Neisseria gonorrhoeae and Neisseria meningitis. Some species of Plasmodium and Chlamydia are sensitive. The use of cotrimoxazole is decreasing due to resistance.

The major side effects associated with the use of sulphonamides are crystalluria, hypersensitivity reactions, haematological disorders and hepatic damage. They should be used with caution in patients with blood dyscrasias, in renal impairment and in patients with G-6-P-D deficiency. They are also contraindicated in infants less than two months of age and in the late third trimester of pregnancy because of the possibility of development of kernicterus.

Trimethoprim on the other hand is bactericidal in action. It is largely effective against many gram positive, anaerobic bacteria and some gram negative anaerobic bacteria. It is inactive against bacteroides and has no established activity against strict anaerobes such as Clostridium or Fusobacterium.

Volume of distribution of trimethoprim is about nine times that of sulphamethoxazole. It has been used alone in the treatment of pneumocystis carinii pneumonia (PCP), uncomplicated urinary tract infection caused by sensitive organisms and in the prophylaxis of chronic and recurrent urinary tract infections in men and women. It has also been used as prophylaxis in pneumocystis carinii pneumonia in HIV positive individuals particularly infants born to HIV positive mothers.

The combination of trimethoprim with sulphamethoxazole enhances activity, decreases resistance and reduces the net frequency of administration of each drug. However some cumulative side effects have been recorded. The combination of sulphamethoxazole/trimethoprim is useful in the treatment of most urinary tract infections, gastro-intestinal infections and pneumocystis carinii infection (high dose).

44 Drugs used in the treatment of infections

CO-TRIMOXAZOLE

Presentation: Tablets containing 400mg sulphamethoxazole and 80mg trimethoprim (480mg). Suspension containing 200mg sulphamethoxazole and 40mg trimethoprim (240mg). Intravenous infusion containing 900mg sulphamethoxazole and 60mg trimethoprim.

Indications: It should be limited to the role of drug of choice for the treatment of pneumocystis carinii pneumonia. It is also indicated for the treatment of toxoplasmosis and nocardiosis. It should only be considered for use in acute exacerbation of chronic bronchitis and infections of the urinary tract where there is good bacteriological evidence of sensitivity. Similarly it should be used in acute otitis media where there is good reason to prefer it.

Dose: By mouth, Adult; 960mg every 12 hours increased to 1.44g in severe infections. 480mg every 8 hours if treated for more than 14 days.

Child, 6 weeks – 5 months; 120mg every 12 twelve hours. 6 months – 5 years; 240mg every 12 hours. 6 – 12 years; 480mg every 12 hours. High dose therapy for pneumocystis carinii pneumonia; 120mg/kg body weight in divided doses for 14 days. Prophylaxis in children born to HIV positive mothers; 240mg daily until HIV status is known. By intravenous infusion, adult; 960mg every 12 hours increased to 1.44g every 12 hours in severe infection.

Child; 36mg/kg daily in divided doses increased to 54mg/kg daily in severe infections.

Side effects: Nausea, vomiting, diarrhoea, glossitis, rashes, erythema multiform (including Stevens-Johnson syndrome), epidermal necrolysis, pancreatitis, eosinophilia, agranulocytosis, leucopenia, granulocytopenia, thrombocytopenia, megaloblastic anaemia due to the trimethoprim component, pseudomembranous colitis, jaundice and hepatic necrosis. Diarrhoea, myocarditis, serum sickness, stomatitis, anorexia are indications for discontinuing treatment.
**Caution:** renal impairment, breast feeding, phototoxic sensitivity, elderly patients, maintain adequate fluid intake during treatment.

**Contra-indications:** Pregnancy, infants under 6 weeks (risk of kernicterus), renal or hepatic failure, jaundice, blood disorders, porphyria.

### TRIMETHOPRIM

**Presentation:** Tablets containing 100mg, 200mg trimethoprim. Injection containing 20mg/ml trimethoprim lactate.

**Indications:** Trimethoprim should be reserved as the drug of choice for the treatment of pneumocystis carinii pneumonia in those who are hypersensitive to sulphonamides, urinary tract infections due to susceptible strains, acute and chronic bronchitis.

**Dose:** Oral; **adult:** acute infections, 200mg every 12 hours. **Child; 2 – 5 months:** 25mg twice daily. **6 months – 5 years:** 50mg twice daily. **6 – 12 years:** 100mg twice daily. Chronic infections and prophylaxis, **adult;** 100mg at night. **Child; 1 - 2mg/kg body weight at night.**

By slow i.v. injection or by infusion, **adult;** 150 – 250mg every 12 hours. **Child; under 12 years;** 6 – 9mg/kg body weight daily in 2 – 3 divided doses

**Side effects:** GIT disturbances including nausea and vomiting, pruritis, rashes, depression of haematopoiesis, erythema multiforme, toxic epidermal necrolysis and aseptic meningitis.

**Caution:** Renal impairment, breast feeding, porphyria and in patients that are predisposed to folate deficiency.

**Contra-indications:** Severe renal impairment, pregnancy, neonates, blood dyscrasia, megaloblastic anaemia due to folate deficiency.

### 4.1.5 Quinolones

These are generally effective against most gram negative bacteria and some gram positive bacteria. Most anaerobic bacteria are resistant. The fluorinated quinolones like ciprofloxacin and norfloxacin have expanded spectrum of activity and increased activity compared with the non-fluorinated quinolones (e.g. nalidixic acid, oxolinic acid and cinoxacin). The pipéraciline group in most fluoroquinolones enhances the antipseudomonas activity.

They should be used with caution in patients with epilepsy, in hepatic or renal impairment, in pregnancy and breast feeding. They should also be used with caution in children or adolescence (because of arthropathy). The major side effects of the quinolones include nausea, vomiting, abdominal pain, diarrhoea, arthralgia and blood disorders. Less frequent side effects include anorexia, restlessness, depression, hallucinations and confusion.

### CIPROFLOXACIN

**Presentation:** Tablets containing 250mg, 500mg, 750mg ciprofloxacin hydrochloride. Intravenous infusion containing 2mg/ml ciprofloxacin lactate.

**Indications:** Gram negative and gram positive infections caused by susceptible bacteria. It is particularly active against gram negative bacteria including **Salmonella, Shigella, Campylobacter, Neisseria and Pseudomonas.** It is used in the treatment of respiratory tract infections (excluding pneumococcal pneumonia), urinary tract infections, infections of the GIT (including thyphoid), gonorrhoea, septicemia and for skin and soft tissue infections.

**Dose:** Oral; **adult:** respiratory tract infection, 250 – 750mg twice daily. Urinary tract infection, 250 – 500mg twice daily. Gonorrhoea, 500mg single dose. Most other infections; 500 – 750mg twice daily by intravenous infusion; 200mg twice daily (over 30 - 60 minutes). In urinary tract infection; 100mg twice daily. Gonorrhoea; 100mg as a single dose. Surgical prophylaxis; 750mg given 60 – 90 minutes before procedure.

**Child;** Not recommended. However where benefits outweigh risk, by mouth, 7.5 – 15mg/kg body weight daily in 2 divided doses or by intravenous infusion, 5 – 10mg/kg body weight daily in 2 divided doses.

**Side effects:** see notes above (4.1.5.)

**Caution:** see notes above (4.1.5.)

**Contra-indications:** Hypersensitivity to 4-Quinolones or quinolone group of antibacterials.

### NALIDIXIC ACID

**Presentation:** Tablets containing 500mg nalidixic acid. Suspension containing 300mg/5ml nalidixic acid.

**Indications:** Dysentery, urinary tract infections caused by susceptible gram-negative microorganisms, including majority of **proteus strains, klebsiella, enterobacterial species and E. Coli.**

**Dose:** **adult:** 1g every 6 hours for 7 days, reduced in chronic infections to 500mg every 6 hours for 7 – 14 days. **Child;** over 3 months, maximum dose 50mg/kg body weight daily in divided doses, reduced in prolonged therapy to 30mg/kg body weight daily.

**Side effects:** see notes above (4.1.5.). Also paraesthesia, cholestasis, metabolic acidosis, increased intracranial pressure and jaundice.

**Caution:** see notes above (4.1.5.). Also avoid exposure to strong sunlight during treatment, avoid in porphyria. Monitor blood counts, liver and renal function if treatment exceeds two weeks.

**Contra-indications:** Hypersensitivity to nalidixic acid, epilepsy or history of epilepsy.
**NORFLOXACIN**

**Presentation:** Tablet containing 400mg norfloxacin.

**Indications:** Urinary tract infections, chronic prostatitis.

**Dose:** Urinary tract infections; 400mg twice daily for 7 - 10 days (3 days for uncomplicated lower urinary tract infection). Chronic relapsing urinary tract infection 400mg twice daily for up to 12 weeks; maybe reduced to 400mg once daily if adequate suppression within first 4 weeks.

Chronic prostatitis; 400mg twice daily for 28 days.

**Side effects:** See notes above; also euphoria, anxiety, tinnitus, polyneuropathy, exfoliative dermatitis, pancreatitis, vasculitis

**Caution:** See notes above. Renal impairment.

**Contra-indications:** Hypersensitivity to 4-Quinolones or quinolone group of antibacterials

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**NITROFURANTOIN**

**Presentation:** Tablets containing 50mg, 100mg nitrofurantoin. Suspension containing 25mg/5ml nitrofurantoin.

**Indications:** Urinary tract infections due to susceptible strains of E. coli, Enterococci, Staphylococcus aureus and certain strains of Klebsiella, Enterobacteriaceae and proteus species.

**Dose:** Adult; acute uncomplicated infection 50mg every 6 hours with food for 7 days. Child, over 3 months; 3mg/kg body weight daily in 4 divided doses. Severe chronic recurrent infection; 100mg every 6 hours with food for 7 days. Prophylaxis, adult; 50 – 100mg at night. Child, over 3 months; 1mg/kg body weight at night.

**Side effects:** see notes above (4.1.6.). Also peripheral neuropathy, angiodema, urticaria, rash and pruritis, exfoliative dermatitis, erythema multiforme, pancreatitis.

**Caution:** Predisposing conditions such as renal impairment, anaemia, diabetes, electrolyte imbalance, vitamin B deficiency may enhance the peripheral neuropathy produced by nitrofurantoin. Monitor Liver Function Test (LFT).

**Contra-indications:** Impaired renal function, infants less than 3 months old, G6PD deficiency, porphyria, late pregnancy and breast feeding.

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4.1.6 Nitrofuran drugs

These are synthetic nitrofuran derivative antibacterial agents. They are bacteriostatic in action mainly at low concentration but bactericidal at higher concentrations. They are mostly used in the treatment of urinary tract infections caused by sensitive gram negative bacilli and gram positive cocci such as Escherischia coli, Klebshiella, Enterobacter species, Entero cocci and some strains of Staphylococci.

They inhibit acetyl co enzyme A interfering with bacterial carbohydrate metabolism. Therapeutic concentration in the serum and tissue is very low after oral administration, hence they are rarely used for the treatment of systemic infections. High concentrations are excreted in the urine and antibacterial activity is greater in acidic urine. Acute urine enhances tubular reabsorption of nitrofuran drugs enhancing their antibacterial activity in the renal tissues. Antibacterial activity is reduced at higher pH.

The major side effects associated with the use of nitrofurans include anorexia, nausea, vomiting, acute and chronic pulmonary reactions, cholestatic hepatitis, jaundice, thrombocytopenia and aplastic anaemia. An example is nitrofurantoin which occurs in two forms; the macrocrystalline form which is absorbed more slowly due to slower dissolution and causes less gastro-intestinal distress and the microcrystalline form which has a higher dissolution rate and is more rapidly absorbed.

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4.1.7 Macrolides

These antibiotics contain many numbered lactone rings to which are attached one or more sugars. They bind irreversibly to the 50S ribosomal subunit and inhibit RNA dependent protein synthesis. They are weak bases and their activity increases in alkaline pH. They enter the pleural fluid, ascitic fluid, middle ear exudates and sputum. Penetration into the CSF is poor but increases in meningitis. They are bacteriostatic but may be bactericidal at higher concentrations. They are used in the treatment of respiratory, genital, gastro-intestinal tract, skin and soft tissue infections especially when Beta-lactam antibiotics or tetracyclines are contra-indicated. They are effective against most strains of Streptococcus, Haemophilus, Bordetella pertussis, Legionella pneumophila, Chlamydia species, Mycoplasma pneumoniae and Ureaplasma urealyticum. Examples include azithromycin, clarithromycin, erythromycin and troleandomycin.

The major side effects include cholestatic jaundice, hepatitis, pseudo membranous colitis and hypersensitivity reactions.

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**ERYTHROMYCIN**

**Presentation:** Tablets or capsules containing 250mg, 500mg erythromycin. Suspension containing 125mg/5ml erythromycin ethyl
succinate. Intravenous infusion (powder for reconstitution) containing 1g erythromycin lactobionate.

**Indications:** Alternative to penicillin in hypersensitive patients; campylobacter enteritis, pneumonia, legionnaires’ disease, syphilis, non gonococcal urethritis, chronic prostatitis, acne vulgaris, diphtheria and whooping cough prophylaxis.

**Dose:** Oral, adult and child over 8 years old; 250 – 500mg every 6 hours or 0.5g – 1g every 12 hours up to 4g daily in severe infections. **Child, up to 2 years;** 125mg every 6 hours. 2 – 8 years; 250mg every 6 hours. Doses may be doubled in severe infections. By intravenous infusion, adult and child; 50mg/kg body weight daily by continuous infusion or in divided doses every 6 hours. In mild infections where oral treatment is not possible; 25mg/kg body weight daily.

**Side effects:** Nausea, vomiting, abdominal discomfort, diarrhoea (pseudomonas colitis), urticaria, rashes, allergic reactions, reversible loss of hearing reported after large doses, cholestatic jaundice and cardiac effects.

**Caution:** Renal or hepatic impairment, pregnancy and breastfeeding, porphyria and in cardiac arrhythmias.

**Contra-indications:** Liver disease, hypersensitivity to erythromycin.

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**AZITHROMYCIN**

**Presentation:** Capsule containing 250mg azithromycin dihydrate. Film coated tablet containing 500mg azithromycin dihydrate. Oral suspension containing 200mg/5ml azithromycin dihydrate.

**Indications:** Respiratory tract infections, otitis media, skin and soft tissue infections, uncomplicated genital chlamydial infections and non gonococcal urethritis.

**Dose:** 500mg once daily for 3 days. **Child over 6 months;** 10mg/kg once daily for 3 days or boy weight 15 - 25kg, 200mg once daily for 3 days, body weight 26 - 35kg, 300mg once daily for 3 days, body weight 36 - 45 kg 400mg once daily for 3 days. Uncomplicated genital chlamydial infections and non gonococcal urethritis 1g as a single dose.

**Side effects:** Anorexia, dyspepsia, constipation, dizziness, headache, drowsiness, photosensitivity, hepatitis, interstitial nephritis, acute renal failure, asthenia, paraesthesia, convulsions and mild neutropenia, rarely tinnitus, hepatic necrosis, hepatic failure and taste disturbances.

**Caution:** See under erythromycin

**Contra-indications:** See under erythromycin

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**CLARITHROMYCIN**

**Presentation:** Film coated tablets containing 250mg, 500mg clarithromycin. Suspension containing 125mg/5ml clarithromycin powder for reconstitution with water.

**Indications:** Respiratory tract infections, mild to moderate skin and soft tissue infections, otitis media.

**Dose:** Orally 250mg every 12 years for 7 days increased in severe infections to 500mg every 12 hours for up to 14 days. **Child;** body weight under 8kg: 7.5mg/kg twice daily, 8 - 11kg (1-2years) 62.5mg twice daily, 12 - 19kg (3 - 6 years) 125mg twice daily, 20 - 29kg (7 - 9 years) 187.5mg twice daily, 30-40kg (10 – 12 years) 250mg twice daily

*By intravenous infusion into larger proximal vein, 500mg twice daily, CHILD not recommended.*

**Side effects:** see under Erythromycin; also reported, dyspepsia, headache, smell and taste disturbances, tooth and tongue discoloration, stomatitis, glossitis, pancreatitis, arthralgia, myalgia, dizziness, vertigo, tinnitus, anxiety, insomnia, nightmares, confusion, psychosis, convulsions, paraesthesia, hypoglycaemia, hepatitis, renal failure, leucopenia, and thrombocytopenia; on intravenous infusion, local tenderness, phlebitis

**Caution:** See under Erythromycin;

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**CHLORAMPHENICOL**

Chloramphenicol is a potent, potentially toxic, broad spectrum antibiotic which should be reserved for the treatment of life threatening infections, particularly those caused by Salmonella species and Haemophilus influenzae. It inhibits protein synthesis and it is bacteriostatic in action. It exhibits high tissue penetration and reasonable concentration is achieved in the CSF even when the meninges are not inflammed. It is effective against a wide range of gram positive and gram negative bacteria and it is also active in vitro against Rickettsiae, Lymphogranuloma psittacosis and Vibrio cholera. Chloramphenicol causes serious and sometimes fatal blood dyscrasias (aplastic anaemia, hypo plastic anaemia, thrombocytopenia). Chloramphenicol must not be used when less potentially toxic antibacterial agents are available. It must not be used to treat trivial infections such as influenza, colds, or throat infections, infections other than indicated or as prophylaxis for bacterial infections. It is essential that adequate blood studies are performed during treatment to detect blood disorders such as cytopenia before they become irreversible.
CHLORAMPHENICOL

**Presentation:** Capsules containing 250mg chloramphenicol. Suspension containing 125mg/5ml chloramphenicol palmitate. Injection containing 1g chloramphenicol sodium succinate.

**Indications:** Potent, potentially toxic broad spectrum antibiotic reserved for the treatment of life threatening infections for which less potentially toxic drugs are ineffective or contraindicated, particularly for salmonella infection and haemophilus influenzae. It could also be used for the treatment of typhoid and life threatening anaerobic infections, *Rickettsiae*, Lymphogranuloma- pitacosis and bacterial infections due to susceptible micro organisms in which the benefit of use outweighs the serious side effects.

**Dose:** Oral or by intravenous injection or by intravenous infusion, adult; 50mg/kg body weight daily in 4 divided doses (exceptionally, can be doubled for severe infections such as septicaemia and meningitis, providing high doses are reduced as soon as clinical condition improves). Child; haemophilus epiglotitis and pyogenic meningitis, 50 – 100mg/kg body weight daily in divided doses (high doses decreased as soon as clinical condition improves).

**Side effects:** See notes above. Bone marrow depression, peripheral neuritis, optic neuritis, erythema multiforme, nausea, vomiting, diarrhoea.

**Caution:** Avoid repeated courses and prolonged (beyond 7 days) treatment, reduce dose in hepatic or renal impairment, blood counts required before and periodically during treatment, avoid concurrent use with other drugs causing bone marrow depression, breast feeding

**Contra-indications:** Pregnancy, porphyria, trivial infections.

CEFOTAXIME

**Presentation:** Injection containing 1g cefotaxime sodium powder.

**Indications:** Lower respiratory tract infections including pneumonia, urinary tract infections, gynaecological infections including pelvic inflammatory disease (PID), endometritis and pelvic cellulitis, septicaemia, skin and skin structure infections, intra abdominal infections including peritonitis, bone or joint infections, CNS infections and pre-operative prophylaxis.

**Dose:** By intramuscular or intravenous injection or by intravenous infusion, moderate to serious infections; 1g every 8 hours. Life threatening infections 2g every 8 hours. Especially, for life threatening infections due to organisms less sensitive to cefotaxime, up to 12g daily. Urinary tract and mild to moderate infections; 1g every 12 hours. In severe renal impairment, dose to be halved after initial dose of 1g. Neonate; 50mg/kg body weight daily in 2 – 4 divided doses, in severe infections 150 – 200mg/kg daily. Child; 100 – 150mg/kg body weight daily in 2 – 4 divided doses, in severe infections, up to 200mg/kg daily.

By intravenous infusion; 1 – 2g over 20 – 60 minutes.

**Side effects:** see notes above. Also diarrhoea (rarely pseudo-membranous colitis), nausea and vomiting, allergic reactions including rashes, pruritis, urticaria, serum sickness like reactions with rashes, fever and arthralgia, anaphylaxis, disturbance in liver enzymes, transient hepatitis, cholestatic jaundice, eosinophilia and blood disorders.

**Caution:** Penicillin hypersensitivity, renal impairment, pregnancy and breast feeding, false positive urinary glucose may occur during treatment.

**Contra-indications:** Cefotaxim hypersensitivity and porphyria.

CEFTRIAXONE

**Presentation:** Injection powder, containing 250mg, 1g ceftriaxone as sodium for reconstitution.

Cephalosporins and cephamycins

They are semi synthetic derivatives of Cephalosporium C and belong to the beta-lactam antibiotics. They are composed of a 7-amino cephalosporinic acid nucleus which is composed of a beta-lactam ring fused with a 6-member dihydrothiazine ring.

They are classified into first, second and third generation. The classification is based on their spectrum of activity. In general progression from first to third generation reveals broadening gram negative activity, loss of efficacy on gram positive organisms, greater efficacy against resistant organisms and increased cost.

They inhibit muco peptide synthesis in the bacterial cell wall. They are broad spectrum antibiotics which are used for the treatment of septicaemia, pneumonia, meningitis, biliary tract infections, peritonitis and urinary tract infections.

The pharmacology of the cephalosporins is similar to that of the penicillins. Excretion is principally through the renal route and is blocked by probenecid.

The principal side effect of the cephalosporins is hypersensitivity and about 10% of the penicillin-sensitive patients will also be allergic to cephalosporins. Haemorrhage due to interference with blood clotting factors has been associated with several cephalosporins. Examples of first generation cephalosporins are cephradine and cephazolin; second generation include cefuroxime and cephamandole; third generation are cefotaxime, ceftriaxone and cefodizime.
Indications: surgical prophylaxis; prophylaxis of meningococcal meningitis [unlicensed indication]

Dose: By deep intramuscular injection, or by intravenous injection over at least 2–4 minutes, or by intravenous infusion, 1 g daily; 2–4 g daily in severe infections; intramuscular doses over 1 g divided between more than one site; single intravenous doses above 1 g by intravenous infusion only

NEONATE by intravenous infusion over 60 minutes, 20–50 mg/kg daily (max. 50 mg/kg daily) INFANT and CHILD under 50 kg, by deep intramuscular injection, or by intravenous injection over 2–4 minutes, or by intravenous infusion, 20–50 mg/kg daily; up to 80 mg/kg daily in severe infections; doses of 50 mg/kg and over by intravenous infusion only; 50 kg and over, adult dose Endocarditis caused by haemophilus, actinobacillus, cardio bacterium, eikenella, and kingella species (‘HACEK organisms’) (in combination with another antibacterial,[unlicensed indication]), by intravenous infusion, 2–4 g daily.

Early syphilis [unlicensed indication], by deep intramuscular injection, 500 mg daily for 10 days. Uncomplicated gonorrhoea, by deep intramuscular injection, 250 mg as a single dose. Surgical prophylaxis, by deep intramuscular injection or by intravenous injection over at least 2–4 minutes, 1 g at induction; colorectal surgery, by deep intramuscular injection or by intravenous infusion, 2 g at induction; intramuscular doses over 1 g divided between more than one site.

Side-effects: calcium ceftriaxone precipitates in urine (particularly in very young, dehydrated or those who are immobilised) or in gall bladder—consider discontinuation if symptomatic; rarely prolongation of prothrombin time, pancreatitis. Caution: severe renal impairment; hepatic impairment if accompanied by renal impairment, premature neonates; may displace bilirubin from serum albumin, administer over 60 minutes in neonates (see also Contraindications); treatment longer than 14 days, renal failure, dehydration—risk of ceftriaxone precipitation in gall bladder. Contra-indications: neonates with jaundice, hyopoalbuminaemia, acidosis or impaired bilirubin binding; concomitant treatment with calcium in children—risk of precipitation in urine and lungs of neonates (and possibly infants and older children) suspected. urinary tract infections; 125 mg twice daily, doubled in pyelonephritis. Child over 3 months; 125 mg twice daily, if necessary doubled in child over 2 years with otitis media.

By i.m. or i.v. injection or by intravenous infusion; 750 mg every 6 – 8 hours. 1.5 g every 6 – 8 hours in severe infections. Child; usual dose 60 mg/kg body weight daily (range, 30 – 100 mg/kg daily) in 3 – 4 divided doses (2 – 3 divided doses in neonates). Surgical prophylaxis; 1.5 g by i.v. injection at induction, may be supplemented with 750 mg by i.m. injection 8 – 16 hours later (abdominal, pelvic and orthopaedic operations) or followed by 750 mg by i.m. injection every 8 hours for a further 24 – 48 hours (cardiac, pulmonary, oesophageal and vascular operations)."
Drugs used in the treatment of infections and pseudo membranous colitis on prolonged benign intracranial hypertension, pancreatitis headache and visual disturbances (may indicate Side effects: maximum 2g daily. By intravenous infusion; 500mg every 12 hours; 4 – 6 hours in severe infection. By i.m. injection; course). 14 days. (21 days if failure or relapse following first severe infections to 500mg every 6 – 8 hours. Non Presentation: Tablets or capsules containing 50mg, 100mg doxycycline hydrochloride. Indications: Exacerbation of chronic bronchitis, brucellosis, gonorrhoea (if allergic or resistant to penicillins), syphilis, chlamydia, balantidium coli, pelvic inflammatory disease, chronic prostatitis and sinusitis. Dose: 200mg on 1 st day, then 100mg daily, in severe infections including chronic urinary tract infections 200mg daily. Acne; 100mg 2 x daily for 6 – 12 weeks or longer. Capsules should be swallowed whole with plenty of fluid during meals while sitting or standing. Side effects: Nausea, vomiting, diarrhoea, headache and visual disturbances (may indicate benign intracranial hypertension), pancreatitis and pseudomembranous colitis on prolonged treatment. Caution: hepatic impairment and history of photosensitivity. Contra-indications: Severe renal impairment, pregnancy, breast feeding, children under 12 years and systemic lupus erythematosus.

TETRACYCLINE Presentation: Tablets or capsules containing 250mg tetracycline hydrochloride. I.m. injection containing 100mg tetracycline hydrochloride. Intravenous infusion containing 250mg tetracycline hydrochloride. Indications: see 4.1.10.1. Also pleural effusion due to malignancy or cirrhosis, mycoplasma and rickettsia. Dose: Oral; 250mg every 6 hours increased in severe infections to 500mg every 6 – 8 hours. Non gonococcal urethritis 500mg every 6 hours for 7 – 14 days. (21 days if failure or relapse following first course). By i.m. injection; 100mg every 8 – 12 hours , or every 4 – 6 hours in severe infection. By intravenous infusion; 500mg every 12 hours maximum 2g daily. Side effects: Nausea, vomiting, diarrhoea, headache and visual disturbances (may indicate benign intracranial hypertension), pancreatitis and pseudo membranous colitis on prolonged treatment. Caution: Hepatic impairment where it should not be administered intravenously, renal impairment (avoid if severe), history of photosensitivity, avoid giving with milk products and antacids since these products reduce absorption of tetracycline. Contra-indications: Severe renal impairment, pregnancy, breast feeding, children under 12 years and systemic lupus erythematosus.

DOXYCYCLINE

VANCOMYCIN

5mg/kg every 6 hours, over 5 years, half adult done Note: Oral paediatric dose is lower than that on product literature but is adequate. By intravenous infusion, 500mg over at least 60 minutes every 6hours or 1g over at least 100 minutes every 12 hours; NEONATE up to 1 week, 15mg/kg initially then 10mg/kg every 12 hour; INFANT 1-4 weeks, 15mg/kg, initially then 10/kg every 8 hours; CHILD over 1 month, 10mg/kg every 6 hours. Side effects: after parenteral administration: nephrotoxicity including renal failure and interstitial nephritis; ototoxicity (discontinue if tinnitus occurs); blood disorders including neutropenia (usually after 1 week or cumulative dose of 25g), rarely agranulocytosis and thrombocytopenia; nausea; chills, fever; eosinophilia, anaphylaxis, rashes (including exfoliative dermatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, and vasculitis); phlebitis (irritant to tissue); on rapid infusion, severe hypotension (including shock and cardiac arrest), wheezing, dyspnoea, urticaria, pruritus, flushing of he upper body (‘red man’ syndrome), pain and muscle spasm of back and chest) Caution: avoid rapid infusion (risk of anaphylactoid reactions, see Side effects); rotate infusion sites; renal impairment; elderly; avoid if history o deafness; all patients require plasma-vancomycin measurement (after 3 r 4 doses if renal function normal, earlier if renal impairment), blood counts, urinalysis, and renal function tests; monitor auditory function in elderly or if renal impairment; pregnancy and breast feeding; systemic absorption may follow oral administration especially in inflammatory bowel disorders or following multiple doses.

5- NITRO IMIDAZOLES The 5-nitro imidazole antimicrobial agents are active against various anaerobic bacteria and protozoa. Their mode of action is not well understood, however they appear to enter the cells of micro organisms that contain nitro reductase where their nitro group is reduced to intermediate compounds which bind to DNA leading to inhibition of synthesis of DNA and cell lysis. They are active against many protozoa such as...
Entamoeba histolytica, Giardia lamblia, Trichomonas vaginalis, and most obligate anaerobes but generally not effective against facultative anaerobes or obligate anaerobes. They have large apparent volume of distribution and are well distributed in the various tissues.

The common side effects associated with the use of 5-nitro imidazoles include nausea, vomiting, unpleasant taste, furred tongue, headache, dizziness, prolonged use may cause peripheral neuropathy, transient epileptiform seizures and leucopenia.

Tinidazole is similar to metronidazole but has a longer duration of action and hence it is administered less frequently. Their major use is in the treatment of amoebiasis, giardiasis, trichomonas, bacterial vaginosis and systemic anaerobic infections. They should generally be used with caution in the first trimester of pregnancy, in breast feeding and in hepatic impairment.

### METRONIDAZOLE

**Presentation:** Tablets containing 200mg, 400mg metronidazole. Suspension containing 200mg/5ml metronidazole benzoate. Intravenous infusion containing 5mg/ml metronidazole. Suppositories containing 500mg metronidazole oral gel and skin cream.

**Indications:** Amoebic dysentery, trichomoniasis, giardiasis, systemic anaerobic infections particularly those due to Bacteroides fragilis and Clostridium perfringens, it is also useful in surgical and gynaecological sepsis in which its activity against colonic anaerobic bacteria is important. Useful in the treatment of antibiotic associated colitis (pseudomembranous colitis) and in anaerobic dental infections due to susceptible organisms.

**Dose:**
- **Oral, adult:** anaerobic infections (usually treated for seven days) 800mg initially then 400mg every 8 hours. By intravenous infusion; 500mg every 8 hours. Child; any route 7.5mg/kg body weight every 8 hours.
- **Bacterial vaginosis:** orally 400mg twice daily for 7 days or 2g as a single dose.
- **Acute ulcerative gingivitis:** orally 200mg every 8 hours for 3 days. Child, 1 – 3 years; 50mg every 8 hours. 3 – 7 years; 100mg every 12 hours. 7 – 10 years; 100mg every 8 hours all for 3 days.
- **Acute dental infections:** orally, 200mg every 8 hours for 3 – 7 days.
- **Trichomoniasis:** adult, 2g as a single dose.
- **Giardiasis:** adult, 200mg every 8 hours for 7 days. Child, 5 – 12 years; 100mg every 8 hours. Less than 5 years; 50mg every 8 hours, all for 7 days.
- **Amoebic dysentery:** adult; 400mg every 8 hours for 7 days. Child, less than 9 years 200mg every 8 hours for 7 days.
- **Surgical prophylaxis:** Oral; 400mg every 8 hours started 24 hours before surgery, then continued post operatively by intravenous infusion or rectally until oral administration can be resumed. Child; 7.5mg/kg body weight every 8 hours. By rectum; 1g every 8 hours or 125 – 250mg every 8 hours. By intravenous infusion; 500mg shortly before surgery then every 8 hours until oral administration can be resumed.

**Side effects:** Nausea, vomiting, unpleasant taste and gastro-intestinal disturbances, rashes, urticaria and angioedema, rarely drowsiness, headache, dizziness, ataxia and darkening of urine. On prolonged or intensive therapy peripheral neuropathy, transient epileptiform seizures and leucopenia.

**Caution:** Disulfiram-like reactions with alcohol, hepatic impairment, pregnancy and breast feeding.

**Contra-indications:** Hypersensitivity to metronidazole, first trimester of pregnancy.

### TINIDAZOLE

**Presentation:** Tablets containing 500mg tinidazole.

**Indications:** see 4.1.11.1. Its longer acting than metronidazole.

**Dose:** Anaerobic infections; 2g stat followed by 1g daily for 5 – 6 days or 500mg twice daily for 5 – 6 days.

**Bacterial vaginosis and acute ulcerative gingivitis:** 2g as single dose.

**Abdominal surgery prophylaxis:** 2g as a single dose approximately 12 hours before surgery.

**Side effects:** see 4.1.11.1.

**Caution:** see 4.1.11.1.

**Contra-indications:** see 4.1.11.1.

### 4.2 Anti-fungal drugs

| 4.1.1 Polyene antifungals |
| 4.1.2 Imidazole antifungals |
| 4.1.3 Triazole antifungals |
| 4.1.4 Penicillin derived antifungals |
| 4.1.5 Fluorinated pyrimidine derivatives |
| 4.1.6 Others |

These are drugs which are used in the treatment of fungal infections. Fungi are pathogenic microorganisms that possess a rigid chitinous cell wall. The treatment of fungal infections is generally more difficult and problematic compared to the treatment of bacterial infections because of the complex method of reproduction, their structure and metabolism.

The nature of therapy will depend on the type of fungus (whether it is a mould, yeast or dimorphic); the location of the infection, (whether it is on the skin, hair, nails, or within the system of the patient). Generally systemic fungal infections is a warning sign of compromised body immunity.
In the treatment of superficial fungal infections, it is generally recommended that oral medication should be supplemented with topical antifungal cream or ointment in order to achieve better results. Generally the duration of therapy will normally last for a minimum of four to six weeks.

Fungal infection of the meninges will normally present with severe complications due to immuno-depression and it is normally advisable to put the patients on parenteral antifungal drugs for quicker action and clinical response. Systemic fungal infections such as candidiasis, blastomycosis, aspergillosis, plasmosis, cryptococcosis and mucormycosis will generally require parenteral or oral treatment depending on the severity of the infection and the condition of the patient. The duration of treatment will normally last two to three weeks. In general antifungal drugs are classified into the following broad groups:

### 4.2.1 Polyene Antifungals

This group includes nystatin (see also section 12 and 13) and amphotericin B. They are not absorbed from the gut and are active against most fungi and yeasts. However, nystatin is recommended principally for the treatment of candidiasis infections of the skin and mucous membranes. It is also used in the treatment of intestinal candidiasis.

#### AMPHOTERICIN

**Presentation:** Tablets containing 100mg amphotericin B. Intravenous infusion containing 50mg amphotericin sodium deoxycholate powder for reconstitution.

**Indications:** Intestinal candidiasis, systemic fungal infection

**Dose:** Oral; intestinal candidiasis, 100 – 200mg every 6 hours.

By intravenous infusion; systemic fungal infection, (0.25mg/kg/250mcg/kg body weight daily, gradually increased if tolerated to 1mg/kg daily. Maximum dose for severe infection, 1.5mg/kg daily or on alternate days.

**Side effects:** Anorexia, nausea, vomiting, diarrhoea, epigastric pain, febrile reactions, renal toxicity, blood disorders, neurological disorders including hearing loss, abnormal liver function (discontinue treatment).

**Caution:** Toxicity common when given parenterally, pregnancy, breast feeding, monitor plasma electrolytes, hepatic and renal functions, concurrent administration with corticosteroids and other nephrotoxic drugs.

#### NYSTATIN

**Presentation:** Sugar coated tablets containing 500,000 units nystatin. Suspension containing 100,000 units/ml nystatin. Vaginal pessaries containing 100,000 i.u. nystatin

**Indications:** Candidiasis

**Dose:** Oral: intestinal candidiasis 500,000 units every 6 hours doubled in severe infections. Child; 100,000 units every 6 hours. Neonate; 100,000 units as a single dose. For use in oral infections see 13.3.1. 6.3. Vaginal candidiasis; insert 1 – 2 pessaries at night for at least 14 nights

**Side effects:** Nausea, vomiting diarrhoea at high doses, local irritation, sensitization, rash may occur.

**Contra-indications:** History of hypersensitivity to nystatin

### 4.2.1 Imidazole antifungals

This group includes clotrimazole, econazole, isoconazole, ketoconazole and tioconazole (see also section 12). They are active against a wide range of fungi and yeasts. Their major indication is in the treatment of vaginal candidiasis and dermatophyte infections.

#### Clotrimazole

**Presentation:** Pessaries containing 100mg, 500mg clotrimazole. Lozenges 1%, Cream 1%, Topical 505, vaginal cream 1 %, Lotions1 % and Solutions 1%

**Indications:** Vaginal and vulval candidiasis

**Dose:** infant; 2 pessaries at night for 3 nights or 1 pessary for 6 nights. For oral 20 drops after meals 3 times and for fungal dermatosis apply twice a day.

**Side effects:** Occasional local irritation

**Caution:** Antibiotic therapy, oral contraceptives, pregnancy and diabetes mellitus may affect the clinical effectiveness of clotrimazole.

**Contra-indications:** Hypersensitivity to imidazole and other antifungal drugs.

#### Ketoconazole

**Presentation:** Tablets containing 200mg ketoconazole. Suspension containing 100mg/5ml ketoconazole.

**Indications:** Systemic mycosis, serious chronic resistant mucocutaneous candidiasis, serious resistant gastro-intestinal mycosis, chronic resistant vaginal candidiasis, resistant dermatophyte of the skin or finger nails (not toe nails) Dose: adult; 200mg once daily with food for 14 days. If response is inadequate after 14 days continue until at least 1 week after symptoms have cleared and culture becomes negative. Maximum dose 400mg daily. Child; 3mg/kg body weight daily. Chronic resistant vaginal candidiasis; 400mg daily with food for 5 days.

**Side effects:** Nausea, vomiting, abdominal pain, headache, rashes, urticaria, pruritis, rarely thrombocytopenia, gynaecomastia, fatal liver
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**4.2.3 Triazole Antifungals**

This group includes fluconazole and itraconazole which are absorbed by mouth. They are indicated for the treatment of local and systemic candidiasis and cryptococcal infections. They are also indicated in aspergillosis and histoplasmosis.

### FLUCONAZOLE

**Presentation:** Capsules containing 50mg, 150mg, 200mg fluconazole. Suspension containing 50mg/5ml, 200mg/5ml fluconazole. Intravenous infusion containing 2mg/ml fluconazole.

**Indications:** acute or recurrent vaginal candidiasis, mucosal candidiasis, tinea pedis, corporis, cruris, versicolor and dermal candidiasis, systemic candidiasis, cryptococcal infections including meningitis.

Prevention of relapse of cryptococcal meningitis in AIDS patients after completion of primary therapy, by mouth or by intravenous infusion, 100-200mg daily.

Prevention of fungial infections in immunocompromized patients following cytotoxic chemotherapy or radiotherapy, by mouth or by intravenous infusion, 50 – 400mg daily adjusted according to risk; 400mg daily if high risk or systemic infections e.g. following bone marrow transplantation; commence treatment before anticipated onset of neutropenia and continue for 7 days after neutrophil count in desirable range; CHILD according to extent and duration of neutropenia, 3-12 mg/kg daily (ever 72 hours in NEONATE up to 2 weeks old, every 48 hours in NEONATE 2-4 weeks old); max. 400mg daily

**Dose:** Acute or recurrent vaginal candidiasis; oral single dose of 150mg. Mucosal candidiasis; oral, 50 – 100mg daily for 7 – 14 days. Tinea pedis, corporis, cruris, versicolor and dermal candidiasis; oral, 50mg daily for 2 – 4 weeks (up to 6 weeks for tinea pedis). Systemic candidiasis; oral or i.v. infusion, 400mg initially then 200mg daily and continued according to patient response. Cryptococcal meningitis, by i.v. infusion; 800mg daily.

**Child,** over 1 year; oral or i.v. infusion 1-2mg/kg body weight daily. Systemic and life threatening infections; 3 – 6mg/kg body weight daily. Can be increased up to 12mg/kg body weight daily in child aged 5 - 13 years.

**Caution:** Renal impairment, pregnancy, breast feeding, children (use only if no alternative treatment), raised liver enzymes.

**Side effects:** vestibular and auditory damage, nephrotoxicity, rarely, hypomagnesaemia on prolonged therapy, antibiotic-associated colitis; also reported, nausea, vomiting, rash.

**Contra-indications:** Child under 1 year

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### GRISEOFULVIN

**Presentation:** Tablets containing 125mg, 500mg griseofulvin. Suspension containing 125mg/5ml griseofulvin.

**Indications:** Treatment of ringworm infection of the skin, hair, nails namely tinea corporis, tinea pedis, tinea cruris, tinea barbae, tinea capitis when caused by one or more of the following fungi, *Tinea rubrum, Tinea tonsurans, Tinea mentagrophytes, Tinea interdigitalis, Tinea verrucosum, Tinea megnini, Tinea schuelei, Microsporum audouini, M. canis, M. gypseum and Epidermophyton floccosum.*

**Dose:** adult; 500mg daily in divided doses or as a single dose, in severe infection dose may be doubled reducing when response occurs. **Child,** 10mg/kg body weight daily in divided doses or as a single dose.

**Side effects:** headache, nausea, vomiting, rashes, photosensitivity, dizziness, fatigue, agranulocytosis and leucopenia, lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, peripheral neuropathy, confusion and impaired co-ordination.

**Caution:** Breast feeding, enhances the effect of alcohol, may impair performance of skilled tasks e.g. driving

**Contra-indications:** Hypersensitivity to griseofulvin, porphyria, hepatic failure, lupus erythematosus and related conditions, pregnancy (avoid pregnancy for one month after treatment).

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### FLUCYTOSINE

**Presentation:** Tablets containing 125mg, 500mg griseofulvin. Suspension containing 125mg/5ml griseofulvin.

**Indications:** Treatment of ringworm infection of the skin, hair, nails namely tinea corporis, tinea pedis, tinea cruris, tinea barbae, tinea capitis when caused by one or more of the following fungi, *Tinea rubrum, Tinea tonsurans, Tinea mentagrophytes, Tinea interdigitalis, Tinea verrucosum, Tinea megnini, Tinea schuelei, Microsporum audouini, M. canis, M. gypseum and Epidermophyton floccosum.*

**Dose:** adult; 500mg daily in divided doses or as a single dose, in severe infection dose may be doubled reducing when response occurs. **Child,** 10mg/kg body weight daily in divided doses or as a single dose.

**Side effects:** headache, nausea, vomiting, rashes, photosensitivity, dizziness, fatigue, agranulocytosis and leucopenia, lupus erythematosus, erythema multiforme, toxic epidermal necrolysis, peripheral neuropathy, confusion and impaired co-ordination.

**Caution:** Breast feeding, enhances the effect of alcohol, may impair performance of skilled tasks e.g. driving

**Contra-indications:** Hypersensitivity to griseofulvin, porphyria, hepctocellular failure, lupus erythematosus and related conditions, pregnancy (avoid pregnancy for one month after treatment).

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**4.2.5 Fluorinated Pyrimidine Derivative antifungals**

These include Flucytosine. This is a synthetic antifungal drug which is only active against yeasts and has been used for the treatment of systemic candidiasis, cryptococcosis and torulopsosis. Side effects are uncommon but bone marrow depression can occur.
adjunct to amphotericin (or fluconazole) in cryptococcal meningitis, adjunct to amphotericin in severe systemic candidiasis and in other severe or long-standing infections.

Caution:  Renal impairment; elderly; blood disorders; liver and kidney function test and blood counts required (weekly in renal impairment or blood disorders); pregnancy, breast feeding.

Side effects:  nausea, vomiting, diarrhoea, rashes; less frequently confusion, hallucinations, convulsions, headache, sedation, vertigo, alterations in liver function tests (hepatitis and hepatic necrosis reported); blood disorders including thrombocytopenia, leucopenia, and aplastic anaemia reported.

Dose:  by intravenous infusion over 20-40 minutes, adult and child, 200mg/kg daily in 4 divided doses usually for not more than 7 days; extremely sensitive organisms, 100-150mg/kg daily may be sufficient; treat for at least 4 months in cryptococcal meningitis.

4.2.5.2 Other antifungals

These include gentian violet, benzoic acid, undecanoic acid, salicylic acid and sulphur. These agents have weak antifungal activity and are used only topically in the treatment of superficial fungal skin infection. However, resistance easily develops. They are mostly used in form of ointments or creams and applied topically to infected surfaces. (See section 12).

4.3 Antiprotozoal Drugs

4.3.1 Antimalarials

High plasmodium falciparum resistance to chloroquine necessitated the Zambian Government to change to malaria treatment policy. The frontline drug of choice for treatment of uncomplicated malaria should be an Artemether Combination Therapy (ACT) Artemether-Lumefantrine has been selected for this purpose. However, wherever Artemether-Lumefantrine is contraindicated or is not available, sulphadoxine-pyrimethamine is the drug of choice. For all cases of severe malaria, quinine id the drug of choice.

The use of artemisinin or its derivatives as a monotherapy is not preferred as the possibility and potential for development of parasites resistance and failure for adherence to treatment is high. Wherever monotherapy of artemisinin or its group of compounds are unavoidable, the doses recommended in this formulary should be used. The dose for artemether-lumefantrine is determined by body weight to avoid or over dosing. It is recommended that the first dose, wherever possible, should possible, should be given by observed therapy (DOTS).

4.3.1.1 Artemether with Lumefantrine

Presentation:  Tablets containing 20mg Artemether + 120mg Lumefantrine (140mg).

Indications:  Treatment of uncomplicated malaria in both adults and children above 10 kg body weight.

Dose:  Adult:  80mg artemether + 480mg Lumefantrine two times a day. 15-24kg body weight (6-8 years) 40mg artemether + 140 lumefantrine two times a day. 10-14kg body (1-5 years) 20mg artemether + 120mg lumefantrine three times a day. Artemether + lumefantrine is not recommended for children below 10kg body weight (1 year). To increase bioavailability, absorption can be enhanced if it is administered after meals (preferably containing fatty foods). See schedule for recommended doses.

Side Effects:  Sleep disorders, headache, dizziness, palpitations, abdominal pain, anorexia, diarrhea, vomiting, nausea, pruritis, rash, cough, arthralgia, myalgia.

Caution:  electrolyte imbalance, use with other drugs known to cause QT interval prolongation, hepatic impairment, renal impairment, pregnancy, patients unable to take food (ris of recrudescence), concomitant use of other drug that are metabolized by enzyme cytochrome P450.

Contraindications:  history of arrhythmias, clinical brady carddia, congestive hear failure accompanied by reduced left ventricular ejection fraction, family history of sudden death or of congenital QT interval prolongation, breast feeding.

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>Age (yrs) (Approx)</th>
<th>No. of tablets per dose. Give twice daily</th>
<th>Coartemâ (A + L)/ dox</th>
<th>Total no. tablets to be given over 3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>&lt;1</td>
<td>Not recommended</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>10-14</td>
<td>1-5</td>
<td></td>
<td>20mg A + 120mg L</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>6-8</td>
<td></td>
<td>40mg A + 240mg L</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>9-12</td>
<td></td>
<td>60mg A + 360mg L</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>³12</td>
<td></td>
<td>80mg A + 480mg L</td>
<td>24</td>
</tr>
</tbody>
</table>
**Side effects:** The common effects reported include, sleep disorders, headache, dizziness, palpitations, abdominal pain, anorexia, vomiting, nausea, pruritis, rash, cough. Arthralgia.

**SULFADOXINE-PRYMETHAMINE (SP)**

**Presentation:** Tablets containing 500mg sulfadoxine and 25mg pyrimethamine suspension.

**Indications:**
1. Treatment of uncomplicated malaria in both adults and children
   - First treatment in the following
     - Children 5-10kg body weight
     - Second and third trimester of pregnancy
     - When artemether-lumefantrine is not available
     - Hypersensitivity to artemether-lumefantrine.
2. Intermittent Presumptive Treatment (IPT) in pregnancy

**Contraindications:** Sulphadoxine-pyrimethamine is contraindicated in patients with hypersensitivity to sulfa drugs or pyrimethamine and in hepatic renal dysfunction.

**Dosage:** Single dose adult treatment containing 25mg/kg body weight sulfadoxine plus 75mg/kg body weight primethamine.

Recommended single adults dose is 1500mg sulfadixine plus 75mg pyrimethamine (i.e. 3 tablets.

(See dosage schedule below):

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Age (years)</th>
<th>No. of Tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>2-11 months</td>
<td>0.5</td>
</tr>
<tr>
<td>10-14</td>
<td>1-2</td>
<td>0.75</td>
</tr>
<tr>
<td>15-20</td>
<td>3-5</td>
<td>1</td>
</tr>
<tr>
<td>21-30</td>
<td>6-8</td>
<td>1.5</td>
</tr>
<tr>
<td>31-40</td>
<td>9-11</td>
<td>2</td>
</tr>
<tr>
<td>41-50</td>
<td>12-13</td>
<td>2.5</td>
</tr>
<tr>
<td>&gt;50</td>
<td>14 and above</td>
<td>3</td>
</tr>
</tbody>
</table>

**Side Effects:** Serious adverse reactions to sulfa drugs are rare. When they occur they include severe cutaneous reactions, such as Stevenson Johnson syndrome and toxic epidermal necrolysis. Toxic epidermal appears to be more common in HIV infected patients. These serious cutaneous adverse reactions are fatal in 10-20% of cases. They are not dose dependant and cannot be predicted by a history of allergy to sulfa drugs. Gastrointestinal disturbances include nausea, vomiting and stomatitis.

**PRIMAQUINE**

**Presentation:** Tablets containing 26.3mg primaquine phosphate (1.5mg primaquine base).

**Indications:** Adjunct in the treatment to eliminate the liver stages of infestation. Recommended only for radical cure of plasmodium ovale and plasmodium vivax in endemic areas.

**Dose:** After full course of treatment with chloroquine, adult; 15mg daily for 14 – 21 days. Child; 0.25mg/kg body weight daily for 14 – 21 days.

**Side effects:** Nausea, vomiting, abdominal pain, less commonly methaemoglobinemia, haemolytic anaemia especially in G6PD deficiency.

**Caution:** G6PD deficiency, pregnancy, breast feeding.

**Contra-indications:** Patients undergoing quinacrine therapy, acutely ill patients suffering from systemic disease manifested by tendency of agranulocytopenia (e.g. rheumatoid arthritis, lupus erythema).

**QUININE DIHYDROCHLORIDE**

**Presentation:** Tablets (coated) containing 200mg and 300mg base injection containing 150mg, 300mg/ml in 2 ml ampoules.

**Indications:**
- Treatment of severe and complicated malaria.
- First line treatment for uncomplicated malaria during first trimester of pregnancy.
- Second line treatment in case of treatment failure with first line treatment.

**Contraindications:** Quinine is contraindicated in haemoglobinuria, optic neuritis and tinnitus.

**Dosage:** Adults; 600mg every 8 hours for 5 – 7 days. by intramuscular injection;10mg/kg body weight diluted in saline or water for injection (to a concentration of 60-100mg salt/ml), repeated after 4 hours and then 8 hourly. A loading dose is not recommended in intramuscular route. **Children:** by intramuscular injection; 10mg/kg body weight diluted in saline or water for injection (to a concentration of 60-100mg salt/ml), repeated after 4 hours and then 8 hourly. A loading dose is not recommended by this route. **Infants** up to 1 year; 250mg daily in divided doses for 5 – 7 days. Child; 1 – 3 years; 400mg daily in divided doses for 5 – 7 days. 3 – 6 years; 650mg daily in divided doses every 4 – 6 hours for 5 – 7 days. 6 – 12 years; 1000mg (1g) daily every 4 – 6 hours for 5 – 7 days. If a patient with chloroquine resistant malaria is seriously ill, quinine should be given by intravenous infusion over 4 hours in a loading dose of 30mg/kg body weight followed by a maintenance dose of 10mg/kg body weight in 500ml 5% glucose over 4 hours every 8 hours until the patient can swallow tablets to complete the course.

**Side effects:** include tinnitus, headache, hot and flushed skin, nausea, abdominal pain, rashes visual disturbances (including temporal
Drugs used in the treatment of infections

4.1.1

Drugs used in the treatment of infections

blindness), confusion, hypersensitivity reactions including angioedema, blood disorders (including thrombocytopenia and intra vascular coagulation), acute renal failure, cardiovascular effects and hypoglycaemia (especially after parenteral administration.

Caution: Atrial fibrillation, conduction defects, heart block, blood glucose concentrate should be monitored, G6PD deficiency.

Contra-indications: Hypersensitivity to quinine, G6PD deficiency, optic neuritis, tinnitus, thrombocytopenic purpura

4.1.2 Amoebicides

METRONIDAZOLE

Presentation: Tablets containing 200mg, 400mg metronidazole. Suspension containing 200mg/5ml metronidazole benzoate. Intravenous infusion containing 5mg/ml (100ml) metronidazole.

Indications: Acute invasive intestinal amoebiasis, extra-intestinal amoebiasis (including liver abscess) and symptomless amoebic cyst passers.

Dose: Oral, invasive intestinal amoebiasis; 800mg every 8 hours for 5 days. Child, 1 – 3 years; 200mg every 8 hours. 3 – 7 years; 200mg every 6 hours . 7 – 10 years; 400mg every 8 hours.

Side effects: Caution, contra-indications: see under 4.1.11.1.

TINIDAZOLE

Presentation: Tablets containing 500mg Tinidazole

Indications: Same as for 4.3.11.1.

Dose: Intestinal amoebiasis; 2g daily for 2 – 3 days. Child, 50 – 60mg/kg body weight daily for 3 days. amoebic involvement of the liver; 1.5 – 2g daily for 3 – 5 days. Child, 50 – 60mg/kg body weight daily for 5 days. Urogenital tract trichomoniasis and giardiasis; single 2g dose (repeat once if necessary).

Child; single dose of 50 – 70mg/kg body weight

Side effects: Caution, contra-indications: see under 4.3.11.1.

4.3.3 Trypanocides

MELARSOPROL

Presentation: Injection containing 3.6% Melarsoprol

Indications: Meningo encephalitic stage of African trypanosomiasis. It is effective in both Gambian and Rhodesian strains of the disease. It is also effective in the early stage of the disease.

Dose: administered by slow i.v. injection through a fine needle and avoid leakage to tissue.

Adult, 50kg or more; 3.5mg/kg daily for 3 – 4 days. The course is repeated after an interval of 7 days. A third course of the same dose can be given if required after 10 – 21 days. Reduce dose accordingly in children and underweight patients

Side effects: Pyrexia, reactive encephalopathy, haemorragic encephalopathy, hypersensitivity reaction, hepatic damage, vomiting, agranulocytosis, dematitits.

Caution: leprosy patients, administration should be under close supervision to monitor response, initial dose should be based on the clinical assessment of the patient rather than on the body weight.

Contra-indications: Known hypersensitivity to the drug.
4.3.4 Anthelmintics

4.4.1 Intestinal anthelmintics

4.4.2 Schistosomicides

4.4.3 Anti-filarials

4.4.1 Intestinal Anthelmintics

**MEBENDAZOLE**

**Presentation:** Tablets containing 100mg mebendazole. Suspension containing 500mg/5ml mebendazole.

**Indications:** For the treatment of *Trichuris trichura* (whipworm), *Enterobias vermicularis* (pinworm), threadworms, *Ascaris lumbricoides* (roundworm), *Ancylostoma duodenal* (common hook worm), or *Necter erythema* (American hookworm), in single or mixed infections.

**Dose:**
- **Threadworm**, adult and child over 2 years; 100mg as a single dose. If reinfection occurs a second dose maybe given after 2 – 3 weeks. Not yet recommended in child under 2 years.
- **Whipworm**; adult and child over 2 years; 100mg twice daily for 3 days or 500mg as single dose.
- **Roundworm**; adult; 100mg twice daily for 3 days.
- **Hookworm**; adult, 100mg twice daily for 3 days

**Side effects:** Abdominal pain, diarrhoea, hypersensitivity reactions including erythema, rash, urticaria and angiodema.

**Caution:** Pregnancy especially the first trimester, breastfeeding, safety for use has not been established in children less than 2 years of age. Use only if benefit outweighs risk.

**Contra-indications:** Hypersensitivity to mebendazole.

**PYRANTEL**

**Presentation:** Tablets containing 125mg pyrantel pamoate. Suspension containing 250mg/5ml pyrantel pamoate.

**Indications:** Ascaris, threadworm and hookworm infestation

**Dose:**
- **Ascaris lumbricoides** alone; a single dose of 5mg/kg body weight. Mixed infections involving *Ascaris lumbricoides*; single dose of 10mg/kg body weight.
- **Hookworm:** 10mg/kg body weight (maximum 1g) given as a single dose for light infestations, heavy infestations may need single daily doses for 3 days.
- **Threadworm:** A single dose of 10mg/kg body weight (maximum 1g); cure rates are improved if one or two further doses are given at intervals of 2 weeks.

**Side effects:** Nausea, retching, abdominal pains, light headedness, and pruritis.

**Caution:** Safety for use in children under 2 years has not been established

**Contra-indications:** Hepatic disease and pregnancy.

**NICLOSAMIDE**

**Presentation:** Tablets (chewable) containing 500mg niclosamide

**Indications:** For the treatment of *Taenia saginata* (beef tape worm), *Diphyllobothrium latum* (fish tape worm), *Hymenolepis nana* (dwarf tape worm) and *Taenia solium*.

**Dose:**
- **Taenia solium**, adult and child over 6 years; 2g as a single dose after a light breakfast followed by a purgative after 2 hours. *Child*, under 2 years; 500mg. 2 – 6 years; 1gram. *Taenia saginata* and *Diphyllobothrium Latum*; as for *Taenia solium* but half the dose maybe taken after breakfast and the remainder one hour later followed by a purgative 2 hours after the last dose.
- **Hymenolepis nana**, adult and child over 6 years, 2g as a single dose on first day then 1 g daily for 6 days.
- **Child** under 2 years; 500mg on first day then 250mg daily for 6 days. 2 – 6 years; 1g on first day then 500mg daily for 6 days. Tablets should be chewed thoroughly or crushed before washing down with water.

**Side effects:** Praziquantel is well tolerated and side effects are usually mild and transient, but more frequent or serious in patients with heavy worm burden. These include malaise, headache, dizziness, abdominal discomfort (with or without nausea), pyresia, rarely urticaria.

**Caution:** Safety for use in children under 4 years

**PRAZIQUANTEL**

**Presentation:** Tablets containing 600mg praziquantel

**Indications:** *Schistosoma japonicum*, *Schistosoma haematobium*, *Schistosoma mansoni* and all other types of bilhaziasis infestation. It is also useful in the treatment of *taenia saginata*, solium and *hymenolepis nana*.

**Dose:**
- **Schistosoma haematobium**, *Schistosoma mansoni*, adult; 40mg/kg body weight as a single dose
- **Schistosoma japonicum**; 60mg/kg body weight divided in 3 doses in one day.
- **Distomiasis**, adult and child; 75mg/kg body weight divided in 3 doses in one day.

**Side effects:** Praziquantel is well tolerated and side effects are usually mild and transient, but more frequent or serious in patients with heavy worm burden. These include malaise, headache, dizziness, abdominal discomfort (with or without nausea), pyresia, rarely urticaria.

**Caution:** Safety for use in children under 4 years
Drugs used in the treatment of infections

is not yet established. May produce drowsiness
observe caution when driving or performing
functions requiring high level of concentration
during course of treatment.

Contra-indications: Previous hypersensitivity
reaction to praziquantel, Since parasitic destruction
in the eye may cause lesions.

4.4.3 Antifilarials

**DIETHYLCARBAMAZINE**

Presentation: Tablets containing 100mg
diethylcarbamazine

Indications: Bancrofti filariasis, topical
eosinophilia, loasis,

Dose: Filariasis; to minimise reactions, treatment
is commenced with a dose of 1mg/kg body weight
on the 1st day and increased gradually over 3 days to
6mg/kg body weight in divided doses. This dosage
is maintained for 21 days. Topical eosinophilia;
13mg/kg body weight per day for 4 – 7 days.

Side effects: Allergic reaction including pruritis,
risk of lethal encephalitis, drowsiness, malaise,
headache, nausea and vomiting.

Caution: Pregnancy and breast feeding, administer
carefully to avoid or control allergic reactions.

**SURAMIN**

Presentation: See 4.3.3.2.

Indications: Eradication of adult filarea in
onchocerciasis

Dose: Normal adult dose is 1g given on days
1,3,7,14, and 21. Weekly doses can be given for
an additional 5 weeks. Child, less than 12 years;
14.2mg/kg body weight. Infants; 10 –11mg/kg
body weight.

Side effects: Caution, and contra-indications: See
4.3.3.2.

4.5 Antituberculosis drugs

Treatment for sputum positive TB, TB meningitis,
massive pleural effusion and TB pericarditis new
and relapse cases is in two phases: Intensive
(initial) phase and the continuation phase using.
The total duration of treatment of the two phases
is eight months.

Intensive phase (Initial):
Concurrent use of four drugs during the initial
phase is designed to reduce the population of viable
bacteria as rapidly as possible and to prevent the
emergence of drug-resistance bacteria. This will
include the daily use of isoniazid, rifampicin and
pyrazinamide and ethambutol under supervision
for 2 months.

Continuation phase:
After intensive phase, treatment is continued for
6 months with isoniazid, ethambutol (Longer
treatment may be necessary for bone and joint
T.B. infections, for T.B. meningitis or resistant
organisms).

a) Recommended dosage for sputum positive
Tuberculosis, Tuberculosis meningitis,
massive pleural effusion and Tuberculosis
pericarditis new cases

2 month regimen:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>300mg daily</td>
</tr>
<tr>
<td>Ethambutol</td>
<td>600mg daily, 50kg and over 800mg daily</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>1.5g daily, 50kg and over 2g daily</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>450mg daily, 50kg and over 600mg daily</td>
</tr>
</tbody>
</table>

Followed by 6 month regimen:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid</td>
<td>300mg daily</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>ADULT under 50kg</td>
</tr>
<tr>
<td>Pyrazinamide</td>
<td>ADULT under 50kg 1.5g daily, 50kg and over 2g daily</td>
</tr>
</tbody>
</table>

b) Recommended dosage for new cases sputum
negative, extra pulmonary Tuberculosis new
cases

2 month regimen:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</th>
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<tbody>
<tr>
<td>Isoniazid</td>
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<tr>
<td>Rifampicin</td>
<td>ADULT under 50kg 450mg daily.</td>
</tr>
<tr>
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<tr>
<td>Ethambutol</td>
<td>ADULT under 50kg 600mg daily, 50kg and over 800mg daily</td>
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</table>

Followed by 6 month regimen:

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</tr>
<tr>
<td>Ethambutol</td>
<td>ADULT under 50kg 600mg daily, 50kg and over 800mg daily</td>
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</tbody>
</table>

Followed by 6 month regimen:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>1g daily</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>ADULT 300mg daily</td>
</tr>
</tbody>
</table>
Rifampicin:  ADULT under 50kg 450mg daily. 50kg and over 600mg
Pyrazinamide:  ADULT under 50kg 1.5g daily, 50kg and over 2g daily.
Ethambutol:  ADULT under 50kg 600mg daily, 50kg and over 800mg daily.

Followed by 1 month regimen:
Isoniazid:  ADULT 300mg daily
Rifampicin:  ADULT under 50kg 450mg daily. 50kg and over 600mg
Pyrazinamide:  ADULT under 50kg 1.5g daily, 50kg and over 2g daily.
Ethambutol:  ADULT 800mg daily.

Followed by 5 month regimen:
Isoniazid:  ADULT 300mg daily
Rifampicin:  ADULT under 50kg 450mg daily. 50kg and over 600mg
Ethambutol:  ADULT 800mg daily.

Pregnancy and Breast Feeding: The standard regimen (above) may be used during pregnancy and breast-feeding; pyridoxine supplements are advisable. Streptomycin should not be given in pregnancy.

Children: As for adults, children are given isoniazid, rifampicin, and pyrazinamide for the first 2 months followed by isoniazid and rifampicin during the next 4 months. If pyrazinamide is omitted from the initial phase, then treatment with isoniazid and rifampicin should be given for 9 months.

Except in exceptional circumstances (e.g. drug resistance), ethambutol should be avoided in young children because of the difficulty in testing eyesight and in obtaining reports of visual symptoms (see below).

Recommended dosage for children
2 month regimen:
Rifampicin: 75mg – 300mg daily
Isoniazid: 50mg – 100mg daily
Pyrazinamide: 250mg – 500mg daily

4 month regimen:
Rifampicin: 75mg – 300mg daily
Isoniazid: 50mg – 100mg daily

Doses in children depend very much on the age, weight and nutritional status of the child.

Immunocompromised Patients: Immunocompromised patients may develop tuberculosis owing to reactivation of previously latent disease or due to new infection. Multi-resistant Mycobacterium tuberculosis may be present or the infection may be caused by other mycobacteria e.g. M avium complex in which case specialist advice is needed. Culture should always be carried out and the type of organism and its sensitivity confirmed. A minimum duration of treatment of 9 months is currently recommended for M. tuberculosis infection.

Monitoring: Since isoniazid, rifampicin and pyrazinamide are associated with liver toxicity hepatic function should be checked before and during treatment with these drugs; those dependent on alcohol or who have pre-existing liver disease require special care.

Renal function: This should be checked before treatment with antituberculous drugs and appropriate dosage adjustments made. Streptomycin or ethambutol should preferably be avoided in-patients with renal impairment, but if used require dose reduction and possibly drug concentration monitoring.

Visual acuity should be tested before ethambutol is used.

Rifampicin is a key component of any antituberculous regimen. Like isoniazid it should always be included unless there is a specific contra-indication.

Caution: Rifampicin induces hepatic enzymes, which accelerate the metabolism of several drugs including oestrogens, corticosteroids, phenytoin, sulphonylureas, and anticoagulants.

Important: the effectiveness of oral contraceptives is reduced and alternative family planning advice should be offered.

Ethambutol is included in a treatment regimen if resistance is suspected; it can be omitted if the risk of resistance is low. For unsupervised treatment ethambutol is given in a dose of 25 mg/kg daily in the initial phase followed by 15 mg/kg daily in the continuation phase (or 15 mg/kg daily throughout).

Side effects: are largely confined to visual disturbances in the form of loss of acuity, colour blindness, and restrictions of visual fields. The earliest features of ocular toxicity are subjective and patients should be advised to discontinue therapy immediately if they develop deterioration in vision and promptly seek further advice. Early discontinuation of the drug is almost always followed by recovery of eyesight. Patients who cannot understand warnings about visual side effects should, if possible, be given an alternative drug in particular, ethambutol should be avoided in children until they are at least 6 years old.
Drugs used in the treatment of infections

and capable of reporting symptomatic visual changes accurately.

Ophthalmic examination should be performed before, and at intervals during, treatment.

**Streptomycin** is now used for resistant organisms and relapses. It is given intramuscularly in a Standard dose of 1 g daily reduced to 500-750 mg in patients under 50 kg or those over 40 years of age. Children are given streptomycin in a dose of 15-20 mg/kg daily. Plasma drug concentrations should be measured, particularly in patients with impaired renal function in which streptomycin must be used with great care.

**Side effects** increase after a cumulative dose of 100g, which should only be exceeded in exceptional circumstances.

**ETHAMBUTOL HYDROCHLORIDE**

**Presentation:** Tablets containing 400 mg ethambutol hydrochloride

**Indications:** Tuberculosis, in combination with other drugs intensive and continuation phase.

**Dose:** Adult and child over 6 years, see notes above (4.2).

**Side effects:** optic neuritis, red/green colour blindness, and peripheral neuritis.

**Caution:** Reduce dose in renal impairment; elderly; pregnancy; warn patients to report visual changes – see above notes.

**Contra-indications:** Young children, optic neuritis, and poor vision.

**PYRAZINAMIDE**

Pyrazinamide is a bactericidal drug only active against intracellular dividing forms of mycobacterium tuberculosis; it exerts its main effect only in the first two or three months. It is particularly useful in tuberculous meningitis because of good meningeal penetration. It is not active against *M. bovis*. Serious liver toxicity may occasionally occur.

**Presentation:** Tablets containing 500 mg pyrazinamide

**Indications:** Tuberculosis in combination with other drugs intensive and continuation phase.

**Dose:** See notes above (4.5.)

**Side effects:** Hepatotoxicity including fever, anorexia, hepateomegaly, jaundice, liver failure; nausea, vomiting, arthralgia, sideroblastic anaemia, urticaria.

**Caution:** Hepatic impairment (monitor hepatic function, see also below); renal impairment; slow acetylator status (increased risk of side-effects); epilepsy; history of psychosis; alcoholism; pregnancy and breast-feeding; porphyria

**Interactions:** anaesthetic, potentiated by isoflurane, antacids reduces absorption, increases toxicity of cyloserine, metabolism of carbamazepine, phenytoin inhibited

**Hepatic disorders:** Patients or their carers should be told how to recognize signs of liver disorders, and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice develop.

**Contra-indications:** Drug-induced liver disease.

**SIDE EFFECTS:** Nausea, vomiting, peripheral neuritis with high doses (pyridoxine prophylaxis, see notes above), optic neuritis, convulsions, psychotic episodes; hypersensitivity reactions including fever, erythema multiforme, purpura; agranulocytosis; hepatitis (especially over age of 15); systemic lupus erythematosus-like syndrome, pellagra, hyperglycaemia, and gynaecomastia reported.

**ETHAMBUTOL + ISONIAZID**

Ethambutol is included in a treatment regimen if resistance is suspected; it can be omitted if the risk of resistance is low. For unsupervised treatment ethambutol is given in a dose of 25 mg/kg daily in the initial phase followed by 15 mg/kg daily in the continuation phase (or 15 mg/kg daily throughout).

**Side effects:** are largely confined to visual disturbances in the form of loss of acuity, colour blindness, and restrictions of visual fields. The
earliest features of ocular toxicity are subjective and patients should be advised to discontinue therapy immediately if they develop deterioration in vision and promptly seek further advice. Early discontinuation of the drug is almost always followed by recovery of eyesight. Patients who cannot understand warnings about visual side effects should, if possible, be given an alternative drug in particular, ethambutol should be avoided in children until they are at least 6 years old and capable of reporting symptomatic visual changes accurately.

Ophthalmic examination should be performed before, and at intervals during, treatment.

Streptomycin is now used for resistant organisms and relapses. It is given intramuscularly in a Standard dose of 1 g daily reduced to 500-750 mg in patients under 50 kg or those over 40 years of age. Children are given streptomycin in a dose of 15-20 mg/kg daily. Plasma drug concentrations should be measured, particularly in patients with impaired renal function in which streptomycin must be used with great care.

Side effects increase after a cumulative dose of 100 g, which should only be exceeded in exceptional circumstances.

Presentation: Tablets containing 400 mg ethambutol, 150 mg isoniazid.

Indication: Tuberculosis continuation phase

Dose: See notes above

Side effects: peripheral neuritis is the most common adverse effect when higher dose are used, skin rashes, ataxia dizziness, optic neuritis and hepatic damage.

Caution: See notes above (ethambutol and isoniazid)

Contra-indications: See notes above (ethambutol and isoniazid)

4.5.3 Other Drugs

4.6 Antileprotic drugs

The World Health Organization has made recommendations to overcome this problem of dapsone resistance and to prevent the emergence of resistance to other antileprotic drugs. These recommendations are based on the same principles as for the chemotherapy of tuberculosis. Drugs recommended are dapsone, rifampicin and clofazimine.

A three-drug regimen is recommended for multibacillary leprosy (lepromatous, borderline-lepromatous, and borderline leprosy) and a two-drug regimen for those suffering from paucibacillary leprosy (borderline tuberculosis, tuberculoid, and indeterminate). These regimens, which are widely applicable throughout the world (with minor local variations), are as follows:

Multibacillary leprosy (3-drug regimen)

Rifampicin 600 mg once-monthly, supervised (450 mg for those weighing less than 35 kg). Dapsone 100 mg daily, self-administered. Clofazimine 300 mg once-monthly, supervised, and 50 mg daily (or 100 mg on alternate days), self-administered.

Treatment for multibacillary leprosy should be given for at least 2 years and be continued, if possible, up to smear negativity. It should be continued unchanged during both type 1 (reversal) or type II (erythema nodosum leprosum) reactions which, if severe, should receive their own specific treatment (e.g. prednisolone or increased clofazimine dosage).

Paucibacillary leprosy (2-drug regimen)

Rifampicin 600 mg once monthly, supervised (450 mg for those weighing less than 35 kg). Dapsone 100 mg daily, self-administered.

Treatment for paucibacillary leprosy should be given for 6 months. If treatment is interrupted the regimen should be recommenced where it was left off to complete the full course.

Neither the multibacillary nor the paucibacillary antileprosy regimen is sufficient to treat tuberculosis, therefore patients who also have tuberculosis should be given appropriate antituberculosis drugs in addition to the antileprosy regimen.

CLOFAZIMINE

Presentation: Capsules containing 50 mg, 100 mg

Clofazimine

Indications: Multibacillary leprosy, in combination with Dapsone, chronic leprae type 2 (ENL) reactions

Caution: hepatic and renal impairment; pregnancy and breast-feeding; may discolor soft contact lenses; avoid if persistent abdominal pain and diarrhoea.

Side-effects: nausea, vomiting (hospitalise if persistent), abdominal pain; headache, tiredness; brownish-black discoloration of lesions and skin including areas exposed to light; reversible hair discoloration; dry skin; red discoloration of faeces, urine and other body fluids; also rash, pruritus, photosensitivity. Acne-like eruptions, anorexia, eosinophilic enteropathy,
Drugs used in the treatment of infections

4.6.2 Dapsone (DDS-Diamino Diphenyl Sulphone)

Presentation: Tablets 10mg, 25mg, 100mg

Indications: Leprosy, dermatitis herpetiformis

Dose: 6-10mg/kg/week divided into single daily dose.

Adult; 50-100mg daily in single dose.

Therapy is generally continued for 3 years after the disease has been inactive in Tuberculoid leprosy 5 to 10 years in borderline leprosy and for life in lepromatous leprosy

prophylaxis of leprosy in children of in-patients: child under 2 years 5mg weekly, over 2 years 10 mg weekly.

Caution: Cardiac or pulmonary disease; anemia (treat severe anemia before starting); G6PD-deficiency (including breast-feeding of affected children, pregnancy; avoid in porphyria

Side-effects: Nausea, vomiting (hospitalise if persistent), abdominal pain, headache, tiredness: brownish-black discoloration of lesions and skin including areas exposed to light; reversible hair discoloration; dry skin; red discoloration of faeces, urine and other body fluids; also rash, pruritus, photosensitivity, acne-like eruptions, anorexia, eosinophilic enteropathy, bowel obstruction, dry eyes, dimmed vision, masular and subepithelial corneal pigmentation; elevation of blood sugar, weight loss, splenic infraction lymphadenopathy.

RIFAMPICIN

Presentation: Capsules containing 150mg, 300mg rifampicin

Indications: In combination with Dapsone in the treatment of multibacillary and paucibacillary leprosy. Tuberculosis, in combination with other drugs.

Dose: See notes above brucellosis, legionnaires’ disease and serious staphylococcal infections, in combination with other drugs, by mouth or by intravenous infusion, 0.6-1.2g daily (in 2-4 divided doses).

Tuberculosis, in combination with other drugs, see notes above.

Side-effects: Gastro-intestinal symptoms including anorexia, nausea, vomiting, diarrhoea (pseudomembranous colitis reported); those influenza syndrome (with chills, fever, dizziness, bone pain), respiratory symptoms (including shortness of breath), collapse and shock, haemolytic anaemia, acute renal failure, and thrombocytopenic purpura; alterations of liver function, jaundice, flushing, urticaria, and rashes; other side-effects reported include oedema, Caution: reduce dose in hepatic impairment (liver function tests and blood counts in hepatic disorders and on prolonged therapy); renal impairment (if above 600mg daily); pregnancy and breast-feeding (see notes above;

Important: advise patients on oral contraceptives to use additional means, discolors soft contact lenses; see also notes above

Note: If treatment is interrupted re-introduce with low dosage and increase gradually; discontinue permanently if serious side effects develop.

hepatic disorders: Patients or their carers should be told how to recognise signs of liver disorder, and advised to discontinue treatment and seek immediate medical attention if symptoms such as persistent nausea, vomiting, malaise or jaundice, porphyria muscular weakness and myopathy, leucopenia, eosinophilia, metrual disturbances; urine, saliva, and other body secretions coloured orange-red; thrombophlebitis reported if infusion used for prolonged period.

Contra-indications: liver failure

4.7 Antiviral drugs

The majority of viral infections resolve spontaneously and do not need specific therapy. Treatment is primarily symptomatic.

4.7.1 Drugs used in Herpes simplex and Varicella zoster infections

Acyclovir is active against herpes viruses but does not eradicate them. It is effective only if started at the onset of infection. Acyclovir can be used either systemically or topically (including the eye) for the treatment of herpes simplex infections of the skin and mucous membranes (including genital herpes) or systemically for the treatment of varicella-zoster. It may be given by mouth to immunocompetent adults and older adolescents for the treatment of chickenpox but not to immunocompetent children in whom the disease is milder. In immunocompromised patients with herpes simplex and varicella-zoster infection it can also be used prophylactically to prevent recurrence.

Valaciclovir, a product of acyclovir, is licensed for use in herpes zoster and herpes simplex infections of the skin and mucous membranes (including genital herpes).
Idoxuridine is only used topically because of its systemic toxicity. It is only effective if used at the onset of infection. It is indicated for use in the treatment of herpes simplex lesions of the skin and external genitalia. It is less effective in herpes zoster infection.

**ACYCLOVIR**

**Presentation:** Tablets containing aciclovir 200mg, 400mg, 800mg. iv infusion vial containing 250mg, 500mg powder for reconstitution. Sugar-free suspension containing aciclovir 200mg/5ml (125ml), 400mg/5ml (50ml)(chickenpox treatment). Cream containing aciclovir 5%, 2g, 10g tube. Eye ointment containing aciclovir 3%, 4.5g tube.

**Indications:** herpes simplex and varicella-zoster

**Dose:** Oral: -herpes simplex, treatment, 200mg (400mg in the immunocompromised or if absorption impaired) 5 times daily, for 5 days; child under 2years, half adult dose, over 2 years, adult dose -herpes simplex, prevention of recurrence, 200mg 4 times daily or 400mg twice daily possibly reduced to 200mg 2 or 3 times daily and interrupted every 6-12 months -herpes simplex, prophylaxis in the immunocompromised, 200-400mg 4 times daily; child under 2 years, half adult dose, over 2 years, adult dose.

-varicella and herpes zoster, treatment, 800mg 5 times daily for 7 days; child, varicella, 20mg/kg (max. 800mg) 4 times daily for 5 days or under 2 years 200mg 4 times daily, 2-5 years 400mg 4 times daily, over 6 years 800mg 4 times daily.

By iv infusion; Give over one hour, herpes simplex or recurrent varicella-zoster 5mg/kg every 8 hours; doubled in primary and recurrent varicella-zoster in the immunocompromised, and in simplex encephalitis (for which it should be continued for at least 10 days); child up to 3 months 10mg/kg every 8 hours; 3 months to 12 months, 250mg/m2 every 8 hours, dose doubled in the immunocompromised and in simplex encephalitis (for which it should be continued for at least 10 days).

**Side-effects:** Rash; gastro-intestinal disturbances; rises in bilirubin and liver enzymes, increases in blood urea and creatinine, decreases in haematological indices, headache, neurological reactions (including dizziness), fatigue; on iv infusion, sever local inflammation (sometimes leading to ulceration), also confusion, hallucinations, agitation, tremors, somnolence, psychosis, convulsions and coma.

**Caution:** Maintain adequate hydration; renal impairment; pregnancy and breastfeeding.

**Contra-indications:** Hypersensitivity to aciclovir

**GANCYCLOVIR**

**Presentation:** Capsules containing ganciclovir 250mg. iv infusion powder for reconstitution containing ganciclovir sodium 500mg per vial.

**Indications:** Life-threatening or sight-threatening cytomegalovirus infections in immunocompromised patients only; prevention of cytomegalovirus disease during immunosuppressive therapy following organ transplantation.

**Dose:** by iv infusion over one hour, initial (induction treatment), 5mg/kg every 12 hour for 14-21 days for treatment or for 7-14 dys for prevention; maintenance (for patients at risk of relapse of cytomegalovirus disease during immunosuppressive therapy following organ transplantation).

**4.7.2 Drugs used in Cytomegalovirus (CMV) infections**

Ganciclovir is related to aciclovir but is more active against cytomegalovirus and is also more toxic. It should therefore only be given when potential benefit outweighs the risks. It is usually given by intravenous infusion but capsules are available for maintenance treatment if CMV retinitis in AIDS patients following IV therapy if the condition is stable. Ganciclovir should not be given together with zidovudine as the combination causes severe myelosuppression.

**IDOXURIDINE**

**Presentation:** Application (with applicator) containing idoxuridine 5% in dimethyl sulphoxide, 5ml

**Indications:** Herpes simplex and herpes zoster

**Dose:** apply to lesions 4 times daily for 4 days, starting at first sign of attack; child under 12 years, not recommended.

**Side-effects:** stinging on application, changes in taste; overuse may cause maceration

**Caution:** avoid contact with eyes, mucous membranes, and textiles; breast-feeding (may taste unpleasant).

**Contra-indications:** Pregnancy (toxicity in animal studies); not to be used in the mouth.

**VALACYCLOVIR**

**Presentation:** Tablets containing valacyclovir hydrochloride 500mg

**Indications:** Treatment of herpes zoster and herpes simplex infections of skin and mucous membranes including initial and recurrent genital herpes.

**Dose:** Herpes zoster, 1g 3 times daily for 7 days; herpes simplex, first episode, 500mg twice daily for 5 days (up to ten days if severe); recurrent infection, 500mg twice daily for 5 days; child-not recommended.

**Side-effects:** As for acyclovir; nausea and headache reported

**Caution:** Maintain adequate hydration; renal impairment; pregnancy and breast-feeding.

**Contra-indications:** Hypersensitivity to valacyclovir
retinitis) 6mg/kg daily on 5 days per week or 5mg/kg daily every day; if retinitis progresses initial
drug treatment may be repeated.
Maintenance in AIDS patients where retinitis is
stable (following at least three weeks of iv
ganciclovir), by mouth, 1g 4 times daily with
food or 500mg 6 times daily with food. In renal
impairment, consult product literature.

Side-effects: Most frequent, leucopenia and
thrombocytopenia; less frequent, includes anaemia,
fever, rash, infections, gastrointestinal haemorrhage,
dizziness, mood disturbances, disturbances in taste
and vision, local inflammation, pain, phlebitis at
injection site (see product literature for full list).

Caution: Close monitoring of blood counts; history
of cytopenia; low platelet count; concomitant use
of myelosuppressants or drugs which inhibit
rapid cell replication; potential carcinogen and
teratogen; renal impairment; ensure adequate
hydration during administration; vesicant-infuse
into vein with adequate flow preferably via a plastic
cannula; limited experience in children—not for
infusion.

Contra-indications: Hypersensitivity to
ganciclovir or aciclovir, pregnancy (effective
contraception should be used during treatment
and barrier contraception for men during and for
90 days after treatment); breastfeeding (until 72
hours after last dose); abnormally low neutrophil
or platelet counts.

4.7.3 Drugs used in human
immunodeficiency virus
(HIV) infection

4.7.3.1. Nucleoside reverse transcriptase
inhibitors
4.7.3.2. Non-Nucleoside Transcrip
tase inhibitors (NNTI’s)
4.7.3.3. Protease inhibitors

While there is currently no known cure for HIV
infection, there is evidence that treating HIV
infected patients with antiretroviral drugs does have
benefits in terms of improved health and quality of
life. The use of antiretroviral drugs to treat HIV
infected patient should only be undertaken by those
experienced in their use.

Monitoring HIV infection/therapy
CD4 count
The CD4 count is useful for staging HIV disease
and for timing the initiation of prophylaxis against
opportunistic infections.

Viral load count
Viral load test measures the amount of HIV RNA
in the blood. Right now, if CD4 count and viral
loads are not available, there is no other way to
define failure of therapy with laboratory tests. The
level of HIV in the blood gives an indication of
a person’s risk of getting sick. The lower the load

the less likely the patient to get sick and the longer
they will live. It is expected that after 6 months of
therapy there should be low viral RNA detectable
in the plasma if treatment is optimal.

Initiating
Clinical decisions on initiating or changing therapy
should be guided by a combination of CD4 count
and viral load count monitoring and consideration
of the clinical condition of the patient. It is
proposed that initiation of treatment be considered
when viral load counts are > 10,000 to 50,000
copies/ml with falling CD4 count (<200-300 cells/
mm³).

Special considerations for starting ARV therapy
should be given to patients with:

- TB: Start with CD4< 200 or total lymphocyte
count < 1200/mm³ or other HIV-related
stage 2 or 3 conditions currently or in past 12
months.

- Kaposi’s Sarcoma: is considered an AIDS
defining condition; start on ARV therapy.
A total lymphocyte count of < 1,200-cells/ mm³
can be substituted for the CD4 count if HIV-
related symptoms exist (WHO stage II and III).
An absolute lymphocyte count is less useful in
the patient without symptoms. If there is no CD4
testing, HIV-infected patients with no symptoms
(WHO stage I) should be treated; observe for the
development of early symptoms and refer for
further evaluation (e.g. CD4 and Viral load testing)
if feasible.

Response to treatment
Change in viral load 8-12 weeks after starting
treatment is considered the best single marker of
therapeutic effect, with predictive value being
increased when viral load and CD4 counts are
combined. The aim of treatment is to reduce the
level of virus in the blood as low as possible and
preferably to undetectable levels and to prevent
the emergence of resistance. However, therapy
goals set should be realistic and will depend on the
stage at which the patient is started on treatment,
the baseline viral load and CD4 counts, previous
exposure to treatment drugs and presence and
extent of drug resistance.

Choice of drugs
Failure of drugs to work has been most frequently
associated with the emergence of resistance. Using
a combination of drugs delays the emergence of
resistance.

It is generally accepted that triple therapy with two
nucleoside analogues and one NNRTIs or protease
inhibitor is the preferred regimen. Monotherapy is
not recommended due to the rapid emergence of
resistance and poor response.

When to change therapy
Decisions to change therapy will depend on a
number of factors - clinical eg. intolerance due to
side effects or adverse events; virological eg. rising
viral load count; and immunological eg. falling CD4 count. Occurrences of pregnancy T.B, New effective drugs

The choice of whether to change all the drugs or to change just one or some of the drugs will depend on previous exposure to treatment drugs, toxicity profile of alternative drugs, availability of viral sensitivity assays, availability of testing facilities for CD4 and viral load counts.

Current practice appears to lean towards changing treatment after 3 months if there is little or no clinical improvement or if CD4 remains the same as dropping or if virus levels are rising after initially falling.

It is preferable, in general, to change at least one class of most likely affected drugs (eg NRTIs) and even better to use an entirely new regimen when class of most likely affected drugs (eg NRTIs) and even better to use an entirely new regimen when there is treatment failure due to drug failure as opposed to drug toxicity. Where drug toxicity is the problem a different drug or drugs of equivalent potency from the same class of agents can be substituted.

4.7.3.1 Nucleoside reverse transcriptase inhibitors

ABACAVIR

Presentation: Oral liquid: 100 mg (as sulfate) / 5 ml tablet: 300 mg (as sulfate).

Uses: HIV infection in combination with at least two other antiretroviral medicines.

Precautions: chronic hepatitis B C, hepatic impairment

Hypersensitivity Reactions: Life-threatening hypersensitivity reactions characterized most commonly by fever or rash and possibly nausea, vomiting, diarrhea, abdominal pain, dyspnoea, cough, lethargy, malaise, headache, and myalgia, less frequently by mouth ulceration, oedema, hypotension, sore throat, adult respiratory distress syndrome, paraesthesia, arthralgia, conjunctivitis, lymphadenopathy, lymphocytopenia, renal failure, and anaphylaxis and rarely by myol6sis have been reported. Laboratory abnormalities may include raised liver enzymes (see Hepatic disease below) and creatine kinase. Symptoms usually appear in the first 6 weeks, but may occur at any time; monitor patients for symptoms every 2 weeks for 2 months; discontinue immediately if any symptom of hypersensitivity develops and do not rechallenge (risk of more severe hypersensitivity reaction); also discontinue if hypersensitivity cannot be ruled out, even when other diagnoses possible (if rechallenge is necessary, it must be carried out in a hospital setting). If abacavir is stopped for any reason other than hypersensitivity, exclude hypersensitivity reaction as the cause and rechallenge only if medical assistance is readily available; care is needed with concomitant use of drugs which are known to cause skin toxicity.

Patient advice: Patients should be told about the importance of regular dosing (interruption therapy may increase sensitization), how to recognize signs of hypersensitivity, and advised to seek immediate medical attention if symptoms develop or before re-starting treatment.

Hepatic disease: Potentially life threatening lactic acidosis and severe hepatomegaly with steatosis have been reported. Exercise caution in patients (particularly obese women) with hepatomegaly, hepatitis, liver enzyme abnormalities or risk factors for liver disease and hepatic steatosis (including alcohol abuse) and discontinue if rapid deterioration in liver function tests, symptomatic hyperlactataemia, progressive hepatomegaly, or lactic acidosis occurs.

Dose: HIV infection in combination with at least two other antiretroviral medicines, by mouth, Adult, 300 mg twice daily; Child 3 months – 16 years, 8 mg/kg twice daily (maximum, 600 mg daily).

Adverse effects: hypersensitivity reactions including nausea, vomiting, diarrhea, anorexia, lethargy, fatigue, fever, headache, insomnia, and dizziness (see also note on Hypersensitivity reactions above); pancreatitis, liver damage and lactic acidosis (see note on Hepatic disease above; very rarely Stevens-Johnson syndrome and toxic epidermal necrolysis, rash and gastrointestinal disturbances more common in children.

TENOFOVIR DISOPROXIL FUMARATE

Presentation: Tablet: 300 mg (tenofovir disoproxil fumarate – equivalent to 245 mg tenofovir disoproxil).

Uses: HIV infection in combination with other antiretroviral medicines.

Precautions: renal impairment hepatic disease, pregnancy, breastfeeding.

Hepatic disease: Potentially life-threatening lactic acidosis and severe hepatomegaly with steatosis have been reported. Exercise caution in patients (particularly obese women) with hepatomegaly, hepatitis (especially hepatitis C treated with interferon alfa and ribavirin), liver enzyme abnormalities, or risk factors for liver disease and hepatic steatosis (including alcohol abuse) and discontinue if rapid deterioration I liver function tests, symptomatic hyperlactataemia, progressive hepatomegaly, or lactic acidosis occurs. Exacerbation of hepatitis in patients with chronic hepatitis B may occur on discontinuation of tenofovir.

Dose: HIV infection (in combination with other antiretroviral medicines), by mouth, Adult, 245 mg (1 tablet) once daily.

Patient advice: Tablets can be dispersed in at least 100 ml water, orange juice or grape juice for patients with difficulty swallowing.
Drugs used in the treatment of infections

Adverse effects: nausea, vomiting, abdominal pain, flatulence, diarrhea, anorexia; hypophosphataemia; dizziness, peripheral neuropathy, headache, dyspnoea, insomnia, depression, asthenia, sweating, myalgia, rash, hypertriglyceridaemia, hyperglycaemia, neutropenia; nephritis, nephrogenic diabetes insipidus, renal impairment, effects on renal proximal tubules (including Fanconi syndrome), proteinuria, polyuria, reduced bone density; pancreatitis, hepatitis, lactic acidosis, raised liver enzymes, creatinine and serum amylase reported.

**LAMIVUDINE (3TC)**

**Presentation:** Tablets (film coated) containing 150mg lamivudine. Oral solution containing 10mg/ml lamivudine.

**Indications:** Advanced HIV infection, in combination with other antiretroviral drugs.

**Dose:** Neonates (<30 days); 2mg/kg body weight twice daily.

Child; 4mg/kg body weight twice daily.

Adolescent/adult; Body weight > or = 50kg; 150mg twice daily. Body weight < 50kg 2mg/kg body weight twice daily

**Side effects:** Most frequent ones include headache, anaemia fatigue, nausea, diarrhea, skin rash and abdominal pain, fever, alopecia, lactic acidosis

**Caution:** Renal impairment, hepatic disease due to chronic hepatitis B infection (risk of rebound hepatitis on discontinuation); pregnancy (avoid in first trimester), Breast-feeding

**ZIDOVUDINE (AZT)**

**Presentation:** Tablets containing 300mg zidovudine, capsules containing 100mg zidovudine. Syrup containing 10mg/ml zidovudine. Injection for dilution or use as i.v. infusion containing 10mg/ml zidovudine.

**Indications:** Management of advanced HIV infection such AIDS in combination or AIDS-related complex; early symptomatic or asymptomatic HIV infection with markers indicating risk of disease progression; symptomatic or asymptomatic HIV-infected children with markers indicating significant immune suppression; consider for prevention of maternal-fetal HIV transmission (by treating pregnant women and their newborn infants in combination with other drugs).

**Dose:** Adolescent/adult; 200mg every 8 hours or 300mg twice a day. Child; usual dose; 90mg – 180mg/m² of body surface area every 6 hours.

**Side effects:** Frequent side effects include headache, gastrointestinal disturbances and skin rashes. Uncommon but more severe side effects include peripheral neuropathy, pancreatitis, hepatic toxicity, oral ulcers, esophageal ulcers, haemotologic toxicity, and skin rashes.

**Caution:** Haematological toxicity (blood tests at least every 2 weeks for first 3 months then at least once a month); vitamin B12 deficiency; renal impairment; hepatic impairment; risk of lactic acidosis; elderly; pregnancy; breastfeeding not recommended during treatment

**Contra-indications:** Abnormally low neutrophil counts or haemoglobin values (see data sheet); neonates with hyperbilirubinaemia requiring treatment other than phototherapy, or with raised transaminase.
4.7.3.1.6 Non-nucleoside reverse transcriptase inhibitors

**EFAVIRENZE**

**Presentation:** Capsule: 50 mg; 100 mg; 200 mg. Oral liquid: 150 mg/5 ml. Tablet: 600 mg.

**Note:** The bioavailability of efavirenz from the oral solution is lower than that from the capsules and tablets; the oral solution is therefore not interchangeable with either the capsules or tablets on a milligram-for-milligram basis.

**Indications:** HIV infection in combination with at least two other antiretroviral medicines.

**Contraindications:** Pregnancy (see introductory note above; Appendix 2; substitute nevirapine for efavirenz in pregnant women or women for whom effective contraception cannot be assured).

**Precautions:** chronic hepatitis B or C; hepatic impairment (avoid if severe; renal impairment. Breastfeeding, the elderly; history of mental illness or seizures.

**Side effects:** Rash, usually occurring in the first 2 weeks, is the most common adverse effect; discontinue if rash is severe or if rash is accompanied by blistering oral lesions, mucosal involvement or fever; if rash is mild or moderate, continue without interruption (rash usually resolves within 1 month).

**Psychiatric disorders:** patients should be advised to seek medical attention if severe, depression, psychosis or suicidal ideation occur.

**NEVIRAPINE**

**Presentation:** Oral liquid: 50 mg/5 ml. Tablet: 200 mg.

**Indication:** HIV infection in combination with at least two other antiretroviral medicines; prevention of mother-to-child HIV transmission.

**Side effects:** severe hepatic impairment; post-exposure prophylaxis.

**Caution:** hepatic impairment; chronic hepatitis B or C, high CD4 cell count, and women (greater risk of hepatic side effects preferably avoid in women with a CD4 cell count greater than 250 cells/mm³ and in men with a CD4 cell count greater than 400 cells/mm³; pregnancy breastfeeding.

**Hepatic disease:** Potentially life-threatening hepatotoxicity, including fatal fulminant hepatitis, reported usually occurring in the first 6 weeks. Close monitoring is required during first 18 weeks; assess liver function before treatment then every 2 weeks for 2 months, then after 1 month, and then regularly. Discontinue permanently if liver abnormalities are accompanied by hypersensitivity reactions for example, rash, fever, arthralgia, myalgia, lymphadenopathy, hepatitis, renal impairment, eosinophilia, and granulocytopenia. If severe liver abnormalities occur without hypersensitivity reactions, suspend, but discontinue permanently if significant liver function abnormalities recur. Monitor patient closely if there are mild to moderate liver abnormalities with no hypersensitivity reactions.

**NOTE:** If treatment is interrupted for more than 7 days, reintroduce at a low dose and increase dose cautiously.

**Side effects:** Rash, usually occurring in first 6 weeks, is the most common side-effect; incidence can be reduced if introduced at low dose and dose increased gradually. Monitor closely for skin reactions during first 18 weeks; discontinue permanently if rash is severe or if rash is accompanied by blistering oral lesions, conjunctivitis, facial oedema, general malaise, or hypersensitivity reactions; if rash is mil or moderate, continue without interruption but dose should not be increased until rash resolves.

**Patient advice:** Patients should be told how to recognize hypersensitivity reactions and advised to discontinue treatment and seek immediate medical attention if symptoms of hepatitis, severe skin reaction, or hypersensitivity reactions develop.

**Dose:**

HIV infection (in combination with other antiretroviral medicines), by mouth, Adult, 200 mg once daily for first 14 days, then (if no rash present) 200 mg twice daily. Infant 15-30 days old, 5 mg/kg once daily for 14 days, then (if no rash present) 120 mg/m² twice daily for 14 days, then 200 mg/m² twice daily; Child 1 month-13 years, 120 mg/m² once daily for first 14 days, then (if no rash present) 120-200 mg/m² twice daily.

Prevention of mother-to-child transmission of HIV (see also introductory note above under Pregnancy), by mouth, Adult, 200 mg as a single dose at onset of labour; NEONATE, 2 mg/kg as a single dose within 72 hours of birth; if the maternal dose is given less than 2 hours before delivery, 2 mg/kg should be given immediately after birth, followed by a further dose within 24-72 hours.

**NOTE:** In adults, if treatment is interrupted for more than 7 days, reintroduce at a dose of 200 mg daily. (Infant 15-30 days old, 5 mg/kg; Child over 1 month, 120 mg/m²) and increase dose cautiously.

**Adverse effects:** rash including Stevens-Johnson syndrome and rarely, toxic epidermal necrolysis (see also note on Rash above); nausea, hepatitis (see also note on Hepatic disease above), headache; less commonly vomiting, abdominal pain, fatigue, fever, and myalgia; rarely diarrhoea, angioedema, anaphylaxis, hypersensitivity reactions (may involve hepatic reactions and rash; see not on Hepatic disease above); arthralgia, anaemia, and granulocytopenia (more frequent in children); very rarely neuropsychiatric reactions.

4.7.3.2 Protease inhibitors

**INDINAVIR**

**Presentation:** Capsules containing 100mg, 333mg idinavir.
Indications: Progressive or advanced HIV infection, in combination with ARVs.

Dose: Adolescent/adult: 800mg every 8 hours.
Child: 500mg/m². Children under 4 years, safety and efficacy not yet established.

Side effects: More frequent include nausea, abdominal pain, headache, metallic taste, dizziness and asymptomatic hyperbilirubinaemia. Unusual but more severe side effects include nephrolithiasis (4%) and exacerbation of chronic liver disease. Rarely spontaneous bleeding episodes in haemophiliacs, hyperglycaemia, ketoacidosis, diabetes, and haemolytic anaemia.

Caution: Hepatic impairment; ensure adequate hydration to reduce risk of nephrolithiasis; haemophilia (possible increased bleeding); pregnancy; metabolism of many drugs inhibited if administered concomitantly (consult product literature), breast-feeding

Ritonavir

Presentation: Capsules containing 100mg ritonavir. Oral solution containing 400mg/5ml ritonavir.

Indications: Progressive or advanced HIV infection, in combination with other ARVs.

Dose: Adult; 600mg twice daily. To minimise nausea/vomiting, initiate therapy starting at 300mg twice daily and increase stepwise to full dose over 5 days as tolerated.

Side effects: Most frequent side effects include nausea, vomiting, diarrhoea, headache, abdominal pain, and anorexia. Rarely spontaneous bleeding in haemophiliacs, pancreatitis, increased levels of triglycerides and cholesterol, hyperglycaemia, ketoacidosis, diabetes, and hepatitis.

Caution: Hepatic impairment; haemophilia (possible increased bleeding); pregnancy; metabolism of many drugs inhibited and toxicity increased if administered concomitantly (consult product literature), breastfeeding.

Contra-indications: Severe hepatic impairment.

Saquinavir

Presentation: Capsules containing 200mg saquinavir mesylate, hard or soft gel and shell capsules.

Indications: Progressive or advanced HIV infection, in combination with nucleoside analogues.

Dose: Adult: 600mg three times daily within 2 hours after a meal. Child: Safety and efficacy not established.

Side effects: Diarrhoea, abdominal discomfort, nausea, headache, paresthesias, and skin rashes. Less common exacerbation of chronic liver disease, spontaneous bleeding in haemophiliacs, hyperglycaemia, ketoacidosis, and diabetes.

Caution: Severe hepatic or renal impairment; haemophilia (possible increased bleeding); pregnancy.

Contra-indications: Breast-feeding
5 Drugs acting on the endocrine system

5.1 Drugs used in diabetes
5.2 Drugs acting on the thyroid
5.3 Corticosteroids
5.4 Drugs used in gynaecology and obstetrics
5.5 Other endocrine drugs
5.6 Androgens and anti-androgens

5.1 Drugs used in diabetes

5.1.1 Insulin
5.1.2 Oral hypoglycaemic drugs
5.1.3 Treatment of hypoglycaemia

5.1.1 Insulin

A polypeptide hormone found naturally in the body which plays an important role in the metabolism of carbohydrates, fats and proteins. It is used for management of insulin dependent diabetes mellitus (IDDM) or type 1 diabetes. IDDM is due to deficiency in insulin synthesis and secretion.

Insulin used for treatment is extracted mainly from pork pancreas and purified by crystallization. Also available are beef/pork and human varieties and biosynthetically made and semisynthetic human varieties. Immunological resistance to insulin is uncommon. Antigenic (immune) response occurs in some individuals. It is inactivated by gastrointestinal enzymes so it is given by injection, mainly subcutaneously. It can also be given continuously by subcutaneous infusion although this is not the preferred route as it requires expert supervision at all times.

Insulin is the drug of choice in patients with a rapid onset of symptoms and most children require insulin from the onset.

Blood glucose concentrations must be monitored for patients receiving insulin treatment. Variations in lifestyles, infection, corticosteroids and oral contraceptives may affect insulin requirements. In pregnancy insulin requirements must be assessed frequently.

Insulin is available in three types of preparations:

5.1.1.1 Short duration, soluble forms, for rapid onset of action

Intermediate action
Long acting, with a slower onset of action but lasting longer.

The duration of action varies considerably from one patient to another and individual assessments are necessary. The type, dose and frequency are based on individual needs. Most patients are best started on intermediate action insulin twice daily and a short-acting can later be added to control any hyperglycaemia which may follow breakfast or supper. It is important to note that variability in absorption within the same individual and between two individuals can happen.

The change of the type of insulin e.g. from bovine to human insulin may result in hypoglycaemia. This should only be done with specialist advice. Change from porcine to human insulin does not normally require a dose change but careful monitoring is advised.

Loss of warning of hypoglycaemia is a common problem with insulin-treated patients. The cause is unknown but patients should be warned of the hazard. Beta-blockers and change to human insulin may blunt hypoglycaemic awareness.

Patients especially drivers and those operating machinery should be strongly advised about the dangers of hypoglycaemia.

Insulin vials should be stored under refrigeration at 2 – 8°C Celsius. Exposure to direct sunlight can accelerate the degradation of insulin.

Discolouration, turbidity or unusual viscosity in soluble insulin indicates deterioration or contamination. Insulin suspensions (intermediate and long –acting) should be discarded if the sediment cannot be suspended, if a clumped, granular precipitate is apparent, or if a deposit of solid particles is seen on the wall of the vial.

5.1.1.1 Short acting Insulin

This is the only type of insulin that can be administered intravenously during the treatment of diabetic emergencies, ketoacidosis, during surgery or during intravenous feeding. It can also be administered intramuscularly when the intravenous route is not available. When injected subcutaneously, it has a rapid onset of action (after
Drugs acting on the endocrine system

5.1.1.1 Soluble Insulin
(insulin injection, neutral insulin, regular insulin, semi lente)

Presentation: Injection containing 100 units/ml of soluble insulin (bovine, porcine or human).
Indications: Diabetes mellitus, diabetic ketoacidosis.
Dose: By subcutaneous, intramuscular, or intravenous injection or infusion according to individual requirement. For maintenance regimens it is usual to inject 15 to 30 minutes before meals.
Side effects: Fat hypertrophy at injection site, hypoglycaemia in overdose, see notes above.
Caution: See notes above. Reduce dose in renal impairment.

5.1.1.2 Intermediate and Long Acting Insulins

When given by intramuscular injection these have an onset of action of approximately 1 – 2 hours, a maximal effect at 4 – 12 hours and a duration of 16 – 35 hours.

The dosing regimen is variable but includes the following:

Single morning injection of intermediate –action insulin. To control mid-morning hyperglycaemia from breakfast this may be combined with a rapid acting insulin. The one –daily dose of intermediate acting insulin is commonly used in elderly patients.

A second dose of the intermediate acting insulin before the evening meal may be given if adequate control is not achieved. This second dose can be given before bed time to prevent nocturnal hyperglycaemia if the peak effect occurs during sleep.

5.1.2 Oral hypoglycaemic drugs

5.1.2.1 Sulphonylureas

There are several sulphonylureas. There is no evidence of any difference in their effectiveness. Chlorpropamide has more side effects mainly because of its long duration of action and potential for accumulation and therefore the increased risk of hypoglycaemia.

The choice of drug depends on the age and renal function of the patient. Elderly patients are prone to hypoglycaemia when a long acting drug is used. In this category of patient chlorpropamide and glibenclamide should be avoided.

Caution: These drugs encourage weight gain. Caution should be exercised when used in the elderly and in hepatic and renal insufficiency because of the risk of hypoglycaemia. Avoid use in porphyria.
Contra-indications: Pregnancy, breastfeeding,
ketoacidosis, intercurrent illness (e.g. myocardial infarction, coma, infection and trauma) and in surgery. Insulin therapy should be administered in these conditions.

CHLORPROPAMIDE

**Presentation:** Tablets containing 100 mg and 250mg chlorpropamide.

**Indications:** Non insulin dependent diabetes mellitus

**Dose:** Initially 250 mg daily, adjusted according to response, maximum 500 mg daily taken with breakfast.

**Side effects:** May cause disulfiram like effect (flushing, dizziness and headache) with alcohol, may enhance antidiuretic hormone and rarely causes hyponatraemia.

**Caution and Contra-indications:** See notes above.

GLICLABNCLAMIDE

**Presentation:** Tablets containing 2.5mg, 5mg glibenclamide.

**Indications:** Diabetes mellitus

**Dose:** Initially 5mg daily adjusted according to response. Maximum dose 15mg daily taken with breakfast

**Side effects:** Hypoglycaemia, rarely gastrointestinal disturbances and headaches.

**Caution and Contra-indications:** See notes above.

GLICLABZIDE

**Presentation:** Tablets containing 80mg gliclazide

**Indications:** Non insulin dependent diabetes mellitus

**Dose:** Initially 40mg – 80mg daily, adjusted according to response up to 160mg as single dose with breakfast. Higher doses should be divided. Maximum 320mg daily.

**Side effects:** Hypoglycaemia, rarely gastrointestinal disturbances, headache.

**Caution and Contra-indications:** See notes above.

GLIPIZIDE

**Presentation:** Tablets containing 2.5mg, 5mg glipizide.

**Indications:** Non insulin dependent diabetes mellitus

**Dose:** Initially 2.5mg – 5mg daily adjusted according to response, maximum 40mg daily. Up to 15mg may be given as single dose before breakfast. Higher doses should be divided.

**Side effects:** Hypoglycaemia, gastro-intestinal disturbances, headache.

**Caution and Contra-indications:** See notes above.

**TOLBUTAMIDE**

**Presentation:** Tablets containing 500mg tolbutamide.

**Indications:** Non insulin dependent diabetes mellitus

**Dose:** 0.5 – 1.5g (max 2g) daily in divided doses.

**Side effects:** Hypoglycaemia, gastrointestinal disturbances and headache.

**Caution and Contra-indications:** See notes above.

5.1.2.2 Biguanides

These are only effective in diabetics with some residual functioning pancreatic islet cells as they only act in the presence of endogenous insulin. They are used in type II diabetes when dieting and exercise have failed to achieve adequate control of hyperglycaemia. They can be used alone or with a sulphonylurea.

**METFORMIN HYDROCHLORIDE**

**Presentation:** Tablets containing 500mg, 850mg metformin hydrochloride.

**Indications:** Non insulin dependent diabetes mellitus

**Dose:** 500mg every 8 hours or 850mg every 12 hours with or after food. Maximum 3g daily in divided doses.

**Side effects:** Metallic taste, nausea, anorexia, vomiting, abdominal pain, diarrhoea, lactic acidosis (withdraw treatment), decreased vitamin B12 absorption.

**Contra-indications:** Hepatic or renal impairment, predisposition to lactic acidosis, heart failure, severe infection or trauma, dehydration, alcohol dependence, pregnancy, breast feeding.

**Caution:** See notes above

5.1.3 Treatment of hypoglycaemia

Hypoglycaemia is a potentially fatal condition requiring immediate treatment. 3 to 4 teaspoons of sugar, with a little water should be taken. This can be repeated if necessary in 10 to 15 minutes. Up to 50 ml of 50% glucose intravenous infusion should be administered in case of unconsciousness.

Alternatively, glucagon, a natural hormone, can be given instead of parenteral glucose. It can be administered subcutaneously, intramuscularly or intravenously. If it is not effective within 20 minutes intravenous glucose should be given.

Chronic hypoglycaemia resulting from excess endogenous secretion of insulin is managed using diazoxide.
5.2 Drugs acting on the thyroid

5.2.1 Thyroid Hormones

They are used in hypothyroidism (myxoedema) and also in diffuse non-toxic goiter and carcinoma. Neonatal thyroidism requires prompt treatment for normal development.

5.2.2 Anti-thyroid drugs

5.5.2 Antithyroid drugs

Antithyroid drugs are used to prepare patients for thyroidectomy and inducing life-long remission.

5.3 Corticosteroids

Corticosteroids permit many biochemical reactions in the body to proceed at optimal rates. They are therefore used as replacement therapy in adrenocortical insufficiency. Their clinical use is dependant on the anti-inflammatory, anti-allergic and lympholytic properties of each active substance.

Corticosteroids have both glucocorticoid and mineralocorticoid properties in varying
proportions. Generally anti-inflammatory agents have high glucocorticoid and low mineralocorticoid effects and those with high mineralocorticoid effects are more suitable for adrenal replacement therapy and topical management of inflammatory skin conditions.

Glucocorticoid effects are responsible for the control of sodium, potassium, protein, carbohydrate and lipid metabolism and also increase haemoglobin and red and white cells in the blood. Betamethasone, dexamethasone, methylprednisolone and prednisolone have high glucocorticoid activity.

Mineralocorticoid effects influence electrolyte and water metabolism. Fludrocortisone, hydrocortisone, cortisone and aldosterone have high mineralocorticoid activity hence their low or moderate anti-inflammatory activity. Their fluid retention property renders them unsuitable for long term use in inflammatory disease suppression.

Betamethasone and dexamethasone, because of their high glucocorticoid and insignificant mineralocorticoid activity are the most suitable for long term administration. Cortisone and hydrocortisone are suitable for adrenal replacement therapy.

Corticosteroids have a poor side effect profile. Their use should only be considered after serious consideration of the risk benefit factors. Prolonged use should only be considered in life-saving or life prolonging situations and only after other therapeutic measures have proved ineffective.

The dosage should be carefully determined and varies from one condition to another and from patient to patient. High doses are associated with necrosis of the femoral head and they may also cause mental disturbances, depression, euphoria and muscle wasting. They may also worsen infection and suppress clinical signs. Infections like TB, septicemia may be masked until they reach an advanced stage. They may also cause peptic ulcer disease and cushing’s syndrome like features with moon face, striae and acne.

High dosage or prolonged use may exaggerate normal physiological actions of corticosteroids. These include sodium and water retention, potassium loss (mineralocorticoid), hyperglycaemia and osteoporosis.

The risks in children are even greater and prolonged use is rarely justified. Corticosteroid use in children may result in the suppression of growth. High doses during pregnancy may affect adrenal development in the child.

It is preferable to use local treatment using creams, intra-articular injections, inhalations, eye drops or enemas to systemic treatment. It is preferable to administer the dose in the morning. The prescriber should consider an alternate day dose regimen e.g. prednisone 40mg orally on alternate days instead of 20mg per day. The lowest dose for the shortest possible course of treatment should be considered.

Withdrawal of treatment should be gradual. The length of withdrawal depends on the dosage and duration of therapy. Too rapid withdrawal can lead to acute adrenal insufficiency, hypertension and death. Withdrawal symptoms like rhinitis, conjunctivitis, loss of weight, arthralgia and painful itchy skin may be experienced.

Patients who have received doses of 50mg or more per day of cortisone for periods of more than 1 month should be considered potential cases of pituitary / adren al suppression for at least one year after corticosteroid withdrawal.

Anaesthetists must be informed of corticosteroid therapy to avoid precipitous fall in BP during anaesthesia or in the immediate post operative period.

If an acute infection, trauma or surgery occurs during a course of corticosteroid treatment, increase rather than reduce the dose, giving it parenterally if necessary. **Side effects:** Electrolyte imbalance leading to sodium retention, oedema, hypertension and increased potassium retention, cushing’s syndrome, with hirsutism, acne, moon face and striae, increased appetite, muscle weakness, osteoporosis, peptic ulcer and gastric upsets, skin thinning. Glucose tolerance may be diminished and diabetes precipitated.

Growth retardation in children, inactivity or atrophy of adrenal cortex, impairment of the immune process, delayed wound healing, increased risk of infection and of thrombosis, pancreatitis, glaucoma, cataract, mental disorder. **Contra-indications:** TB (combine with anti-TB treatment if unavoidable), local and systemic infections if not controlled by chemotherapy, active peptic ulcer, psychoses, osteoporosis, renal dysfunction, diabetes mellitus, glaucoma, hypertension, myasthenia gravis, thromboembolic disorders, congestive heart failure, pregnancy and herpes infections.

**Caution:** Concomitant use with cardiac glycosides, thiazide diuretics, antidiabetic drugs, coumarins, rifampicin, phenytoin, barbiturates and NSAIDS.

Perform routine ophthalmic checks with long-term use.

Patients should carry “steroid cards” where available.

**Replacement therapy**

This is necessary in situations where the adrenal cortex does not secrete adequate hydrocortisone. Physiological replacement is best achieved with a
Drugs acting on the endocrine system

**FLUDROCORTISONE ACETATE**

**Presentation:** Tablets containing 100mcg fludrocortisone acetate.

**Indications:** Mineralocorticoid replacement in adrenocortical insufficiency (see 5.3.1.)

**Dose:** Adult: 50 – 100mcg daily. Child: 5mcg/kg body weight daily.

Addison’s disease or adrenalectomy 50 to 300mcg daily.

**Side effects, Contra-indications:** Caution: see notes above

**HYDROCORTISONE**

**Presentation:** Tablets containing 10mg, 20mg hydrocortisone, injection: powder for reconstitution containing 100mg hydrocortisone as sodium succinate.

**Indications:** Adrenocortical insufficiency (See 5.3.1.), Addison’s disease or following adrenalectomy, suppression of inflammatory and allergic disorders, shock.

**Dose:** Replacement therapy; 20 to 30mg daily orally in 2 divided doses. Larger dose in the morning and smaller in the evening. Optimal dose determined according to clinical response.

In acute adrenocortical insufficiency; 100mg every 6 to 8 hours intravenous in 9% sodium chloride infusion.

In suppression of inflammatory and allergic disorders; intramuscular or slow intravenous Adult injection or infusion, 100 – 500mg given 3 to 4 times in 24 hours or as required.

Child; By slow iv injection, up to 1 year; 25mg. 1 – 5 years; 50mg. 6 – 12 years; 100mg. In anaphylactic shock; as adjunct to adrenaline 100 to 300mg intravenous injection.

**Side effects, contra-indications:** Caution, See notes above. Perineal irritation may follow intravenous administration of phosphate ester

**BETAMETHASONE**

**Presentation:** Tablets containing 500mcg betamethasone; injection containing 4 mg/ml betamethasone as sodium phosphate.

**Indications:** Suppression of inflammatory and allergic disorders, congenital adrenal hyperplasia, cerebral oedema.

**Dose:** Oral; 0.5 – 5mg daily. Injection; intramuscular or slow intravenous, or infusion; 4 – 20mg repeated up to 4 times in 24 hours.

Child; By slow intravenous injection, up to 1 year; 1mg. 1 – 5 years; 2mg. 6-12 years; 4 mg.

**Side effects, Caution, Contra-indications:** see notes above

**DEXAMETHASONE**

**Presentation:** Tablets containing 500mcg, 2mg dexamethasone, injection containing 4mg/ml, 20mg/ml dexamethasone sodium phosphate.

**Indications:** Suppression of inflammatory and allergic disorders; shock, diagnosis of cushing’s disease; congenital adrenal hyperplasia, cerebral oedema.

**Dose:** Oral; 0.5 – 9mg daily. By intramuscular, slow intravenous injection or infusion; initially 0.5 – 20mg. Child; 200 – 500mcg/kg body weight daily.

Cerebral oedema; intravenous injection 10mg initially then 4 mg every 6 hours as required for 2 – 10 days.

**Side effects, contra-indications, Caution:** See notes above. Perineal irritation may follow intravenous administration of the phosphate ester.

**METHYLPREDNISOLONE**

**Presentation:** Tablets containing 2mg, 4mg, 16mg methylprednisolone, injection – powder for reconstitution containing methylprednisolone as sodium succinate 125mg, 500mg.

**Indications:** Suppression of inflammatory and allergic disorders, cerebral oedema.

**Dose:** Oral; 2 – 40mg daily. intramuscular or slow intravenous injection or infusion; initially 10 – 500mg.

Graft rejection; up to 1g daily by intravenous infusion up to 3 days.

**Side effects, Contra-indications, Caution:** See notes above, rapid intravenous administration of large doses has been associated with cardiovascular collapse

**PREDNISOLONE**

**Presentation:** Tablets containing 1mg, 2.5mg, 5mg, 25mg prednisolone.

**Indications:** Suppression of anti inflammatory and allergic disorders.

**Dose:** Oral; initially up to 10–20mg daily (severe condition up to 60mg daily) preferably after breakfast. Can be reduced within few days but may need to be continued for several weeks or months.

Maintenance dose 2.5 – 15mg daily.

**TRIAMCINOLONE**

**Presentation:** Tablets containing 2mg, 4mg triamcinolone; injection (aqueous suspension) containing 40mg/ml triamcinolone acetone intramuscular/intra-articular

**Indications:** Suppression of anti-inflammatory and allergic disorders.

**Dose:** Oral; 2 – 24 mg daily. By deep intravenous injection into gluteal muscle 40mg of acetone for depot effect, repeated at intervals according to
patient’s response. Maximum single dose 100mg. **Side effects, Caution:** See notes above. In high dosage may cause proximal myopathy. **Contra-indications:** See notes. **Caution:** Avoid in chronic therapy.

### 5.4 Drugs used in gynaecology and obstetrics

#### Prostaglandins and Oxytocics

**Myometrial relaxants**

**Progestogens**

**Oestrogens**

**Anti-oestrogens**

### 5.1.1 Contraceptives

### 5.1.1 Prostaglandins and Oxytocics

These drugs are used to induce abortion or induce or augment labour, in management of incomplete abortion and to prevent post partum haemorrhage in the third stage of labour. They include oxytocin, ergometrine, ergometrine + oxytocin and prostaglandins.

#### OXYTOCIN

**Presentation:** Injection containing 5 units, 10 units per ml of oxytocin  
**Indications:** Induction or augmentation of labour, management of third stage of labour.  
**Dose:** By slow intravenous infusion delivering 1 – 3 milli units per minute adjusting according to uterine response. Augmentation of labour, Management of third Stage; 5 to 10 units postpartum haemorrhage, i.e. normal saline.  
**Side effects:** Hyperstimulation leading to uterine rupture and foetal asphyxia, maternal hypertension and sub arachnoid hemorrhage, water intoxication and pulmonary oedema.  
**Caution:** High parity, previous caesarean section, concomitant use with prostaglandins.  
**Contra-indications:** Obstruction, foetal distress, placenta praevia.

#### ERGOMETRINE + OXYTOCIN

**Presentation:** Injection containing ergometrine maleate 500mcg + oxytocin 5 units/ml ampoule  
**Indications:** Management of third stage of labour, incomplete abortion to prevent haemorrhage  
**Dose:** 1ml, intramuscular for incomplete abortion and management of third stage of labour  
**Side effects:** Vomiting, nausea and hypertension  
**Contra-indications:** Severe heart disease, severe hypertension

#### ERGOMETRINE MALEATE

**Presentation:** Injection containing 500mcg ergometrine maleate; tablets containing 250mcg, 500mcg ergometrine maleate.  
**Indications:** Incomplete abortion; management of third stage of labour, post partum haemorrhage.  
**Dose:** Oral; 500mcg – 1mg, intramuscular injection; 200 – 500mcg, intravenous injection; 100 – 500mcg.  
**Side effects:** Nausea, vomiting and transient increase in blood pressure  
**Caution:** Hepatic and renal impairment, multiple pregnancy.  
**Contra-indications:** Severe hypertension, cardiac disease, eclampsia

#### GEMEPROST

**Presentation:** Pessaries containing 1mg gemeprost  
**Indications:** Induction of abortion, cervical ripening for induction of labour in intra uterine foetal death.  
**Dose:** 1mg vaginal pessary inserted in posterior fornix 3 hours before surgery or every 3 hours to maximum of 5mg.  
**Side effects:** Nausea, vomiting, diarrhoea, flushing, muscle weakness, dyspnoea, chest pain, mild pyrexia, uterine rupture.  
**Caution:** Obstructive airway disease, cardiovascular insufficiency, raised intraocular pressure.

#### DINOPROSTONE

**Presentation:** Pessaries containing 3mg dinoprostone, Tablets containing 500mcg dinoprostone.  
**Indications:** Induction and augmentation of labour  
**Dose:** By vaginal induction of labour insert pessary high into posterior fornix 3mg followed after 6 hours by 3mg, maximum 6 mg. Oral; 500mcg followed by 0.5 – 1 mg (1.5mg maximum) at hourly intervals.  
**Side effects:** Nausea, vomiting, diarrhea, flushing, muscle weakness, dyspnoea, chest pain, mild pyrexia, uterine rupture, hypertonus amniotic fluid embolism, abruptio placenta, fever, stillbirth.  
**Caution:** Glaucma, cardiac, hepatic, renal impairment, hypertension and epilepsy.  
**Contra-indications:** Active cardiac, pulmonary, renal or hepatic disease, placenta praevia cephalopelvic disproportion, fetal distress, major uterine surgery.

#### Myometrial relaxants

Beta2 adrenoceptor stimulants relax uterine muscle and are used in selected cases of premature labour.
No statistically significant effects on perinatal mortality have been observed. Their use permits a delay for transfers or use of corticosteroids for fetal lung maturity.

**SALBUTAMOL**

**Presentation:** Tablets containing 2mg, 4mg salbutamol sulphate. Intravenous infusion containing 1mg/ml salbutamol as sulphate.

**Indications:** uncomplicated premature labour, foetal asphyxia due to hypertonic uterine action.

**Dose:** Intravenous infusion premature labour starting with 50mcg/minute gradually increase to 150 –350mcg/minute and continue for 12 – 24 hours after contractions have stopped. Oral; 4mg every 6 – 8 hours

**Side effects:** Nausea, vomiting, flushing, sweating, tremor, hypokalaemia, tachycardia and hypotension, rarely pulmonary oedema.

**Caution:** Hypertension, hypokalemia, diabetes mellitus moderate pre eclampsia, pulmonary oedema , concomitant use of beta blockers, sympathomimetics.

**Contra-indications:** Cardiac disease, eclampsia, intra uterine infection, antepartum hemorrhage, not for use in 1st and 2nd trimesters (not effective).

**MAGNESIUM SULPHATE**

**Presentation:** Injection containing 50% (5g) ampoule.

**Indications:** Fulminant pre-eclampsia, Eclampsia.

**Dose:** Intravenous administration; 4g over up to 20 minutes followed by an intravenous rate of 1g every hour. intramuscular regime; 4g intravenous. slowly over 5 minutes then 5g in each buttock. Total loading dose 14g. Maintenance dose; 5g magnesium sulphate in alternate buttock every 4 hours. A total of six maintainance doses are recommended. Side effects: Hypermagnesaemia, nausea, vomiting, thirst, flushing, hypotension, arrhythmias, coma, respiratory depression, loss of tendon reflexes, muscle weakness, drowsiness, confusion.

**Caution:** Vital signs and magnesium sulphate blood levels must be closely monitored.

**Antidote:** 10cc of 10% calcium gluconate intravenous slowly

**5.4.3 Progestogens**

These modify some effects of and act mainly on tissues sensitised by oestrogens. There are two main groups of progestogens, the naturally occurring hormone progesterone and its analogues (dydrogesterone, hydroxyprogesterone, medroxyprogesterone) and yestosterone analogues (norethisterone and norgestrel). Progestogens are used in dysmenorrhoea menorrhagia, endometriosis, premenstrual syndrome, in contraceptive pills, in hormone replacement therapy together with oestrogens.

**MEDROXYPROGESTERONE ACETATE**

**Presentation:** Tablets containing 2.5mg, 5mg medroxyprogesterone acetate, injection containing 50mg/ml medroxyprogesterone acetate

**Indications:** as above

**Dose:** Oral; 2.5 mg – 10 mg daily for 10 days beginning on 16 – 21st day of cycle. Endometriosis; 10mg 3 times daily for 3 months or i.m. 50mg weekly, contraception: 150 mg every 3 months.

**Side effects:** acne, weight gain, changes in libido, premenstrual symptoms, irregular menstrual cycles.

**Caution:** Diabetes, hypertension, hepatic, cardiac, renal disease

**Contra-indications:** Undiagnosed vaginal bleeding, mammary carcinoma, porphyria.

**NORETHISTERONE**

**Presentation:** Tablets containing 5mg norethisterone

**Indications:** see notes above, primary and secondary amenorrhoea.

**Dose:** Endometriosis 10mg daily starting on 5th day of cycle (increase to 25mg daily if spotting occurs and reduce once bleeding has stopped). Menorrhagia 5mg 3 times daily for 10 days. Dysmenorrhoea 5mg 3 times daily from 5th to 24th day for 4 cycles. Postponement of menstruation 5mg 3 times daily starting 3 days before anticipated onset.

**Side effects:** As in 5.4.3.1. but more virilising exacerbation of epilepsy and migraine, liver disturbances and jaundice, gastro-intestinal disturbances.

**Caution:** Conditions associated with fluid retention.

**Contra-indications:** Thrombophlebitis, thromboembolic disorders, undiagnosed vaginal bleeding, carcinoma of the breast.

**OESTROGENS**

**Conjugated Oestrogens**

**Presentation:** Tablets containing 16mcg conjugated oestrogens

**Indications:** Hormone replacement therapy in menopausal symptoms

**Dose:** 0.625mg – to 1.25mg daily ( with progesterone for 10 – 12 days per cycle if uterus is intact). Hormone replacement therapy, dysmenorrhoea.

**Side effects:** Nausea and vomiting, weight changes, pre menstrual like syndrome, cholestatic jaundice, depression, headache.
Drugs acting on the endocrine system

5.4.5 Anti-oestrogens

The anti-oestrogens clomiphene citrate, cyclofenil, tamoxifen are used in the treatment of female infertility due to anovulation. They induce gonadotrophin release by occupying oestrogen receptors in the hypothalamus thereby interfering with feedback mechanisms.

**CLOMIPHENE CITRATE**

**Presentation:** Tablets containing 50mg clomiphene citrate  
**Indications:** Anovulatory infertility  
**Dose:** 50mg daily for 5 days starting from 2nd day of cycle. Second course of 100mg daily for 5 days if ovulation is absent for 3 cycles only.  
**Side effects:** Visual disturbances, ovarian hyperstimulation (withdraw), hot flushes, abdominal discomfort, vomiting, breast tenderness, weight gain.  
**Contra-indications:** Hepatic disease, ovarian cysts, endometrial carcinoma, pregnancy, abnormal uterine bleeding.

5.4.6 Contraceptives

The criteria by which contraceptive methods should be judged are effectiveness, acceptability and freedom from side effects. There are hormonal contraceptives, intrauterine devices, barrier methods and spermicides.

**5.4.6.1 Combined oral contraceptives**

These contain oestrogens and a progestogen. The oestrogen content ranges from 20 to 50 micrograms and preparations with lowest oestrogen and progestogen and which give a good cycle and minimal side effects are chosen. The effectiveness of oral hormonal contraceptives may be reduced by drugs that induce hepatic enzyme activity e.g. carbamazepine, phenytoin, phenobarbitone, primidone, rifampicin or antibiotics. They are available in monophasic and triphasic preparations.  
**Indications:** Contraception, menstrual symptoms.  
**Dose:** 1 tablet daily for 21 days starting on 1st day of cycle repeated after 7 days interval (during which withdrawal bleeding occurs).  
**Side effects:** Nausea, vomiting, headache, weight gain, thrombosis, breast tenderness, depression, reduced menstrual loss, hypertension, changes in libido.  
**Caution:** Diabetes mellitus with vascular complication, sickle cell disease.  
**Contra-indications:** Pregnancy, undiagnosed vaginal bleeding, liver adenoma, severe arterial disease, porphyria, breast and genital carcinoma.

Emergency contraception

**Presentation:** Tablets containing Ethinyloestradiol 50mcg and levonorgestrel 250mcg  
**Indications:** Post coital contraception as occasional emergency measure  
**Dose:** 2 tablets stat as soon as possible after coitus up to 72 hours then repeat 12 hours later.  
**Side effects:** see under 5.4.6.1.  
**Caution:** see under 5.4.6.1. should not be administered if menstrual bleeding is overdue or if unprotected intercourse occurred more than 72 hours previously.  
**Contra-indications:** see under 5.4.6.1.

Oral progestogen only contraceptives

Oral progestogen only contraception may offer a suitable alternative when oestrogens are contraindicated, e.g. heavy smokers, valvular heart disease, diabetes mellitus, migraine and before major surgery.

The tablet is taken continuously from 1st day of the cycle and taken at the same time of the day. If one misses a tablet, it must be taken immediately one remembers and abstain or use a sheath for the next 7 days while continuing normal pill taking.  
**Presentation:** Tablet containing either of the following: Ethinyloestradiol 500micrograms  
Norethisterone 350micrograms  
Levonorgestrel 30 micrograms  
Norgestrel 75 micrograms  
**Indications:** Contraception  
**Dose:** 1 tablet daily at same time starting on 1st day of cycle and then continuously.  
**Side effects:** menstrual irregularities, nausea, vomiting, headache, breast discomfort, weight gain, depression.  
**Caution:** heart disease, past ectopic pregnancy, functional ovarian cysts, Jaundice in active liver disease.  
**Contra-indications:** Pregnancy, undiagnosed vaginal bleeding, liver adenoma, severe arterial disease, porphyria, breast and genital carcinoma.

Caution: In women with intact uterus increased risk of myometrial cancer  
**Contra-indications:** Pregnancy, oestrogen dependent cancer.
5.4.6.4 Injectable Progestogen only contraceptives

Medroxyprogesterone acetate and norethisterone enanthate are long acting progestogen given intramuscularly and which provide effective contraception.

**MEDROXYPROGESTERONE**

**Presentation:** Injection containing Medroxyprogesterone 150mg/ml

**Indications:** Long term contraception

**Dose:** By deep i.m. injection 150 mg within the first 5 days of menstrual cycle, repeat every 3 months.

**Side effects:** as in 5.4.6.1. delayed return of fertility, irregular cycles, heavy menstrual bleeding, headache, uterine bleeding.

**Contra-indications:** as for progestogen only pill

**NORETHISTERONE**

**Presentation:** Injection containing Norethisterone enanthate 200mg/ml

**Indications:** Short term contraception

**Dose:** By deep i.m. injection 200mg within the first 5 days of menstrual cycle immediately after parturition, repeat every 2 months.

**Side effects:** see 5.4.6.2.2.1. more virilising effects, greater possibility of liver disturbances and jaundice, gastro-intestinal disturbances, oedema, weight gain, breast discomfort, and irregular menstrual cycles.

**Contra-indications:** as for progestogen only pill, severe obesity, pre-menopause.

**Progesterone implants**

**LEVONORGESTREL**

**Presentation:** Subcutaneous implant containing 38mg Levonorgestrel

**Indications:** Contraception.

**Dose:** By subdermal implantation, set of 6 implant capsules inserted within the first 5 days of the menstrual cycle (preferably on 1st day after which additional precaution will be necessary for the following 7 days) or on 21st day after parturition (after this day additional precaution will be necessary for the following 7 days). Remove within 5 years of insertion.

**Caution, contra-indications:** as for progestogen only contraception.

5.4.6.6 Spermicidal Contraceptives

Spermicidal contraceptives e.g. nonoxyl “9” are useful additional safeguards but do not give adequate protection if used alone. Use with barrier methods.

5.4.6.7 Contraceptive devices

5.4.6.7.1 Intra Uterine Devices

**Indications:** Contraception

**Side effects:** Uterine perforation, displacement, pelvic infection, menorrhagia, dysmenorrhea.

**Caution:** Menorrhagia, previous or present pelvic infection, diabetes, valvular heart disease, remove if pregnancy occurs.

**Contra-indications:** Anaemia, menorrhagia, history of ectopic pregnancy, pelvic infection, immunosuppressive therapy.

Other contraceptive devices

These include the CAP, diaphragm, female and male condoms.

5.5 Other endocrine drugs

**BROMOCRIPTINE**

Dopamine receptor stimulant in the brain and inhibits release of prolactin and lactation, inhibits growth hormone release.

**Presentation:** Tablet containing 1mg, 2.5mg bromocriptine mesylate

**Indications:** Suppression of lactation, galactorrhoea, cyclical benign breast disease, prolactinoma, rarely acromegaly.

**Dose:** Suppression of lactation 2.5mg on 1st day, then 2.5mg twice daily for 14 days, galactorrhoea/infertility 1.25mg at bedtime, increase gradually to 7.5mg daily in divided doses – maximum 30 mg daily dose should be taken with food.

**Side effects:** Nausea, vomiting, headache, postural hypotension, drowsiness, high doses confusion, psychomotor excitation, pleural effusions, muscle cramps.

**DANAZOL**

Inhibits pituitary gonadotrophins. It combines androgenic with antioestrogenic and progestogenic activity. It is used in endometriosis, menorrhagia, menstrual disorders, mammary dysplasia, gynaecomastia, hereditary angioedema, or pre
operative preparations for fibroids, endometrial resection.

**Presentation:** Capsule containing 100mg, 200mg danazol

**Indications:** as above

**Dose:** 200 – 300mg daily in divided doses, starting during menstruation.

**Side effects:** Nausea, dizziness, weight gain, backache, headache, menstrual disturbance, muscle spasm androgenic effects, insulin resistance, alopecia, leukaemia, emotional liability.

**Caution:** Cardiac, hepatic, renal impairment, polycythæmia, epilepsy, breast feeding, thromboembolic disease, uninvestigated vaginal bleeding, androgen dependant tumours.

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### BUSERELIN

Being a gonadotrophin analogue, after an initial stimulation phase, buserelin down regulates pituitary gonadotrophin secretion leading to inhibition of ovarian steroid secretion.

**Presentation:** Nasal spray containing 150mcg buserelin as acetate, injection 1mg/ml

**Indications:** Endometriosis, pituitary desensitization before ovulation induction with gonadotrophins, pre-operative thinning of endometrium.

**Dose:** 150mcg spray in each nostril 3 times daily starting on 2nd day of menstruation for 6 months.

**Side Effects:** Break through bleeding, menopause like symptoms, decreased bone density, ovarian cysts, leucorrhoea.

**Contra-indications:** Pregnancy, undiagnosed vaginal bleeding, breast feeding.

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### TESTOSTERONE

**Presentation:** capsules containing 40mg testosterone undecanoate; injection containing 20mg, 50mg testosterone propionate, 40mg testosterone phenylpropionate, 250mg testosterone enantate, implant 100mg testosterone.

**Indication:** Androgen deficiency, delayed puberty, breast cancer, male hypogonadism

**Dose:** According to the manufacturers preparations.

**Side effects:** prostate abnormalities and cancer, headache, depression, cholestatic jaundice, electrolyte disturbances, increased bone growth, androgenic effects.

**Caution:** Cardiac, renal, hepatic impairment, Ischaemic heart disease, elderly, migraine, hypertension.

**Contra-indications:** Breast cancer in men, prostate cancer, liver tumours, hypercalcaemia, pregnancy, breast feeding, nephrosis.

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### CYPROTERONE ACETATE

Cyproterone Acetate is an anti-androgen used in the treatment of severe hypersexuality and sexual deviation in male, is also used as an adjunct in prostrate cancer and in treatment of acne and hirsutism in women.

**Presentation:** Tablets containing 50mg

**Indications:** (see notes above); prostate cancer

**Dose:** 50mg twice daily after food.

**Side effects:** Fatigue, breathlessness, weight changes.

**Caution:** Chronic alcoholism, monitor blood count, hepatic function, adrenocortical function, diabetes mellitus

**Contraindications:** Hepatic disease, severe diabetes, sickle cell anaemia, severe depression, thrombo-embolic disorders; youth under 18 years.

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### SILDENAFIL

**Presentation:** Tablets containing 25mg sildenafil.

**Indications:** erectile dysfunction

**Dose:** initially 50mg (elderly 25mg) approximately 1 hour before sexual activity, subsequent doses adjusted according to response to 25 – 100mg as a single dose as needed; max 1 doze in 24 hours, (max. single dose 100mg).

**Side Effects:** Dyspepsia, headache, flushing, dizziness, visual disturbances, priapism.

**Caution:** Cardiovascular disease, predisposition to prolonged erection, renal impairment.

**Contraindication:** Treatment with nitrates, recent stroke and myocardial infarction, hypertension, hereditary degenerative retinal disorders.
6 Drugs used in the treatment of diseases of the respiratory system

6.1 Bronchodilators
6.2 Corticosteroids
6.3 Cromoglycate and related substances
6.4 Antihistamines
6.5 Allergic emergencies
6.6 Oxygen
6.7 Cough preparations
6.8 Systemic nasal decongestants
6.9 Mucolytics
6.10 Aromatic inhalations

6.1 Bronchodilators

6.1.1 Adrenoceptor stimulants
6.1.1.1 Selective beta₂-adrenoceptor stimulants
6.1.1.2 Other adrenoceptor stimulants

Most mild to moderate attacks of asthma respond rapidly to aerosol administration of selective beta₂-adrenoceptor stimulants such as salbutamol. In frequently occurring moderate asthma, the introduction of a corticosteroid by inhalation, cromoglycate or oral theophylline may stabilize the asthma. For more severe attacks a short course of an oral corticosteroid may be necessary to bring the asthma under control. In severe acute asthma or airways obstruction it is safer to treat patients in hospitals where oxygen and resuscitation facilities are available.

The beta₂-adrenoceptor stimulants such as salbutamol are the safest and most effective. They even partially give relief of irreversible airway obstruction in chronic bronchitis and emphysema. Hence beta₂-adrenoceptor stimulants remain the drugs of choice.

The aerosol inhaler is an effective and convenient method of administration for mild to moderate airway obstruction. Sort acting beta₂-agonists are not useful on a regular basis in patients with mild or moderate asthma as there is no clinical benefit. Longer acting beta₂-agonists salbutamol and formoterol are of benefit for these patients.

6.1.1.1 Selective beta₂-adrenoceptor Stimulants

**SALBUTAMOL**

**Presentation:** Tablet containing 2mg, 4mg salbutamol sulphate. Syrup containing 2mg/5ml salbutamol sulphate. Aerosol injection containing 500mcg, 500mcg salbutamol sulphate. Aerosol inhalation containing 100mcg salbutamol metered. Nebules containing 0.1% (1mg/ml) salbutamol.

**Indications:** Asthma, reversible airway obstruction.

**Dose:** 2mg to be taken 3-4 times a day; maximum single dose 8mg. Child: under 2 years 100mcg/kg 4 times a day. 2-6 years; 1-2mg 3-4 times a day. 6-12 years; 2mg 4 times a day. Aerosol inhalation: 100-200mcg (or 1-2 puffs) up to 3-4 times a day for persistent symptoms; Child: 100mcg (1 puff) increase to 200mcg (2 puffs) if necessary. Prophylaxis: in exercise induced bronchospasms 200mcg (2 puffs). Child; 100mcg (1 puff).

Injection; subcutaneously or intramuscularly 500mcg repeated every 4 hours if necessary, Slow intravenous injection 250mcg, repeated if necessary.

**Side effects:** fine tremor, nervous tension, headache, peripheral vasodilatation, tachycardia, hypokalaemia after high doses, hypersensitivity reaction.

**Caution:** Hyperthyroidism, myocardial insufficiency, arrhythmias, hypertension, pregnancy and breastfeeding, intravenous administration in diabetes.

**Contraindications:** Hypersensitivity to salbutamol.

**TERBUTALINE**

**Presentation:** Tablet containing 5mg terbutaline sulphate, syrup containing 1.5mg/5ml terbutaline sulphate, injection containing 500mcg/ml terbutaline sulphate, aerosol inhalation containing 250mcg/metered puff terbutaline sulphate, powder for inhalation containing 500mcg/inhalation of terbutaline sulphate, nebulised solution for inhalation containing 2.5mg/ml of terbutaline sulphate.

**Indications:** Asthma and other conditions associated with reversible airway obstruction.

**Dose:** Inhalation of nebulised solution; Adult, 5
Drugs used in the treatment of diseases of the respiratory system

6.1.1.2 Other adrenoceptor stimulants

These stimulants are now regarded as less suitable and less safe for use as bronchodilators than the selective beta2-adrenoceptors, as they are likely to cause arrhythmias and other side effects. They should be avoided whenever possible. Adrenaline injection (1 in 1000) is used in emergency treatment of acute allergic and anaphylactic reaction.

ADRENALINE

Presentation: Injection containing adrenaline 1 in 1000, 1ml ampoule.
Indications: Emergency treatment of acute allergic and anaphylactic reactions.
Dose: asthma; 0.2 – 0.5ml as a single dose by slow subcutaneous injection. In anaphylactic shock; 1ml. Child; 0.01ml/kg body weight, maximum 0.5ml, repeated 4 hourly if necessary.
Side effects: Hypertension, anxiety and tachycardia
Caution: Avoid in asthma if pulse is 120 and above per minute.

EPHEDRINE HYDROCHLORIDE

Presentation: Tablet containing 15mg ephedrine hydrochloride. Syrup containing 15mg/5ml ephedrine hydrochloride
Indication: Reversible airway obstruction
Dose: 15 – 60 mg 3 times daily. Child; up to 1 year; 7.5 mg 3 times daily. 1 – 5 years; 15mg 3 times daily, 6 – 12 years; 30 mg 3 times daily.
Side effects: Tachycardia, anxiety, restlessness, insomnia, tremor, arrhythmias, dry mouth and cold extremities.
Caution: Hyperthyroidism, diabetes mellitus, ischaemic heart disease, hypertension, renal impairment, elderly, prostatic hypertrophy, interaction with MAOIs.

6.1.2 Xanthine Derivatives

Xanthine derivatives are used for the relief of bronchospasm. Theophylline is the principal compound with additive effect when used with small doses of beta2-adrenoceptor stimulants; however, the combination may increase the risk of side effects, including hypokalaemia.

Theophylline has a narrow therapeutmic index. It is therefore important to be cautious in patients with liver diseases, heart failure, and those on drugs that affect liver metabolism such as cimetidine, ciprofloxacin, erythromycin and oral contraceptives. Its half-life is increased as the
Drugs used in the treatment of diseases of the respiratory system

THEOPHYLLINE

Theophylline is metabolised by the liver. However, the half-life is decreased in smokers, heavy drinkers and by drugs such as phenytoin, carbamazepine, rifampicin and barbiturates. Aminophylline is a stable combination of theophylline and ethylenediamine. The ethylenediamine improves the solubility of the aminophylline in water. Aminophylline must be given by very slow intravenous injection (over at least 20 minutes).

Presentation: Tablet containing 125mg, 300mg theophylline, liquid containing 60mg/5ml theophylline, capsule containing 60mg theophylline

Indications: Reversible airway obstruction, Severe, acute asthma

Dose: Tablet, Adult; 125mg 3 – 4 times daily after food, increased to 250mg if required. Child; 7 - 12 years 62.5 - 125mg 3 - 4 times daily. Liquid, Adult: 120 - 240mg 3 - 4 times daily after food. Child, 2 - 6 years 60 - 90mg 3 – 4 times daily, 7 - 12 years 90 - 120mg 3 - 4 times daily. Capsule, Adult; 250 - 500mg every 12 hours. Child; 2 - 6 years 60 - 120mg every 12 hours, 7 - 12 years 125 - 250mg every 12 hours. As for aminophylline below.

Caution: Theophylline has a narrow therapeutic window, the plasma concentration for optimum response is 10 – 20 mg/litre (55-110 micromol/litre). Also caution in liver and cardiac diseases, epilepsy, disease, pregnancy in breast feeding.

Counselling: Swallow capsule whole with fluids or swallow granules enclosed in soft food such as yogurt.

AMINOPHYLLINE

Presentation: Tablets containing 100mg aminophylline. Injection containing 25mg/ml aminophylline, forte tablets (film coated) containing 350mg aminophylline, paediatric tablets containing 100mg aminophylline.

Indications: Reversible airway obstruction, severe acute asthma.

Dose: Oral, Adult; 100 – 300mg, 3 – 4 times daily, after food. Child, Above 3 years 6mg/kg twice daily initially, increased after 1 week to 12mg/kg twice daily. The slow release tablets are mainly beneficial to smokers. Slow intravenous injection (over 20 minutes) 250 - 500mg (5mg/kg) when necessary. Maintenance 500mg in dextrose 5% infusion given over 8 – 12 hours. Child, slow intravenous injection (over 20 minutes) 5mg/kg.

Side effects: Tachycadia, palpitations, nausea, gastro intestinal disturbances, headache, insomnia, arrhythmias and convulsions if given rapidly by intravenous injection.

Caution: Aminophylline is too irritant for intramuscular use, intravenous injection must be given very slowly (over 20 minutes).

ANTIMUSCARINICS

MANAGEMENT OF ACUTE SEVERE ASTHMA IN GENERAL PRACTICE

Mild asthma in adults

- Speech normal
- Pulse < 100 beats/minute
- Respiration > 25 breaths/minute
- Peak flow < 80% of predicted or best, treat at home but response to treatment must be assessed before doctor leaves.

Treatment:
Nebulised salbutamol 5mg or nebulised terbutaline 10mg.
Monitor response 15 – 30 minutes after nebulisation.
If peak flow 50 – 75% of predicted or best give:
Oral prednisolone 30 – 60 mg and step up usual treatment.
Alternatively if peak flow > 75% of predicted or best:
Step up usual treatment

Follow up
Monitor symptoms and peak flow, set up self management plan.
Review in hospital/clinic setting within 48 hours.
Modify treatment at review according to guidelines for chronic asthma.

IMPORTANT:
Regard each emergency consultation as being for acute asthma until shown otherwise.

Acute Severe Asthma in Adults

- Cannot complete sentence
- Pulse ≥ 120 beats/minute
- Respiration ≥ 30 breaths/minute
- Peak flow ≤ 50% of predicted or best

Seriously consider hospital admission if more than one of above feature present.

Treatment:
Oxygen 40 - 50% if available.
Nebulised salbutamol 5mg or nebulised terbutaline 10mg
Oral prednisolone 30 – 60 mg or i.v hydrocortisone 200mg.
Monitor response 15 – 30 minutes after nebulisation if any signs of acute asthma persist:
Arrange hospital admission while awaiting ambulance repeat nebulised beta, stimulant and give with nebulised ipratropium 500 micrograms or give subcutaneous terbutaline or give slow intravenous aminophylline 250mg. Alternatively if symptoms have improved, respiration and pulse settling, and peak flow > 50% of predicted or best:
step up usual treatment and continue prednisolone

DRUGS IN THE TREATMENT OF DISEASES OF THE RESPIRATORY SYSTEM
**Follow up**
Monitor symptoms and peak flow.
Set up self management, plan review in hospital/clinic setting within 24 hours.
Modify at review.

**Life threatening asthma in adults**

- Silent chest
- Cyanosis
- Tachycardia or exhaustion
- Peak flow <33% of predicted or best arrange IMMEDIATE hospital admission.

**Treatment:**
Oxygen driven-nebuliser in ambulance.
hydrocortisone 200 mg (immediately).
Nebulised<sup>1</sup> beta<sub>2</sub> stimulant with nebulised ipratropium or subcutaneous terbutaline or slow intravenous aminophylline 250mg.
oral prednisolone 30–60 mg or intravenously

**STAY WITH PATIENT UNTIL AMBULANCE ARRIVES**

1. If no nebuliser available give 2 puffs of beta<sub>2</sub> stimulant using large-volume spacer and repeat 10–20 times

**IMPORTANT:**
Do not give bolus aminophylline to patient already taking oral theophylline.

**IMPORTANT:**
Patients with severe or life-threatening attacks may not be distressed and may not have all these abnormalities, the presence of just one of the signs should alert doctor.

**Signs of Acute Asthma in children**

**Acute severe asthma:**

- Too breathless to talk
- Too breathless to feed
- Respiration ≥50 breaths/minute
- Peak flow ≤50% of predicted or best

**IMPORTANT:**
Failure to respond at any time requires immediate referral to hospital.

**Life threatening features**

- Peak flow <33% of predicted or best
- Cyanosis, silent chest, or poor respiratory effort
- Fatigue or exhaustion
- Agitation or reduced alertness

**IMPORTANT:**
Failure to respond adequately at any time requires immediate referral to hospital.

**Treatment of acute asthma in children**

- Short acting beta<sub>2</sub> stimulant from metered dose inhaler using large-volume spacer device may be as effective as use of nebuliser; dose is one puff every few seconds until improvement occurs (max. 20 puffs), using face mask in very young child.
- Terbutaline may be given subcutaneously in severe episodes.
- Oxygen is of benefit.
- A child requiring high-dose inhaled bronchodilators should also receive soluble tablets prednisolone 1–2 mg/kg body weight (maximum 40mg) once daily for up to 5 days if necessary; child needs immediate referral to hospital if fails to respond.
- Aminophylline should no longer be used in children at home.

**6.2 Corticosteroids**
Corticosteroids are recommended for prophylactic treatment in patients using beta<sub>2</sub>-stimulants more than once daily. The aerosol preparation must be used regularly to obtain maximum benefit which is normally obtained after 3–7 days after initiation. Beclomethasone dipropionate is the drug of choice. High doses of corticosteroids are associated with some adrenal suppression and affect the body metabolism. Oral preparations should be used for short duration starting with high doses and lasting for about 5–7 days. For example oral prednisolone should be given in adequate doses i.e. 1–2 mg/kg/day given in divided doses, gradually reduced once the attack has been controlled.

Corticosteroids can be used in chronic continuing asthma when the response to other antiasthmatic drugs has been relatively small. Inhaled doses should be increased to reduce on oral preparation dose. Oral doses could be taken as a single dose in the mornings.

**BECLOMETHASONE DIPROPIONATE**

**Presentation:** Aerosol containing, 50mcg, 100mcg and 200mcg metered doses beclomethasone dipropionate

**Indication:** Prophylaxis of asthma not controlled by bronchodilators.

**Dose:** 200mcg (2 puffs) 2 times a day or 100mcg (1 puff) 3–4 times a day. In more severe cases initial dose of 600–800mcg (6–8 puffs) daily may be required.

**Child:** 50–100mcg (1–2 puffs of 50mcg metered inhaler) 2–4 times a day.
Side effects: see notes above, and hoarseness and candidiasis of mouth and throat (usually with high doses), rarely hypersensitivity reaction including rash and angioedema.
Caution: See notes above, and also active or quiescent tuberculosis and may need systemic treatment when airway are obstructed with mucus, and in stress, paradoxical bronchospasm, (calls for discontinuation and alternative therapy). If mild, prevention is by inhalation of beta2 adrenoreceptor stimulants or transfer to a dry powder inhalation

6.3 Sodium cromoglycate and related substances

Sodium cromoglycate has no value in the treatment of acute attack of asthma. However regular inhalation of the drug can reduce the frequency of attacks of asthma. This would necessitate a reduction in use of beta2-bronchodilators and corticosteroids.

Cromoglycate is also of value in the prevention of exercise-induced asthma, a single dose inhalation 30 minutes beforehand. The nebuliser solution is useful for young children who cannot manage the powdered aerosol.

KETOTIFEN

Ketotifen is an antihistamine with action similar to cromoglycate but has no value in treatment of acute asthma.

Presentation: Tablet containing 1mg ketotifen, Capsule containing 1mg ketotifen, Elixir containing 1mg/5ml ketotifen

Indications: Allergic asthma poorly controlled with bronchodilators. See appendix on antihistamines. Also manifestations advises to avoid oral anti diabetics (fall in Thrombocyte count reported.

Dose: 1 – daily with food, increase if necessary to 2mg twice daily with food. Initial treatment in readily sedated patients 0.5 - 1mg at night. Child, over 2 years; 1mg 2 times daily with food.

Side effects: dry mouth and sedation, slight dizziness, drowsiness, CNS stimulation, weight gain also reported.

Caution: previous anti asthmatic treatment should be continued for a minimum of two weeks after initiation of ketotifen treatment. Drowsiness may affect performance of skilled tasks, enhances alcohol effects.

ANTIHISTAMINES

All antihistamines are of potential value in the treatment of nasal allergies, particularly in seasonal (hay fevers), and may be of some value in vasomotor rhinitis. Oral antihistamines are also of value in preventing urticaria and used for treatment of urticaria rashes, pruritis and insect bites and stings; they are also used in drug allergies. Injection of Promethazine and chlorpheniramine may be used as adjunct to adrenaline in the emergency treatment of anaphylaxis and angioedema. Antihistamines are also useful in nausea and vomiting.

There is no evidence of superiority of any of the older antihistamines over another. They only differ in the extent of sedativeness and duration of action.

Most of the antihistamines cause drowsiness and sedation. Patients must be warned that their ability to drive or perform any activity that requires high alertness may be affected. Antihistamines also may potentiate alcohol effect. Other side effects include headache, psychomotor impairment, antimuscarinic effects such as urinary retention, dry mouth, blurred vision and gastro intestinal disturbances, photosensitivity, occasional rashes. Antihistamines should be used with caution in epilepsy, prostatic hypertrophy, glaucoma and hepatic disease.

Most antihistamines should be avoided in porphyria although chlorpheniramine has been used. For further information on contra-indications and special problems, refer to specific sections, e.g., breastfeeding, pregnancy.

CHLORPHENIRAMINE MALEATE

Presentation: Tablets containing 2mg, 4mg chlorpheniramine maleate; Syrup containing 2mg/5ml chlorpheniramine maleate; injection10mg/ ml.
**Indication:** Symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylactic reactions.

**Dose:** 4mg every 4 – 6 hours, maximum 24mg a day. *Child,* 1 – 2 years; 1 mg 2 times a day, maximum 6 mg a day. 6 – 12 years; 2 mg every 4 – 6 hours a day, maximum 12 mg a day. Not recommended for children under 1 year.

**Side effects and Caution:** see above. In addition, exfoliating dermatitis and tinnitus have been reported. Injection may cause transient hypertension or CNS stimulation and may be irritant.

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**PROMETHAZINE HYDROCHLORIDE**

**Presentation:** Tablets containing 10mg, 25mg promethazine hydrochloride. Injection containing 25mg/ml promethazine hydrochloride. Elixir containing 5mg/5ml promethazine hydrochloride.

**Indication:** Symptomatic relief of allergy such as hay fever, urticaria, emergency treatment of anaphylactic reactions, pre-operative medication, sedation and motion sickness.

**Dose:** 
- **By mouth:** 25mg at night increased to 50mg twice daily if necessary or 10 – 20mg taken 2 – 3 times a day. *Child,* 1 – 5 years; 5 – 15mg per day. 5 – 10 years; 10 – 25mg per day.
- **Injection:** i.m. 25 – 50 mg; maximum 100 mg. *Child,* Not recommended in children under 2 years of age; 2.5mg daily in 1-2 divided doses; 5 – 10 years; 10 – 25mg daily in 1-2 divided doses.

**Premedication, Child under 2 years not Recommended, 2.5- 20mg, 5-10years; 20-25mg.**

**In Emergencies; i.v. fluids, intravenous aminophylline or nebulised beta 2 agonist should be given.** Further more, oxygen and respiratory with emergency tracheostomy may be required in some situations. Intravenous hydrocortisone 100 -300mg may be necessary to prevent further deterioration in severe conditions. If there is doubt about the adequacy of the circulations, the initial injection of adrenaline may be given intravenously as a dilute solution.

**Side effects:** see notes above.

**Caution:** i.m. injection may be painful. See notes above; also pregnancy and breastfeeding.

**Contraindications:** See notes above.

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**DIPHENHYDRAMINE HYDROCHLORIDE**

**Presentation:** Tablets containing 25 mg diphenhydramine hydrochloride. Liquid 10mg/5mls

**Indications:** Symptomatic relief of allergy such as hay fever, urticaria

**Dose:** 25 mg?? 2 times a day.

**Side effects:** see notes above

**Caution:** Use with caution in hypertrophy, urinary retention, dry mouth, blurred vision, GIT disturbances, palpitations and Arrhythmias.

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**6.5 Allergic emergencies**

Adrenaline has the potential to reverse the immediate physiological symptoms associated with hypersensitivity reaction such as anaphylaxis, and angioedema.

Laryngeal oedema, bronchospasms and hypotension in anaphylactic shock require urgent treatment. The major causes of anaphylactic shock are as follows:

- Insect bites and stings such as bees and wasps
- Foods and food additives including eggs, milk protein, nuts, arachis oil (peanuts),
- Medicinal products such as blood products, vaccines, antibiotics (particularly penicillins), aspirin, chloroquine, iron injections, heparin;
- First-aid treatment may be offered on site by securing the airway, restoration of blood pressure by laying down the patient flat, and raising the feet. Adrenaline injection may be administered by i.m in a dose of 0.5-1mg. A dose of 300mg may be appropriate for immediate self-administration. The dose may repeated until improvement occurs.
- Oxygen and an antihistamine (chlorpheniramine) may be give as essential adjuncts. If the patient continues to deteriorate, i.v fluids, intravenous aminophylline or nebulised beta 2 agonist should be given.

Further more, oxygen and respiratory with emergency tracheostomy may be required in some situations. Intravenous hydrocortisone 100 -300mg may be necessary to prevent further deterioration in severe conditions. If there is doubt about the adequacy of the circulations, the initial injection of adrenaline may be given intravenously as a dilute solution.

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**6.6 Oxygen**

Oxygen is prescribed for hypoxaemic patients to increase alveolar oxygen tension and reduce effort breathing to maintain the necessary arterial oxygen tension. The concentration depends on the condition being treated.

High concentrations of up 60% are necessary for short periods in pneumonia, pulmonary thromboembolism, and fibrosing alveolitis. In acute asthmatic attacks high concentrations of oxygen are necessary. But where blood gas measuring facilities are not available 35% to 50% oxygen concentrations are adequate. In asthmatic patients with long history of chronic bronchitis and probable respiratory failure about 24 – 28% may be needed to limit oxygen-induced reduction of respiratory drive.

Oxygen treatment is to provide the patient with just enough oxygen to improve the hypoxaemia without worsening pre-existing carbon-dioxide retention and respiratory acidosis. Only 24 – 28% is reserved
for patients with ventilatory failure due to chronic obstructive airway diseases and other causes. Repeated gas administrations should be measured to determine the required correct concentrations.

**Intermittent Oxygen Therapy**

Oxygen can be given intermittently for hypoxaemia of short duration. For example, asthma, advanced irreversible respiratory disorders (e.g. Chronic obstructive airways disease). It may be supplied as oxygen cylinders. The cylinders can have medium (2 liters/min) or high (4 liters/ min) setting. There are special masks, which are preset to deliver a specific percentage of oxygen irrespective of the flocculate and breathing pattern.

**6.6.2 Long-term Oxygen therapy**

Long-term administration of oxygen for at least 15 hours daily prolongs survival for some patients with chronic obstructive airway disease.

**6.7 Cough preparations**

**6.7.2 Cough expectorants and demulcents**

A cough is generally a useful reflex which serves to get rid of inhaled foreign bodies or clear the air passages of sputum. Such a cough is described as productive. A cough which is dry and irritating serves no purpose and is called unproductive. In most cases of acute cough no medicine is needed, unless there is evidence of more serious lower respiratory illness.

Most of the compound preparations on the market contain three or more active ingredients that may some times have opposing pharmacological action. They may contain antitusives as well as compounds with expectorant action and anti muscarinic effects. Such compounds have no place in the treatment of cough.

**6.7.1 Cough suppressants**

Opioid cough suppressants such as codeine, dextromethorphan and pholcodeine are effective in severe cough although they can cause constipation and rarely dependence in some patients. These drugs are not recommended in children and should be avoided all together in those under one year.

Sedative antihistamines are used as cough suppressants ingredients and they all tend to cause drowsiness, which may reflect their main mode of action.

The use of cough suppressants containing codeine or similar opioid analgesics are not generally recommended in children, and should be avoided altogether in those under 1 year of age.

**CODEINE PHOSPHATE**

**Presentation:** Linctus containing 15mg/5ml codeine phosphate. Paediatric preparation containing 3mg/5ml codeine phosphate.

**Indication:** dry painful cough

**Dose:** 5 – 10ml 3 – 4 times a day, Child 5 – 12 years 2.5 – 5 ml ( but not generally recommended)

Paediatric preparations, 1 – 5 years 5 ml 3 – 4 times a day ( but not generally recommended).

**Side effects:** constipation, respiratory depression sensitive patients or if given in large doses respiratory depression

**Caution:** asthma, Hepatic and renal impairment, history of drug abuse. See interaction: Appendix 2 ( opioid analgesics).

**Contraindications:** Liver disease, ventilatory Failure.

**PHOLCODINE**

**Presentation:** Linctus containing pholcodeine 5mg/5ml ; paediatric Linctus (sugar free) containing pholcodine 2mg/5ml.

**Indication:** dry irritating and painful cough

**Dose:** Linctus 5mg/5ml 5 – 10ml 3 times daily, Child (but not generally recommended; 5 – 12 years 2.5 – 5 ml 3 times daily. Linctus 10mg/5ms; 5mls, 3 times daily. Paediatrics Linctus; Child (but not generally recommended) 1-5 years, 5 ml 3 times daily; 6-12 years 5-10mls 3 times daily.

**Side effects:** Caution and contra-indication:

See under Codeine phosphate

**MORPHINE HYDROCHLORIDE**

**Presentation:** Solution containing 10mg/5ml morphine hydrochloride

**Indication:** Distressful cough in terminal Disease

**Dose:** Initially 5 mg every 4 hours

**Side effects:** Constipation, sedation, Drowsiness, nausea, vomiting, euphoria, tachycardia, bradycardia, palpitations, mental detachment, micturition difficulty, sweating, dry mouth and respiration depression.

**Caution:** Drowsiness may affect performance of skilled tasks, may enhance effect of alcohol, hypotension, hypothyroidism, asthma (avoid during attack) elderly and debilitated (reduced dose).

**Interactions:** See Appendix (. opioid analgesic)

**Contraindications:** Avoid in acute respiratory
depression, acute alcoholism, paralytic ileum, head injury, raised intracranial pressure, avoid injection in phaeochromocytoma.

### 6.7.2 Expectorants

Expectorants supposedly help to expel the bronchial secretions more easily, but there is no evidence to support this myth. They may serve as simple placebo function for there is no rationale for their use.

#### AMMONIA AND IPECACUANHA

**Presentation:** Ammonia and ipecacuanha mixture BP, containing; ammonia bicarbonate 200mg, liquorice liquid extract 0.5ml, ipecacuanha tincture 0.3ml, Camphar water 0.1ml, conc. Anise water 0.05ml, double-strength chloroform water 5ml, water to 10ml. (Reserve for hospital use as it should be freshly prepared extramorporaneously)

**Indication:** Productive cough

**Dose:** 10-20ml 3-4 times a day

**Caution and side-effects:** May cause nausea, vomiting

#### 6.7.3.1 Guaiphenesin, pseudophedrine, triprolidine

#### 6.7.3 Demulcent preparations

These preparations have soothing preparations believed to have relieving effect of dry irritating cough. The contain substances such as syrup and glycerol that are harmless and inexpensive.

#### 6.8 Systemic nasal decogestants

There is little evidence whether these preparations have value. However they do not cause rebound nasal congestion. They contain sympathomimetics and produce constriction of other blood vessels in the body and cause rise in blood pressure. They are best avoided in patients with hypertension, hyperthyroidism, coronary heart disease and patients taking monoamine-oxidase inhibitors; many preparations also contain antihistamines, which may cause drowsiness and affect ability to drive and maintain alertness.

### 6.8.1 Pseudoephedrine

**Presentation:** Tablets containing 60mg pseudoephedrine hydrochloride. Linctus/elixir containing 30mg/5ml pseudoephedrine hydrochloride

**Indication:** Nasal congestion

**Dose:** 1 tablet 4 times a day; 10ml 3 times a day. *Child,* 2-6 years; 2.5ml. 6-12-years 5ml

**Caution:** Use with caution in diabetes, hypertension, hyperthyroidism, ischaemic heart disease and in patients taking monoamine oxidase inhibitor.

**Side effects:** See under ephedrine, may cause rare incidences of visual hallucination in children.

**Interactions:** See Appendix (sympathomimetics)

### 6.9 Mucolytics

Mucolytics reduce sputum viscosity and may be of some benefit in patients with chronic obstructive pulmonary disease.

### 6.10 Aromatic inhalations

Inhalations containing volatile substances like eucalyptus oil encourage deliberate inspiration of warm moist air, which is often comforting in bronchitis.

In children, the use of strong aromatic decongestants is not advised under the use of 3 months. The mother should however, be advised on alternative methods of soothing mucus from the nostrils.

#### 6.10.1 Menthol and Eucalyptus Inhalation

Inhalation capsules, Levomenthol 35.55mg with chlorobutanal, pine oils, terpineol and thymol.

Inhalation, racementhol or levomenthol 2g, eucalyptus oil 10ml, light magnesium carbonate 7g, water to 100ml.

**Administration:** Check instructions on the manufactures advise.
Drugs used in the treatment of diseases of the cardiovascular system

7.1 Cardiac glycosides
7.2 Diuretics
7.3 Anti-arrhythmic drugs
7.4 Antianginal drugs
7.5 Anti-hypertensive drugs

**Cardiac glycosides**

Cardiac glycosides are a small group of drugs that improve contractility of diseased hearts. They also reduce the heart rate in such hearts. They occur widely in nature and they can also be prepared synthetically.

They are prepared from two plants called *digitalis lanata* and *digitalis purpurea*. The term *digitalis* applies to the entire class of glycosides which consist of digoxin, digitoxin. They are useful in congestive heart failure, atrial fibrillation and paroxysmal atrial tachycardia. They are useful in sinus tachycardia caused by congestive heart failure but are ineffective in the treatment of sinus tachycardia such as that due to fever, anaemia or hyperthyroidism which are not associated with heart failure.

**DIGOXIN**

**Presentation:** Tablet containing digoxin 0.25mg, 0.125mg; Elixir containing digoxin 0.05mg/ml; Injection containing digoxin 0.25mg/ml.

**Indications:** Heart failure, cardiac arrhythmias (particularly atrial fibrillation)

**Dose:** Digoxin is normally administered orally as a single dose except in children under the age of 10 years where it may be given in divided doses. Intravenous digoxin can be given undiluted over a period of 5 minutes or diluted in a four-fold volume of 5% dextrose, water for injection or normal saline over a period of 5 minutes. Digoxin intravenous should not be mixed with other drugs.

**Rapid Digitalisation:** Digoxin has a low therapeutic index and therefore cautious dosage determination is of paramount importance. Rapid digitalisation should not be given in somebody who has taken digoxin in the past two weeks.

**Digitalisation doses for Oral Digoxin; Premature neonates;** 0.02mg to 0.03mg/kg body weight. Full term neonates; 0.025mg to 0.035mg/kg body weight. 1 to 24 months; 0.03mg to 0.05mg/kg body weight. 2 to 5 years; 0.025mg to 0.035mg/kg weight. 5 to 10 years; 0.015mg to 0.03mg/kg body weight. Older than 10 years; 0.01mg to 0.015mg/kg body weight.

**Digitalisation doses for intravenous digoxin (with normal renal function); Premature neonates;** 0.015mg to 0.025mg/kg body weight. Full term neonates; 0.02mg to 0.03mg/kg body weight. 1 to 24 months; 0.03mg to 0.05mg/kg body weight. 2 to 5 years; 0.025mg to 0.035mg/kg weight. 5 to 10 years; 0.015mg to 0.03mg/kg body weight. Older than 10 years; 0.008mg to 0.012mg/kg body weight.

**Maintenance dose:** 20 to 30% of the digitalisation dose. In patients under 10 years give in divided doses.

Loading doses are administered in divided doses as follows;

**Oral:** 50% of the total dose given as first dose; the remaining portion is given in fractions of 25% of the loading dose at 6 to 8 hour intervals.

**Intravenous:** 50% of the total dose given as first dose; the remaining portion is given in fractions of 25% of the loading dose at 4 to 8 hour intervals.

Patient’s clinical response should be carefully assessed before each additional dose is given. If the desired therapeutic response has been achieved or the patient has toxic effects then the remaining portion of the full digitalisation dose should not be administered. Patients with renal failure should be given a much lower dose. Patients with hypokalaemia should not be given digoxin until after the hypokalaemia has been corrected. Digoxin should be avoided in patients with conduction abnormalities including severe bradycardia.

**Side effects:** Usually associated with excessive dosage, include: nausea, vomiting, anorexia, diarrhoea, abdominal pain, visual disturbances, headache, fatigue, drowsiness, confusion, delirium, hallucinations, arrhythmias, heart block.

**Caution:** Recent infarction, hypothyroidism, reduce dose in the elderly and in renal impairment.

**Contra-indications:** Supraventricular arrhythmias caused by Wolff-Parkinson-White syndrome.
7.2 Diuretics

7.2.1 Thiazide diuretics
7.2.2 Loop diuretics
7.2.3 Potassium sparing diuretics with other diuretics

7.2.4 Osmotic diuretics

Diuretics are used in fluid retention resulting from cardiac, renal or hepatic failure. They cause electrolyte loss, especially potassium and sodium in addition to water. They should not be used in conditions like kwashiorkor. Different types are available and their potency varies according to the site of action.

7.1 Thiazide

Thiazides act at the beginning of the distal convoluted tubule and are moderately potent diuretics. Small doses of thiazides are used long term to control hypertension alone in mild hypertension, and with other drugs in more severe hypertension.

HYDROCHLOROTHIAZIDE

Presentation: Tablet containing 25mg, 50mg hydrochlorothiazide
Indications: Oedema, hypertension
Dose: Adult, oedema; initially 50 – 100mg daily, maintenance 25 – 50mg on alternate days. Hypertension: 25mg daily which can be increased to 100mg daily if necessary
Child: 2.5mg/kg body weight daily in two divided doses.
Side effects: Hypokalaemia, sensitisation
Caution: Avoid in diabetes and gout, hypercalcaemia
Contra-indications: Severe renal and hepatic impairment, hypercalcaemia

7.2.2 Loop Diuretics

These inhibit reabsorption from the ascending loop of henle in the renal tubule and are powerful diuretics. Hypokalaemia frequently develops and care should be taken to avoid hypotension.

FRUSEMIDE

Presentation: Tablet containing 20mg, 40mg frusemide. Injection containing 10mg/ml frusemide.
Indications: Oedema, oliguria due to renal failure
Dose: Adult, oedema; orally initially 40mg in the morning; maintenance 20mg daily or 40mg on alternate days, increased in resistant oedema to 80mg daily. Child; 1 – 3mg/kg body weight daily.
Oliguria, adult; orally 250mg daily initially, increasing by steps of 250mg to a maximum of a single daily dose of 2g. By intramuscular or slow intravenous injection, initially 20 – 50mg. Child; 0.5 – 1.5mg/kg body weight to a maximum daily dose of 20mg.
Oliguria, intravenous infusion; initially 250mg over 1 hour (rate not exceeding 4mg/minute). If satisfactory urine output is not obtained in the subsequent 1 hour, a further 500mg over 2 hours, if no satisfactory response within the subsequent 1 hour, a further 1g over 4 hours can be given, if no satisfactory response is obtained, dialysis is probably required.
Side effects: Hypokalaemia, fluid depletion
Caution: Pregnancy, liver failure, aggravates diabetes and gout.

7.2.3 Potassium Sparing Diuretics With Other Diuretics

AMILORIDE WITH HYDROCHLOROTHIAZIDE

Presentation: Tablet containing 5mg amiloride hydrochloride and 50mg hydrochlorothiazide
Indications: Oedema and mild hypertension
Dose: 2 – 4 tablets daily in two divided doses
Side effects: see under 7.2.1. dry mouth, hypotension
Caution: May precipitate diabetes mellitus and gout, do not give potassium supplements
Contra-indications: Diabetes mellitus, hyperuricaemia

7.2.1 Osmotic Diuretics

MANNITOL

Presentation: Intravenous infusion containing 10%, 20% solution, 500ml
Indications: Fluid retention, cerebral oedema, and induction of forced diuresis
Dose: 50 – 200g over 24 hours, preceded by a test 200mg/kg body weight by slow intravenous injection.
Side effects: Chills, fever, fluid depletion
Caution: intravenous solution should be kept at room temperature
Contra-indications: dehydration, congestive heart failure
7.3 Anti-arrhythmic drugs

Beta-adrenoceptor blocking drugs

Beta-adrenoceptor blocking drugs (beta-blockers) block the beta-adrenoceptors in the heart, peripheral vasculature, bronchi, pancreas, and liver. Many beta-blockers are now available and in general they are all equally effective. There are, however, differences between them which may affect choice in treating particular diseases or individual patients.

Intrinsic sympathomimetic activity (ISA, partial agonist activity) represents the capacity of beta-blockers to stimulate as well as to block adrenergic receptors.

Beta-blockers with a relatively short duration of action have to be given two or three times daily. Many of these are, however, available in modified-release formulations so that administration once daily is adequate for hypertension.

For angina twice-daily treatment may sometimes be needed even with a modified-release formulation. Some beta-blockers such as atenolol and carvedilol, have an intrinsically longer duration of action and need to be given only once daily.

Beta-blockers slow the heart and can depress the myocardium; they are contra-indicated in patients with second- or third-degree heart block. Beta-blockers should also be avoided in patients with worsening unstable heart failure; care is required when initiating a beta-blocker in those with stable heart failure. (important: particular care is required to avoid hypokalaemia in patients taking sotalol). Carvedilol has, in addition, an arteriolar vasodilating action, by diverse mechanisms, and thus lower peripheral resistance.

Beta-blockers can precipitate asthma and this effect can be dangerous. Beta-blockers should be avoided in patients with a history of asthma or bronchospasm; if there is no alternative, a cardioselective beta-blocker can be used with extreme caution under specialist supervision. Atenolol and metoprolol, have less effect on the beta (bronchial) receptors and are, therefore, relatively cardioselective, but they are not cardioselective.

Beta-blockers are also associated with fatigue, coldness of the extremities and sleep disturbances with nightmares (may be less common with the water-soluble betablockers, Beta-blockers are not contra-indicated in diabetes; however, they can lead to a small deterioration of glucose tolerance and interfere with metabolic and autonomic responses to hypoglycaemia.

Cardioselective betablockers may be preferable and beta-blockers should be avoided altogether in those with frequent episodes of hypoglycaemia. Beta blockers, especially when combined with a thiazide diuretic, should be avoided for the routine treatment of uncomplicated hypertension in patients with diabetes or in those at high risk of developing diabetes.

7.3.1 Atenolol

Presentation: Tablet containing 25mg, 50mg, 100mg atenolol. Injection containing 500mcg/ml atenolol.

Indications: Hypertension, angina, arrhythmias

Dose: Oral, hypertension; 50mg daily. Angina; 100mg daily in 1 or 2 doses. arrhythmias; 50 – 100mg daily. By intravenous injection, arrhythmias; 2.5mg at a rate of 1mg/minute, repeated at 5 minutes intervals to a maximum of 5mg.

By intravenous infusion, arrhythmias; 150mcg/kg body weight over 20 minutes, repeated every 12 hours if necessary.

Side effects: Bradycardia, heart failure, conduction disorders, bronchospasms, peripheral vasoconstriction, gastro-intestinal disturbances, sleep disorders, fatigue.

Caution: Reduce dose in renal impairment, late pregnancy and breast feeding, avoid abrupt withdrawal in angina, diabetes, myasthenia gravis.

Contra-indications: Asthma or history of obstructive airways disease, uncontrolled heart failure, marked bradycardia, 2nd or 3rd degree AV block, cardiogenic shock.

CARVEDILOL

Presentation: Tablets containing Carvedilol 3.125 mg

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

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 max. 50 mg daily in single or divided doses; ELDERLY initial dose of 12.5 mg daily may provide satisfactory control 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; increase to highest dose tolerated, max. 25 mg twice daily in patients with severe heart failure or bodyweight less than 85 kg and 50 mg twice daily in patients over 85 kg

Side-effects: see 7.3.1

Cautions see 7.3.1 monitor renal function during dose titration in patients with heart failure who also have renal impairment, low blood pressure, ischaemic heart disease, or diffuse vascular disease; severe heart
Drugs used in the treatment of diseases of the cardiovascular system

**MECOPROLOL TARTRATE**

**Presentation:** Tablets, metoprolol tartrate 50 mg, metoprolol tartrate 200 mg SR tablets, metoprolol tartrate 1 mg/mL injection.

**Indications:** See see under Dose

**Dose:** By mouth, hypertension, initially 100 mg daily, increased if necessary to 200 mg daily in 1–2 divided doses; max. 400 mg daily (but high 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 doses if necessary. Migraine prophylaxis, 100–200 mg daily in divided doses. Hyperthyroidism (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, by slow intravenous injection 2–4 mg at induction or to control arrhythmias developing during anaesthesia; 2-mg doses may be repeated to a max. of 10 mg Early intervention within 12 hours of infarction, by intravenous injection 5 mg every 2 minutes to a max. of 15 mg, followed after 15 minutes by 50 mg by mouth every 6 hours for 48 hours; maintenance 200 mg daily in divided doses.

**Side effects:** See 7.3.1

**Cautions:** See 7.3.1

**Contraindications:** see 7.3.1

**PROPRANOLOL**

**Presentation:** Tablet containing 10mg, 40mg, 80mg propranolol hydrochloride. Solution containing 5mg/5ml, 10mg/5ml, 50mg/5ml propranolol hydrochloride. Injection containing 1mg/ml propranolol hydrochloride.

**Indications:** See 7.3.1.

**Dose:** Oral, hypertension, initially 80mg twice daily increased as required to a maintenance dose of 160–320mg daily.

**Arrhythmias:** 10–40mg daily.

**Side effects:** See 7.3.1.

**Caution:** See 7.3.1.

**Contraindications:** See 7.3.1.

**Digoxin (See under 7.1.1.)**

**Lignocaine Hydrochloride**

**Presentation:** Infusion solution, 0.1% containing 1mg/ml lignocaine hydrochloride. 0.2% containing 2mg/ml lignocaine hydrochloride and 5% containing 50mg/ml lignocaine hydrochloride all in glucose intravenous infusion. Injection, containing 1% (10mg/ml) lignocaine hydrochloride, 2% (20mg/ml) lignocaine hydrochloride.

**Indications:** arrhythmias, especially frequent ventricular extra systoles

**Dose:** 1mg/kg body weight by slow intravenous injection given in 1–2 minutes, maybe repeated after 10–20 minutes. Alternatively a loading dose of 1–2mg/kg body weight maybe given followed by 0.1–0.2% infusion at 1–2mg per minute for 12–48 hours.

**Side effects:** Dizziness, paraesthesia, drowsiness (particularly when given too rapidly), confusion, respiratory depression and convulsions, hypotension and bradycardia (which may lead to cardiac arrest), hypersensitivity has been reported.

**Caution:** Lower doses in congestive heart failure, hepatic impairment, following cardiac surgery.

**Contra-indications:** Heart block, porphyria

**QUINIDINE**

**Presentation:** Tablet containing 250mg quinidine bisulphate

**Indications:** Ventricular arrhythmias, supraventricular tachycardia

**Dose:** 250–500mg 3–4 times daily

**Side effects:** Nausea, diarrhoea, ventricular arrhythmias, thrombocytopenia, haemolytic anaemia, rarely cinchonism, granulomatous hepatitis.

**Caution:** Test for hypersensitivity can be done by giving a 200mg test dose initially.

**Contra-indications:** Heart block

**7.4 Anti-anginal drugs**

**7.4.1 Atenolol (see under 7.3.1.)**

**GLYCERYL TRINITRATE**

**Presentation:** Sublingual tablet containing 300mcg, 500mcg glyceryl trinitrate

**Indications:** Prophylaxis and treatment of angina pectoris, left ventricular failure

**Dose:** Sublingually; 300mcg – 1.20mg repeated as required

**Side effects:** Throbbing headache, dizziness, flushing, hypotension, tachycardia

**Caution:** Severe hepatic or renal impairment, malnutrition, hypothermia, hypothyroidism.

**Contra-indications:** Hypersensitivity to nitrates, hypotensive conditions and hypovolaemia, mitral stenosis, marked anaemia, head trauma, cerebral haemorrhage, closed angle glaucoma.
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7 ISOSORBIDE MONONITRATE

Presentation: Tablet containing 10mg, 20mg, 40mg isosorbide mononitrate

Indications: acute attacks of angina pectoris, prophylaxis of angina pectoris, adjunct in treatment of congestive heart failure

Dose: Initially 20mg 2 – 3 times daily or 40mg twice daily (10mg twice daily for those who have not previously received nitrates); up to 120mg daily in divided dose if required.

Side effects: See 7.4.2.

Caution: See 7.4.2

Contra-indications: See 7.4.2

7.5.1.1 Amiloride + Hydrochlorthiazide (See notes in 7.2.3.1.)

7.5.2 BETA BLOCKERS

7.5.3.1 Atenolol (See notes in 7.3.1.)

7.5.3 VASODILATORS

7.5.4 ACE Inhibitors

7 HYDRAZINE

Presentation: Tablet containing 12.5mg, 25mg, 50mg captopril

Indications: Alone or in combination with thiazides in essential hypertension, adjunct in heart failure

Dose: Hypertension; Used alone, initially 12.5mg twice daily, if used in addition to diuretic, in the elderly and in renal impairment, initially 6.25mg twice daily. Usual maintenance dose is 25mg twice daily to a maximum of 50mg twice daily (rarely up to 3 times daily in severe hypertension).
Side effects: Hypotension, dizziness, dry cough, voice changes, throat discomfort, fatigue, headache, gastrointestinal disturbances, renal impairment, hypersensitivity reactions, blood disorders. 

Caution: May cause profound hypotension at induction, monitor renal function before and during treatment, reduce dose in renal impairment, breast feeding. Monitor for possible hyperkalemia

Contra-indications: Hypersensitivity to ACE inhibitors, aortic stenosis, or left ventricle outflow tract obstruction, pregnancy, porphyria.

AMIODARONE HYDROCHLORIDE

Presentation: Tablet 100mg, containing Aamiodarone hydrochloride, injection 50mg/ml amiodarone hydrochloride

Indication: Paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation/flutter, ventricular fibrillation

Dose: Oral 200mg 3 times daily for a week, reduced to 200mg twice daily for a further week; maintenance usually 100-200mg daily to control arrhythmia. Intravenous infusion via venal catheter, 5mg/kg over 20 – 120 minutes with ECG monitoring; maximum 1.2g in 24 hours.

Side effects: Reversible corneal microdeposits, peripheral neuropathy and myopathy, thyroid dysfunction, diffuse pulmonary alveolitis, pneumonitis, lung fibrosis, jaundice, hepatitis, cirrhosis, phototoxicity, nausea, vomiting, nightmares, tremors, fatigue, alopecia impotence, hematological disorders, ataxia hypersensitivity

Caution: Should be initiated in hospital or under specialist supervision. Chest x-ray, Liver function and thyroid function tests required before treatment and then every 6 months. Heart failure, renal impairment, elderly, severe bradycardia and conduction disturbances, porphyria.

7.5.6 Inotropic sympathomimetics

DOPAMINE HYDROCHLORIDE

Presentation: Sterile concentrate, dopamine hydrochloride 40mg/ml. For dilution and use as an intravenous infusion.

Indication: Cardiogenic shock, renal failure.

Dose: 2 – 5mkg/kg/minute, slow intravenous infusion, BP monitoring

Side effects: Nausea and vomiting, peripheral vasoconstriction, hypertension, hypotension, tachycardia.

Caution: Correct hypovolaemia.

Contraindication: Tachyarrhythmia, phaeochromocytoma.

DOBUTAMINE HYDROCHLORIDE

Presentation: Sterile solution 12.5mg/ml dobutamine hydrochloride. For dilution and use as an intravenous infusion.

Indication: Inotropic support in infarction, cardiac surgery, cardiomyopathies, septic and, cardiogenic shock.

Side effects: Tachycardia and marked increase in systolic blood pressure indicate overdose.

Caution: Severe hypotension.

7.5.7 Anti-hypertensive aceinhibitor

LISINOPRIL

Presentation: Tablet 2.5mg, 10mg, 20mg containing lisinopril.

Indications: Hypertension, heart failure, diabetic nephropathy, prophylaxis after myocardial infarction.

Dose: Hypertension, initially 2.5mg daily, usual maintenance dose 10-20mg daily; max 40mg daily, heart failure (adjunct), initially 2,5mg daily, usual maintenance dose 5-20mg daily. Prophylaxis after myocardial infarction 2.5 – 10mg daily. Diabetic nephropyathy 2.5 – 10mg daily

Side effects: See Captopril

Caution: See Captopril

Contraindications: See Captopril

7.5.8 Other antihypertensives

ADRENALINE

(Can be added to sympathomimetics Depaum)

Presentation: Injection containing 100 micrograms/ml adrenaline (epinephrine) hydrogen tartrate

Indication: Cardiac arrest, severe anaphylactic reaction, severe angioedema.

Dose: In cardiac arrest 1mg by intravenous injection through a central line (if one is in place) otherwise through a peripheral vein then flushed with some sodium chloride 0.9%. Repeat every 3 minutes according to the response or subcutaneous. In anaphylaxis: By intramuscular injection, adult and adolescent, 500 micrograms, infant under 6
months 50 micrograms, child 6 months – 6 years 120 micrograms, 6-12 years 250 micrograms. The above doses may be repeated several times if necessary at 5 minutes intervals, according to blood pressure, pulse and respiratory function.

**Side effects:** Anxiety, tremor, tachycardia, arrhythmias, hypertension (risk of cerebral hemorrhage) and pulmonary oedema, nausea, vomiting, sweating, dizziness, weakness.

**Caution:** Hypertension, hyperthyroidism, diabetes mellitus, ischaemic heart disease, elderly.

**Note:** See also Local anaesthesia/Eye preparation.
Drugs used in the treatment of malignant disease

The interdisciplinary approach in the treatment of cancer patients of specific surgery, sophisticated multi-cytostatic treatment and radiation is only possible in specialised clinics where different types of treatments are available.

The therapy for malignant tumour demands qualified and experienced personnel – both Doctors and nurses. A laboratory should offer valid and reproducible tests. Only if these conditions are guaranteed should oncology treatment be performed.

For most neoplasms, combination therapy is considered superior to single drug treatment. But timing of doses and selection of cytotoxic drugs (often in combination with prednisolone) is very important and depends not only on the type of tumour but also on the general condition of the patient being treated.

Chemotherapy may cure some malignant diseases in their early stages. Often it is said that chemotherapy improves the quality of life of the patient (especially in the reduction of pain caused by the tumour) but this is an evaluation which only the patient can make. In the later stages of the tumour the chemotherapy has to be balanced carefully between the palliative effect of the drugs and the toxic side effects.

General contraindications for cytotoxic drugs include signs of infection (bacterial or viral) especially where there is fever and anaemia.

Note: In cancer therapy, treatment doses are usually calculated according to skin surface area rather than per kg body weight.

Prescriptions should not be repeated except on the instructions of the specialist.

8.1 Alkylating drugs

**CHLORAMBUCIL**

*Presentation:* Tablet containing 2mg, 5mg Chlorambucil

*Indications:* Chronic lymphocytic leukemia

*Dose:* 4mg – 10mg per day

*Side effects:* Neutropenia, thrombocytopenia, nausea, vomiting, liver damage

*Caution:* Should not be used within one month of radiation therapy, Pregnancy.

**CYCLOPHOSPHAMIDE**

*Presentation:* Tablet containing 50mg Cyclophosphamide. Injection containing 200mg, 500mg, 1g cyclophosphamide in sodium chloride for dilution with water for injection.

*Indications:* Hodgkins disease, lymphomas, multiple myeloma, acute leukemia Chronic myeloid leukemia, carcinoma of the breast, neurastroma sarcoma

*Dose:* 600mg/M² intravenously or 20 – 50mg/M² daily depending on the condition being treated and tolerance

*Side effects:* Alopecia, anorexia, fever, nausea, vomiting, aspermia, permanent sterility, haemorrhagic cystitis, myelosuppression.

*Caution:* High serum uric acid and potassium levels may need treatment during therapy. Ensure high fluid intake.

*Contraindications:* Pregnancy

**MELPHALAN**

*Presentation:* Tablet containing 2mg, 5mg Melphalan

*Indications:* Multiple myeloma, chronic lymphocytic leukemia, lymphoma.

*Dose:* 1mg/kg body weight every 4 weeks.

*Caution:* myelosuppression, renal impairment, pregnancy and alopecia. Frequent blood counts advisable.

**MUSTINE**

*Presentation:* Vials containing 10mg powder for preparation for intravenous injection.

*Indications:* Lymphoma, Hodgkin disease, mycoses fungoides, solid tumour, brain tumour

*Dose:* Single dose 400mg/kg or 100mg/kg intravenously daily for 4 – 5 days

*Side effects:* Nausea, vomiting alopecia, myelosuppression, bone marrow depression.
**8.1 Nitrogen Mustard**

**Presentation:** Powder for dilution  
**Indications:** Hodgkin's lymphoma, lymphoma carcinoma of the lung  
**Dose:** 6mg/m² intravenously  
**Side effects:** Alopecia, nausea, vomiting,
combination with other drugs
Side effects: Gastrointestinal ulceration, megaloblastic anaemia, hepatic impairment
Caution: Renal disease.

8.4 Vinca alkaloids

8.5 Other neoplastic drugs

8 HYDROXYUREA

Presentation: Capsule containing 500mg hydroxyurea
Indications: Chronic myeloid leukaemia and malignant melanoma
Dose: 30 – 50mg/kg body weight in 2 divided doses
Side effects: Bone marrow depression, nausea and vomiting, dizziness, confusion, skin rashes and diarrhoea
Caution: Not to be used in pregnancy and in patients with renal impairment

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disturbances (may include cataracts, corneal changes, retinopathy), leucopenia (sometimes with anaemia and thrombocytopenia), rarely neutropenia, hypertriglyceridaemia, thromboembolic events, liver enzyme changes, interstitial pneumonitis, hypersensitivity reactions including angiodema, stevens-Johnson syndrome, bullous pemphigoid. 

**Caution:** Occassionally, cystic ovarian swellings in premenopausal women, hypercalcaemia if bony metastases; increased risk of thromboembolic events when used with cytotoxics; breastfeeding, porphyria.
Drugs acting on the eye

Preparations for the eye should be sterile. Single use containers should therefore never be re-used. Combination preparations containing an antibiotic and a steroid should only be used under specialist supervision. They should not be used in undiagnosed “red eye” which may be caused by a viral infection.

Prescribers are advised to bear in mind the possibility of drugs which are administered as eye drops being absorbed into the general circulation via conjunctival vessels or from the nasal mucosa after the excess of the preparation has drained down through the tear ducts.

When two different preparations of eye drops are required at the same time of day an interval of a few minutes should be left between the two applications. This is to avoid dilution and overflow. Application of an ointment at night reduces the problem.

9.1 Fluorescein sodium

Presentation: Single use sterile eye drops containing 1% or 2% fluorescein sodium.
Indications: Diagnostic agent for detecting corneal abrasions and foreign bodies in the eye. Also used in the fitting of hard contact lenses.
Administration: Sufficient solution should be applied to stain the damaged areas. Excess should be washed away with sterile saline
Side effects: The skin and urine may be transiently coloured.
Caution: Not to be used with soft contact lenses, may cause transient blurring of vision, patients should not drive or operate hazardous machinery until vision is clear.

9.2 Aciclovir eye ointment

Presentation: Eye ointment containing 3% aciclovir
Indications: Local treatment of herpes simplex
Administration: Apply five (5) times daily. Continue for at least 3 days after complete healing
Side effects: Mild stinging immediately after application may occur; local irritation and inflammation have been reported
Contra-indications: Not to be used with steroids

9.3 Chloramphenicol

Presentation: Eye drops containing 0.5% chloramphenicol, eye ointment containing 1% chloramphenicol.
Indications: Superficial bacterial infections of the eye.
Administration: Eye drops; instill at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing.
Eye ointment; apply either at night (if eye drops used during day) or 3 – 4 times daily (if ointment alone used).
Side effects: Transient irritation, burning, stinging, itching and dermatitis. Adverse haematological events (bone marrow depression, aplastic anaemia and death) have been reported following ocular use of chloramphenicol.
Caution: Avoid prolonged use (sensitization and resistance), remove contact lenses during period of treatment, use only when essential in pregnancy.
Contra-indications: Hypersensitivity to chloramphenicol

9.4 Tetracycline

For mass control of communicable ophthalmia, WHO recommends the application of tetracycline eye ointment to both eyes twice daily for 5 days every 4 weeks for 6 months.

9.4.1 Tetracycline Hydrochloride

Presentation: Eye ointment containing 1% tetracycline hydrochloride.
Indications: Superficial bacterial infections, particularly treatment of chlamydial infections including trachoma.
Administration: As per other ointments above. Trachoma; three times daily for six weeks
Side effects: Allergic reactions, irritation, stinging, burning, itching, dermatitis may occur, transient loss of vision.
Contra-indications: Hypersensitivity to tetracycline.

9.5 Betamethasone

Presentation: Eye drops, eye ointment containing 0.1% betamethasone sodium phosphate.
Indications: Local treatment of inflammation (Short term)
Administration: Eye drops: apply every 1 – 2 hours until controlled then reduce frequency. Eye ointment; apply 2 – 4 times daily or at night when
used with eye drops.

**Side effects:** Hypersensitivity reactions (usually of delayed type) may occur (itching, stinging, irritation, burning and dermatitis) and may result in increased intra ocular pressure.

Intensive or prolonged use may lead to formation of posterior subcapsular cataracts.

**Contra-indications:** Viral, fungal, tuberculosis or purulent conditions of the eye, glaucoma and herpetic keratitis.

### 9.6 Pilocarpine hydrochloride

**Presentation:** Eye drops containing 0.5%, 1%, 2%, 3%, 4% Pilocarpine hydrochloride.

**Indications:** Glaucoma

**Side effects:** Small pupil, sweating, bradycardia, hypersalivation, bronchospasm and intestinal colic

**Administration:** Induction of miosis; 1 - 2 drops.

Emergency treatment of acute narrow angle glaucoma; 1 drop every 5 minutes until miosis is achieved.

**Caution:** Use only when essential in pregnancy and lactation. Do not drive or machinery until vision is clear.

### 9.7 Timolol Maleate

**Presentation:** Eye drops containing 0.25%, 0.5% of timolol as maleate

**Indications:** Chronic simple glaucoma.

**Side effects:** Transitory dry eyes, skin rashes.

**Contra-indications:** In patients with bradycardia, heart failure, heart block, bronchial asthma, chronic obstructive pulmonary disease, hypersensitivity to timolol or other beta blockers.

**Caution:** Concomitant use with drugs like verapamil and other beta blockers.

### 9.8 Atropine sulphate

**Presentation:** Eye drops, eye ointment containing 1% atropine sulphate.

**Indications:** As a mydriatic and cycloplegic used in refraction procedures in young children.

**Administration:** 1 drop three times daily

**Side effects:** Contact dermatitis, toxic systemic reactions may occur in the very young and very old.

**Caution:** Patients advised not to drive for one or two hours after mydriasis

**Contra-indications:** In narrow angle glaucoma, soft contact lenses.

### 9.9 Homatropine hydrobromide

**Presentation:** Eye drops containing 1%, 2% homatropine hydrobromide.

**Indications:** Mydriatic and cycloplegic

**Administration:** 1 drop as required

**Side effects:** As for atropine sulphate

**Contra-indications:** As for atropine, not to be used in patients hypersensitive to atropine.

### 9.10 Acetazolamide

**Presentation:** Tablet containing 250mg acetazolamide, injection (iv) containing 500mg acetazolamide as sodium salt.

**Indications:** Tablets; glaucoma of all types

**Administration:** Orally or intravenous injection 0.25 – 1g daily in divided doses.

**Side effects:** Diuresis and hypokalaemia, appetite loss, drowsiness and depression.

### 9.11 Betaxolol hydrochloride

**Presentation:** Eye drops containing 0.5% betaxolol as hydrochloride

**Indications:** Treatment of chronic simple glaucoma.

**Administration:** Apply twice daily

**Side effects:** May be absorbed systemically, so side effects of beta-blockers may be experienced, transitory dry eyes.

**Caution:** In concomitant use with drugs such as verapamil

**Contra-indications:** In bradycardia, heart block or heart failure. In asthma, history of obstructive Airways disease, unless no alternative treatment is available.

### 9.12 Gentamicin eye drops

**Presentation:** Eye/ear drops containing 0.3% gentamicin sulphate.

**Indications:** Blepharitis; bacterial conjunctivitis.

**Administration:** Mild to moderate infection, by instillation into the eye, adult and child 1 drop every 2 hours, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete.

Severe infection, by instillation into the eye, Adult and Child 1 drop every hour, reducing frequency as infection is controlled, then continue for 48 hours after healing is complete

**Side effects:** Burning, stinging, itching, dermatitis.

**Caution:** Prolonged use may lead to skin sensitization and emergence of resistant organisms including fungi; discontinue if purulent discharge, inflammation or exacerbation of pain.

**Contraindications:** Hypersensitivity to aminoglycoside group of antibiotics.
9.13 Lignocaine hydrochloride

**Presentation:** Eye drops containing 4% lignocaine hydrochloride, fluorescein sodium 0.25%

**Indications:** Short acting local anaesthesia of cornea and conjunctiva

**Administration:** Local anaesthesia by instillation into the eye, Adult and Child 1 drop.

**Side effects:** Burning, stinging, redness; rarely, allergic reactions may occur.

**Caution:** Avoid prolonged use (cause of severe keratitis, permanent corneal opacification, scarring, delayed corneal healing); protect eye from dust and bacterial contamination until sensation fully restored.
10.1 Anti-coagulants

Anticoagulants are of little value in the prevention of arterial thrombosis. However, they are useful in the management of venous thromboembolism. Anticoagulant therapy carries the risk of haemorrhage which is increased in the following circumstance: severely ill patients taking other drugs such as phenylbutazone, aspirin, salicylates and clofibrate concomitantly. Care should be taken with patients who are also taking glutethimide or phenobarbitone, as these drugs accelerate the degradation of the anticoagulants and the dose needs to be re-adjusted if they are withdrawn.


10.2 Anti-haemorrhagics

AMINO APROIC ACID

Presentation: Tablet containing 500mg amino caproic acid. Syrup containing 250/500mg/ml amino caproic acid. Injection containing 5g/20ml per dilution and 24g/96ml for infusion.

Indications: Treatment and prophylaxis of haemorrhage due to excessive fibrinolysis

Dose: Oral or slow intravenous infusion; 4 – 5g initially followed by 1 – 1.25g every hour for up to 8 hours. If treatment is necessary for more than 8 hours then the total dose should not exceed 30g over 24 hours. Dosage should be reduced in patients with renal impairment

Side effects: Gastro-intestinal disturbances (dose related), dizziness, tinnitus, headache, generalized thrombosis, nasal and conjunctival congestion and skin rashes. Hypotension, bradycardia and arrhythmias may occur when aminocaproic acid is given by rapid intravenous injection or infusion

Caution: Renal or cardiac impairment, when treatment is prolonged, it is advisable to monitor creatine phosphokinase value for signs of muscle damage. Oral contraceptives increase probability of hypercoagulability.

FIBRINOGEN

Presentation: Dry or freeze dried powder for reconstitution containing fibrinogen concentrate alone or in combination with other factors such as Human factor III, thrombin or human albumin. When reconstituted the preparation will contain not less than 60g/litre of clottable protein

Indications: Control of haemorrhage associated with low blood fibrinogen concentration.

HUMAN ANTI-HAEMOPHILIAC FRACTION (DRIED) (FACTOR VIII)

Presentation: Freeze dried concentrate containing 3 units/ml and not less than 0.1units/mg of total protein when dissolved

Indications: Control of haemorrhage in
haemophilia A including those under going surgery such as dental or general surgery.

**Dose:** By slow intravenous infusion. The dosage should be determined for each patient and will vary according to the circumstances involving bleeding or type of surgery to be performed.

Adult; a dose of 1 unit/kg body weight raises the plasma concentration of plasma factor VIII by approximately 2%. Suggested formula to calculate the dose needed approximately for a given effect is:

\[ \text{Dose (in units)} = \text{weight (kg)} \times 0.5 \times \% \text{ desired increase (of normal) of plasma concentration of factor VIII} \]

**Side effects:** Allergic reactions including chills and fever. Hyperfibrinogenaemia may occur after massive doses with factor VIII products. This is less likely with newer products whose fibrinogen content has been reduced.

**Caution:** Intravascular haemolysis may occur with large or frequently repeated doses in patients with blood group A, B, or AB. This is less likely to occur with high potency concentrates.

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**FACTOR IX FREEZE DRIED CONCENTRATE**

**Presentation:** Powder for solution for infusion

**Indications:** Haemophilia B

**Dosage:** Haemophilia B, by slow intravenous infusion, Adult and Child according to patient’s needs and specific preparation used.

**Caution:** Risk of thrombosis

**Side effects:** Allergic reactions, including chills, fever.

**Contraindications:** Disseminated vascular coagulation

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**PHYTOMENADIONE (VITAMIN K)**

**Presentation:** Injection containing 10mg/ml Phytomenadione. Tablet (sugar coated) containing 10mg phytomenadione

**Indications:** Vitamin K deficiency particularly in neonates and also in liver disease. Reversal of effects of anti-coagulants.

**Dose:** Neonatal prophylaxis 1mg immediately after birth. Liver disease 1-2mg repeated as desired.

**Side effects:** Shock-like reactions, cyanosis, bronchospasm, rapid pulse, pain and swelling at injection site.

**Caution:** Pregnancy, store in the dark, do not use if separation has occurred or oil droplets have appeared.

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**ASPIRIN (ANTIPLATELET)**

**Presentation:** Tablet containing 75mg aspirin

**Indication:** Prophylaxis of cerebrovascular disease or myocardial infarction.

**Dose:** A low dose of aspirin is used for secondary prevention of thrombotic cerebrovascular or cardiovascular disease. 150-300mg is given after myocardial infarction and 300mg is given after ischaemic (not haemorrhagic) stroke. Initial dose is followed by maintenance treatment with aspirin 75 – 300mg daily. A low dose of aspirin is also of benefit in the primary prevention of vascular events when the estimated 10 year coronary heart disease risk is 15% or greater and provided that blood pressure is controlled. A low dose of aspirin (75-100mg) is also given following coronary bypass surgery.

**Side effects:** bronchospasm; gastro-intestinal haemorrhage (occasionally major).

**Caution:** Asthma; uncontrolled hypertension; pregnancy.

**Contraindications:** children under 12 years and in breast-feeding, active peptic ulceration, haemophilia and other bleeding disorders.

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**10.3 Haemopoetics**

**IRON**

Haemopoetics should not be given until an accurate diagnosis has been made. They should be introduced singly. A response is shown by a rise in reticulocyte count in a week. If a patient with apparent iron deficiency anaemia fails to respond to treatment with either oral or parental iron preparations, the diagnosis should be reviewed.

**FERROUS SULPHATE**

**Presentation:** Tablet containing 200mg ferrous sulphate. Paediatric mixture containing 60mg/5ml ferrous sulphate.

**Indications:** Treatment and prevention of iron deficiency anaemia.

**Dose:** Adult; 600 – 800mg daily in three divided doses. Maintenance; 200 – 400mg daily. Take after food.

Child; up to 1 year 5ml well diluted with water three times daily. 1 – 5 years 10ml well diluted with
water three times daily.  
**Side effects:** Gastro-intestinal disturbances.  
**Caution:** Do not use with tetracycline, could be poisonous to children.  
**Contraindications:** Aplastic anaemia and megaloblastic anemia.

### FERROUS GLUCONATE

**Presentation:** Tablet containing ferrous gluconate 300mg (35mg iron).  
**Indications:** Iron-deficiency anaemia.  
**Dose:** Prophylactic, 2 tablets daily before food, therapeutic, 4-6 tablets daily in divided doses before food; Child 6-12 years, prophylactic and therapeutic 1 – 3 tablets daily.  
**Side effects:** Gastro-intestinal irritation may occur with iron salts, nausea and epigastric pain, constipation or diarrhoea  
**Caution:** Pregnancy.

### FERROUS FUMERATE

**Presentation:** Tablet containing 322mg (100mg) iron  
**Indications:** Iron-deficiency anaemia  
**Dose:** prophylaxis 1 tablet daily; therapeutic, 1 tablet twice daily.  
**Side effects:** See 10.3.3  
**Caution:** Pregnancy

### FERROUS GLYCINE SULPHATE

**Presentation:** Syrup containing ferrous glycine sulphate equivalent to 25mg iron per 5ml  
**Indications:** Iron-deficiency anaemia  
**Dose:** 5 – 10mls 3 times daily. Child; 2.5 – 5mls 1-3 times daily according to age.  
**Side effects:** See10.3.3  
**Caution:** Pregnancy

### FOLIC ACID

**Presentation:** Tablet containing 5mg folic acid  
**Indications:** Prevention and treatment of folic acid deficiency  
**Dose:** 5 – 20mg daily  
**Contraindications:** Sub acute combined degeneration of spinal cord.

### HYDROXOCOBALAMIN (VITAMIN B₁₂)

**Presentation:** Injection containing 1mg/ml hydroxocobalamin  
**Indications:** Pernicious anaemia  
**Dose:** Initially 1mg intramuscularly repeated 5 times at intervals of 2-3 days. Maintainance dose 1mg every three months. Child; as for adult  
**Caution:** Should not be given before diagnosis is fully established
11.1 Vitamin, minerals and dietary supplements

Vitamins are used for the prevention and treatment of specific deficiency states or where the diet is inadequate. They may be prescribed to prevent or treat deficiency but not as a dietary supplement.

**ASCORBIC ACID (VITAMIN C)**

**Presentation:** Tablet containing 50mg, 100mg, 200mg, ascorbic acid. Effervescent tablet containing 1g ascorbic acid. Injection containing ascorbic acid 100mg/ml.

**Indications:** Supplementation and deficient states. Prevention and treatment of Scurvy.

**Effects of deficiency:** Scurvy, irritability, slow growth, decreased resistance to infections, haemorrhagic tendencies, poor wound healing.

**Physiological requirements:** Up to 1 year; 35mg daily. 1 – 12 years; 40mg daily. Over 12 years; 40 – 60mg daily.

**Therapeutic dose:** 200 – 400mg daily.

**Natural sources:** Citrus fruits, tomatoes, green vegetables, black currant and rose fruit.

**Side effects:** Large doses cause diarrhoea, other GIT disturbances, hyperoxaluria, renal calcium, oxalate calculi, haemolysis in patients with G6PD deficiency.

**Caution:** Destroyed by usual cooking temperatures. Hyperoxaluria, deficiency of G6PD.

**CALCIUM GLUCONATE**

**Presentation:** Injection ampoules containing 10% calcium gluconate. Tablet containing 600mg calcium gluconate. Effervescent tablet containing 1g calcium gluconate. Chewable tablet containing 1.5mg calcium gluconate.

**Indications:** Adjunct in the treatment of hypocalcaemia. Hyperkalaemia, hypermagnesaemia, hyperphosphataemia (to prevent development of real osteodystrophy).

**Dose:** Calcium supplementation is usually required only where there is dietary calcium intake deficiency. This requirement varies with age and is relatively greater in childhood, pregnancy and lactation due to an increased demand and in old age due to decreased absorption. Oral, osteoporosis; 800mg calcium (20mmol)

Simple deficiency states – orally 400mg to 2mg daily adjusted according to patient’s requirements.

Severe acute hypocalcaemia or hypocalcaemic tetany – by slow intravenous injection 2.25mmol followed by continuous intravenous infusion of 9mmol daily.

Hyperkalaemia and hypermagnesaemia – by intravenous injection 2.25 – 4.5mmol.

Hyperphosphataemia – orally 2.5g daily titrated slowly to a maximum of 17g.

By slow intravenous injection in hypocalcaemic tetany; 10ml (2.5 mmol) initially followed by continuous infusion of 40ml (9 mmol) daily.

**Side effects:** Excess amounts could lead to hypercalcaemia especially in renal failure. Other side effects include GIT irritation especially with calcium chloride.

**Caution:** Renal impairment; plasma calcium during intravenous treatment should be monitored. Calcium chloride injections are irritant, therefore take extra care during intravenous injection. Renal impairment, sarcoidosis, patients with renal calculi.

In these conditions plasma calcium concentrations should be monitored closely.

**Contraindications:** Conditions associated with hypercalcemia and hypercalcuria (e.g. some form of malignant diseases).

**ERGOCALCIFERAL (VITAMIN D)**

Vitamin D comprises compounds used in treatment and prevention of rickets. The margin of safety between therapeutic and toxicity concentration is narrow. Therefore, vitamin D dietary supplementation may be detrimental in patients already receiving adequate dietary intake. Furthermore, Vitamin D is the most likely of all vitamins to cause toxicity.

**Presentation:** Effervescent and chewable tablet containing 10,000 units (250mcg), 50,000 units (1.25mg) ergocalciferal. Injection containing 300,000 units/ml ergocalciferal in oil.

**Indications:** Vitamin D deficiency including that caused by intestinal malabsorption, chronic liver disease, hypoparathyroidism.

**Dose:** therapeutic dose – deficiency due to malabsorption or liver disease – up to 40,000 units daily. Hypocalcaemia due to hypothyroidism – doses up to 100,000 units daily. Monitor calcium levels initially weekly then every 2 to 4 weeks to optimize clinical response and avoid hypercalcaemia.

**Effects of deficiency:** Rickets and osteomalacia

**Physiological requirements:** Child; 400i.u. daily. Adult; 100 i.u. daily

**Therapeutic dose:** 40,000 – 100,000 units daily

**Natural sources:** Milk, fish, liver, oil, sunlight

**Side effects:** Excess leads to hypercalcaemia, hypercalcuria, renal damage and cardiovascular damage.

**Caution:** Infants, renal and heart disease,
hypercalcaemia. Infants breast-fed by mothers taking therapeutic doses of vitamin D.

Contraindications: Hypercalcaemia

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**RETINAL (VITAMIN A)**

Retinol (Vitamin A) is a fat soluble vitamin and essential for growth, development and maintenance of epithelial tissue and for vision. Deficiency state develops with inadequate dietary intake. This is common in children.

Presentation: Capsule containing 50,000 i.u., 100,000 i.u., 200,000 i.u. vitamin A

Indications: Night blindness, xerophthalmia, xeromalacia. Adjunct treatment in measles, diarrhoea, malnutrition and primary biliary cirrhosis.

Effects of deficiency: Night blindness, xerophthalmia, xeromalacia, abnormal bone and teeth formation, dry skin and mucous membrane, retarded growth, decreased resistance to infections, significant increased risk of child mortality.

Physiological requirements: Up to 1 year, 1500 i.u. daily. 1 – 12 years; 2000 – 4500 i.u. daily. Over 12 years; 5000 – 8000 i.u. daily.

In deficient populations children should receive a high dose supplement every 6 months as follows; 6 – 11 months, 100,000 i.u. 1 – 6 years 200,000 i.u.

Therapeutic dose: 50,000 daily.

Dose:
- Primary biliary cirrhosis
  - Intravenous doses of 10,000 units every 2 to 4 months Xerophthalmia.
  - Over 1 year of age 200,000 units by mouth immediately on diagnosis.
  - 6 – 12 months 100,000 units
  - Less than 6 months 50,000 units (given by mouth immediately on diagnosis, then on the following day and repeated 2 weeks later.

Effects of overdose: Drying and cracking of skin, pain in long bones, sparse hair growth, growth retardation, increased intracranial pressure.

Natural sources: Dietary vitamin is derived from two sources, namely animal and plan. Animal sources include Liver, kidney, dried fish, oils, whole milk, egg yolk. Plant sources include carrots, whole grain, yellow fruits, dry/dark green or yellow vegetables.

Side effects:
- Excessive amounts may lead to hyper vitaminosis A, raised intracranial pressure, tinnitus, visual disturbances, acute vitamin A intoxication.

Caution: Destroyed by exposure to strong sunlight. Pregnancy, women of child-bearing age and breast feeding. Resistant to usual cooking temperatures.

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**VITAMIN B GROUP**

The Vitamin B Group comprises the following substances Vitamin B1 (Thiamine), Vitamin B2 (Riboflavin), Vitamin B6 (pyridoxine and derivatives) and Vitamin B12 (cobalamines). To these are added nicotinic acid and derivatives, folic acid and panthothenic acid.

The term vitamin B complex is a term generally used when individual Vitamin B substances and other components are commercially prepared. The ingredients and doses, are according to the manufacturers' instructions. Indications, side effects and Caution are as for the individual components of the formulation. The presentation of the Vitamin B complex is in form of tablets, capsules, elixir and injection.

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**NICOTINAMIDE**

Naturally occurs as a water-soluble vitamin B substance which is converted to nicotinamide odemine dinucleotide (NADP). These co-enzymes play a major role in electron transfer reactions in the respiratory chain. Their deficiency leads to a syndrome of pellagra which is characterised by skin lesions especially to areas exposed to sunlight with hyperpigmentation and hyperkeratination.

Nicotinic acid deficiency may occur in association with other Vitamin B complex deficiency states e.g. in alcoholism.

Presentation: Tablet containing 50mg nicotinamide

Indications: Pellagra, especially in alcoholism.

Effects of deficiency: Pellagra

Natural sources: Milk, fish, poultry, liver, whole grain, green vegetables and groundnuts.

Dose: Daily requirements are not definitely known but daily human requirement is required for optimum amounts of nicotinic acid to be absorbed.

Side effects: Vasodilation, dryness of the skin, pruritus hyperpigmentation, abdominal cramps, peptic ulcer disease, ambylopia, jaundice, impaired liver function, decrease in glucose tolerance, hyperglycaemia, hyperuricaemia.

Caution: Peptic ulcer disease, diabetes mellitus, gout or impaired liver function.

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**PYRIDOXINE (VITAMIN B6)**

A water soluble vitamin involved principally in amino acid, carbohydrate and fat metabolism and also required for haemoglobin formation. Deficiency is rare but may occur during drug therapy e.g. isoniazid therapy. Deficiency causes sideroblastic anaemia, dermatitis, cheliosis and neurologic symptoms such as peripheral neuritis, convulsions especially in neonates.

Presentation: Tablet containing 10mg, 20mg, 50mg pyridoxine hydrochloride
**Indications:** Pyridoxine deficiency such as may occur in isoniazid therapy or metabolic disorders e.g. hyperoxaluria, in sideroblastic anaemia, peripheral neuropathy.

**Effects of deficiency:** Irritability, convulsions especially in neonates, hypochromic anaemia, polyneuritis.

**Side effects:** Large dose and long term therapy leads to severe peripheral neuritis (neuropathies).

**Physiological requirements:** Up to 1 year; 200 – 400 micrograms. 1 – 12 years; 500mcg. Over 12 years; 1.2 – 1.8mg daily.

**Deficiency states:** 50 – 150mg daily in divided doses. Prophylaxis of isoniazid neuropathy; 10mg daily.

**Natural sources:** Meat, liver, kidney, whole grain, groundnuts and soya beans.

**Caution:** Destroyed by heat, intestinal synthesis occurs.

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**RIBOFLAVIN (VITAMIN B2)**

It is a water-soluble vitamin. It is used as a coenzyme in the various metabolic reactions. It is also necessary for the normal functioning of pyridoxine and nicotinic acid. Riboflavin deficiency mainly results from insufficient intake. The deficiency state is called ariboflavinosis. In addition, there may also be normocytic anaemia and some ocular symptoms. It may also occur in other deficiency states with other B vitamins.

**Presentation:** Tablet containing 5mg riboflavin

**Indications:** Aroboflavinosis characterized by conditions such as glossitis, stomatitis, photophobia and blurred vision.

**Physiological requirements:** Up to 1 year; 400 – 600micrograms. 1 – 12 years; 600mcg – 3mg. Over 12 years; 1.3mg – 1.5mg daily.

**Therapeutic dose:** 5 – 10mg daily

**Natural sources:** Milk, cheese, liver, meat, eggs, fish, green vegetables, whole grain.

**Caution:** Resistant to normal cooking temperatures.

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**THIAMINE (VITAMIN B1)**

This is a water-soluble vitamin. It is essential in carbohydrate metabolism. Its deficiency leads to a syndrome known as beri-beri.

**Presentation:** Tablet containing 25mg, 50mg, 100mg, 300mg thiamine hydrochloride. In high potency vitamin B Co. injections containing 25mg/ml (intravenous), 50mg/ml (intramuscular)

**Indications:** Treatment of thiamine deficiency, beri-beri, adjunct in treatment of alcohol abuse.

**Physiological requirements:** Up to 1 year; 200 – 500mcg daily. 1 – 12 years; 500mcg – 1.3mg. Over 12 years; 1.5mg daily

**Therapeutic dose:** 25 – 100mg intramuscularly or orally. In severe cases up to 300mg, higher doses acceptable in Wernicke-Korsakoff syndrome by intravenous route.

**Effects of overdose:** Sudden death with injection. Hypersensitivity reactions which may be fatal.

**Natural sources:** Liver, meats, milk, legumes, cereals and nuts.

**Caution:** Destroyed by normal cooking heat. Because of possibility of potentially serious allergic reaction, use by injection should be restricted to those patients in whom parenteral treatment is essential, intravenous injection should be given slowly (over 10 minutes).

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**VITAMIN B12**

This is a water-soluble vitamin. It occurs in various forms of cobalamins. Deficiency is commoner in those strict vegetarians who do not ingest any animal and dairy products. It is also common in patients after gastrectomy or ileal resection. Deficiency causes megaloblastic anaemia, demyelination and other neurological damage.

**Presentation:** Oral form of cyanocobalamin. Injectable forms of cyanocobalamin and hydroxy cobalin.

**Therapeutic dose:** (I) Pernicious anaemia and other macrocytic anaemia without neurological involvement: intramuscular cyanocobalamin and hydroxy cobalamin 250 - 1000mcg on alternate days for one to two weeks. Then 250mcg weekly until blood levels are normal.

**Maintenance doses:** 1000mcg cyanocobalamin monthly or 1000 mcg hydrocobalamin every 2 to 3 months.

**Prophylaxis for Vitamin B12 deficiency following parenteral administration, arrhythmias secondary to hypokalaemia.

**Caution:** Avoid use in hebers disease or tobacco amblyopia since these optic neuropathies may degenerate further.

**Interactions:** (see Appendix II) absorption of Vitamin B12 is reduced when administered together with neomycin, aminosalicylic acid, H² receptor antagonist, and colchicines.

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**MULTIVITAMIN TABLETS AND SYRUP**

These are available in different formulations. The constituents and dose are according to manufacturer’s instructions. Indications and side effects are as for constituents mentioned above.
HYDROLISED PROTEIN

Presentation: Powder containing lactose free protein without vitamins and minerals

Indications: Lactose intolerance (e.g. in kwashiorkor) and protein supplementation

Dose: Adults: 1 – 2 teaspoonfuls 3 times daily. Child: Use as milk.

Caution: Use for short a period as necessary

HIGH ENERGY PROTEIN SUPPLEMENT (HEPS)

Presentation: Powder containing dried skimmed milk, corn, soya, milk and sugar

Indications: Prevention and treatment of protein calorie malnutrition, expectant mothers in third trimester, during breastfeeding.

Dose: 3 tablespoons mixed with 2 tablespoons of oil in boiled water or mixed with porridge three timed daily.

11.2 Electrolyte and water replacement

Fluid and electrolyte therapy should be considered as replacement therapy and maintenance therapy.

Replacement therapy

Dehydration may result from either inadequate intake (thirst or fasting) or from excessive loss (diarrhoea). Rehydration fluid should replace sodium bicarbonate, potassium and water in amounts roughly equivalent to the loss and should contain glucose. (See rehydration chart in 2.3.4.).

Maintenance therapy

Any patient deprived of normal dietary intake requires water and electrolytes to replace obligatory losses in urine, stool, sweat and evaporation in exhaled air. Protein and calories are also required, but complete parenteral replacement is difficult and rarely essential if therapy is required for a limited period of time. The water, sodium and potassium requirements for normal maintenance therapy are 115ml, 3MEQ, 2.5MEQ respectively for every 100 calories metabolised. Supplemental therapy is needed where loss of fluid and electrolyte are specific. Inappropriate use may lead to fluid and electrolyte imbalance.

11.2.1 Oral administration

ORAL REHYDRATION SALTS (ORS)

Presentation: WHO formula containing 3.5g/l sodium chloride, trisodium citrate 2.9g/l, potassium chloride 1.5g/l, glucose (anhydrous) 20.00g/l.

Indications: Correction or maintenance of fluid and electrolyte balance

Dose: depends on clinical condition of patient

POTASSIUM CHLORIDE

Potassium is an essential electrolyte.

Presentation: Tablet containing 600mg potassium chloride. 15% potassium chloride injection in 10mls ampoules.

Indications: Prevention and treatment of potassium deficiency or hypokalaemia and prevention of diuretic-induced hypokalaemia.

Dose: 1,200 – 3,600mg daily in three divided doses. Swallow whole with fluid in an upright position. Up to 50 mmol daily orally. In severe acute hypokalaemia give an infusion containing 20mmol of potassium in 500ml over 2-3 hours under ECG control. Max; dose 2-3mmol potassium/kg/body weight in 24 hours

Side effects: After oral administration, nausea, vomiting, diarrhoea, abdominal cramps, gastric ulcer perforation and GIT bleeding may also occur. Hyperkalaemia especially in renal impairment, cardiac toxicity especially after intravenous administration.

Caution: Avoid in renal failure, ensure adequate fluid intake, intestinal stricture, history of peptic ulcer, cardiac disease.

Contraindications: Hyperkalaemia

11.2.2 Intravenous administration

DEXTROSE (GLUCOSE)

Presentation: Solution containing 2.5% glucose in water (200ml), 5% glucose in water (1 litre), 10% glucose in water (1 litre), 50% glucose in water (100ml), 50% glucose in normal saline (1 litre).

Indications: Fluid replacement, provision of energy, hypoglycaemia.

Dose: Depends on clinical condition of patient

Side effects: Injection especially if hypertonic may cause venous irritation and thrombophlebitis.

Caution: Diabetes mellitus and insipidus, 50% dextrose should be given into a large vein
**POTASSIUM CHLORIDE**

**Presentation:** Concentrated solution containing 15% potassium chloride in 10ml ampoules.

**Indications:** Potassium deficiency

**Dose:** By slow intravenous infusion depending on the deficit or the daily maintenance requirements.

**Side effects:** Rapid intravenous infusion may be toxic to the heart.

**Caution:** Renal impairment, adrenal insufficiency, administer slowly

**Contraindications:** Hyperkalaemia

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**SODIUM BICARBONATE**

**Presentation:** Solution containing 4.2% sodium bicarbonate, 50ml, 500ml. Capsule containing sodium bicarbonate 500mg.

**Indications:** Correction of metabolic acidosis, cardiac arrest. (i) chronic acidotic states such as uraemic acidosis or renal tubular acidosis, (ii) to make pH of the urine alkaline.

**Dose:** Slow intravenous injection or continuous intravenous infusion according to requirements. Acidosis; 3 – 5MEQ/kg. In cardiac arrest larger doses are required, 500ml vials must be diluted in the ratio of 2 parts of bicarbonate to 5 parts of dextrose 5%

Orally for correction of metabolic acidosis, 4.8g daily (8 tablets). Orally for correction of urinary pH, 3gram in water, every 2 hours until urine exceeds PH 11.

**Side effects:** Alkalosis. Most serious side effects are due to hypernatraemia. This may lead to pulmonary and peripheral oedema and dehydration of the brain. GIT effects are nausea, vomiting, diarrhoea and abdominal cramps.

**Caution:** Cardiac failure, hypertension, renal failure, peripheral and pulmonary oedema and toxicaemia of pregnancy.

**Contraindications:** Routine use of intravenous sodium bicarbonate.

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**SODIUM CHLORIDE (NORMAL SALINE)**

**Presentation:** Solution containing 3.9% sodium chloride, 200ml, 1litre packs, 500m packs of sodium chloride.

**Indications:** Correction of electrolyte imbalance. Sterile irrigation in eye, bladder, general skin or wound cleansing.

**Dose:** Replacement therapy; 8 10mcg/kg body weight. In severe sodium depletion, 2-3 litres of 0.9% solution over 2-3 hours, thereafter a slower rate. Maintenance therapy; 2.5mcg/kg body weight.

**Side effects:** Sodium accumulation (electrolyte imbalance) and oedema. Hypernatraemia if large doses are administered and oedema.

**Caution:** Restrict intake in renal, cardiac impairment, hypertension, peripheral and pulmonary oedema and toxicaemia of pregnancy.

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**SODIUM LACTATE AND GLUCOSE**

**Presentation:** Full strength and half strength solution containing sodium chloride and potassium bicarbonate. Half strength also contains dextrose 2.5%

**Indications:** Dehydration

**Dose:** Mild dehydration; 50ml/kg body weight. Moderate dehydration; 70 – 100mg/kg body weight. Severe dehydration; 120 – 150ml/kg body weight.

**Side effects:** Fluid overload and electrolyte imbalance

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**SODIUM LACTATE COMPOUND (RINGER-LACTATE SOLUTION)**

**Presentation:** Solution containing sodium chloride 0.6%, sodium lactate 0.25%, potassium chloride 0.04%, calcium chloride 0.027%, 500ml, 1000ml packs

**Indications:** Diabetic coma, severe dehydration due to acute diarrhoea and burns

**Dose:** Acidosis; 60ml/kg body weight. Alkalisation of urine; 30ml/kg body weight. Severe dehydration; 30ml/kg body weight per hour. Dose maybe adjusted according to patients needs.

**Side effects:** Salt and water overload

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**WATER FOR INJECTION**

**Presentation:** 1ml, 2ml, 5ml, 10ml, 20ml, 50ml

**Indications:** For reconstitution of injections

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**11.2.3 Plasma substitutes**

**DEXTRAN 70**

**Presentation:** Solution containing dextran 70 in 5% dextrose or in 0.9% sodium chloride in 500ml packs.

**Indications:** Predominantly for blood volume expansion in shock arising from conditions such as burns or septicaemia and following acute haemorrhage.

**Dose:** By intravenous infusion after haemorrhage or in the shock phase of burns injury (initial 48 hours), 500ml to 1000ml rapidly, followed by 500ml later if necessary given slowly. The total dose and rate of flow will depend on the clinical state of the patient.

**Side effects:** urticarial and other hypersensitivity reactions, fluid overload

**Caution:** Congestive heart failure, renal impairment, coagulation defects, blood samples should be taken before infusion, as dextran 70 may interfere with blood group cross matching or other biochemical measurements.

**Contraindications:** Severe congestive heart failure, renal failure.
**GELATIN**

**Presentation:** Solution containing gelatin polygeline, 500ml

**Indications:** Low blood volume

**Dose:** By i.v. infusion; initially 500 – 1000ml of a 3.5 – 4% solution.

**Side effects:** see under 11.2.3.1 above, increased risk of hypersensitivity reactions.

**Caution:** See under 11.2.3.1. above

**Contraindications:** See under 11.2.3.1. above

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**Peritoneal dialysis fluid**

Dialysis should only be undertaken where adequate laboratory facilities exist.

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**DEXTROSE**

**Presentation:** Solution containing 1.5% , 4.5% dextrose

**Indications:** Severe uraemia, hyperkalaemia, severe acidosis, fluid overload.

**Dose:** Up to 36 cycles is adequate initially. The need for further dialysis is determined by the patient’s needs.

**Caution:** Use proper and sterile procedure in starting the peritoneal dialysis.
12 Drugs acting on the skin

12.1 Antipruritics
12.2 Topical Corticosteroids
12.3 Preparations for Eczema and Psoriasis
12.4 Preparations for Acne
12.5 Preparations for warts
12.6 Anti-infective skin preparations
12.7 Parasiticidal preparations
12.8 Surgical antiseptics

Dermatological preparations for several conditions are available in various suitable vehicles. The choice of vehicle i.e. cream, lotion, application, aqueous or oily base is important as the vehicle may affect the degree of hydration of the skin or aid the penetration of the active drug in the preparation and thereby affect the treatment outcome.

Some additives in topical preparations may be associated with sensitization. These include wool fat, some fragrances, propylene glycol etc.

Preparations containing an antibacterial should be avoided unless bacterial infection is present. The choice of such drugs should be limited to those not used systematically.

12.1 Antipruritics

**CALAMINE**

- **Presentation:** Lotion containing calamine 15% and zinc oxide 5%. Ointment containing calamine 15% in white soft paraffin.
- **Indications:** Pruritis

12.2 Topical corticosteroids

For the treatment of inflammation of the skin, particularly eczematous disorders. Corticosteroids are only for the relief of symptoms and suppression of signs. They are of no use in the treatment of infections and urticaria. They are contraindicated in rosacea and in ulcerative conditions as they worsen the condition. They should not be used indiscriminately in pruritis. Systemic or potent corticosteroids should be avoided or given only under specialist supervision.

The most potent topical corticosteroids should be reserved for recalcitrant dermatoses. Use in children should be avoided or, if necessary should be used with great care and only for short periods.

**HYDROCORTISONE**

- **Presentation:** Cream containing 0.5% and 1% hydrocortisone, ointment containing 0.5% and 1% hydrocortisone.
- **Indications:** Mild inflammatory skin disorders such as eczema.
- **Side effects:** Thinning of skin with prolonged use, increased hair growth, peri-oral dermatitis, acne at site of application, mild pigmentation and vellus hair.
- **Contraindications:** Untreated bacterial, fungal or viral infections.
- **Administration:** Apply thinly 2 – 3 times daily, reducing frequency as condition responds.

**BETAMETHASONE**

- **Presentation:** Cream containing betamethasone valerate 0.05% and 0.1% in water-miscible base, ointment containing betamethasone valerate 0.05% and 0.1% in anhydrous paraffin base, lotion containing betamethasone valerate 0.05% - 0.1%. Scalp application containing betamethasone valerate 0.1%.
- **Indications:** Severe inflammatory skin disorders such as eczema unresponsive to less potent corticosteroids, psoriasis.
- **Side effects:** Severe pituitary – adrenal – axis suppression and hypercorticism and immunosuppression on prolonged use.
- **Contra-indications:** See hydrocortisone. Do not use in infants and children.
- **Administration:** Apply thinly 2 – 3 times daily reducing frequency as condition responds.

**CLOBETASOL**

- **Presentation:** Cream, ointment, scalp application containing 0.05% clobetasol propionate.
- **Indications:** Short term treatment of severe resistant inflammatory skin disorders such as recalcitrant eczema unresponsive to less potent corticosteroids, psoriasis.
- **Side effects:** See betamethasone
- **Contra-indications:** See betamethasone
- **Caution:** This is a high potency corticosteroid.
- **Administration:** Apply thinly 1 – 2 times daily for up to 4 weeks reducing frequency as condition responds.

**FLUOCINOLONE**

- **Presentation:** Cream, ointment containing 0.025% fluocinolone acetonide.
Indications: Inflammatory skin disorders such as eczema, psoriasis.

Side effects: See betamethasone

Contraindications: See betamethasone

Administration: Apply thinly 2 – 3 times daily reducing frequency as condition responds.

12.3 Preparations for eczema and psoriasis

ECZEMA

Eczema (dermatitis) is due to a particular type of epidermal inflammation. Where possible the causative factor should be established and removed before commencing medication. Emollients and preparations containing zinc oxide and calamine may be sufficient to treat dry, fissured, scaly lesions. Chronic eczematous conditions where there is marked thickening of the skin and pronounced scaling may require treatment with other substances like keratolytics.

COAL TAR

Presentation: Ointment, lotion, cream containing coal tar extract 1%, 5% or 10%. Also available in combination with calamine and zinc oxide.

Indications: Chronic eczema and psoriasis

Side effects: Skin irritation and acne-like eruptions, photosensitivity, stains skin, hair and fabric.

Caution: Avoid eyes and broken or inflamed skin.

Administration: 1 – 3 times daily starting with low strength preparation.

SALICYLIC ACID

Presentation: Ointment containing salicylic acid 2% in wool alcohol ointment Paste containing salicylic acid 2% and zinc oxide 24%.

Indications: Chronic eczema

Side effects: Irritant contact sensitivity, systemic effects if used extensively, excessive drying of skin.

Caution: Avoid broken or inflamed skin.

Administration: Apply twice daily.

12.3.2 Psoriasis

Psoriasis is characterized by epidermal thickening and scaling. Preparations containing coal tar, salicylic acid and dithranol are commonly used to treat psoriasis. Some patients are intolerant to dithranol even in low concentrations. Fair skin is more sensitive than dark skin. It is important to recognise the problem of intolerance early in treatment.

CYCLOSPORIN

Cyclosporin may be used, under specialist supervision, in severe resistant psoriasis. Corticosteroids should be avoided and if used specialist supervision is necessary. Only weaker corticosteroids like hydrocortisone should be used and only for short periods.

12.3.2.2 Coal Tar: See section on eczema

DITHRANOL

Presentation: Ointment containing 0.1% to 5% dithranol.

Indications: Subacute and chronic psoriasis

Side effects: Local burning sensitization and irritation, stains skins, hair and fabrics.

Caution: Intolerance in some patients, wash hands thoroughly after use, avoid use near eyes.

Administration: Apply to the lesion, cover with a dressing and leave for an hour. It is preferable to leave the application over night but short contact applications are also effective.

SALICYLIC ACID

Presentation: See under eczema

Indications: psoriasis

Side Effects: See under Eczema

Caution: See under eczema

Administration: Apply twice daily

12.3 Preparations for acne

Treatment involves removing follicular plugs and reducing skin flora. The skin should be cleaned regularly with detergent solutions. Antiseptics and keratolytics are applied after cleansing. Topical antibiotics may also be used for mild to moderately severe acne.

Preparations are those containing erythromycin (refer to systemic anti infectives), tetracycline or clindamycin. Topical neomycin is unsuitable owing to sensitization. Topical corticosteroids should not be used in acne. Thick, greasy preparations should not be used.

BENZOYL PEROXIDE

Presentation: Gel containing 2.5%, 5% benzoyl peroxide in aqueous alcoholic base, cream containing 5% benzoyl peroxide in a non-greasy basis, lotion containing 5% benzoyl peroxide in a non greasy basis.

Caution: Avoid contact with eyes, mouth, mucous membranes. May bleach fabrics.
Indications: Acne vulgaris
Side effects: Skin irritation which subsides with continued treatment.
Administration: Apply 1 – 2 times daily to clean skin, starting with lower strength preparations.

12.6 Anti infective skin preparations

This section includes antibacterial, anti fungal and antiviral preparations.

Some infections particularly if they are widespread, may require systemic treatment, as topical applications may not achieve adequate penetration.

12.6.1 Anti-Bacterial Preparations

Antibacterial drugs should only be considered in skin conditions involving infection by a sensitive organism. To minimize the development of resistant organisms topical preparations should, as far as possible, contain drugs that are not used systemically.

12.6.1 Anti-Fungal Preparations

These are available as lotions, ointments and dusting powders. Lotions are preferred for application to large and hairy areas. Ointments are best avoided on moist surfaces because of their occlusive properties. Dusting powders are not effective and may cause skin irritation.
12.6.3 Antiviral preparation

Topical preparations are not effective for the treatment of buccal or vaginal infections. Systemic preparations should be used in these cases. Herpes Zoster also requires systemic treatment.

ACICLOVIR

Presentation: Cream containing 5% aciclovir
Indications: Initial and recurrent labial and genital herpes simplex infections.
Side effects: Transient stinging or burning, occasionally erythema or drying of the skin.
Caution: Avoid contact with eyes and mucous membranes, pregnancy.
Contraindications: Hypersensitivity to acyclovir
Administration: Start treatment at first sign of attack, apply to lesions every 4 hours (5 times daily) for 5 days. Continue up to 10 days if necessary.

12.7 Parasiticidal preparations

To effectively treat parasitic infections like scabies, all members of the affected household should be treated. The itching of scabies may persist for days after the infection has been eliminated. Antipruritic treatment may be administered.

BENZOIC ACID

Presentations: Ointment containing benzoic acid 6% and salicylic acid 3%
Indications: Ringworm (tinea)
Administration: Apply twice daily

CLOTRIMAZOLE

Presentation: Cream containing 1% clotrimazole
Indications: Fungal skin infections
Side effects: Occasional skin irritation or sensitivity.
Contraindications: Hypersensitivity to clotrimazole.
Administration: Apply once daily until a few days after disappearance of all symptoms.

MICONAZOLE NITRATE

Presentation: Cream containing miconazole nitrate 2%, lotion containing miconazole nitrate 2%
Indications: Fungal infections of skin, hair and nails.
Side effects: Occasional skin irritation or sensitivity.
Contraindications: Hypersensitivity to miconazole.
Administration: Apply twice daily and continue for 10 days after lesions have healed. For nail infections apply daily under occlusive dressing.

ACICLOVIR

Presentation: Cream rinse containing aciclovir 1%. Dermal cream containing aciclovir 5%
Indications: (Cream rinse) head lice and (dental cream) scabies.
Side effects: Pruritis, erythema, and stinging; rarely rashes and oedema.
Caution: Avoid contact with eyes, pregnancy and breast feeding, children under 6 months.
Administration: Cream Rinse (Head lice). Apply to clean damp hair, leave on for 10 minutes, rinse and dry.
Dermal Cream (Scabies) – Apply over whole body (excluding head in adults) and wash off after 8 – 24 hours. Child apply over whole body, including face, neck, scalp and ears. If hands are washed with soap within 8 hours of application, cream

MALATHION

Presentation: Lotion containing malathion 0.5% in alcoholic basis or liquid containing malathion 0.5% in aqueous basis.
Indications: Crab lice, head lice and scabies.
Side effects: Skin irritation.
Caution: Avoid contact with eyes, alcoholic lotions not recommended for pediculosis in asthmatics or small children, or for scabies or crab lice. Do not use lotion for more than once a week for 3 weeks at a time; medical supervision required when used in children under six months.
Administration: Pediculosis – rub lotion into dry hair, scalp, and affected area, comb, allow to dry naturally, remove by washing after 12 hours. Scabies – apply liquid preparation over whole body, omitting head and neck, and wash off after 24 hours.

PERMETHRIN

Presentation: Cream rinse containing permethrin 1%. Dermal cream containing permethrin 5%
Indications: (Cream rinse) head lice and (dental cream) scabies.
Side effects: Transient stinging or burning, occasionally erythema or drying of the skin.
Caution: Avoid contact with eyes and mucous membranes, pregnancy.
Contraindications: Hypersensitivity to acyclovir
Administration: Start treatment at first sign of attack, apply to lesions every 4 hours (5 times daily) for 5 days. Continue up to 10 days if necessary.
12.8 Surgical antiseptics

Some of these preparations are used in minor burns and abrasions while others are used for general cleansing of skin and wounds. Preparations containing camphor and sulphonamides should be avoided.

**CETRIMIDE**

*Presentation:* Cream containing cetrimide 0.5% in water miscible basis. Solution containing cetrimide 0.15% and chlorhexidine 0.015%.
*Indications:* Used in minor burns and abrasions, for cleansing and disinfecting wounds and burns.

**ALCOHOL**

*Presentation:* As surgical spirit or industrial methylated spirit.
*Indications:* Skin preparation before injection.
*Caution:* Flammable, avoid broken skin.

**SODIUM CHLORIDE**

*Presentation:* Solution containing sodium chloride 0.9%.
*Indications:* General cleansing of skin and wounds.

**CHLORHEXIDENE**

*Presentation:* Solution containing chlorhexidine gluconate 0.05%.
*Indications:* For cleansing and disinfecting wounds and burns.

**BENZALKONIUM CHLORIDE**

*Presentation:* Solution containing benzalkonium chloride 1%.
*Indications:* Skin disinfection as pre-operative skin preparation.
*Caution:* Avoid contact with eyes.

**IODINE COMPOUNDS**

*Presentation:* Antiseptic solution containing povidone-iode 10% in aqueous solution, antiseptic paint containing povidone-iode 10%.
*Indications:* For disinfecting minor wounds and infections.
*Side effects:* Rarely sensitivity, may interfere with thyroid function tests.
*Caution:* Pregnancy, breast feeding, broken skin. Application to large wounds or severe burns may produce systemic adverse effects such as metabolic acidosis, hypernatremia and impairment of renal function.

**CRYSTAL VIOLET (GENTIAN VIOLET)**

*Presentation:* Paint containing crystal violet 0.5% in purified water.
*Indications:* Impetigo.
*Side effects:* Mucosal ulceration.
*Caution:* Stains skin and clothes. Not recommended for application to mucous membrane or open wounds.

**POTASSIUM PERMANGANATE**

*Presentation:* Solution containing potassium permanganate 0.1% in water.
*Indications:* Cleansing and deodorizing suppurating eczematous reactions and wounds.
*Caution:* Irritant to mucous membrane, stains clothes and skin. Administration: Wet dressing, or baths, approximately 0.01% solution.

12.8.7 Effervescent Tablet for disinfecting

Sodium Dichlorisocyanurate (Presept™)

Produce a rapid acting wide spectrum disinfectant solution effective against vegetative bacteria, fungi, viruses and bacterial spores.

*Presentation:* Tablet, containing Sodium Dichlorisocyanurate 0.5g, 2.5g, 5.0g and Granules 500g.
*Indication:* For disinfection of working surfaces, utensils, glassware and equipment in maternity units, nurseries, surgeries and laboratories, together with general hospital disinfection.
*Caution:* Warning! Do not use together with other products. May release dangerous gases (chlorine). If swallowed, wash mouth out thoroughly with water and drink plenty (500mg) of water or milk. Do not immerse animal fibers such as wool or silk due to strong proeolytic action. Avoid prolonged contact with stainless steel items. Do not form sprays or aerosols. Contact with combustible material may cause fire. Avoid contact with skin and eyes. Thoroughly rinse eyes with water if need be. Direction for use: See Annex.

Note:-Granules can be sprinkled onto spillage resulting in the hazard being rapidly solidified and
made safe for disposal.

### SODIUM HYPOCHLORITE

**Presentation:** stabilized solution containing sodium hypochlorite 1%.

**Indications:** Disinfection of hard surfaces, food utensils, feeding bottles and teats.

**Administration:** Immense for 3 hours.

**Caution:** Dilute before use

### CHLOROXYLENOL

**Presentation:** liquid containing chloroxylenol 4.8%.

**Indications:** General antisepsis and disinfectant.

**Caution:** Dilute with water
13.1. Drugs acting on the ear

13.1.1 Anti-inflammatory preparations

**BETAMETHASONE SODIUM PHOSPHATE**

- **Presentation:** Eye/ear/nose drops containing 0.1% betamethasone sodium phosphate. Eye/ear/nose drops containing 0.1% betamethasone sodium phosphate, 0.5% neomycin sulphate
- **Indications:** Eczematous inflammation in otitis externa (see notes above)
- **Dose:** 2 – 3 drops in the ear every 2 – 4 hours, reduce frequency when relief is obtained.
- **Eye, nose - see relevant sections**
- **Side effects:** Local sensitivity reactions
- **Caution:** Avoid prolonged use
- **Contraindications:** Untreated infection

**DEXAMETHASONE SODIUM PHOSPHATE**

- **Presentation:** Eye/ear drops containing 0.1% Dexamethasone sodium phosphate.
- **Indications:** Inflammation in otitis externa with eczema present; short term treatment.
- **Dose:** Instill 2-3 drops every 2-3 hours; reduce frequency when relief is obtained
- **Caution:** Use under expert supervision, avoid prolonged use.
- **Contraindications:** Untreated infection

**HYDROCORTISONE**

- **Presentation:** Eardrops containing 1% hydrocortisone acetate, 0.3% gentamycin sulphate. Eye/ear drops containing 1.5% hydrocortisone acetate, 0.5% neomycin sulphate. Eye/ear ointment containing 1.5% hydrocortisone acetate, 0.5% neomycin sulphate
- **Indications:** Eczematous inflammation in otitis externa (see notes above)
- **Dose:** Eardrops; 2 – 4 drops in the ear every 6 – 8 hours
- **Side effects:** Local sensitivity reactions
- **Caution:** Avoid prolonged use
- **Contraindications:** Untreated infection

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13.2. Drugs acting on the Nose

13.3. Drugs acting on the Oropharynx
13.1.2 Anti-infective preparations

13.1.2.1 Drugs used in the treatment of diseases of Chloramphenicol

Presentation: Eardrops containing 5% chloramphenicol in propylene glycol
Indications: Bacterial infection in otitis externa (refer to notes above).
Dose: Instill 2-3 drops into the ear 2-3 times a day
Side effects: Sensitivity to propylene glycol
Caution: Avoid prolonged use.
Contraindications: Perforated tympanic membrane

GENTAMYCIN

Presentation: Eye/Ear drops containing gentamicin sulphate 0.3%
Indications: Bacterial infection in otitis externa
Dose: Instill 2-4 drops in the ear 3-4 times daily and at night
Side effects: Local sensitivity
Caution: Avoid prolonged use.
Contraindications: Perforated tympanic membrane.

NEOMYCIN SULPHATE:
SEE UNDER 13.1.1.2. AND 13.1.1.3.

NOTE: For systemic treatment of infection see section 4

13.1.3 Wax softeners

Earwax provides protection to the meatal skin and need only be removed if it causes deafness or interferes with a proper view of the eardrum. As a general rule syringing is best avoided in patients with a history of recurring otitis externa, perforated eardrum or previous ear surgery. Wax may be removed by syringing with warm water. If necessary wax can be softened with simple remedies such as vegetable oil.

SODIUM BICARBONATE

Presentation: Eardrops containing sodium bicarbonate 5%
Indications: Excessive ear wax
Dose: Instill 3-4 drops in the ear. Keep ear uppermost for 5-10 minutes. Syringe with warm water.
Caution: The drops should be recently prepared.

VEGETABLE OIL

Presentation: Eardrops
Indications: Earwax
Dose: Warm to body temperature and instill 4-5 drops into the ear, wait 5-10 minutes with ear upwards and then syringe with warm water.
Caution: Hypersensitivity to oil report

13.2 Drugs acting on the nose

13.2.1 Drugs used in nasal allergy

13.2.2 Topical nasal decongestants

13.2.1 Drugs used in nasal allergy

Oral antihistamines and systemic nasal decongestants are used to control mild cases. Topical corticosteroids and sodium cromoglycate may be used in severe cases. (see section 6).

13.2.2 Topical nasal decongestants

The common cold has no effective treatment at the moment and the temptation to use nasal drops should be resisted. Sodium chloride 0.9% given as nasal drops may relieve nasal congestion by helping to liquify mucus secretions.

SODIUM CHLORIDE

Presentation: Solution containing 0.9% sodium chloride administered as nasal drops
Indications: Nasal congestion
Dose: Use as required

13.3.1 Drugs acting on the oropharynx

13.3.1.1 Drugs for oral ulceration and inflammation

Ulceration of the oral mucosa maybe caused by trauma (physical or chemical), recurrent aphthae, infection, carcinoma, dermatological disorders, nutritional deficiencies, gastro-intestinal disease,
Drugs used in the treatment of Diseases of the ear, nose and Oropharynx

It is important to establish the diagnosis in each case as the majority of these lesions require specific management in addition to local treatment. Patients with unexplained mouth ulcers of more than three weeks duration require urgent referral to hospital for further diagnosis to exclude other more serious conditions such as oral cancer. Local treatment is aimed at protecting the ulcerated area, relieving pain and reducing inflammation.

13.3.1.2 Mouth washes, gargles and dentifrices

Simple mouth washes

A saline or compound thymol glycerine mouth wash may relieve pain.

**SODIUM CHLORIDE**

Presentation: Mouth wash containing sodium bicarbonate 1%, sodium chloride 1.5% in a suitable vehicle with peppermint flavour.

Indications: Oral hygiene

**THYMOL**

Presentation: Mouth wash containing glycerol 10%, thymol 0.05% with colouring and flavouring (compound thymol glycerine B.P. 1988). Mouth wash solution tablets which may contain antimicrobial, colouring and flavouring agents in a suitable effervescent basis to make a mouth wash suitable for dental purposes.

Indications: Oral hygiene (see notes above)

Dose: Mouth wash; To be used undiluted or diluted with 3 volumes of warm water as necessary. Mouth wash solution tablets; dissolve 1 tablet in a glass of warm water and rinse when necessary.

**CARBENOXOLONE SODIUM**

Presentation: Mouth gargle containing carbenoxolone sodium 1% (20mg/sachet). Gel containing 2% carbenoxolone odium in adhesive base.

Indications: Mild oral and peri oral lesions

Dose: For mouth ulcers rinse 1 sachet in 30-50ml of warm water 3 times a day and at bedtime. Gel: Apply after meals and at bedtime.

Side effects: May produce sodium and water retention and hypokalaemia.

Caution: Contraindicated in patients with hypokalaemia.

13.3.1.3 Antiseptic mouth washes

Use of a chlorhexidine mouth wash is often beneficial in any mucosal ulceration with secondary bacterial infection and healing of aphthae is often accelerated. There is evidence that chlorhexidine has a specific effect inhibiting the formation of plaque on the teeth. Mouth washes have a mechanical cleansing action and freshen the mouth. Those containing an oxidising agent may be useful in the treatment of acute ulcerative gingivitis.

**CETYLPYRIDINIUM CHLORIDE**

Presentation: Solution containing cetylpyridinium chloride 0.5%

Indications: Oral hygiene

Dose: Use undiluted or diluted with an equal volume of water.

13.3.1.4 Chlorhexidine Gluconate

Presentation: Solution containing chlorhexidine gluconate 0.1%, 0.12%, 0.2%, 0.5%. Dental gel containing 0.1% chlorhexidine gluconate. Oral spray containing 0.2% chlorhexidine gluconate.

Indications: Oral hygiene. Plaque inhibition

Dose: Rinse mouth with 10 - 15ml for 30 seconds to 1 minute 2 to 3 times a day. Brush teeth with gel once or twice a day. Spray teeth and gingival surfaces using up to 12 actuations twice a day.

Caution: Chlorhexidine gluconate maybe incompatible with some ingredients in toothpaste; an interval of at least 30 minutes should be left between using toothpaste and chlorhexidine mouth wash

**HEXETIDINE**

Presentation: Mouth wash or gargle containing 0.1% hexetidine

Indications: Oral hygiene

Dose: Use 15ml undiluted 2 - 3 times a day

**OXIDISING AGENTS**

**HYDROGEN PEROXIDE**

Presentation: Mouth wash containing 6% hydrogen peroxide

Indications: Oral hygiene (see notes above)

Dose: Rinse the mouth for 2-3 minutes with 15ml in half a glass of warm water 2 - 3 times a day.
POVIDONE IODINE

Presentation: Mouth wash or gargle containing 1% povidone iodine.
Indications: Oral hygiene
Dose: Adults and children over 6 years; Up to 10ml undiluted or diluted with an equal volume of warm water for up to 30 seconds up to 4 times a day for up to 14 days.
Side Effects: Idiosyncratic mucosal irritation and hypersensitivity reactions, may interfere with the thyroid function tasks and with tests for occult blood.
Caution: Pregnancy, breast feeding
Contraindications: Avoid regular use in patients with thyroid disorders or those receiving lithium therapy.

MECHANICAL PROTECTION

Some gelatin based pastes such as carmellose gelatin gel relieve discomfort by protecting the ulcer site through adhering to the mucosa.

CARMELLOSE SODIUM

Presentation: Oral paste containing carmellose sodium 16.5% in gelatin base. Powder containing carmellose sodium, pectin and gelatin in equal parts.
Indications: Mechanical protection of oral and peri oral lesions.
Dose: Paste; apply a thin layer on the lesion when necessary after meals, powder; sprinkle on the affected area when necessary
Side effects: Occasional exacerbation of local infection.

CHOLINE SALICYLATE

Presentation: Oral gel containing choline salicylate 8.7% in a flavoured gel base
Indications: Mild oral and peri oral lesions
Dose: Apply 1.25cm of gel with gentle massage not more often than every 3 hours. Child over 4 months old; apply 0.60cm of gel not more often than every 3 hours. Maximum 6 applications a day.

CORTICOSTEROIDS

Some forms of oral ulcerations respond to corticosteroid therapy. Aphthous ulcers especially in the prodromal phase appear to respond well to this kind of therapy. Thrush and other types of candidiasis are recognised complications of corticosteroid treatment.

Triamcinolone dental paste is made in such a way that the paste is in contact with the mucosa for long enough to allow penetration of the lesion by the corticosteroid. However application of the paste is not easy for some patients.

TRIAMCINOLONE ACETONIDE

Presentation: Oral paste containing triamcinolone acetonide 0.1% in adhesive base.
Indications: Oral and peri oral lesions
Dose: Apply a thin layer 2 - 4 times a day; do not rub in; use should be limited to 5 days in children and short term treatment is also advised in adults.
Side effects: Occasional exacerbation of local infection.

LOCAL ANAESTHETICS

Because of their relatively short duration of action when applied topically local anaesthetics have a limited role in the management of oral ulcers. They may be useful in relieving pain of intractable oral ulceration particularly that of major aphthae. Lignocaine 5% ointment or lozenges may be applied to the ulcer. Care should be taken to avoid anaesthesia of the pharynx especially before meals as this may lead to choking.

Presentation: Ointments, gels, mouthwashes, sprays and lozenges.
Indications: Relief of pain in oral lesions
Caution: Avoid prolonged use.

13.3.1.5 Oropharyngeal anti-infective drugs

The commonest cause of sore throat is viral infection which does not benefit from antibiotic treatment. Streptococcal sore throats require systemic penicillin therapy (see section 4.). Systemic metronidazole is used in acute ulcerative gingivitis (see section 4.). Dental surgery local treatment of periodontal diseases include administration of gels of metronidazole and of minocycline.

13.3.1.6 Oral antifungal drugs

Oral thrush maybe caused by candida albicans and sometimes even other forms of stomatitis which maybe a sequel to the use of broad spectrum antibiotics or cytotoxics. Usually withdrawal of the causative drug may lead to resolution of the condition; otherwise an antifungal drug may be effective.

Of the antifungal drugs used for infections of the oral cavity, amphotericin and nystatin are not absorbed from the gastro-intestinal tract and are used by local application in the mouth. Fluconazole
and itraconazole are absorbed when taken orally and are available for administration by mouth for oropharyngeal candidiasis (see section 4.4.).

### AMPHOTERICIN

**Presentation:** Lozenges containing 10mg amphotericin B, sugar free suspension containing 100mg/ml amphotericin B, 12ml supplied with a pipette.

**Indications:** Oral and peri oral fungal infections.

**Dose:** **Lozenges:** dissolve 1 lozenge slowly in the mouth 4 times a day. May require 10 – 15 days treatment. Continue for 48 hours after lesions have resolved. Increase dose to 8 times daily if infection is severe. **Oral suspension:** place 1ml in the mouth after food and retain near lesions 4 times daily for 14 days. Continue for 48 hours after lesions have resolved.

**Side effects:** Local irritation, pruritis.

### MICONAZOLE

**Presentation:** Sugar free oral gel containing 24mg/ml miconazole.

**Indications:** Prevention and treatment of oral fungal infection.

**Dose:** **Adult:** place 5 – 10ml in the mouth after food and retain near lesions 4 times daily. **Child**, under 2 years; 2.5ml twice a day; 2 - 6 years; 5ml twice a day. Over 6 years; 5ml 4 times a day. Continue treatment for 48 hours after lesions have resolved.

**Side effects:** Nausea, vomiting, diarrhoea and rarely allergic reactions.

**Caution:** Pregnancy and breast-feeding, avoid in porphyria.

**Contra-indications:** Hepatic impairment.

### NYSTATIN

**Presentation:** Pastilles containing nystatin 100,000 units/ml. Oral suspension (sugar free) containing nystatin 100,000 units/ml.

**Indications:** Oral and peri oral fungal infections.

**Dose:** **Pastilles/suspension:** 100,000 units 4 times a day after food for 7 days. Continue for 48 hours after lesions have resolved. **Note:** immunosuppressed patients may require higher doses e.g. 500,000 units 4 times a day.

**Side effects:** Nausea, oral irritation and sensitisation.

### VIRAL INFECTION

Herpes infections of the mouth may be managed by a soft diet, adequate fluid intake, analgesics as required and use of chlorhexidine mouthwash to control plaque accumulation if tooth brushing is painful. In the case of severe herpetic stomatitis, systemic acyclovir is required (see section 4.).

#### LOZENGES AND SPRAYS

There is no convincing evidence that antiseptic lozenges and sprays have a beneficial action. They sometimes irritate and cause sore tongue and sore lips. Some of these products also contain local anaesthetics, which relieve pain but may cause sensitisation.

### 13.3.2 Treatment of dry mouth

Dry mouth (xerostomia) may be caused by drugs’ antimuscarinic (anticholinergic) side effects e.g. antispasmodics, tricyclic antidepressants and some antipsychotics, by irradiation of the head or neck region or by damage to or disease of the salivary glands. Patients with a persistently dry mouth may develop a burning or scalding sensation and have poor oral hygiene, they develop increased dental caries, periodontal diseases, intolerance of dentures and oral infections (particularly candidiasis). Dry mouth may be relieved in many patients by simple measures such as frequent sips of cool drinks or sucking pieces of ice or sugar free pastilles. Artificial saliva can provide useful relief of dry mouth. Properly balanced artificial saliva should be of a neutral pH and contain electrolytes (including fluorride) to correspond approximately to the composition of saliva. Pilocarpine tablets are restricted to use in xerostomia following irradiation for head and neck cancer. They are effective only in patients who have some residual salivary gland function and therefore should be withdrawn if there is no response.

#### PILOCARPINE HYDROCHLORIDE

**Presentation:** Tablets (film coated) containing pilocarpine hydrochloride 5mg.

**Indications:** Salivary glands hypofunction in xerostomia following irradiation for head and neck cancer (see also notes above)

**Dose:** 5mg 3 times a day with or immediately after meals (last dose always with an evening meal); if dose is tolerated but if response is not sufficient after 4 - 8 weeks may be increased to maximum 50mg daily in divided doses (but associated with increased side effects); Discontinue if no improvement after 3 months. Not recommended in children.

**Side effects:** Sweating, chills, diarrhoea, nausea, vomiting, lacrimation, abdominal pain, ambylopia, hypertension, constipation, abnormal vision, dizziness, rhinitis, asthma, increased urinary frequency, headache, dyspepsia, vasodilation, flushing.

**Caution:** Close medical supervision in asthma (avoid if uncontrolled) and in cardiovascular disease, biliary tract disease, peptic ulcer, hepatic impairment, there is risk of increased urethral smooth tone and renal colic, eye examination...
before treatment (decreased visual acuity more likely at night and in patients with central lens changes); maintain adequate fluid intake to avoid dehydration associated with excessive seating; cognitive or psychiatric disturbances.

**Contraindications:** Uncontrolled asthma and chronic obstructive pulmonary disease (increased bronchial secretion and increased airway glaucoma);
### 14 Drugs used in the treatment of musculoskeletal disorders

#### 14.1 Drugs used in rheumatic diseases

14.1.1 **Non-steroidal anti-inflammatory Drugs (NSAIDs)**

Most rheumatic diseases require symptomatic treatment to relieve pain and stiffness. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used and in certain circumstances corticosteroids may be required to suppress inflammation.

Drugs are available which may affect the disease process itself and favourably influence outcome of rheumatoid arthritis. These include penicillamine, gold salts, antimalarials, immunosuppressants and sulphasalazine.

#### 14.1.1 Non-steroidal anti-inflammatory Drugs (NSAIDs)

In single dose NSAIDs have analgesic activity comparable to that of paracetamol and can therefore be taken on demand for mild or intermittent pain.

In full dosage they have an analgesic and anti-inflammatory effect which is lasting and therefore makes them suitable for use in inflammatory conditions such as rheumatoid arthritis and in some cases of advanced osteoarthritis.

The differences in anti-inflammatory activity between different NSAIDs are small but there are considerable differences in the incidence and type of side effects. The prescriber should, therefore, weigh efficacy against possible side-effects.

A feature of NSAIDs is the considerable variation in individual patient response. It is, therefore, often necessary to change from one NSAID to another until a suitable one is found for a particular patient.

Most NSAIDs produce an effect within a few days. If no response is obtained then the drug should be changed – after one week if used for analgesia alone, after 3 weeks if used for its anti-inflammatory action.

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#### ACETYL SALICYLIC ACID (ASPIRIN)

**Presentation:** Tablet containing acetyl salicylic acid 300mg, dispersible tablets containing acetyl salicylic acid 300mg.

**Indications:** Acute pain and inflammation in rheumatic disease (e.g. rheumatoid arthritis, osteoarthritis) and other musculoskeletal disorders including juvenile arthritis. Not recommended for use in minor illness in children under 12 years.

**Dose:** 0.3 – 1g every 4 hours, maximum in acute conditions 8g daily, child/juvenile arthritis; up to 80mg/kg body weight daily in 5 – 6 divided doses, increased in acute exacerbation to 130mg/kg body weight. **Doses should be taken after food.**

**Side effects:** Common with anti-inflammatory doses; gastro-intestinal discomfort or nausea, ulceration with occult bleeding and occasionally major haemorrhage, other haemorrhage e.g. subconjunctival, tinnitus, vertigo, mental confusion, hypersensitivity reactions (angioedema, bronchospasm and rashes), increased bleeding time rate. Rare side effects include oedema, myocarditis, blood disorders particularly thrombocytopenia.

**Caution:** Asthma, allergic disease, uncontrolled hypertension, hepatic or renal impairment (avoid if severe), may worsen these conditions, dehydration, pregnancy particularly at term, elderly, G6PD deficiency.

**Contraindications:** Gastro-intestinal ulceration, children under 12 years (except for juvenile arthritis) due to association with Reye’s syndrome, breastfeeding haemophilia and other bleeding disorders, not for treatment of gout; history of hypersensitivity to aspirin and other NSAIDs includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or other NSAIDs.

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#### IBUPROFEN

**Presentation:** Film coated, sugar coated tablet containing 200mg and 400mg ibuprofen, syrup containing ibuprofen 100mg/5ml, gel/cream containing ibuprofen 5%.

**Indications:** Pain and inflammation in rheumatic diseases (including juvenile arthritis) and other musculoskeletal disorders.

**Dose:** 1.2 – 1.8g daily in 3 – 4 divided doses, with food or milk, increased if necessary to maximum of 2.4 g daily; maintenance dose of 0.6 – 1.2g daily.
Child; 20mg/kg body weight daily in divided doses (juvenile arthritis, up to 40mg/kg body weight daily), not recommended for children under 7kg. Cream gel; Apply up to 3 times daily – apply with gentle message.

**Side effects:** Has fewer side effects than other NSAIDs and is usually well tolerated. Side effects include gastro-intestinal discomfort, nausea, diarrhoea, occasionally bleeding and ulceration; hypersensitivity reactions (angioedema, bronchospasm, rashes) headache, dizziness, vertigo, hearing disturbances e.g. tinnitus, haematuria, blood disorders, fluid retention (rarely precipitating congestive heart failure in elderly patients); reversible acute renal failure in patients with pre-existing renal impairment.

**Caution:** Elderly, allergic disorders, patients with renal, cardiac or hepatic impairment since use of NSAIDs may result in deterioration of renal function, asthma. Gel/cream; avoid contact with eyes, mucous membranes, inflamed or broken skin.

**Contraindications:** Patients with a history of hypersensitivity to aspirin or other NSAIDs include those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAIDs; patients with active peptic ulceration.

### DICLOFENAC

**Presentation:** Enteric coated tablet containing diclofenac sodium 25mg, 50mg, modified release tablet containing diclofenac sodium 75mg, 100mg. Injection 3ml ampoules containing diclofenac sodium 25mg/ml. Suppositories containing diclofenac sodium 12.5mg, 100mg. Gel containing diclofenac diethylammonium salt 1.16% (equivalent to diclofenac sodium 1%).

**Indications:** Pain and inflammation in rheumatic diseases (including juvenile arthritis) and other musculoskeletal disorders, acute gout.

**Dose:** Orally; 75 – 150mg daily in 2-3 divided doses, after food. By deep intramuscular injection into the gluteal muscle, acute exacerbations and is usually well tolerated. Side effects include gastro-intestinal discomfort, nausea, diarrhoea, occasionally bleeding and ulceration; hypersensitivity reactions (angioedema, bronchospasm, rashes) headache, dizziness, vertigo, hearing disturbances e.g. tinnitus, haematuria, blood disorders, fluid retention (rarely precipitating congestive heart failure in elderly patients); reversible acute renal failure in patients with pre-existing renal impairment.

**Caution:** Elderly, allergic disorders, patients with renal, cardiac or hepatic impairment since use of NSAIDs may result in deterioration of renal function, asthma. Gel/cream; avoid contact with eyes, mucous membranes, inflamed or broken skin.

**Contraindications:** Patients with a history of hypersensitivity to aspirin or other NSAIDs include those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAIDs; patients with active peptic ulceration.

### NAPROXEN

**Presentation:** Tablet containing naproxen 250mg, 500mg. Suspension containing naproxen 125mg/5ml. Suppositories containing naproxen 500mg.

**Indications:** Pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders; acute gout.

**Dose:** Orally with food; 0.5 – 1g daily in 2 divided doses or 1g once daily. Child (over 5 years) juvenile arthritis; 10mg/kg body weight daily in 2 divided doses. Acute musculoskeletal disorders; 500mg initially, then 250mg every 6 - 8 hours as required, maximum dose after first day 1.25g daily.

**Acute gout:** 750mg initially, then 250mg every 8 hours until attack has passed. rectally (suppositories); 500mg at bedtime, if necessary 500mg in the morning as well.

**Side effects:** See under ibuprofen. has lower incidence of side effects.

**Caution:** See under Ibuprofen. suppositories may cause rectal irritation and occasional bleeding.

**Contraindications:** See under Ibuprofen.

### INDOMETHACIN

**Presentation:** Capsule or tablet containing indomethacin 25mg, 50mg. Suspension containing indomethacin 25mg/5ml. Suppositories containing indomethacin 100mg.

**Indications:** Pain and moderate to severe inflammation in rheumatic disease and other acute musculoskeletal disorders, acute gout.

**Dose:** Orally, rheumatoid arthritis; 50 – 200mg daily in 3 divided doses with food. Acute gout; 150 – 200mg daily in 3 divided doses. Rectally in suppositories; 100mg at night and in the morning if required. Combined oral and rectal treatment; maximum total daily dose 150 – 200mg.

**Side effects:** High incidence of side effects, frequently gastrointestinal disturbances (including diarrhoea) headache, dizziness, and light-headedness, gastro-intestinal ulceration and bleeding, rarely, drowsiness, confusion, insomnia, convulsions, psychiatric disturbances, depression, syncope, thrombocytopenia, hypertension, hyperglycaemia, blurred vision, corneal deposit, peripheral neuropathy. Suppositories may cause pruritus, discomfort, bleeding.

**Caution:** See under ibuprofen, breast feeding, epilepsy, parkinsonism, psychiatric disturbances; during prolonged therapy ophthalmic and blood examination are particularly advisable, avoid rectal administration in proctitis and haemorrhoids. Dizziness may affect performance of skilled tasks e.g. driving.

**Contraindications:** See under ibuprofen.
**PIROXICAM**

**Presentation:** Capsule or tablet containing piroxicam 10mg, 20mg. Injection containing piroxicam 20mg/ml. Suppositories containing piroxicam 20mg. Gel containing piroxicam 0.5%.

**Indications:** Pain and inflammation in rheumatic disease (including juvenile arthritis) and other musculoskeletal disorders, acute gout.

**Dose:** Orally or rectally, rheumatic disease; initially 20mg daily with food, maintenance 10 – 30mg daily in single or divided doses. *Child* (over 6 years) orally, juvenile arthritis; less than 15kg; 5mg daily. 16-25kg; 10mg daily. 26 – 45kg; 15mg daily. Over 46kg; 20mg daily. *Acute musculoskeletal disorders*; 40mg daily in single or divided doses for 2 days, then 20mg daily for 7 – 14 days.

**Acute gout:** 40mg initially, then 40mg daily in single or divided doses for 4 – 6 days. By deep intramuscular injection into gluteal muscle, for initial treatment of acute conditions, as dose by mouth (on short term basis).

**Side effects:** See under ibuprofen, pain at injection site (occasionally tissue damage occurs), pancreatitis.

**Caution:** See under ibuprofen, avoid in porphyria.

**Contraindications:** See under ibuprofen.

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**METHYPREDNISOLONE**

**Presentation:** Injection powder for reconstitution containing methylprednisolone as sodium succinate 40mg, 125mg, 200mg, 1g, 2g or injection, aqueous suspension containing methylprednisolone acetate 40mg/ml.

**Indications:** sodium succinate preparation; suppression to highly active inflammatory disease while longer term and slower acting medication is being started.

**Acetate preparation:** local inflammatory of joints and soft tissue.

**Dose:** Sodium succinate preparation; by slow intravenous injection or infusion, up to 1g on 3 consecutive days.

**Acetate preparation:** by intra-articular or soft-tissue injection 4 – 80mg according to size, where appropriate may be repeated at intervals of 7 – 35 days.

**Side effects:** See under prednisolone; flushing may occur with intra-articular injections.

**Caution:** See under prednisolone, full aseptic preCaution should be observed, rapid intravenous administration of large doses has been associated with cardiovascular collapse

**Contraindications:** See under prednisolone

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**PREDNISOLONE**

**Presentation:** Tablet containing prednisolone 1mg, 5mg, 25mg.

**Indications:** Suppression of inflammation in rheumatic disease when other drugs are unsuccessful, polymyalgia rheumatica, temporal (giant cell) arteritis, polyarthritis nodosa, polymyositis, systemic lupus erythematosus.

**Dose:** Polymyositis rheumatica; initially 10 – 15mg daily, temporal arteritis; 40 - 60mg daily. Treatment should be continued until remission occurs, then the dose gradually reduced to a maintenance dose of 7.5 – 10mg.

**Polyarthritis nodosa:** 60mg daily, reduce to maintenance dose of 10 – 15mg daily.

**Side effects:** Cushing's syndrome, diabetes, osteoporosis at high doses avascular necrosis, mental disturbances, euphoria, muscle wasting, peptic ulceration, suppression of clinical symptoms of infection leading to spread of infection, growth suppression in children, adrenal suppression (so dosage should be gradually reduced), risk of steroids cataract (75%) if more than 15mg prednisolone is given daily for several years, acne.

**Caution:** Should not be withdrawn abruptly as this may lead to acute adrenal insufficiency, hypotension and death. Other withdrawal symptoms rhinitis, conjunctivitis, loss of weight, arthralgia, painful and itchy skin nodules.

**Contraindications:** Viral infection e.g. herpes simplex, herpes zoster, measles, chicken pox, septicemia, tuberculosis.

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**HYDROCORTISONE**

**Presentation:** Injection (aqueous suspension) containing hydrocortisone acetate 25mg/ml.

**Indications:** Local inflammation of joints and soft tissues.
Drugs used in the treatment of musculoskeletal disorders

**Dose:** By intra-articular or soft-tissue injection; 5 – 50mg according to size, where appropriate may be repeated at intervals of 21 days. Not more than 3 joints should be treated on any one day. **Child:** 5 – 30mg (divided)

**Side effects:** See under prednisolone, flushing may occur with intra-articular injection of corticosteroids.

**Caution:** See under prednisolone; full aseptic precaution should be observed.

**Contra-indications:** Avoid infected areas.

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**DEXAMETHASONE**

**Presentation:** Injection containing dexamethasone sodium phosphate 5mg/ml.
Injection containing dexamethasone phosphate 4mg/ml.

**Indications:** See under prednisolone.

**Dose:** 0.4 – 4 mg according to size, where appropriate may be repeated at intervals of 3 – 21 days according to response by intra-articular or soft tissue injection.

**Side effects:** See under prednisolone

**Caution:** See under prednisolone

**Contraindications:** See under prednisolone

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**14.1.3 Drugs which suppress the rheumatic disease process**

Certain drugs may suppress the disease process in rheumatic arthritis (gold, penicillamine hydroxychloroquine, chloroquine, immuno suppressants and sulphasalazine) and in psoriatic arthritis (gold, immuno suppressants). These drugs should only be used on expert advice. Full therapeutic response is produced after 4 – 6 months of treatment. If no response is seen within 6 months, the drug should be discontinued.

These drugs are used when treatment with NSAIDs has been unsuccessful and if there is evidence of disease progression, treatment should be initiated before joint damage becomes irreversible.

Penicillamine has similar action to gold and more patients are able to continue treatment than with gold. Chloroquine and hydroxychloroquine have similar action to and are better tolerated than gold or penicillamine. Immunosuppressants have similar action to gold and are alternatives where response has not been obtained with gold, penicillamine, chloroquine or hydroxychloroquine.

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**PENICILLAMINE**

**Presentation:** Tablet containing penicillamine 50mg, 125mg, 250mg.

**Indications:** Severe active rheumatoid arthritis including juvenile arthritis, palindromic rheumatism.

**Dose:** Adult; initially 125 – 250mg daily before food for 1 month increased by similar amount at intervals of not less than 4 weeks to usual maintenance dose of 500 – 750mg daily. Maximum dose, 1.5g daily. **Child:** initially 50mg daily before food for 1 month increased at intervals of not less than 4 weeks to maintenance at 15 – 20mg/kg daily. **Elderly:** initially 50 – 125mg daily before food increased at intervals of not less than 4 weeks, to a maximum of 1g daily.

**Side effects:** Nausea, transient loss of taste, rashes which may necessitate discontinuation of treatment, anorexia, fever, blood disorders (thrombocytopenia, neutropenia, agranulocytosis, aplastic anaemia), proteinuria, haematuria, haemolytic anaemia, nephrotic syndrome, lupus erythematosus like syndrome, myasthenia gravis-like syndrome, pemphigus, Goodpasture’s syndrome, Steven–Johnson syndrome.

**Caution:** Renal impairment, pregnancy; avoid concurrent treatment with gold, chloroquine, hydroxychloroquine, or immunosuppressive treatment, avoid oral iron preparations within 2 hours of a dose, blood counts including platelets and urine examinations should be done every 1 or 2 weeks in the first 2 months then every 4 weeks to detect blood disorders and protein-urea.

**Contraindications:** Psoriatic arthritis
AZATHIOPRINE

Presentation: Tablet containing azathioprine 25mg, 50mg, injection, powder for reconstitution containing azathioprine (as sodium salt) 50mg.

Indications: Rheumatoid arthritis when no response is obtained with gold, penicillamine, chloroquine, hydroxychloroquine.

Dose: 1.5 to 2.5mg/kg daily in divided doses.

Side effects: Irritation at injection site; myelosuppression, hepatic toxicity, nausea, vomiting, diarrhoea.

Caution: Reduce dose when given concurrently with allopurinol, blood counts should be done every 4 weeks to detect possible neutropenia and/or thrombocytopenia, patients will be prone to atypical infections, herpes zoster infections may occur; reduce dose in severe hepatic or renal impairment.

Contraindications: Psoriatic arthritis, hypersensitivity to azothiopine, pregnancy

4.2 Drugs used in gout

It is important to distinguish drugs used for the treatment of acute attacks of gout from those used in the long term control of the disease. The latter exacerbate and prolong the acute manifestations if started during an attack

Acute attacks of gout are treated with high dose NSAIDs or with colchicine. Aspirin should not be used for gout.

Allopurinol is not effective in treating acute attacks of gout and may prolong the attack if started during the acute episode. Initial treatment with allopurinol may precipitate an acute attack of gout and the patient should therefore be given colchicine or an anti-inflammatory analgesic for about three months.

14.2.1 NSAIDs - See under 14.1.1

14.2.2 Colchicine

Colchicine is as effective as NSAIDs but its toxicity at higher doses limits its usefulness. However, it is of value in patients with heart failure as it does not induce fluid retention like NSAIDs. It is also useful in patients receiving anticoagulants.

Presentation: Tablet containing colchicine 500 micrograms.

Indications: Acute gout, short term prophylaxis during initial therapy with allopurinol, pregnancy, breast feeding.

Dose: Acute gout; 1mg initially, then 500 micrograms every 2 – 3 hours until pain is relieved or vomiting or diarrhoea occurs or until a total of 10mg has been reached. Do not repeat course within 3 days. Prevention of attacks during initial treatment with allopurinol – 500 micrograms 2 – 3 times daily.

Side effects: Nausea, vomiting, diarrhoea, abdominal pain, excessive doses may cause profuse diarrhoea, gastro-intestinal haemorrhage, rashes and renal damage. Rarely peripheral neuritis, alopecia, on prolonged treatment blood disorders.

Caution: Gastro-intestinal disease, renal impairment.

4.2.3 Allopurinol

allopurinol is especially useful in patients with renal impairment or urate stones where uricosuric drugs cannot be used. It is usually given once daily but doses over 300mg daily should be divided.

Presentation: Tablet containing allopurinol 100mg, 300mg.

Indications: Prophylaxis of gout and of uric acid and calcium oxalate renal stones.

Dose: Initially 100 mg daily as a single dose, after food, gradually increased over 1 – 3 weeks according to plasma or urinary uric acid concentration, to about 300mg daily, usual maintenance dose 200 – 600 mg, rarely 900 mg daily divided into 300mg doses.

Side effects: Rashes (withdraw therapy), skin reactions, fever, lymphadenopathy, arthralgia, eosinophilia, gastro-intestinal disorders, rarely malaise, headache, vertigo, drowsiness, taste disturbances, hypertension, symptomless xanthine deposits in muscle, alopecia, hepatotoxicity, paraesthesia, neuropathy.

Caution: Give prophylactic colchicine or NSAIDs (not aspirin or salicylates) until at least 1 month after hyperuricaemia is corrected, ensure adequate fluid intake (2 litres per day), hepatic and renal impairment.

Contraindication: Not for treatment of acute gout.

4.2.4 Probenecid

Presentation: Tablet containing 500mg probenecid

Indications: Gout prophylaxis (correction of hyperuricaemia)

Dose: Uricosuric therapy; 250mg twice daily after food initially, increased after one week to 500mg twice daily which can further be increased up to 2g daily in 2 – 4 divided doses according to plasma uric acid concentration and then reduced for maintenance.

Side effects: Occasionally nausea and vomiting, urinary infrequency, headache, flushing, dizziness, rashes. Rarely hypersensitivity, nephrotic syndrome, hepatic necrosis, aplastic anaemia.

Caution: Ensure adequate fluid intake (at least 2
Drugs used in the treatment of musculoskeletal disorders

14.2.5 Sulphinpyrazone

Presentation: Tablet containing 100mg, 200mg sulphinpyrazone
Indications: Prophylaxis of gout, hyperuricaemia
Dose: 100 – 200mg initially, daily taken with food or milk. Increasing over a period of 2 – 3 weeks to 600mg daily (rarely 800mg). Therapy should be continued until the serum uric acid concentration has reached normal, after which the dose can be reduced to the maintenance dose which can be as low as 200mg daily.
Side effects: Gastro-intestinal disturbances, salt and water retention, gastro-intestinal ulceration and bleeding, acute renal failure, jaundice, hepatitis, occasionally allergic skin reactions, rarely blood disorders.
Caution: See under probenecid. Regular blood counts advisable
Contraindications: avoid in NSAIDs hypersensitivity and cardiac diseases.

14.3 Drugs used in neuromuscular disorders

14.3.1 Drugs which enhance neuromuscular transmission
Skeletal muscle relaxants

14.3.2 Corticosteroids

ANTICHOLINESTERASES

Myasthenia gravis is treated using anticholinesterases as first line treatment and corticosteroids as concomitant treatment when anticholinesterases treatment is failing. Anticholinesterases enhance neuromuscular transmission in voluntary and involuntary muscles in myasthenia gravis. They prolong the action of acetylcholine by inhibiting the action of the enzyme acetylcholinesterases.

The two most commonly used drugs are neostigmine and pyridostigmine. Neostigmine has pronounced muscarinic action and may cause colic, excessive salivation or diarrhoea which need to be treated with an antimuscarinic drug such as atropine or probanthine. Pyridostigmine has less pronounced muscarinic effects, is less powerful and slower in action than neostigmine, but is of longer duration. It is preferred to neostigmine because of its smoother action and less frequent dosage.

Because of its brief duration of action, edrophonium is used mainly in the diagnosis of myasthenia gravis and to determine whether the patient already on treatment is receiving inadequate or excess doses of cholinergic drugs. A single test dose gives marked improvement in muscle power for about 5 minutes in patients who have the disease. If treatment is excessive, an injection of edrophonium will either have no effect or will intensify the symptoms. Transient improvement will be seen in patients receiving inadequate treatment. The above procedure should be performed only in conjunction with someone skilled at intubation if there is respiratory impairment in the patient.

NEOSTIGMINE

Presentation: Tablet containing neostigmine bromide 15mg; Injection containing neostigmine methylsulphate 0.5/2.5mg/ml.
Indications: Myasthenia gravis
Dose: Orally, adult; 15 – 30mg at suitable intervals throughout the day, total daily dose 75 – 300mg, neonate: 1 – 5mg every 4 hours, half an hour before feeds. Child up to 6 years initially 7.5mg; 6 – 12 years initially 15mg, usual total daily dose 15-90mg. By subcutaneous or intramuscular injection; 1 – 2.5mg at suitable intervals throughout the day (usual total daily dose 5 – 20mg). Neonate; 50 – 250micrograms every 4 hours half an hour before feeds, child; 200 – 500micrograms as required.
Side effects: Nausea, vomiting, increased salivation, diarrhoea, abdominal cramps especially at higher doses.
Caution: Asthma, bradycardia, recent myocardial infarction, epilepsy, hypotension, parkinsonism, vagotonia, peptic ulcers, pregnancy, breast feeding.
Contraindications: Intestinal and urinary obstruction.

PYRIDOSTIGMINE BROMIDE

Presentation: Tablet containing pyridostigmine bromide 60mg.
Indications: Myasthenia gravis
Dose: Orally, adult; 30 – 120mg at suitable intervals throughout the day, total daily dose 0.3 – 1.2g but it is inadvisable to exceed a daily dose of 720mg, neonate; 5 – 10mg every 4 hours, ½ to 1 hour before feeds, child up to 6 years; initially 30mg, 6 – 12 years; initially 60mg. Usual total daily dose 30 – 360mg.
Side effects: See under neostigmine. Has weaker
14.3.1 Drugs used in the treatment of musculoskeletal disorders

14.3.2 Corticosteroids

Corticosteroids are useful in the treatment of myasthenia gravis where thymectomy is inappropriate or to reduce risk of surgery. The initial dose may be high (100mg prednisolone) but it is advised to start with a smaller dosage (20mg prednisolone) and increase the dose gradually. Myasthenia gravis may be exacerbated during the initial stages of treatment with corticosteroids, it is therefore advised to conduct the treatment under supervision (inpatient).

14.3.3 Skeletal muscle relaxants

Drugs used for relief of chronic muscle spasm or spasticity include baclofen and benzodiazepines such as diazepam. They act on the CNS and differ from muscle relaxants used in anaesthesia which block transmission at the neuromuscular junction. The underlying cause of spasticity should be identified and treated.

**EDROPHONIUM CHLORIDE**

**Presentation:** Injection containing 10mg/ml edrophonium chloride

**Indications:** Diagnosis of myasthenia gravis, detection of under or over dose of cholinergic drugs

**Dose:** Diagnosis; by intravenous injection 2mg followed after 30 seconds if no adverse reaction occurs by 8mg. In adults without suitable veins 10mg is given intra muscularly. Detection of under or overdose of cholinergic drugs; by intravenous injection 2mg (best given before the next dose of anticholinesterases)

**Child:** by intravenous injection 20mcg/kg body weight followed after 30 seconds (if no adverse reaction occurs) by 80mcg/kg body weight.

**Side effects:** See under neostigmine

**Caution:** See under neostigmine, Resusitation facilities should be at hand; extreme caution in respiratory distress and asthma.

**Contraindications:** See under neostigmine.

**BACLOFEN**

**Presentation:** Tablet containing baclofen 10mg,
sugar free liquid containing 5mg/5ml baclofen.

**Indications:** Chronic severe spasticity of voluntary muscle.

**Dose:** 5mg 3 times daily, after food, gradually increased to maximum 100mg daily; child 0.75 – 2mg/kg daily (over 10 years, maximum 2.5mg/kg daily) or 2.5 mg 4 times daily increased gradually.

**Maintenance:** 1 – 2 years; 10 – 20 mg daily. 2 – 6 years; 20 – 30mg daily. 6 – 10 years; 30 – 60mg daily.

**Side effects:** Frequently sedation, drowsiness, nausea, hypotonia. Other adverse events are rare.

**Caution:** Psychiatric illness, cerebrovascular disease, elderly patients, diabetes mellitus, hepatic and renal impairment, history of peptic ulcer, avoid abrupt withdrawal as it may cause autonomic dysreflexia, porphyria, enhances effects of alcohol, drowsiness may cause impairment performance of skilled tasks such as driving.

**Contraindications:** peptic ulceration

**DIAZEPAM**

**Presentation:** Tablet containing diazepam 2mg, 5mg, oral solution containing diazepam 2mg/5ml, 5mg/5ml, injection containing solution diazepam 5mg/ml, emulsion 5mg/ml.

**Indications:** Muscle spasm

**Dose:** Orally; 2 – 15mg daily in divided doses increased to 60mg daily if necessary and according to response in spastic conditions. Cerebral spasticity in selected cases, child; 2 - 4mg daily in divided doses by intramuscular or slow intravenous injection (into a large vein at a rate of not more than 5mg/min), in acute muscle spasm; 10mg repeated if necessary after 4 hours.

**Side effects:** Sedation, drowsiness and lightheadedness next day, extensor hypotonus, confusion and ataxia, amnesia, dependence.

**Caution:** Respiratory disease, muscle weakness, history of drug abuse, marked personality disorder, pregnancy and breast feeding reduce dose in elderly, in hepatic and renal impairment, when given iv facilities for reversing respiratory depression with mechanical ventilation must be at hand, risk of venous thrombophlebitis when given intravenously-this risk can be reduced by using an emulsion.

**Contraindications:** Respiratory depression, acute pulmonary insufficiency, chronic psychosis.
**15 Immunological products and vaccines**

15.1 Active immunity

**Vaccines** may consist of:
1. A live attenuated form of a virus (e.g. rubella or measles vaccine) or bacteria (e.g. BCG vaccine).
2. Inactivated preparations of the virus (e.g. influenza vaccine) or bacteria or
3. Extracts of or detoxified exotoxins produced by a micro-organism (e.g. tetanus vaccine).

They stimulate production of antibodies and other components of the immune mechanism.

For **live attenuated** vaccines, immunisation is generally achieved with a single dose (but 3 doses are required with oral poliomyelitis and oral typhoid vaccines). Live attenuated vaccines usually produce a durable immunity but not always as long as that of the natural infection. When two live virus vaccines are required (and are not available as a combined preparation) they should be given either simultaneously at different sites or with an interval of at least 3 weeks.

**Inactivated** vaccines may require a primary series of injections of vaccine to produce adequate antibody response and in most cases booster (reinforcing) injections are required: the duration of immunity varies from months to many years.

**Extracts of or detoxified exotoxins** are more immunogenic if absorbed onto an adjuvant (such as aluminium hydroxide). They require a primary series of injections followed by booster doses.

**Side effects:** Some vaccines (e.g. poliomyelitis) produce very few reactions, while others (e.g. measles and rubella) may produce a very mild form of the disease. Some vaccines may produce discomfort at the site of injection and mild fever and malaise.

Anaphylactic reactions (see section for management) are very rare but can be fatal. Occasionally, there are more serious …… reactions and those should always be reported to the pharmacovigilance centre. For full details of side effects, the product literature should always be consulted.

**Contraindications:** Most vaccines have some basic contra-indication to their use, and the product literature should always be consulted. In general, vaccination should be postponed if the subject is suffering from an acute illness. Minor infections without fever or systemic upset are not contra-indications. A definite severe reaction to a preceding dose is a contra-indication to further doses.

Some viral vaccines contain small quantities of antibiotics such as neomycin or polymyxin (or both). Such vaccines may need to be withheld from individuals who are sensitive to the antibiotic. Hypersensitivity to egg contra-indicates influenza vaccine (residual egg protein present) and, if evidence of previous anaphylactic reaction, also yellow fever vaccine.

Live vaccines should not be routinely administered to pregnant women because of possible harm to the foetus but where there is a significant risk of exposure (e.g. to poliomyelitis or yellow fever), the need for vaccination outweighs any possible risk to the foetus. Live vaccines should not be given to individuals with impaired immune response, whether caused by disease (for special reference to AIDS, see below) or as a result of radiotherapy or treatment with high doses of corticosteroids or other immunosuppressive drugs (see points 3,4 below). They should not be given to those suffering from malignant conditions such as leukaemia and tumours of the reticulo-endothelial system.

The intramuscular route should not be used in patients with bleeding disorders such as haemophilia or thrombocytopenia.

1. Poliomyelitis virus may be excreted for longer periods in HIV subjects than in normal subjects after vaccination: contacts should be warned of this and of the need for washing hands after changing a vaccinated infant’s nappies: HIV-positive contacts are at greater risks than normal contacts. For HIV positive symptomatic subjects inactivated poliomyelitis vaccine may be used at the discretion of the clinician.

2. For those with impaired immune response including those who have received corticosteroids within the last 3 months and chemotherapy within the last 6 months, consideration should be given to use of normal immunoglobulin after exposure to measles and to varicella-zoster immunoglobulin after exposure to chickenpox or herpes zoster.

3. Live vaccines should be postponed until at least 3 months later after stopping corticosteroids and 6 months after stopping chemotherapy.

4. BCG, yellow fever and oral typhoid vaccines should be avoided in HIV positive subjects because
insufficient evidence of safety.

**IMMUNISATION SCHEDULE (See schedule in appendix 1)**

**During first year of life**

**Adsorbed Diphtheria, Tetanus and Pertussis Vaccine** (triple vaccine)

3 doses at intervals of 4 weeks: first dose at 2 months of age.

If pertussis component omitted from earlier immunisations 3 doses of Pertussis Vaccine can be given at monthly intervals to provide protection. If basic course against diphtheria and tetanus incomplete, triple vaccine (DPTer/Vac/Ads) may be used to begin or to complete course against pertussis to avoid more injections than necessary.

*plus* **Haemophilus Influenza type b Vaccine** (Hib) 3 doses at intervals of 4 weeks: first dose at 2 months of age

*also* **Poliomyelitis Vaccine, Live (Oral)** 3 doses at intervals of 4 weeks: first dose at 2 months of age.

*Also* **BCG Vaccine**

See section 15.4, BCG Vaccines.

*Also* **Measles vaccine**

* Single dose at 9 months. See 15.4.11 Measles vaccine

**During second year of life**

**Measles, Mumps and Rubella Vaccine, Live (MMR)**

Single dose at 12-15 months of age.

*In developing countries (including Zambia) as part of the WHO Expanded Programme on Immunisation, measles vaccine is given to infants at 9 months of age.

**In most developed countries MMR is administered to children at 12 - 15 months of age.

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**BEFORE NURSERY SCHOOL OR SCHOOL ENTRY**

**Adsorbed Diphtheria and Tetanus Vaccine**

Single booster dose

Preferably allow interval of at least 3 years after completing basic course; give at same session as MMR Vaccine but use separate syringe and needle, and give after MMR (MMR less painful) in different limb.

*also* **Poliomyelitis Vaccine, Live (Oral)**

Single booster dose

Preferably allow interval of at least 3 years after completing basic course.

*also* **Measles vaccine or Measles, Mumps and Rubella Vaccine, Live (MMR)**

Single booster dose

Give at same session as Adsorbed Diphtheria and Tetanus Vaccine but use separate syringe and needle; give MMR first (less painful) and use different limb - alternatively, second appointment can be made.

**BETWEEN 10 - 14 YEARS OF AGE**

**BCG Vaccine** (for tuberculin - negative children)

Single dose

May be given simultaneously with another live vaccine: otherwise an interval of at least 3 weeks should be allowed between the two.

**BEFORE LEAVING SCHOOL OR BEFORE EMPLOYMENT OR FURTHER EDUCATION**

Adsorbed Diphtheria and Tetanus Vaccine used at school entry should not be used for children aged over 10 years and adults. Instead a special low dose version combined in a single injection with tetanus vaccine should be used.

*also* **Poliomyelitis Vaccine, Live (Oral)**

Single booster dose.

**DURING ADULT LIFE**

**Poliomyelitis Vaccine, Live (Oral) (if not previously immunised)**

3 doses at intervals of 4 weeks

*No adult should remain unimmunised; health care workers in possible contact with poliomyelitis require booster dose if they have not received immunisation within last 10 years.*

**Rubella Vaccine, Live** (for susceptible women of child-bearing age)

Single dose

Women of child bearing age should be tested for rubella antibodies and offered rubella immunisation if sero-negative - exclude pregnancy before immunisation, but see also section 15.4, Rubella Vaccine.

**Adsorbed Tetanus Vaccine** (if not previously immunised)
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3 doses at intervals of 4 weeks

Booster dose 10 years after primary course and again 10 years later maintains satisfactory level of protection if diphtheria cover also needed give Adsorbed Diphtheria and tetanus Vaccine for adults and Adolescents.

Adsorbed Diphtheria Vaccine for Adults and Adolescents (if not previously immunised)

3 doses at intervals of 4 weeks.

Booster dose 10 years after primary course. If tetanus cover also needed give Adsorbed Diphtheria and Tetanus Vaccine for Adult and adolescents.

HIGH RISK GROUPS

For information on high-risk groups, see section 15.4 under individual vaccines.

Hepatitis A Vaccine
Hepatitis B Vaccine
Influenza Vaccine
Pneumococcal Vaccine

Post-immunisation pyrexia

The doctor should advise the parent that if pyrexia develops after immunisation with triple vaccine the child can be given a dose of paracetamol followed, if necessary, by a second dose 4 to 6 hours later. The dose of paracetamol for post-immunisation pyrexia in an infant aged 2 - 3 months is 60mg; an oral syringe can be obtained from a pharmacy to give the small dose-volume required. The doctor should warn the parent that if the pyrexia persists after the second dose medical advice should be sought.

15.2 Passive Immunity

Immunity with immediate protection against certain infective organisms can be obtained by injecting preparations made from the plasma of immune individuals with adequate levels of antibody to the disease for which protection is sought. This passive immunity lasts only a few weeks; where necessary passive immunisation can be repeated.

Antibodies of human origin are usually termed immunoglobulins. The term antiserum is applied to material prepared in animals. Because of serum sickness and other allergic type reactions that may follow injections of antiserum, this therapy has been replaced wherever possible by the use of immunoglobulins. Reactions are theoretically possible after injection of human immunoglobulins but reports of such reactions are very rare.

15.3 Storage and use

Care must be taken to store all vaccines and other immunological products under the conditions recommended in the product literature, otherwise the preparation may become denatured and totally ineffective. Refrigerated storage is usually necessary; many vaccines need to be stored at 2-8 degrees C and not allowed to freeze. Vaccines should be protected from light. Unused vaccine in multidose vials without preservative (most live virus vaccines) should be discarded within 1 hour of first use; those containing a preservative (including oral poliomyelitis vaccine) should be discarded within 3 hours or at the end of a session. Unused vaccines should be disposed of by incineration at a registered disposal contractor.

Particular attention must be paid to instructions on the use of diluents. Vaccines which are liquid suspensions or are reconstituted before use should be adequately shaken to ensure uniformity of the material to be injected.

Note: The use of jet guns for vaccination is not advised owing to the risk of transmitting blood-bone infections, such as HIV.

15.4 Vaccines and antisera

15.4.1 Anthrax Vaccine

Anthrax immunisation is indicated for individuals who handle infected animals, for those exposed to imported infected animal products, and for laboratory staff who work with Bacillus anthracis. The vaccine is the alum precipitate of an antigen from Bacillus anthracis and, following the primary course of injections, booster doses should be given at about yearly intervals. In the event of possible Contract with B anthracis post exposure Immunisation may be indicated in addition to antimicrobial prophylaxis (obtain from Public Health Centre)

Dose: initial course 3 doses of 0.5ml. by intramuscular injection at intervals of 3 weeks followed by a 4th dose after an interval of 6 months. Booster doses: 0.5 ml annually.

15.4.2 BCG Vaccine

BCG (Bacillus Calmette-Guerin) is a live attenuated strain derived from Mycobacterium bovis which stimulates the development of hypersensitivity to M. tuberculosis. BCG vaccine should be given intradermally by operators skilled in the technique (see below).

Within 2-6 weeks a small swelling appears at the injection site which progresses to a papule or to a benign ulcer about 10 mm in diameter and heals in
6-12 weeks. A dry dressing may be used if the ulcer discharges, but air should not be excluded. BCG is recommended for the following groups if BCG immunisation, as evidenced by a characteristic scar, has not previously been carried out and they are negative for tuberculoprotein hypersensitivity:

i. Contacts of those with active respiratory tuberculosis.

ii. Immigrants (including infants and children) from countries with a high incidence of tuberculosis should be immunised without delay. Their infants born in the Country should be immunised within a few days of birth, or at two months of age at the same time as the first dose of routine childhood vaccines.

iii. Health service staff (including medical students, hospital medical staff, nurses, physiotherapists, radiographers, technical staff in pathology departments and any others considered to be at special risk because of the likelihood of contact with infective patients or their sputum:

It is particularly important to test staff in contact with the immuno compromised, e.g. in transplant, oncology and HIV units, staff in maternity and paediatric departments).

iv. Children between 10 and 14 years of age.

v. Veterinary and other staff who handle animal species known to be susceptible to tuberculosis.

vi. Staff working in prisons, in residential homes and in hostels for refugees and the homeless.

vii. Those intending to stay for more than 1 month in countries with a high incidence of tuberculosis.

viii. Newly-born infants, children or adults where the parents or the adults request immunisation.

Apart from infants of up to 3 months, any person being considered for BCG immunisation must first be given a skin test hypersensitivity to tuberculoprotein (see under Diagnostic agents, below).

BCG vaccine may be given simultaneously with another live vaccine (see also section 15.1), but if they are not given at the same time, an interval of at least 3 weeks should normally be allowed between them. However, when BCG is given to infants, there is need to delay the primary immunisations. See section 15.1 for general contra-indications. BCG is also contra-indicated in subjects with generalised septic skin conditions (in the case of eczema, a vaccination site free from lesions should be chosen).

### Intradermal

**Bacillus Calmette-Guerin Vaccine** BCG Vaccine, Dried Tub/Vac.BCG. A freeze-dried preparation of live bacteria of a strain derived from the bacillus of Calmette and Guerin.

**Dose:** 0.1 ml. (Infant under 3 months 0.05 ml) by intradermal injection.

**INTRADERMAL INJECTION TECHNIQUE.** After swabbing with spirit and allowing to dry, skin is stretched between thumb and forefinger and needle (25G or 26G) inserted (bevel upwards) for about 2 mm into superficial layers of dermis (almost parallel with surface). Needle should be short with short bevel (can usually be seen through epidermis during insertion). Raised blanched bleb showing tips of hair follicles is sign of correct injection: 7 mm bleb = 0.1 ml injection: if considerable resistance not felt, needle is removed and reinserted before giving more vaccine.

Injection site is at insertion of deltoid muscle onto humerus (sites higher on arm more likely to lead to keloid formation); tip of shoulder should be avoided: for cosmetic reasons, upper and lateral surface of thigh may be preferred and this is an acceptable alternative.

### Percutaneous

The percutaneous multiple puncture technique is an acceptable alternative only for young infants in whom the technique of intradermal injection may be difficult (18-20 puncture points are required).

**Bacillus Calmette-Guerin Vaccine, Percutaneous** Tub/Vac/BCG (Perc). A preparation of live bacteria of a strain derived from the bacillus of Calmette and Guerin (important: this preparation must not be confused with the intradermal preparation).

**Dose:** about 0.03 ml by percutaneous administration but only recommended as an alternative for infants. see notes above.

### Diagnostic agents

In the Mantoux test, the diagnostic dose is by intradermal injection of Tuberculin Purified Protein Derivative (PPD):

**Routine.** 10 units PPD i.e. 0.1 ml of 100 units/ml (1 in 1000).

**Special** (hypersensitive or TB suspected) 1 unit PPD i.e. 0.1 ml of 10 units/ (1 in 10 000)

**Special (low sensitivity)** 100 units PPD i.e. 0.1 ml of 1 000 units/ml (1 in 100).

In the Heaf test (multiple puncture) a solution containing Tuberculin Purified Protein Derivative 100 000 units/ml is used; 1 ml is sufficient for up to about 20 tests.
Note: tuberculin testing should not be carried out within 4 weeks of receiving a live viral vaccine since response to tuberculin may be inhibited.

**Tuberculin PPD** Prepared from the heat treated products of growth and lysis of the appropriate species of mycobacterium, and containing 100,000 units/ml. Also available diluted 1 in 100 (1000 units/ml), 1 in 1000 (100 units/ml), and 1 in 10,000 (10 units/ml).

### 15.4.3 Botulism antitoxin

A trivalent botulism antitoxin is available for the post-exposure prophylaxis of botulism and for the treatment of persons thought to be suffering from botulism. It specifically neutralises the toxins produced by *Clostridium botulinum* types A, B, and E.

It is not effective against infantile botulism as the toxin (type A) is seldom, if ever, found in the blood in this type of infection.

Hypersensitivity reactions are a problem. It is essential to read the contra-indications, warnings, and details of sensitivity tests on the package insert. Prior to treatment checks should be made regarding previous administration of any antitoxin and history of any allergic conditions, e.g. asthma, hay fever, etc. All patients should be tested for sensitivity (diluting the antitoxin if history of allergy).

Botulism Antitoxin is a preparation containing the specific antitoxic globulins that have the power of neutralising the toxins formed by types A, B, and E of *Clostridium botulinum*.

**Note:** The BP title Botulism Antitoxin is not used because the preparation currently available has a higher phenol content (0.45% against 0.25%).

**Dose:** prophylaxis, 20ml by intramuscular injection as soon as possible after exposure; treatment 20ml (diluted to 100ml with sodium chloride 0.9%) by slow intravenous infusion followed by 10ml 2-4 hours later if necessary, and further doses at intervals of 12-24 hours.

### 15.4.4 Cholera vaccine

Cholera Vaccine contains heat-killed Inaba and Ogawa sub-types of *Vibrio cholerae*, Serovar O1. Cholera vaccine provides little protection and cannot control the spread of the disease. Laboratory staff who have direct contact with the cholera organism should be advised of the possible risk, and the need for vaccination determined. Cholera vaccine is no longer required for international travel.

Travellers to regions where cholera exists should be warned that scrupulous attention to food and water and personal hygiene is essential.

### 15.4.5 Diphtheria vaccines

Protection against diphtheria is essentially due to antitoxin, the production of which is stimulated by vaccines prepared from the toxin of * Corynebacterium diphtheriae*. Adsorbed diphtheria vaccines are recommended for the routine immunisation of babies and are usually given in the form of a triple vaccine, **adsorbed diphtheria, tetanus, and pertussis vaccine** (see Appendix 1). Adsorbed diphtheria and tetanus vaccine is used in place of the triple vaccine when immunisation against pertussis is contra-indicated.

A booster dose of **adsorbed diphtheria and tetanus vaccine** is recommended before school entry (4-5 years of age). This should preferably be given after an interval of at least 3 years from the last dose of the basic course. A further booster dose is now recommended before school leaving: for this purpose **adsorbed diphtheria and tetanus vaccine for adult and adolescents** (a special low-dose version combined in a single injection with tetanus vaccine) is available. For details on booster doses of diphtheria vaccine in a child over 13 years who requires treatment of a tetanus-prone wound, see under Tetanus Vaccine. If there is documented history of a fifth dose of tetanus vaccine having been given when the school leaving booster dose of adsorbed diphtheria and tetanus vaccine for adults and adolescents is due, then a booster dose of single antigen adsorbed diphtheria vaccine for adults and adolescents should be given instead.

Other booster doses of adsorbed diphtheria vaccine are not recommended as a routine except for staff in contact with diphtheria patients, or handling clinical specimens which may be pathogenic, or working directly with *Corynebacterium diphtheriae*: they should be considered for a booster or for primary immunisation following a risk assessment. A low dose vaccine, **adsorbed diphtheria vaccine for adults and adolescents**, is available for this purpose: immunity should be checked by antibody testing at least 3 months after completion of immunisation.

Unimmunised contacts of a diphtheria case require a primary course of 3 doses of adsorbed diphtheria vaccine at monthly intervals.

1. **Immunised** contacts require a single booster dose (important: adults and children over 10 years must be given a low dose vaccine); those also requiring tetanus cover can be given the appropriate strength of adsorbed diphtheria vaccine combined with tetanus vaccine.

2. **Previously immunised** travellers to countries where diphtheria is endemic or epidemic require a booster dose if their primary immunisation was more than 10 years ago.
3. Unimmunised travellers require a full course of 3 doses at monthly intervals (**important**: adults and children over 10 years requiring either a primary course or a booster should be given a **low-dose** vaccine - those also requiring tetanus cover can be given the special low-dose version combined with tetanus vaccine).  

**See section 15.1 for general contra-indications.**

**Diphtheria vaccines for children**  
**IMPORTANT**: Not recommended for persons aged 10 years or over (use diphtheria vaccines for adults and adolescents instead).

### ADSORBED DIPHTHERIA, TETANUS, AND PERTUSSIS VACCINE

**DTPer/Vac/Ads.** Prepared from diphtheria formol toxoid, tetanus formol toxoid, and pertussis vaccine adsorbed on a mineral carrier.  
**Dose:** primary immunisation of children, 0.5ml by intramuscular or deep subcutaneous injection at 2 months followed by second dose after 4 weeks and third dose after another 4 weeks (see schedule).  

**Note:** Adsorbed diphtheria, tetanus and pertussis vaccine is available in combination with Haemophilus influenzae type b vaccine, see under Haemophilus Influenzae type b Vaccine.

### ADSORBED DIPHTHERIA AND TETANUS VACCINE

**DT/Vac/Adst(Child)*** Prepared from diphtheria formol toxoid and tetanus formol toxoid adsorbed on a mineral carrier.  
**Dose:** primary immunisation of children omitting pertussis component, 0.5 ml by intramuscular or deep subcutaneous injection at 2 months followed by second dose after 4 weeks and third dose after another 4 weeks (see schedule).  

**Note:** Children require the same dose as adults, depending on the severity of the case.

### ADSORBED DIPHTHERIA VACCINE

**Dip/Vac/Adst (Child).** Prepared from diphtheria formol toxoid adsorbed on a mineral carrier.  
**Note:** Used only for contacts of a diphtheria case or carrier, *immunised children under 10 years* are given one dose of 0.5 ml by intramuscular or by deep subcutaneous injection, *unimmunised children under 10 year* are given three doses of 0.5ml with an interval of 4 weeks between first and second doses and another 4 weeks between second and third: adults and children over 10 years must be given adsorbed diphtheria vaccine for adults and adolescents (see below).

### 15.4.6 Diphtheria antitoxin

**Diphtheria Antitoxin** is used for passive immunisation: it is prepared in horses therefore reactions are common after administration.  

It is now only used in suspected cases of diphtheria (without waiting for bacteriological confirmation); tests for hypersensitivity should be first carried out.  

It is no longer used for prophylaxis because of the risk of hypersensitivity: unimmunised contacts should be promptly investigated and given erythromycin prophylaxis and vaccine (see notes above).

### 15.4.7 Haemophilus influenza type b vaccine

Children under the age of 13 months are at high risk of *Haemophilus influenzae* type b infection.  
**Haemophilus influenzae type b (Hib) vaccine** is a component of the primary section (15.1). The course consists of 3 doses of haemophilus influenzae type b vaccine with an interval of 1 month between each dose. If primary immunisations against diphtheria, tetanus, pertussis and poliomyelitis have already been commenced or completed, children under the age of 13 months should still receive 3 doses of haemophilus influenzae type b vaccine at monthly intervals. Children over the age of 13 months are at a lower risk of infection and, if not previously immunised, need receive only 1 dose of the vaccine. The risk of infection falls sharply after the age of 4 years therefore the vaccine is not normally required for children over 4 years. However, it may be given to those over 4 years who are considered to be at increased risk of invasive *Haemophilus influenzae* type b disease (such as those with sickle cell disease and those receiving treatment for malignancy). Also, asplenic children and adults, irrespective of age or the interval from splenectomy, should receive a single dose of haemophilus influenzae type b vaccine; those under one year should be given three doses. For elective splenectomy, the vaccine should ideally be given at least 2 weeks before the operation. Side-effects reported include fever, headache, malaise,
irritability, prolonged crying, loss of appetite, vomiting, diarrhoea and rash (including urticaria); convulsions, erythema multiform, and transient cyanosis of the lower limbs have been reported. See section 15.1 for general contra-indications.

### Single component

Each single component may be used to complete a course started with any other single component product listed below.

#### HIB TITER (WYETH)

**Injection**, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier).  
**Dose:** by intramuscular injection, 0.5 ml; for primary immunisations, 3 doses are required at intervals of 1 month (see schedule, section 15.1).  
**Note:** If required, haemophilus influenzae type b vaccine is available in combination with adsorbed diphtheria, tetanus and pertussis vaccine (see below); alternatively, *Hib TITER* may be combined with *Trivax-AD* brand of adsorbed diphtheria, tetanus and pertussis vaccine in the same syringe (final combined volume = 1 ml).  
Available, as part of childhood immunisation schedule.

#### ACT-HIB (PASTEUR MERIEUX)

**Injection** powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier).  
**Dose:** By intramuscular or deep sub-cutaneous injection, 0.5 ml; for primary immunisation, 3 doses are required at intervals of 1 month (see schedule, section 15.1).  
**Note:** If required, haemophilus influenzae type b vaccine is available in combination with adsorbed diphtheria, tetanus and pertussis vaccine (see below); alternatively, *ACT-HIB* may be reconstituted with 0.5 ml of Pasteur Merieux brand of adsorbed diphtheria, tetanus, and pertussis vaccine.  
Available as part of childhood immunisation schedule.

### With diphtheria, tetanus and pertussis vaccines

Each combined product may be used to complete a course started with any other combined product listed below; important see also under Adsorbed Diphtheria, Tetanus and Pertussis Vaccine.

#### ACT-HIB DTP DC (PASTEUR MERIEUX).

**Injection**, powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to a protein carrier) with diluent containing diphtheria toxoid, tetanus and *Bordetella pertussis* cells.  
**Dose:** *Child* under 4 years, by intramuscular or deep sub-cutaneous injection, 0.5 ml; for primary immunisation, 3 doses are required at intervals of 1 month (see schedule, section 15.1).

Available, as part of childhood immunisation schedule.

#### TRIVAX-HIB (SMITHKLINE BEECHAM)

**Injection**, powder for reconstitution, capsular polysaccharide of *Haemophilus influenzae* type b (conjugated to protein carrier) with diluent containing diphtheria toxoid, tetanus toxoid and *Bordetella pertussis* cells.  
**Dose:** *Child* under 10 year, by intramuscular injection.  0.5ml; for primary immunisation, 3 doses are required at intervals of 1 month (see schedule, section 15.1).  
Available, as part of childhood immunisation schedule.

#### HEPATITIS A VACCINE

**Hepatitis A vaccine** is prepared from formaldehyde-inactivated hepatitis A virus grown in human diploid cells.

Immunisation is recommended for:

- Staff and residents of homes for those with severe learning difficulties.
- Prevention of secondary cases in closed contacts of confirmed cases of hepatitis A, with seven days of onset of disease in the primary case.
- Laboratory staff who work directly with the virus:
  - Haemophiliacs treated with Factor VIII or Factor IX concentrates or who have liver disease or who have been infected with hepatitis B or hepatitis C:
  - Travellers to high-risk areas, individuals who are at risk due to their sexual behaviour. Immunisation should be considered for: patients with chronic liver disease:
  - Workers at risk of exposure to untreated sewage.

Haemophiliacs and patients with chronic liver disease should be checked for previous exposure before immunisation.  
Normal immunoglobulin (section 15.5) provides short-term protection against hepatitis A, but anti-
body titres after 3 primary course of hepatitis A vaccine are well in excess of those found after the administration of normal immunoglobulin.

**Side-effects:** of hepatitis A vaccine, usually mild, include transient soreness, diarrhoea, erythema, and induration at the injection site. Less common effects include fever, malaise, fatigue, headache, nausea, and loss of appetite; generalised rashes are occasionally reported.

See section 15.1 for general contra-indications.

- **Single component**

### AVAXIM (PASTEUR MERIEUX)

Injection suspension of formaldehyde-inactivated hepatitis A virus (GBM grown in human diploid cells) 320 antigen units/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below), 0.5 ml as a single dose; booster dose 0.5 ml 6-12 months following the initial dose; further booster doses, 0.5 ml every 10 years: child under 16 years, not recommended.

**Note:** The deltoid region is the preferred site of injection. The subcutaneous route may be used for patients with haemophilia.

### HAVRIX MONODOSE (SMITHKLINE BEECHAM)

Injection suspension of formaldehyde-inactivated hepatitis A virus (HM 175 grown in human diploid cells) 1440 ELISA units/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below), 1 ml as a single dose; booster dose, 1 ml 6-12 months following the initial dose. Child, 1-15 years; 0.5ml, booster dose for child, 0.5ml 6-12 months after initial dose. If booster dose is not given after the recommended interval, it may be delayed by up to 3 years after primary dose.

**Note:** The deltoid region is the preferred site of injection adults. The subcutaneous route may be used for patients with haemophilia.

### VAQTA PAEDIATRIC AND ADOLESCENT (PASTEUR MERIEUX)

Injection of suspension of formaldehyde-inactivated hepatitis A virus (grown in human diploid cells) 50 antigen units/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below) child 2-17 years 0.5 ml as a single dose; booster dose 0.5 ml 6-18 months following the initial dose; under 2 years of age, not recommended.

**Note:** The deltoid region is the preferred site of injection.

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**With hepatitis B vaccine Twinrix See Hepatitis B Vaccine**

### 15.4.9 Hepatitis B vaccine

**Hepatitis B vaccine** contains inactivated hepatitis B virus surface antigen (HBsAg) adsorbed on aluminium hydroxide adjuvant. It is made biosynthetically using recombinant DNA technology. The vaccine is used in individuals at high risk of contracting hepatitis B. High risk groups include: parenteral drug abusers; individuals who change sexual partners frequently; close family contacts of a case or carrier; infants born to mothers who either have had hepatitis B during pregnancy, or positive for both hepatitis B surface antigen and hepatitis B e-antigen or are surface antigen positive without e markers (or where they have not been determined); active immunisation of the infant is started immediately after delivery and hepatitis B immunoglobulin is given at the same time as the vaccine. Infants born to mothers who are positive for hepatitis B surface antigen and for e-antigen antibody should receive the vaccine but not the immunoglobulin; haemophiliacs, those receiving regular blood transfusions or blood products, and carriers responsible for the administration of such products.

Patients with chronic renal failure including those on haemodialysis. Haemodialysis patients should be monitored for antibodies annually and re-immunised if necessary: health care personnel who have direct contact with blood or blood-stained body fluids or with patients’ tissues; trainee health care workers; other occupational risk groups such as morticians and embalmers; staff and patients of day-care or residential accommodation for those with severe learning difficulties; inmates of custodial institutions; those travelling to areas of high prevalence who are at increased risk or who plan to remain there for lengthy periods; families adopting children from countries with a high prevalence of hepatitis B.

Immunisation takes up to 6 months to confer adequate protection; the duration of immunity is not known precisely, but a single booster 5 years after the primary course may be sufficient to maintain immunity for those who continue to be at risk.

Immunisation does not eliminate the need for commonsense preCaution for avoiding the risk of infection from known carriers by the routes of infection which have been clearly established, consult Guidance for Clinical Health Care Workers: Protection against Infection with HIV and Hepatitis Viruses and Protecting Health Care Workers and Patients from Hepatitis B. Accidental inoculation of hepatitis B virus-infected blood into a wound, incision, needle-prick, or abrasion may lead to infection, whereas it is unlikely that indirect exposure to a carrier will do so.
Specific hepatitis B immunoglobulin (‘HBIG’) is available for use with the vaccine in those accidentally infected and in infants (section 15.5).

A combined hepatitis A and hepatitis B vaccine is also available. See section 15.1 for general contraindications.

- Single component

**ENGERIX B (SMITHKLINE BEECHAM)**

Injection of suspension of hepatitis B surface antigen (rby, prepared from yeast cells by recombinant DNA technique) 20 micrograms/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below), 3 doses of 1ml (20 micrograms), the second 1 month and the third 6 months after the first dose; more rapid (e.g. for travellers), third dose 2 months after first dose with booster at 12 months: child birth to 12 years; 3 doses of 0.5 ml (10 micrograms). *infants* born to HBsAg-positive mother (see also above); 3 doses of 0.5ml (10 micrograms), first dose at birth with hepatitis B immunoglobulin injection (separate site).

**Note:** Deltoid muscle is preferred site of injection in adults; anterolateral thigh is preferred site in infants and children: not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia.

- With hepatitis A vaccine

**B-VAX II (PASTEUR MERIEUX)**

Injection of suspension of hepatitis B surface antigen (prepared from yeast cells by recombinant DNA technique) 10 micrograms/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below) 3 doses of 1ml (10 micrograms), the second 1 month and the third 6 months after the first dose; more rapid (e.g. for travellers), third dose 2 months after first dose with booster at 12 months. *Child* birth to 15 years; 3 doses of 0.5 ml (10 micrograms). *infants* born to HBsAg-positive mother (see also above); 3 doses of 0.5ml (10 micrograms), first dose at birth with hepatitis B immunoglobulin injection (separate site).

**Note:** Deltoid muscle is preferred site of injection in adults; anterolateral thigh is preferred site in infants and children: not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia.

- Single component

**HB-VAX II 40 (PASTEUR MERIEUX)**

A suspension of hepatitis B surface antigen (prepared from yeast cells by recombinant DNA technique) 40 micrograms/ml adsorbed onto aluminium hydroxide.

**Dose:** By intramuscular injection (see note below) 3 doses of 1ml (40 micrograms), the second one month and the third 6 months after the first dose; booster doses may be required in those with low antibody concentration.

**Note:** Deltoid muscle is preferred site of injection in adults; subcutaneous route used for patients with haemophilia.

- Single component for dialysis and predialysis patients

**TWINRIX (SMITHKLINE BEECHAM)**

Inactivated hepatitis A virus 720 ELISA units and recombinant (DNA) hepatitis B surface antigen 20 micrograms/ml adsorbed onto aluminium hydroxide and aluminium phosphate.

**Dose:** By intramuscular injection onto deltoid muscle (see note below); primary course of 3 doses of 1ml, the second 1 month and the third 6 months after the first dose; 1ml booster dose 5 years after the start of primary course for those at continued risk: *child*, 1-15 years; 0.5ml.

**Note:** Primary course should be completed with TWINRIX (single component vaccines given at appropriate intervals may be used for booster dose); not to be injected into the buttock (vaccine efficacy reduced); subcutaneous route used for patients with haemophilia (but immune response may be reduced).

**IMPORTANT.** TWINRIX is **not** recommended for post-exposure prophylaxis following percutaneous (needle-stick), ocular or mucous membrane exposure to hepatitis B virus.

**15.4.10 Influenza vaccine**

While most viruses are antigenically stable, the influenza viruses A and B (especially A) are constantly altering their antigenic structure as indicated by changes in the haemagglutinins (H) and neuraminidases (N) on the surface of the viruses. It is essential that influenza vaccines in use contain the H and N components of the prevalent strain or strains. Every year the World Health Organization recommends which strains should be included.

The recommended strains are grown in the allantoic cavity of chick embryos (therefore **contraindicated** in those hypersensitive to eggs).
Interactions: See appendix (Influenza Vaccine)

Since influenza vaccines will not control epidemics they are recommended only for persons at high risk. Annual immunisation is strongly recommended for those of all ages, especially the elderly, with any of the following conditions:

- chronic respiratory disease, including asthma;
- chronic heart disease;
- chronic renal failure;
- diabetes mellitus;
- immunosuppression due to disease or treatment, including asplenia or splenic dysfunction.

Influenza immunisation is also recommended for residents of nursing homes, residential homes for the elderly, and other long-stay facilities.

**INACTIVATED INFLUENZA VACCINE (SPLIT VIRION) (PASTEUR MERIEUX)**

Inactivated influenza vaccine (split virion) Flu/Vac/Split.

*Dose:* 0.5ml by deep subcutaneous or by intramuscular injection. *Child 6-17 months,* 0.25ml repeated once after 4-6 weeks; 0.5ml repeated once after 4-6 weeks; single doses are appropriate for children who have already been immunised.

**BEGRIVAC (WYETH)**

Inactivated influenza vaccine (split virion) Flu/Vac/Spli.

*Dose:* 0.5ml by deep subcutaneous or by intramuscular injection. *Child 6-36 months,* 0.25ml or 0.5ml repeated once after 4-6 weeks. *Child 3-12 years,* 0.5ml repeated once after 4-6 weeks; single doses are appropriate for children who have already been immunised.

**FLUARIX (SMITHKLINE BEECHAM)**

Inactivated influenza vaccine (split virion) Flu/Vac/split.

*Dose:* 0.5ml by deep subcutaneous or by intramuscular injection. *Child 6 months to 35 months* 0.25-0.5ml, *6-12 years* 0.5ml repeated once after 4-6 weeks, single doses are appropriate for children who have already been immunised.

**FLUVIRIN (MEDEVA)**

Inactivated influenza vaccine (surface antigen) flu/Vac/SA.

*Dose:* 0.5ml by deep subcutaneous or by intramuscular injection. *Child 6 months to 35 months* 0.25-0.5ml, *6-12 years* 0.5ml repeated once after 4-6 weeks, single doses are appropriate for children who have already been immunised.

### 15.4.11 Measles Vaccine

Measles vaccine are used for active immunisation against measles. In most developed countries children are immunised against measles using a combined Measles, Mumps and Rubella (MMR) vaccine during the second year of life. In developing countries including Zambia a measles vaccine is administered at 9 months (can be given in certain circumstances from 7 months) and forms part of WHO Expanded Programme on Immunisation (EPI). In both instances a second dose is often given later on in childhood.

Administration of a measles-containing vaccine to children may be associated with a mild measles like syndrome with a measles-like rash and pyrexia about a week after injection. Much less commonly, convulsions and, very rarely, encephalitis have been reported. Convulsions in infants are much less frequently associated with measles vaccines than with other conditions leading to febrile episodes.

Both the Measles and MMR vaccines may be used in the control of outbreaks of measles (see under MMR Vaccine).

- Single antigen vaccine

**Measles vaccine;** routine vaccination against measles is recommended for all children in the country at 9 months or at least during the first year of life from 9 months of age. A second dose is given at 18 months and a third dose at school entry (see schedule in 15.1.)

Measles vaccine is generally not recommended in children less than 9 months in whom maternal
antibodies may prevent a response. However, it has been administered in infants at 7 months in certain circumstances e.g. during a measles outbreak.

Measles vaccine can be given as prophylaxis after exposure to measles such as during an outbreak as long as it is given within 72 hours of exposure.

**Immunological products and vaccines**

**15.4.12 MMR vaccine**

A combined measles/mumps/rubella vaccine (MMR vaccine) has been introduced with the aim of eliminating rubella (and congenital rubella syndrome), measles, and mumps. Every child should receive two doses of MMR vaccine by entry to primary school, unless there is a valid contraindication (see below) or parental refusal.

The first dose of MMR vaccine is given to children aged 12-15 months. A second (booster) dose has been given before starting school at 3-5 years of age (see schedule, section 15.1). Children presenting for their pre-school booster who have not received their first dose of MMR vaccine should be given a dose of MMR vaccine followed 3 months later by a second dose. At school-leaving age or at entry into further education. Individuals of both sexes who have not received either MR or MMR vaccines should be offered MMR immunisation.

MMR vaccine may also be used in the control of outbreaks of measles and should be offered to susceptible children within 3 days of exposure to infection (important: MMR vaccine is not suitable for prophylaxis following exposure to mumps or rubella since the antibody response to the mumps and rubella components is too slow for effective prophylaxis).

Children with partially or totally impaired immune responsiveness should not receive live vaccines (for advice on vaccines and AIDS see section 15.1). If they have been exposed to measles infection they should be given normal immunoglobulin (section 15.5).

Malaise fever or a rash may occur following the first dose of MMR vaccine, most commonly about a week after immunisation and lasting about 2 to 3 days. Parotid swelling occasionally occurs, usually in the third week. After a second dose of MMR vaccine, adverse reactions are considerably less common than after the first dose. Post-vaccination meningoencephalitis was reported (rarely and with complete recovery) following immunisation with MMR vaccine containing Urabe mumps vaccine, which has been discontinued; no cases have been confirmed in association with the currently-used Jeryl Lynn mumps vaccine. Children with post vaccination symptoms are not infectious.

**Contra-indications** to MMR include: Children with untreated malignant disease or altered immunity (for advice on vaccines and AIDS see section 15.1), and those receiving immunosuppressive drugs or radiotherapy, or high-dose corticosteroids, children who have received another live vaccine by injection within 3 weeks, children with allergies to neomycin, kanamycin and Gelatin children with acute febrile illness (vaccination should be deferred):

**Adverse reactions:** Include idiopathy, thrombocytopenia purpura within six weeks, “leaflets are available to provide parents with advice for reducing fever” (including the use of Paracetamol).

If given to women, pregnancy should be avoided for 1 month (as for rubella vaccine); should not be given within 3 months of an immunoglobulin injection.

It should be noted that; children with a personal or close family history of convulsions should be given MMR vaccine, provided the parents understand that there may be a febrile response: immunoglobulin must not be given with MMR vaccine since the immune response to rubella and mumps may be inhibited; doctors should seek specialist paediatric advice rather than withhold vaccination;

There is increasing evidence that MMR vaccine can be given safely even when the child has had an anaphylactic reaction to food containing egg (dislike of egg or refusal to eat is not a contra-indication).

**MMR VACCINE**

Live measles, mumps, and rubella vaccine. 

**Dose:** 0.5ml deep subcutaneous or by intramuscular injection. Available as MMR II (Pasteur Merieux) or Priorix (SmithKline Beecham).

**5.4.13 Meningococcal polysaccharide vaccine**

Meningococcal Polysaccharide vaccine is indicated for visits of longer than 1 month to areas of the world where there is risk of acquiring meningococcal infection particularly for travellers proposing to travel 'rough'. Travellers with asplenia (or severe dysfunction of the spleen) also particularly require protection.

These areas include Delhi, Nepal, Burma, Pakistan, Mecca (see below), and the meningitis belt of Africa, which encompasses southern sub-Saharan Africa.
parts of Senegal, Mali, Niger, Chad and Sudan; all of Gambia, Guinea, Togo and Benin; South-west Ethiopia; northern part of Sierra Leone, Liberia, Ivory Coast, Nigeria, Cameroon, Central African Republic, Uganda and Kenya. Saudi Arabia requires vaccination of pilgrims to Mecca during the Hajj annual pilgrimage; this may apply to others visiting Saudi Arabia in the months leading up to August.

The need for immunisation of laboratory staff who work directly with Neisseria meningitidis should be determined by assessing the risk. See section 15.1 for general contra-indications.

**AC VAX (SMITHKLINE BEECHAM)**

Meningococcal polysaccharide vaccine, Neimen/Vac. Prepared from *Neisseria meningitidis* (meningococcus) groups A and C.

**Dose:** Adult and child aged 2 months and over, 0.5ml by deep subcutaneous or intramuscular injection.

**MENGIVAC (A + C) (PASTEUR MERIEUX)**

Meningococcal polysaccharide vaccine, Neimen/Vac. Prepared from *Neisseria meningitidis* (meningococcus) group A and C.

**Dose:** Adult and child aged over 18 months 0.5ml by deep subcutaneous or intramuscular injection.

**Note:** The lower age range for AC Vax and Mengivac (A+C) differ; in the case of Mengivac (A+C) the product literature states that young children and infants respond less well to the vaccine than older children and adults with little response to the Group C polysaccharide under 18 months of age and a poor response to Group A polysaccharide under 3 months of age. Additionally, protection in infants under 18 months of age is of shorter duration.

### 15.4.14 Mumps Vaccine

Mumps vaccine consists of a live attenuated strain of virus grown in chick-embryo tissue culture. See under MMR vaccine and section 15.1 for contra-indications.

**MUMPSVAX (PASTEUR MERIEUX)**

Mumps vaccine (Jeryl Lynn strain).

**Dose:** Adult and child over 1 year; 0.5ml by subcutaneous injection.

- Combined vaccines
  - With measles and rubella see MMR Vaccine.

15.4.15 Pertussis Vaccine

**Pertussis vaccine** is usually given combined with diphtheria and tetanus vaccine (in triple vaccine) starting at 2 months of age (see section 15.1).

Convulsions and encephalopathy have been reported as rare complications, but such conditions may arise from other causes and be falsely attributed to the vaccine. Neurological complications after whooping cough itself are considerably more common than after the vaccine.

As with any other elective immunisation procedure it is advisable to postpone vaccination if the child is suffering from any acute illness, until fully recovered. Minor infections, without fever, or systemic upset are not reasons to delay immunisation. Immunisation should not be carried out in children who have a history of severe general reaction to a preceding dose: in these children immunisation should be completed with adsorbed diphtheria and tetanus vaccine. Where there has been a severe local reaction or pyrexia, a cellular pertussis vaccine may be used. The following reactions should be regarded as severe:

**Local** - an extensive area of redness and swelling which becomes indurated and involves most of the antero-lateral surface of the thigh or a major part of the circumference of the upper arm.

**General** - temperature of 39.5 degrees C or more within 48 hours of vaccine, anaphylaxis, bronchospasm, laryngeal oedema, generalised collapse, prolonged unresponsiveness, prolonged inconsolable screaming, and convulsions occurring within 72 hours.

A personal or family history of allergy is not a contra-indication to immunisation against whooping cough; nor are stable neurological conditions such as cerebral palsy or spina bifida.

**Children with problem histories.** When there is a personal or family history of febrile convulsions, there is an increased risk of these occurring after pertussis immunisation. In such children, immunisation is recommended but advice on the prevention of fever should be given at the time of immunisation.

In a British study, children with a family history of epilepsy were immunised with pertussis vaccine without any significant adverse events. These children's developmental progress has been normal. In children with a close family history (first degree relatives) of *idiopathic epilepsy*, there may be a risk of developing a similar condition, irrespective of vaccine Immunisation is recommended for these children.

Where there is a still evolving neurological
problem, immunisation should be deferred until the condition is stable. Children whose epilepsy is well controlled may receive pertussis vaccine. When there has been a documented history of cerebral damage in the neonatal period, immunisation should be carried out unless there is evidence of an evolving neurological abnormality. If immunisation is to be deferred, this should be stated on the neonatal discharge summary. Where there is doubt, appropriate advice should be sought from a consultant paediatrician, district immunisation co-ordinator or consultant in communicable disease control rather than withholding vaccine.

Older children: there is no contra-indication to administration of pertussis vaccine to unimmunised older children in order to protect the individuals and siblings under the age of immunisation; there is no upper age limit. However, no suitable vaccine is available for children over 7 years. Guidance for immunisation against pertussis in the absence of single antigen pertussis vaccine is available at www.doh.gov.uk.

15.4.16 Pneumococcal vaccine

A polyvalent pneumococcal polysaccharide vaccine is recommended for the immunisation of persons over the age of 2 years with any of the following conditions:

- Homozygous sickle cell disease;
- Asplenia or severe dysfunction of the spleen;
- Chronic renal disease or nephronic syndrome;
- Coeliac syndrome;
- Immunodeficiency or immunosuppression due to disease or treatment, including HIV infection;
- Chronic heart disease;
- Chronic lung disease;
- Chronic liver disease including cirrhosis;
- Diabetes mellitus.

Where possible, the vaccine should be given at least 2 weeks before splenectomy and before chemotherapy; patients should be given advice about increased risk of pneumococcal infection. Prophylactic antibiotic therapy against pneumococcal infection should not be given in pregnancy, or when breast feeding, or when there is infection. Hypersensitivity reactions may occur. Prophylactic antibacterial therapy against pneumococcal infection should not be stopped after immunisation. The vaccine is effective in a single dose if the types of pneumonia in the Community are reflected in the polysaccharides contained in the vaccine. A polyvalent (7-valent) pneumococcal polysaccharide conjugated vaccine has been introduced recently for the prevention invasive pneumococcal disease in children aged between 2 months and 2 years. Who are at special risk because of the condition shown below; the number of doses required for primary Immunisation varies according to age. Children aged over 2 years at high risk of pneumococcal disease who have previously received pneumococcal polysaccharide conjugated vaccine may receive the UN Conjugated (23-valent pneumococcal polysaccharide vaccine.)

REVACCINATION. Revaccination with the previously available 12 or 14-valent vaccines produced severe reactions in some subjects, especially if undertaken less than 3 years after the first injection; the same is likely to apply to revaccination with the currently available 23-valent vaccines. Revaccination is therefore not recommend except after 5-10 years, in individuals in whom the antibody concentration is likely to decline more rapidly (e.g. asplenia, splenic dysfunction and nephronic syndrome). If there is doubt about the need for revaccination, this should be discussed with haematologist and measurement of antibody concentration considered.

IMPORTANT. Not for intradermal injection which may cause severe local reactions. See section 15.1 for general contra-indications.

PNEUMOVAX II (PASTEUR MERIEUX)

Polysaccharide from each of 23 capsular types of pneumococcus.

Dose: 0.5ml by subcutaneous or intramuscular injection. Child under 2 years, not recommended (suboptimal response and also safety and efficacy not established).

PNU-IMUNE (WYETH)

Polysaccharide from each of 23 capsular types of pneumococcus.

Dose: 0.5ml subcutaneous or intramuscular injection. Child under 2 years not recommended. See Appendix 1.

Prevenar

Polysaccharide of each of 7 capsular type of pneumococcus adsorbed into aluminium phosphate.

Dose: Intramuscular injection, infant 2-6 months. 3 doses each of 0.5ml separated by intervals of 1 month and a further dose in second year of life, 7-11 months 2 doses each of 0.5ml separated by a interval of 1 month and a further dose in second year of life; child 1-2 years 2 doses each of 0.5ml separated by an interval of 2 months.

Note: Reltoid muscle is preferred site of injection in young children anterolateral thigh is preferred site in infants.
15.4.17 Poliomyelitis vaccines

There are two types of poliomyelitis vaccine. Poliomyelitis vaccine, live (oral) (Sabin) and poliomyelitis vaccine, inactivated (Salk). The oral vaccine consisting of a mixture of attenuated strains of virus type 1, 2 and 3 is at present generally used in Zambia.

A course of primary immunisation consists of 3 doses of poliomyelitis vaccine, live (oral), starting at two months of age with an interval of 1 month between each dose (see schedule, section 15.1). The initial course of 3 doses should also be given to all unimmunised adults; no adult should remain unimmunised against poliomyelitis.

Two booster doses of poliomyelitis vaccine, live (oral), are recommended, the first before schools entry and the second before leaving school (see schedule, section 15.1). Booster dose for adults are not necessary except for those at special risk such as travellers to endemic areas, or laboratory staff likely to be exposed to the viruses, or health care workers in possible contact with cases: booster dose should be given to such individuals every 10 years.

Vaccine-associated poliomyelitis and poliomyelitis in-contacts of vaccines are rare. The need for strict personal hygiene must be stressed; the contacts of a recently vaccinated baby should be advised particularly of the need to wash their hands after changing the baby’s napkins.

Contra-indications include vomiting and diarrhoea, and immunodeficiency disorders (or household contacts of patients with immunodeficiency disorders). See section 15.1 for further contra-indications.

Poliomyelitis vaccine (inactivated) may be used for those in whom poliomyelitis vaccine (oral) is contra-indicated because of immunosuppressive disorders (for advice on AIDS see section 15.1).

Either live (oral) vaccine or inactivated vaccine may be used to complete a course started with the other except that live (oral) vaccine must not be used for immunosuppressed individuals or their household contacts (see also contra-indications).

TRAVELLERS. Travellers to areas other than Australia, New Zealand, Northern and Western Europe and North America should be given a full course of oral poliomyelitis vaccine if they have not been immunised in the past. Those who have not received immunisation within the last 10 years should be given a booster dose of oral poliomyelitis vaccine.

15.4.18 Rabies vaccine

Pre-exposure, prophylactic immunisation with human diploid cell rabies vaccine should be offered to those at high risk – laboratory staff who handle the rabies virus, those working in quarantine stations, animal handlers, veterinary surgeons and field workers who are likely to be exposed to bites of possibly infected wild animals, certain port officials, and health workers who are likely to come into close contact with patients with rabies. Pre-exposure immunisation is also recommended for those living or travelling to enzootic areas who may be exposed to unusual risk.

For prophylactic use the vaccine produces a good antibody response when given in a 3-dose schedule on days 0, 7, and 28, with a booster dose every 2-3 years to those at continued risk. For travellers to enzootic areas who are not animal handlers, 2 doses given 4 weeks apart may be acceptable provided that post-exposure treatment is readily available; for those who remain at continued risk a booster dose should be given 6-12 months later followed by a booster every 2-3 years.
Post-exposure treatment depends on the level of risk in the country concerned and the individual’s immune status. For post-exposure treatment of fully immunised patients: countries with no risk, generally no treatment required; countries with low risk and high risk, two booster doses are needed (one on day 0 and one on day 3-7). For post-exposure treatment of previously immunised patients (or those whose prophylaxis is possibly inadequate): countries with no risk, generally no treatment required; countries with low risk, a course of injections should be started as soon as possible after exposure (days 0, 3, 7, 14 and 30); countries with high risk, as for countries with low risk, plus rabies immunoglobulin on day 0 (section 15.1). The course may be discontinued if it is proved that the patient was not at risk.

Staff in attendance on a patient who is highly suspected of, or known to be suffering from, rabies should be offered immunisation. Four intradermal doses of 0.1ml of human diploid cell vaccine (Pateur Merieux) given on the same day at different sites (ensuring correct intradermal technique) has been suggested for this purpose (unlicensed route).

There are no specific contra-indications to this diploid cell vaccine and its use should be considered whenever a patient has been attacked by an animal even if there is no direct evidence of rabies in the attacking animal.

Rabies Vaccine BP Pasteur Merieux (Pasteur Merieux)

Freeze-dried inactivated Wistar rabies virus strain PM/WI 38 1503-3M cultivated in human diploid cells. Single dose vial with syringe containing diluent.

IMPORTANT. Studies have shown that when this vaccine is injected into the gluteal region there is a poor response. Concomitant administration of chloroquine may also affect the antibody response. Because of the potential consequences of inadequately treated rabies exposure and because there is no indication that foetal abnormalities have been associated with rabies vaccination, pregnancy is not considered a contra-indication to post-exposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy.

Dose: Prophylactic, 1ml by deep subcutaneous or intramuscular injection in the deltoid region, on days 0, 7, and 28; also booster doses every 2-3 years to those at continued risk; see above for 2 dose schedule.

Post-exposure, 1ml by deep subcutaneous or intramuscular injection in the deltoid region, see notes above. Staff in attendance, see notes above.

15.4.19 Rubella vaccine

The selective practice of protecting women of child bearing age from the risk of rubella (German measles) in pregnancy has been replaced by a practice of eliminating rubella in children; the single-antigen rubella immunisation programme for 10-14 year old girls has been discontinued. All children should be immunised with rubella-containing vaccine (measles, mumps and rubella) at 12-15 months and at 3-5 years (see MMR vaccine).

Rubella vaccine may conveniently be offered to previously immunised and seronegative post-partum women. Immunising susceptible post-partum women a few days after delivery is important as far as the overall reduction of congenital abnormalities is concerned, for about 60% of these abnormalities occur in the babies of multiparous women.

PREGNANCY. Rubella immunisation should be avoided in early pregnancy, and women of child-bearing age should be advised not to become pregnant within 1 month of immunisation. However, despite active surveillance in the UK, the USA, and Germany, no case of congenital rubella syndrome has been reported following inadvertent immunisation shortly before or during pregnancy. There is thus no evidence that the vaccine is teratogenic, and routine termination of pregnancy following inadvertent immunisation should not be recommended; potential parents should be given this information before making a decision about termination.

See section 15.1 for general contra-indications.

Rubella Vaccine, Live Rub/Vac (Live).

Prepared from Wistar RA 22/3 strain propagated in human diploid cells. Dose: 0.5ml by deep subcutaneous or by intramuscular injection (see schedule, section 15.1 and notes above).

Combined vaccines, see under MMR vaccine.

15.4.20 Smallpox vaccine

Smallpox immunisation in no longer required routinely because global eradication has been achieved.
15.4.21 Anti-snake venom sera

- Polyvalent

Anti-snake venom sera is a lyophilised powder. It is effective against venoms of the following corresponding poisonous snakes:
- Black Mamba (Dendroaspis Polylepis)
- Gaboon Viper (Bitis Gabonica Rhinoceros)
- Russel’s Viper (Vipera Russelli)
- Saw-Scaled Viper (Echis Carinatus)

Snake bite should be treated immediately. The following first aid measures are of great value in snake bite management:

- Institute measures to combat shock which has a major physiological element in it.
- A ligature should be bound at some moderate distance above the bitten part to prevent the venom form spreading to the upper part of the limb.
- The bite wound should be cleaned in the usual surgical way. The bitten part should be immobilised as in fracture cases.
- In order to derive the greatest benefit out of the anti-snake venom serum treatment, the serum should be injected as soon as possible after the snake bite.
- It is advisable to check the manufacturer’s instructions before administering the serum.

ANTI-SNAKE VENOM SERUM POLYVALENT

Presentation: A white or pale yellow lyophilised powder in 10ml vials

Indications: Antitoxic therapy in bites from the above mentioned snakes. It can also be used in cases where specific antiserum is not available or when the species is not known.

Dose: As a first dose 20ml of the reconstituted serum should be injected intravenously very slowly (1ml per minute). The second dose should be given after 1 hour if symptoms persist. If symptoms persist, (these vary depending on the venom) further doses can be given every 6 hours until symptoms disappear completely. In viper cases some serum should be injected around the site of the bite to prevent gangrene which results due to the destructive effect of the localised viper venom on tissue.

Side effects: Serum sickness, thermal reactions and acute anaphylaxis.

Caution: Before administration of the anti-snake serum it is necessary to find out from the patient of any allergies and if possible test for sensitivity by injecting the patient 0.1ml of the serum diluted 1:10 in normal saline or saline/glucose. The patient should then be observed for 30 minutes for local or general reaction. If the test dose produces reaction, this should be countered immediately with 1:100 adrenaline and if necessary corticosteroids. But if the symptoms of snake bite are severe it may not be advisable to wait for 30 minutes to observe reactions to the test dose. In such cases it may be better to inject 1ml of adrenaline 1:1000 intramuscularly at the same time as the serum in order to minimise the risk of anaphylaxis.

15.4.22 Tetanus vaccines (tetanus toxoids)

Tetanus vaccines stimulate the production of the protective antitoxin. In general, adsorption on aluminium hydroxide, aluminium phosphate, or calcium hydroxide, aluminium phosphate, or calcium phosphate improves antigenicity. Adsorbed tetanus vaccine is offered routinely to babies in combination with adsorbed diphtheria vaccine (DT/Vac/AdsaChild), and more usually also combined with killed Bordetella pertussis organisms as a triple vaccine, adsorbed diphtheria, tetanus, and pertussis vaccine (DTP/Per/Vac/Adsa). See schedule, section 15.1).

In children, the triple vaccine not only gives protection against tetanus in childhood but also gives the basic immunity for subsequent booster doses of adsorbed tetanus vaccine at school entry and at school leaving (combined with low-dose adsorbed diphtheria vaccine) and also when a potentially tetanus-contaminated injury has been received. Normally, booster doses of adsorbed tetanus vaccine should not be given unless more than 10 years have elapsed since the last booster dose because of the possibility that hypersensitivity reactions may develop. If a child over the age of 13 years requires a tetanus booster for a tetanus-prone wound then, provided more than 10 years have elapsed since the school-entry booster, adsorbed tetanus vaccine combined with low-dose adsorbed diphtheria vaccine can be given; the routine booster at school leaving age is omitted.

Active immunisation is important for persons in older age groups who may never have had a routine or complete course of immunisation when younger. In these persons a course of adsorbed tetanus vaccine may be given. Very rarely, tetanus has developed after abdominal surgery; patients awaiting elective surgery should be asked about tetanus immunisation and immunised if necessary. All laboratory staff should be offered a primary course if unimmunised.

Any adult who has received 5 doses is likely to have life-long immunity; booster doses on injury should only be required if more than 10 years have elapsed since the last dose.
Wounds are considered to be tetanus-prone if they are sustained either more than 6 hours before surgical treatment or at any interval after injury and are puncture-type or show much devitalised tissue or are septic or are contaminated with soil or manure. All wounds should receive thorough surgical toilet. For clean wounds, a booster dose of adsorbed tetanus vaccine is given if the primary course (or booster dose) was given more than 10 years previously; non-immunised individuals (or whose immunisation status is not known) should be given a full course of the vaccine. For tetanus prone wounds, treatment is as for clean wounds with the addition of a dose of tetanus immunoglobulin (section 15.5); in an immunised individual who has received a dose of adsorbed tetanus vaccine within the previous 10 years the immunoglobulin may only be needed if the risk of infection is considered to be especially high (e.g. contamination with manure). Antibiotic treatment (with benzyl penicillin or amoxycillin + clavulanic acid) may also be required for tetanus-prone wounds. See section 15.1 for general contra-indications.

Single antigen vaccines

The BP directs that when Tetanus Vaccine is prescribed or demanded and the form is not stated, Adsorbed Tetanus Vaccine may be dispensed or supplied.

**ADSORBED TETANUS VACCINE TET/VAC/ADS.**

Prepared from tetanus formol toxoid with a mineral carrier (aluminium hydroxide). Dose: 0.5ml or as stated on the label, by intramuscular or deep subcutaneous injection followed after 4 weeks by a second dose and after a further 4 weeks by a third. Combined vaccine, see Diphtheria Vaccines.

**15.4.23 Typhoid vaccines**

Typhoid immunisation is advised for travellers to countries where sanitation standards may be poor, although it is not a substitute for scrupulous personal hygiene (see section 14.6). Immunisation is also advised for laboratory workers handling specimens from suspected cases.

Capsular polysaccharide typhoid vaccine is given by intramuscular or deep subcutaneous injection with booster dose every 3 years on continued exposure. Local reactions, including pain, swelling or erythema may appear 48-72 hours after administration. An oral typhoid vaccine is also available. It is a live attenuated vaccine contained in an enteric coated capsule. It is taken by mouth as three doses of one capsule on alternate days, providing protection 7-10 days after the last dose. Protection may persist for up to 3 years in those constantly (or repeatedly) exposed to *Salmonella typhi*, but occasional travellers require a repeat course at intervals of 1 year.

**Contra-indications:** Individuals who are immunosuppressed (whether due to disease or its treatment) and is inactivated by concomitant administration of antibiotics or sulphonamides. Oral typhoid vaccine and oral poliomyelitis vaccine should be given at least 3 weeks apart on theoretical grounds. Administration of a dose of oral typhoid vaccine should be coordinated so that mefloquine is not taken for at least 12 hours before or after a dose (vaccination with oral typhoid vaccine should preferably be completed at least 3 days before the first dose of mefloquine).

Side-effects: Abdominal cramps, diarrhoea, headache, fever and hypersensitivity reactions including rarely, anaphylaxis.

For general contra-indications to vaccines, see section 15.1.

**Polysaccharide vaccine for injection**

**TYPHIM VI (PASTEUR MERIEUX)**

Vicapsular polysaccharide typhoid vaccine, 50 micrograms/mL virulence polysaccharide antigen of *salmonella typhi*. Dose: 0.5ml by deep subcutaneous or intramuscular injection: Child under 18 months, may show suboptimal response.

**VIVOTI (MEDEVA)**

Capsules, enteric coated, live attenuated *salmonella typhi* Dose: Adult and child over 6 years; 1 capsule on days 1, 3 and 5. Under 6 years, not recommended.

COUNSELLING: Swallow as soon as possible after placing in mouth with a cold or lukewarm drink; it is important to store in refrigerator.

**15.4.24 Yellow fever vaccine**

Yellow fever vaccine consists of a live attenuated yellow fever virus (17D strain) grown in developing chick embryos. Immunisation is indicated for those travelling or living in areas where infection is endemic and for laboratory staff who handle the virus or who handle clinical material from suspected cases. Infants under 9 months of age should only be vaccinated if the risk of yellow fever is unavoidable since there is a small risk of encephalitis. The vaccine should not be given to those with impaired immune responsiveness, or who have had an anaphylactic reaction to egg; it
should not be given during pregnancy (but where there is a significant risk of exposure the need for immunisation outweighs any risk to the foetus). See section 15.1 for further contra-indications. Reactions are few. The immunity which probably lasts for life is officially accepted for 10 years starting from 10 days after primary immunisation and for a further 10 years immediately after revaccination.

Yellow Fever Vaccine, Live Yel/Vac A suspension for chick embryo proteins containing attenuated 17D strain virus

**Dose:** 0.5ml by subcutaneous injection

### 15.5 Immunoglobulins

Human immunoglobulins have replaced immunoglobulins of animal origin (antisera) which were frequently associated with hypersensitivity. Injection of immunoglobulins produces immediate protection lasting for several weeks.

The two types of human immunoglobulin preparation are normal immunoglobulin and specific immunoglobulins.

#### 15.5.1 Normal immunoglobulin

*(Gamma Globulin)*

Human normal immunoglobulin (‘hnig’) is prepared from pools of at least 1000 donations of human plasma; it contains antibody to measles, mumps, varicella, hepatitis A, and other viruses that are currently prevalent in the general population.

**Caution and side effects.** Side effects of immunoglobulins include malaise, chills, fever, and rarely anaphylaxis.

**Contra-indications:** Patients with known class specific antibody to immunoglobulin A (IgA).

Normal immunoglobulin may **interfere with immune response to live viruses vaccines** which should therefore only be given **at least 3 weeks before or 3 months after** an injection of normal immunoglobulin (this does not apply to yellow fever vaccine since normal immunoglobulin does not contain antibody to this virus). For travellers, if there is insufficient time, the recommended interval may have to be ignored.

**Intramuscular**

Normal immunoglobulin is administered by intramuscular injection for the protection of susceptible contacts against hepatitis A virus (infectious hepatitis), **measles** and, to a lesser extent, rubella.

**HEPATITIS A.** Control of hepatitis A depends on good hygiene and many studies have also shown the value of normal immunoglobulin in the prevention and control of outbreaks of this disease. It is recommended for controlling infection in contacts in closed institutions and also, under certain conditions, in school and home contacts, and for occasional or short-term travellers going to areas where the disease is highly endemic (all countries excluding Northern and Western Europe, North America, Australia, and New Zealand). Hepatitis A vaccine is preferred for those visiting such countries frequently or who stay for longer than 3 months.

**MEASLES.** Normal immunoglobulin may be given for prophylaxis in children with compromised immunity (and in adults with compromised immunity who have no measles antibodies); it should be given as soon as possible after contact with measles. It should also be given to children under 12 months with recent severe illness for whom measles should be avoided; MMR vaccine should then be given (after an interval of **at least 3 months**) at around the usual age.

**RUBELLA.** Immunoglobulin after exposure does not prevent infection in non-immune contacts and is not recommended for protection of pregnant women exposed to rubella. It may however, reduce the likelihood of a clinical attack which may possible reduce the risk to the fetus. It should only be used when termination of pregnancy would be unacceptable when it should be given as soon as possible after exposure. Serological follow-up of recipients is essential. For routine prophylaxis, see Rubella Vaccine.

**REPLACEMENT THERAPY.** Normal immunoglobulin may also be given intramuscularly for replacement therapy, but intravenous formulations (see below under intravenous) are normally preferred.

Normal immunoglobulin. Normal immunoglobulin injection containing 250mg vial; 750mg vial

**Dose:** By deep intramuscular injection, Hepatitis A travel prophylaxis (2 months or less abroad), 250mg: Child under 10 years 125mg: longer travel prophylaxis (3-5 months broad, but see notes above) and to control outbreaks, 500mg. Child under 10 years 250mg. Measles prophylaxis, Child under 1 year; 250 mg. 1 – 2 years 500mg, 3 years and over; 750mg. To allow attenuated attack, Child under 1 year 100mg. 1 year and over; 250mg.

**Gammabulin (immuno)** Normal immunoglobulin injection 16%. **Dose:** see below

Kabiglobulin (Pharmacia & Upjohn)

Normal immunoglobulin injection 16%. See dose below

Kabiglobulin (Pharmacia & Upjohn)

Normal immunoglobulin injection 16%. **Dose:** see below

**Note:** Doses for Gammabulin and Kabiglobulin are expressed in terms of volume:
Dose: By intramuscular injection
Hepatitis A prophylaxis, adult and child; 0.02 – 0.04ml/kg body weight. Greater exposure risk; 0.06 – 0.12ml/kg body weight.
Measles prophylaxis; 0.2ml/kg body weight. To allow attenuated attack, 0.04ml/kg body weight.

Rubella in pregnancy, prevention of clinical attack, 750ml.
Antibody deficiency syndromes, consult product literature.

Intravenous
Special formulations for intravenous administration are available for replacement therapy for patients with congenital agammaglobulinaemia and hypogammaglobulinaemia, for the treatment of idiopathic thrombocytopenic purpura and Kawasaki syndrome, and for the prophylaxis of infection following bone marrow transplantation.

- For intravenous use
Normal Immunoglobulin for Intravenous Use
Available as: Alphaglobin \(^{(k)}\) (2.5g, 5g, 10g – Grifols); Human Immunoglobulin (3g, 5g, 10g – SNBTS); Octagam (2.5g, 5g, 10g – Octapharma); Sandoglobulin \(^{(a)}\) (1g, 3g, 6g, 12g – Sandoz); Vigam \(^{(a/S)}\) (2.5g, 5g – BPL); vigam \(^{(a)}\) liquid (5g – BPL)
Dose: consult product literature

15.5.2 Specific Immunoglobulins
Specific immunoglobulins are prepared by pooling the plasma of selected donors with high levels of the specific antibody required.

Although a hepatitis B vaccine is now available for those at high risk of infection, specific hepatitis B immunoglobulin (‘HBIG’) is available for use in association with the vaccine for the prevention of infection in laboratory and other personnel who have been accidentally inoculated with hepatitis B virus, and in infants born to mothers who have become infected with this virus in pregnancy or who are high-risk carriers.

Following exposure of an unimmunised individual to an animal in or from a high-risk country, specific rabies immunoglobulin of human origin should be injected at the site of the bite should be washed with soap water and also given intramuscularly. Rabies vaccine should also be given (for details see Rabies Vaccine).

For tetanus-prone wounds, tetanus immunoglobulin of human origin (‘HTIG’) should be used in addition to wound toilet, antibiotic treatment and, where appropriate, adsorbed tetanus vaccine (for details see Adsorbed tetanus).

Varicella-zoster immunoglobulin (VZIG) is recommended for individuals who are at risk of severe varicella and who have no antibodies to varicella-zoster virus and who have significant exposure to chickenpox or herpes zoster. Those at increased risk include neonates of women who develop chickenpox 7 days before or 28 days after delivery, women exposed at any stage or pregnancy, and the immunosuppressed including those who have received corticosteroids in the previous 3 months at the following dose equivalents of prednisolone: children 2mg/kg daily for at least 1 week or 1mg/kg daily for 1 month; adults about 40 mg daily for more than 1 week
Varicella vaccine is available on a named-patient basis from SmithKline Beecham or Pasteur Merieux.

Cytomegalovirus immunoglobulin (available on a named-patient basis from Grifols as Alphaglobin CMV\(^{(c)}\)) is indicated for prophylaxis in patients receiving immunosuppressive treatment.

- Hepatitis B
Hepatitis B Immunoglobulin (see notes above
Dose: By intramuscular injection (as soon as possible after exposure), Adult 500 units. Child under 4 years 200 units. 5 –9 years; 300 units. Neonate; 200 units as soon as possible after birth.

- Rabies
Rabies Immunoglobulin (Antirabies Immunoglobulin Injection). See notes above
Dose: 20units/kg, half by intramuscular injection and half by infiltration around wound.

- Tetanus
Tetanus Immunoglobulin (Antitetanus Immunoglobulin Injection). See notes above
Dose: By intramuscular injection, prophylactic; 250 units, increased to 500 units if more than 24 hours have elapsed or there is risk of heavy contamination.
Therapeutic, 150 units/kg (multiple sites)
Tetabulin \(^{\text{(immuno)}}\)
Tetanus immunoglobulin.
Dose: by intramuscular injection, prophylactic, 250 units, increased to 500 units if wound older than 12 hours or if risk of heavy contamination or if patient weighs more than 90 kg: second dose of 250 units given after 3-4 weeks if patient immunosuppressed or if active immunisation with tetanus vaccine contra-indicated.
Therapeutic, 30-300 units/kg

Tetanus immunoglobulin for intravenous use
Used for proven or suspected clinical tetanus.
Dose: by intravenous infusion, 5000-10 000 units

- Varicella-Zoster
Varicella-Zoster Immunoglobulin (Antivaricella-zoster Immunoglobulin) See notes
Anti-D (Rh0) immunoglobulin

Anti-D (Rh0) immunoglobulin is available to prevent a rhesus-negative mother from forming antibodies to foetal rhesus-positive cells which may pass into the maternal circulation. The objective is to protect any subsequent child from the hazard of haemolytic disease of the new born. Anti-D immunoglobulin should be administered following any sensitising episode (e.g. abortion, miscarriage and birth); it should be injected within 72 hours of the episode but even if a longer period has elapsed it may still give protection and should be administered. The dose of anti-D immunoglobulin is determined according to the level of exposure to rhesus-positive blood.

**Note.** Rubella vaccine may be administered in the postpartum period simultaneously with anti-D (Rh0) immunoglobulin injection providing separate syringes are used and the products are administered into contralateral limbs. If blood is transfused, the antibody response to the vaccine may be inhibited and test for antibodies should be formed after 8 weeks and the subject revaccinated if necessary.

**MMR vaccine should not be given within 3 months of an injection of anti-D (Rh0) immunoglobulin injection.**

**Dose:** By deep intramuscular injection, prophylaxis (as soon as possible—not later than 10 days after exposure), child up to 5 years; 250mg. 6-10 years; 500mg. 11-14 years; 750mg. Over 15 years; 1g. second dose required if further exposure occurs after 3 weeks.

**Note.** No evidence that effective in treatment of severe disease. An intravenous preparation of normal immunoglobulin (see Intravenous Therapy) may be used to provide an immediate source of antibody.

---

### Partobulin® (immuno)

Anti-D (Rh0) immunoglobulin 1250 units/ml. 1-ml prefilled syringe.

**Dose:** By intramuscular injection, to rhesus-negative woman for prevention of Rh0(D) sensitisation.

Following abortion, miscarriage or birth or rhesus-positive infant, 1250 units immediately or within 72 hours; for transplacental bleed in excess of 25ml foetal blood (% of foetal erythrocytes), 5000 units (or 50 units per ml foetal blood).

Following any potentially sensitising episode (e.g. amniocentesis) 1250 units immediately or within 72 hours.

Following Rh(D) incompatible blood transfusion, at least 50 – 100 units per ml transfused rhesus-positive blood. Antenatal prophylaxis, 1250 units may be given at weeks 28 and 34 of pregnancy; a further dose is still needed immediately or within 72 hours of delivery.

**Interferons**

**Interferon gamma-1b** is indicated for chronic granulomatous disease to reduce the frequency of serious infection.

**Interferon gamma-1b** (Immune interferon)

**Indications:** Adjunct to antibiotics to reduce frequency of serious infection in patients with chronic granulomatous disease

**Side effects:** Fever, headache, chills, myalgia, fatigue; nausea, vomiting, arthralgia, rashes and injection-site reactions reported.

**Caution:** Severe hepatic or renal impairment; seizure disorders or compromised central nervous system function; pre-existing cardiac disease (including ischaemia, congestive heart failure, and arrhythmias); monitor before and during treatment: haematological tests (including full blood count, differential white cell count, and platelet count), blood chemistry tests (including renal and liver function tests) and urinalysis.

**Driving:** May impair ability to drive or operate machinery; effects may be enhanced by alcohol.

**Immukin®** (Boehringer Ingelheim)

Injection, recombinant human interferon gamm-1b 200 micrograms/ml.

**Dose:** by subcutaneous injection, 50 micrograms/m² 3 times a week; patients with body surface area of 0.5m² or less, 1.5 micrograms/kg 3 times a week: not yet recommended for children under 6 months.

---

### 15.6 International travel

No particular immunisation is required for travellers to the United States, Europe, Australia, or New Zealand although all travellers should have immunity to tetanus and poliomyelitis (and childhood immunisations should be up to date). In Non-European areas surrounding the Mediterranean, in Africa, the Middle East, Asia, and South America, certain special pre-caution are

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### Immunological products and vaccines

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**15.5.2** Anti-D (Rh0) immunoglobulin

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**Partobulin® (immuno)**

Anti-D (Rh0) immunoglobulin 1250 units/ml. 1-ml prefilled syringe.

**Dose:** By intramuscular injection, to rhesus-negative woman for prevention of Rh0(D) sensitisation.

Following abortion, miscarriage or birth or rhesus-positive infant, 1250 units immediately or within 72 hours; for transplacental bleed in excess of 25ml foetal blood (% of foetal erythrocytes), 5000 units (or 50 units per ml foetal blood).

Following any potentially sensitising episode (e.g. amniocentesis) 1250 units immediately or within 72 hours.

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**Caution:** Severe hepatic or renal impairment; seizure disorders or compromised central nervous system function; pre-existing cardiac disease (including ischaemia, congestive heart failure, and arrhythmias); monitor before and during treatment: haematological tests (including full blood count, differential white cell count, and platelet count), blood chemistry tests (including renal and liver function tests) and urinalysis.

**Driving:** May impair ability to drive or operate machinery; effects may be enhanced by alcohol.

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**Dose:** by subcutaneous injection, 50 micrograms/m² 3 times a week; patients with body surface area of 0.5m² or less, 1.5 micrograms/kg 3 times a week: not yet recommended for children under 6 months.
Immunological products and vaccines

15

required.

Long term travellers to areas that have high incidence of poliomyelitis or tuberculosis should be immunised with the appropriate vaccine; in the case of poliomyelitis previously immunised adults may be given a booster dose of oral poliomyelitis vaccine. BCG immunisation is recommended for travellers proposing to stay for longer than one month (or in close contact with the local population) in Asia, Africa, or Central and South America; it should preferably be given three months or more before departure.

Yellow Fever immunisation is recommended for travel to much of Africa and South America. Many countries require an International Certificate of Vaccination for individuals arriving from, or who have been travelling through endemic areas, whilst other countries require a certificate from all entering travellers. Immunisation against meningococcal meningitis is recommended for a number of areas of the world. (for details see 15.4.13).

Protection against hepatitis A is recommended for travellers to high risk areas. Hepatitis A vaccine (see 15.4.8.) is preferred particularly for frequent travellers or for stays longer than 3 months. Normal immunoglobulin can be used in as an alternative for short or infrequent travel. Those who require immunisation less than 10 days before departure may be given the single dose vaccine plus normal immunoglobulin at a different injection site. Administration of normal immunoglobulin at the same time as the vaccine, at different injection sites, does not affect rate of seroconversion but the level of antibody may be reduced (see also 15.5.1.)

Hepatitis B vaccine is recommended for those travelling to areas of high prevalence who intend to seek employment as health care workers or who plan to remain there for lengthy periods and who may therefore be at increased risk of acquiring infection as a result of medical or dental procedures carried out in those Countries. Short term tourists or business travellers are not generally at increased risk of infection but may place themselves at risk by their sexual behaviour when abroad.

Prophylactic immunisation against rabies is recommended for travellers to enzootic areas on long journeys to remote areas out of reach of immediate medical attention.

Typhoid vaccine is indicated for travellers to those countries where typhoid is endemic but the vaccine has no substitute for personal preCaution. Food should be freshly prepared and hot, and uncooked vegetables (including green salads) should be avoided. Only fruits which can be peeled should be eaten. Only suitable bottled water or tap water that has been boiled or treated with sterilising tablets should be used for drinking. This advice applies to cholera and other diarrhoeal diseases, including cholera vaccine has little value in preventing infections and should not be given for international travel.
16 General treatment of poisoning

Antidotes

Chloroquine overdosage
Corrosive substances
Some commonest poisons in Zambia are organophosphates, drug injection (e.g. chloroquine, septrin, paracetamol), alcohol, carbon monoxide.
All cases of poisoning or suspected poisoning must be admitted to a Health facility. Most cases of poisoning do not require specific antidotes or active removal of the poison. Most patients must be treated symptomatically.

Only few poisons like opioids, paracetamol and iron require specific antidotes.

16.1 Antidotes

ACETYLCYSTEINE

Presentation: Injection containing 200mg/ml of acetylcysteine in ampoules of 10 ml
Indications: Paracetamol overdose
Dose: intravenous infusion initially 150mg/kg in 200 ml over 15 minutes, followed by 50mg/kg in 500ml over 4 hours, then 100mg/kg in 1000ml over 16 hours.
Side effects: Rashes, anaphylaxis, nausea and vomiting, bronchospasm
Caution: Asthma, in elderly patients with severe respiratory insufficiency.

METHIONINE

Presentation: Tablets containing 250mg methionine
Indications: Paracetamol overdose.
Dose: Adult; 2.5g initially, followed by three further doses of 2.5g every 4 hours.
Child; 1g every 4 hours for 4 doses
Side effects: Nausea, vomiting, drowsiness and irritability
Caution: May precipitate hepatic encephalopathy in patients with established liver disease.

16.2 Chloroquine overdosage

Prompt treatment
Induce emesis
Empty stomach by aspiration or lavage
Administer activated charcoal
Induce diuresis in doses of up to 8g daily by mouth to enhance urinary excretion.
Ringer injection to counter depressant effects on the heart.

6.3 Corrosive substances

Do not induce vomiting in case of ingestion of corrosive substances (like acid, petroleum products or gastric lavage).
## General treatment of poisoning

<table>
<thead>
<tr>
<th>Vaccines</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatitis B+</strong></td>
<td></td>
</tr>
<tr>
<td>Hep B-1 (EPI)</td>
<td></td>
</tr>
<tr>
<td>Diphtheria, Tetanus toxoids &amp; Pertussis</td>
<td></td>
</tr>
<tr>
<td>vaccine†</td>
<td></td>
</tr>
<tr>
<td><strong>Haemophilus influenzae type b</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Poliovirus++</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Measles, mumps, rubella $$</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Measles alone</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Varicella zoster virus</strong></td>
<td></td>
</tr>
</tbody>
</table>

### Dose Schedule

<table>
<thead>
<tr>
<th>Age</th>
<th>Birth</th>
<th>1 mo</th>
<th>2 mos.</th>
<th>4 mos.</th>
<th>6 mos.</th>
<th>12 mos.</th>
<th>15 mos.</th>
<th>18 mos.</th>
<th>4-6 years</th>
<th>11-12 years</th>
<th>14-16 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hep B-1 (EPI)</strong></td>
<td></td>
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<tr>
<td><strong>DTP</strong></td>
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<tr>
<td><strong>Hep B-2</strong></td>
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</tr>
<tr>
<td><strong>DTP (EPI)</strong></td>
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<tr>
<td><strong>Hep B-3</strong></td>
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<tr>
<td><strong>DTP (DtaP at &gt;/=15 mos.)</strong></td>
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<tr>
<td><strong>Hib</strong></td>
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<td><strong>OPV</strong></td>
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<tr>
<td><strong>MMR</strong></td>
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<tr>
<td><strong>Measles at 9 mos (EPI)</strong></td>
<td></td>
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<tr>
<td><strong>Varicella</strong></td>
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<tr>
<td><strong>Varicella</strong>*</td>
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</tr>
</tbody>
</table>

† EPI: Expanded Programme of Immunisation

**Hep B-1 (EPI)**

- 1st dose: Birth
- 2nd dose: 1 month
- 3rd dose: 6 months
- Booster: 12 months

**DTP or DtaP**

- 1st dose: Birth
- 2nd dose: 4 months
- 3rd dose: 11 months
- Booster: 15 months

**OPV**

- 1st dose: Birth
- 2nd dose: 2 months
- 3rd dose: 4 months

**MMR**

- 1st dose: Birth
- 2nd dose: 12 months

**Hib**

- 1st dose: Birth
- 2nd dose: 6 months

**Measles, Varicella**

- 1st dose: 12 months
- 2nd dose: 15 months (for measles)
- 3rd dose: 15 months (for varicella)

**Td**

- 1st dose: 15 months

**Or MMR**

- 1st dose: 15 months
APPENDIX 1

TABLE 1 INFANT/CHILD IMMUNISATION TABLE

Key to table 1
+ If mother HBsAg neg.’ recommended 1st dose is 2.5ug of Recombivax HB (Smith Kline Beecham). If mother HBsAg pos.’ give infant 0.5ml HBIG within 12 hours of birth and either 5ug of Recombivax HB or 10ug Engerix-B at separate site.

1 Acellular pertussis vaccine licensed for 4th and 5th dose for children aged >15 months.

** 3 licensed H. influenza protein conjugate vaccines. A 4th, available in 1997, combines Haemophilus B with Hepatitis B.
++ Inactivated polio vaccine acceptable alternative for patients with congenital or acquired immunodeficiency.
$$ Second dose anytime > 1 month after 1st dose.
11 Anytime after age 12 months. If no reliable history of chickenpox, vaccinate at age 11-12 years.

<table>
<thead>
<tr>
<th>AGE GROUP (Years)</th>
<th>Td2</th>
<th>Measles</th>
<th>Mumps</th>
<th>Rubella</th>
<th>Influenza</th>
<th>Pneumococcal</th>
<th>Hepatitis B4</th>
<th>Individuals at high risk regardless of age</th>
<th>See table for post-exposure Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 - 24</td>
<td>xx</td>
<td>xx</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>25 - 64</td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
<td>x</td>
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<td></td>
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<tr>
<td>&gt;65</td>
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</tr>
</tbody>
</table>

Table 2
Key to table 2

2. Td = tetanus + diphtheria toxoids, adsorbed for adult use (contains 5fl units tetanus + 2fl units diphtheria vs childhood vaccine, which contains 5fl units tetanus + 12.5 Fl u diphtheria).
3. Indicated for persons born in 1957 or later. Serotest and immunize especially during outbreaks.
4. Screen all pregnant women for HBsAg (give HBIG and vaccine to infants born to HBsAg-positive mothers). Those at h exposure, other sexually transmitted diseases, household and sexual contacts or HBV carriers, health care and public safety workers with exposure to blood, residents and staff or institutions for retarded, haemodialysis patients, recipients of Factor VII or IX concentrates, morticians.

ADMINISTRATION SCHEDULE FOR ABOVE PLUS OTHER SELECTED VACCINES ($)

Hepatitis A (Havrix, Vagta): 1.0ml IM and repeat in 6 – 12 months. Antibodies detectable after 15 days; use immune serum globulin. 0.02ml/kg IM for immediate protection. Indication: for travellers to endemic areas. (Med. Letter 37:51, 1995; IDCP 5:122, 1996)

Hepatitis B (Engerix B, Recombivax HB): 3 doses; initial, 1 month later, 6 months after 1st. Give IM in deltoid (not in buttocks), use 1 ½ inch needle; give SC only in patients at risk of bleeding (hemophiliacs). (Seroprotection associated with titers – 10mIU/ml.)

Influenza (killed virus): One dose (0.5ml) IM. Annual reimmunization with current vaccine recommended.

Measles (Attenuvax) (live virus vaccine): Unless contraindicated. $ one dose (0.5ml) sc preferably in outer aspect upper arm. Booster not required.

Measles + Rubella + Mumps (MMR) (live virus): Unless contraindicated $ (do not give to pregnant women), one dose (0.5ml) sc as with measles. Booster not required.

Pneumococcal (Pneumovax 23, Pnu-Immune 23) (pure antigens, 23): One dose (0.5ml) sc. Booster not required except possibly individuals at high risk (nephrotic syndromes, renal failure, transplant recipients, splenectomy patients, HIV positive who received vaccine > 6 years before).

Td (toxoids, not live): Primary: Two doses IM at least 4 weeks apart, 3rd dose 6 – 12 months after 2nd. Booster: every 10 years.

Typhoid (Typhim Vi): A single IM dose of 25micrograms yields 95% seroconversion. Minimal side effects. For travellers and lab. Workers.

Varicella (Varivax): 0.5ml sc. Repeat 4 – 8 weeks later. For susceptible adolescents/adults who are: (1) health care workers (2) susceptible household contact immunocompromised persons, (3) work in schools/day care centres, (4) College students/military, (5) non-pregnant women of child bearing age.

$ Review package insert for specific product being administered.
## Table 3

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Tetanus Prone</th>
<th>Non-Tetanus Prone</th>
<th>History of Tetanus Immunisation</th>
<th>Tetanus-Prone Wound</th>
<th>Non-Tetanus Prone Wound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of wound</td>
<td>&gt; 6 hours</td>
<td>&lt;= 6 hours</td>
<td>Unknown or &lt; 3 doses</td>
<td>TD1 2</td>
<td>TIG</td>
</tr>
<tr>
<td>Configuration</td>
<td>Stellate, avulsion</td>
<td>Linear</td>
<td>3 or more doses</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Depth</td>
<td>&gt; 1 cm</td>
<td>&lt;= 1 cm</td>
<td>No 3</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Mechanisms of injury</td>
<td>Missile, crush burn,</td>
<td>Sharp surface (glass, knife)</td>
<td>No 4</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

1. Td = Tetanus & Diphtheria toxoids absorbed (adult)  
   TIG = Tetanus immunoglobulin (human)  
2. Yes if wound > 24 hours old.  
   For children < 7 years, DPT (DT if pertussis vaccine contraindicated;  
   For persons > /= 7 years, TD preferred to tetanus toxoids alone.  
3. Yes if > 5 years since last booster  
4. Yes if > 10 years since last booster.  

(from ACS Bull, 69:22, 23, 1984, No. 10)
### RABIES POST-EXPOSURE PROPHYLAXIS (1)

All Wounds should be cleaned immediately and thoroughly with soap and water.

#### Table 4

<table>
<thead>
<tr>
<th>Animal Type</th>
<th>Evaluation and disposition of Animal</th>
<th>Recommendations for Prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dogs, cats</td>
<td>Health and available for 10 day observation.</td>
<td>Do not start unless animal develops symptoms, then immediately begin HRIG + HDCV or RVA.</td>
</tr>
<tr>
<td></td>
<td>Rabid or suspected rabid</td>
<td>Immediate vaccination.</td>
</tr>
<tr>
<td></td>
<td>Unknown (escaped)</td>
<td>Consult public health officials.</td>
</tr>
<tr>
<td>Skunks, hyenas, bats, foxes, most carnivores</td>
<td>Regard as rabid</td>
<td>Immediate vaccination.</td>
</tr>
<tr>
<td>Livestock; rabbits, hares, hamsters, guinea pigs,</td>
<td></td>
<td>Almost never require anti-rabies treatment.</td>
</tr>
<tr>
<td>rats, mice, monkeys</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Post-Exposure Immunisation Schedule (Unvaccinated Persons)

<table>
<thead>
<tr>
<th>Immunizing Product</th>
<th>Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRIG</td>
<td>20 IU/kg, if feasible infiltrate ½ of dose around the wound(s), the rest IM in gluteal area. Not in same syringe as vaccine. (3)</td>
</tr>
<tr>
<td>Vaccine: HDCV or RVA</td>
<td>1.0 ml IM in deltoid area (only acceptable site in adults and older children; younger children, outer aspect of thigh) (never in gluteal area). Days 0, 3, 7, 14, 28.</td>
</tr>
</tbody>
</table>

#### Key to Table 4

2. HRIG = Human rabies immunoglobulin (Hyperab, Imogan Rabies);
   HDCV = Human diploid cell vaccine, rabies (inactivated) Imovax Rabies;
   RVA = Rabies vaccine absorbed (inactivated), liquid (should not be used intradermally)
3. In reported post-exposure treatment failure, only identified deficiency was failure to infiltrate wound(s) with HRIG *(CID 22:228, 1996)*
HEPATITIS B POST-EXPOSURE PROPHYLAXIS FOR ADULTS (Percutaneous, Permucosal, Sexual)

Table 5

<table>
<thead>
<tr>
<th>EXPOSED PERSON</th>
<th>EXPOSURE SOURCE</th>
<th>HBsAg+</th>
<th>HBsAg</th>
<th>Status Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unvaccinated</td>
<td></td>
<td></td>
<td></td>
<td>Do HBsAg test on source of exposure</td>
</tr>
<tr>
<td>HBIG 5.0ml IM*++</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HB vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test exposed for anti-HBs, if &gt;/= 10 mIU/ml no treatment, if &lt; 10mIU/ml: HBIG + 1 dose HB vaccine</td>
<td></td>
<td></td>
<td>No treatment</td>
<td>Test exposed for anti-HBs if &lt;10mIU/ml give 1 dose HB vaccine, if &gt;/= 10 no treatment.</td>
</tr>
</tbody>
</table>

APPENDIX 2

DRUG INTERACTIONS

Interactions can occur either between one drug and another drug or between a drug and food or drink. When two drugs have similar side effects, they can also interact. The interaction may be potentiation or antagonism of one drug by another or occasionally some other effect. Drug interaction may be pharmacodynamic or pharmacokinetic.

Pharmacodynamic interactions
These are interactions between drugs that have similar or antagonistic pharmacological effects or side effects. This may be due to competition at receptor sites or occurs between drugs acting on the same physiological system.

Pharmacokinetic interactions
These interactions occur when one drug alters the absorption, distribution, metabolism or excretion of another, thus increasing or decreasing the amount of drug available to produce its pharmacological effects. Pharmacokinetic interactions occurring with one drug in a related group cannot be assumed to occur with related drugs unless their pharmacokinetic properties are known to be similar. Pharmacokinetic interactions are of several types:

Affecting absorption: The rate of absorption or the total amount of drug absorbed can both be altered by drug interactions. Reductions in the total amount absorbed however, may result in ineffective therapy. Delayed absorption however, is rarely of clinical importance unless high peak plasma concentrations are required.

Due to changes in protein binding: Most drugs are loosely bound to plasma protein. Protein binding sites are non-specific and one drug can displace another thereby increasing its proportion free to diffuse from plasma to its site of action. Displacement rarely produces more than transient potentiation because this increased concentration of free drug results in an increased rate of elimination. Displacement from protein binding plays a part in the potentiation of warfarin by phenylbutazone, sulphonamides and tolbutamide, but the importance of these interactions is due mainly to the fact that warfarin metabolism is also inhibited.

Affecting metabolism: Many drugs are metabolized in the liver. Induction of the hepatic microsomal enzyme system by one drug can gradually increase the rate of metabolism of another, resulting in lower plasma concentrations and a reduced effect. On withdrawal of the inducer, plasma concentrations increase and toxicity may occur. Barbiturates, griseofulvin, most antiepileptics and rifampicin are the most important enzyme inducers in man. Drugs affected include warfarin and the oral contraceptives.

Affecting renal excretion: Drugs eliminated through the kidney by both glomerular filtration and active tubular secretion. Competition occurs between those that share active transport mechanisms in proximal tubule. Thus probenecid delays the excretion of any drugs including penicillins and some cephalosporins, indomethacin and dapsone. Aspirin may increase the toxicity of methotrexate by a similar mechanism.

Many drug interactions are harmless, and the severity of an interaction varies from one patient to another. Drugs with a small therapeutic ratio (e.g. phenytoin) and those that require careful control of dosage (e.g. anticoagulants, antihypertensives and antidiabetics) are most often involved. Patients at increased risk from drug interactions include the elderly and those with impaired renal or hepatic function.
## DRUG INTERACTION TABLE

<table>
<thead>
<tr>
<th>AFFECTED DRUG</th>
<th>INTERACTS WITH</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiabetics</td>
<td>Analgesics</td>
<td>NSAIDs may enhance effects of sulphonylureas</td>
</tr>
<tr>
<td></td>
<td>Antibacterials</td>
<td>Chloramphenicol, co-trimoxazole, 4-quinolones, sulphonamidesand</td>
</tr>
<tr>
<td></td>
<td></td>
<td>trimethoprim enhance effect of sulphonylureas</td>
</tr>
<tr>
<td></td>
<td>Antifungals</td>
<td>Fluconazole and miconazole increase plasma concentrations of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>sulphonylureas.</td>
</tr>
<tr>
<td></td>
<td>Uricosurics</td>
<td>Sulphinpyrazone enhances effect of sulphonylureas</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>Anaesthetics</td>
<td>Anaesthetics enhance hypotensive effect of ACE inhibitors</td>
</tr>
<tr>
<td></td>
<td>Analgesics</td>
<td>Antagonism of hypotensive effect</td>
</tr>
<tr>
<td></td>
<td>Cyclosporin</td>
<td>Increased risk of hypokalaemia</td>
</tr>
<tr>
<td></td>
<td>Diuretics</td>
<td>Enhanced hyporensive effect which can be extreme.</td>
</tr>
<tr>
<td></td>
<td>Lithium</td>
<td>Reduced excretion of lithium</td>
</tr>
<tr>
<td></td>
<td>Potassium salts</td>
<td>Hyperkalaemia</td>
</tr>
<tr>
<td>Amantadine</td>
<td>Alcohol</td>
<td>Enhanced effects of extrapyramidal side effects.</td>
</tr>
<tr>
<td></td>
<td>Antimuscarinics</td>
<td>Enhanced effects of antimuscarinics</td>
</tr>
<tr>
<td></td>
<td>Antiparkinsonism agents</td>
<td>Enhanced effects of antiparkinsonism agents</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Antifungals</td>
<td>Increased risk of nephrotoxicity with amphoterin cin</td>
</tr>
<tr>
<td>(cont.)</td>
<td>Cyclosporine</td>
<td>Increased risk of nephrotoxicity</td>
</tr>
<tr>
<td></td>
<td>Diuretics</td>
<td>Increased risk of ototoxicity with loop diuretics.</td>
</tr>
<tr>
<td></td>
<td>Non polarising muscle relaxants</td>
<td>Effect of non polarising muscle relaxants enhanced</td>
</tr>
<tr>
<td></td>
<td>Radiographic contrast</td>
<td>Increased risk of nephrotoxicity</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>Increased risk of ototoxicity and nephrotoxicity</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Beta-blockers (Note: systemic absorption following topical application possible)</td>
<td>Anaesthetics</td>
<td>Enhanced hypotensive effect. Increased risk of bupivacaine toxicity with propranolol..</td>
</tr>
<tr>
<td></td>
<td>Antiarrhythmics</td>
<td>Increased risk of myocardial depression and bradycardia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased risk of lignocaine toxicity with propranolol</td>
</tr>
<tr>
<td></td>
<td>Antihypertensives</td>
<td>Enhanced hypotensive effect. Increased risk of withdrawal hypertension with clomidine</td>
</tr>
<tr>
<td></td>
<td>Calcium channel blockers</td>
<td>Increased risk of bradycardia and AV block with diltiazem.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Occasionally severe hypotension and heart failure with nifedipine.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asystole, severe hypotension and heart failure with verapamil.</td>
</tr>
<tr>
<td></td>
<td>Sympathomimetics</td>
<td>Severe hypertension with adrenaline and noradrenaline.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe hypertension also possible with sympathomimetics contained in anorectics and cough and cold remedies</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>-------------------------------------</td>
<td>-----------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Calcium channel blockers (Note: Grapefruit increases plasma concentrations of dihydopyridine calcium channel blockers except amlodipine)</td>
<td>Anaesthetics</td>
<td>Verapamil increases hypotensive effect of general anaesthetics and risk of AV delay.</td>
</tr>
<tr>
<td>Calcium channel blockers (cont.)</td>
<td>Antiarrhythmics</td>
<td>Amiodarone-induced risk of bradycardia, AV block. Myocardial depression increased by diltiazem and verapamil. Plasma concentration of quinidine reduced by nifedipine. With verapamil raised plasma concentration of quinidine which may cause extreme hypotension.</td>
</tr>
<tr>
<td></td>
<td>Antihypertensives</td>
<td>Enhanced hypotensive effect. Increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers such as prazosin.</td>
</tr>
<tr>
<td></td>
<td>Beta-blockers</td>
<td>Increased risk of bradycardia and AV block with diltiazem. Occasionally severe hypotension and heart failure with nifedipine. Asystole, severe hypotension and heart failure with verapamil.</td>
</tr>
<tr>
<td></td>
<td>Cardiac glycosides</td>
<td>Plasma concentration of digoxin increased by diltiazemnicardipine, verapamil and possibly nifedipine. Increased AV block and bradycardia with verapamil.</td>
</tr>
<tr>
<td></td>
<td>Cyclosporin</td>
<td>Plasma concentrations of cyclosporin increased by diltiazem, nicardipine and verapamil.</td>
</tr>
<tr>
<td></td>
<td>Theophylline</td>
<td>Diltiazem, verapamil and possibly other calcium channel blockers enhance the effect of theophylline.</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>----------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Cardiac glycosides (cont.)</td>
<td>Antiarrhythmics</td>
<td>Plasma concentration of digoxin increased by amiodarone and quinidine (halve maintenance dose of digoxin).</td>
</tr>
<tr>
<td></td>
<td>Antifungals</td>
<td>Increased toxicity of hypokalaemia occurs with amphotericin. Plasma concentration of digoxin increased by itraconazole.</td>
</tr>
<tr>
<td></td>
<td>Antimalarials</td>
<td>Quinine and possibly chloroquine raises plasma concentration of digoxin (maintenance dose of digoxin should then be halved). Possible increased risk of bradycardia with mefloquine.</td>
</tr>
<tr>
<td></td>
<td>Calcium channel blockers</td>
<td>Plasma concentration of digoxin increased by diltiazem, nicardipine, verapamil and possibly nifedipine. Increased AV block and bradycardia with verapamil.</td>
</tr>
<tr>
<td></td>
<td>Diuretics</td>
<td>Increased toxicity of hypokalaemia occurs with acetazolamide, loop diuretics and thiazides. Effects of digoxin enhanced by spironolactone.</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Oral anticoagulants</td>
<td>Effects of warfarin and nicoumalone enhanced by cefamandole and possibly others.</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
<td>Disulfiram like reactions (tachycardia, flushing, diarrhoea) with cefamandole</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Phenobarbitone</td>
<td>Chloramphenicol may be less effective due to lower levels in the body</td>
</tr>
<tr>
<td></td>
<td>Rifampicin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iron salts, vitamin B₁₂</td>
<td>Response to vitamin B₁₂ reduced</td>
</tr>
<tr>
<td>Cotrimoxazole and sulphonamides</td>
<td>Anticoagulants</td>
<td>Effect of nicoumalone and warfarin enhanced.</td>
</tr>
<tr>
<td></td>
<td>Antidiabetics</td>
<td>Effect of sulphonylureas enhanced</td>
</tr>
<tr>
<td></td>
<td>Anticonvulsants</td>
<td>Antifolate effect and plasma concentration of phenytoin increased.</td>
</tr>
<tr>
<td></td>
<td>Antimalarials</td>
<td>Increased risk of antifolate effect with pyrimethamine.</td>
</tr>
<tr>
<td></td>
<td>Cyclosporin</td>
<td>Increased risk of nephrotoxicity</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------------------</td>
<td>-------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Carbamazepine</td>
<td>Increased levels of carbamazepine resulting in nausea, vomiting, ataxia</td>
</tr>
<tr>
<td></td>
<td>Theophyllines</td>
<td>Increased serum levels of theophyllines resulting in nausea, vomiting, seizures, apnea</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td>Enhanced effects of corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Clozapine</td>
<td>Increased serum levels of clozapine, CNS toxicity</td>
</tr>
<tr>
<td></td>
<td>Cyclosporine</td>
<td>Increased serum levels of cyclosporine</td>
</tr>
<tr>
<td></td>
<td>Digoxin</td>
<td>Increased serum levels of digoxin</td>
</tr>
<tr>
<td></td>
<td>Cisapride</td>
<td>Peripheral ischemia</td>
</tr>
<tr>
<td></td>
<td>Ergot alkaloids</td>
<td>May increase prothrombin time</td>
</tr>
<tr>
<td></td>
<td>Oral anticoagulants</td>
<td>Increased levels of valproic acid</td>
</tr>
<tr>
<td></td>
<td>Valproic acid</td>
<td>Increased cardiotoxicity</td>
</tr>
<tr>
<td>Erythromycin (cont.)</td>
<td>Astemizole</td>
<td></td>
</tr>
<tr>
<td>Ethambutol</td>
<td>Aluminium salts</td>
<td>Absorption of ethambutol reduced</td>
</tr>
<tr>
<td>Ganciclovir</td>
<td>Probenecid</td>
<td>Metabolism of ganciclovir probably reduced (increased plasma half life)</td>
</tr>
<tr>
<td></td>
<td>Zidovudine</td>
<td>Increased toxicity (myelosuppression) of ganciclovir</td>
</tr>
<tr>
<td>Halofantrine</td>
<td>Chloroquine, mefloquine, quinine, Antiarrhythmics, Antidepressants, Antihistamines, Antipsychotics, Beta-blockers, Diuretics</td>
<td>Halofantrine in combination with any of these drugs is dangerous as fatal cardiac arrhythmias can occur. If patient has taken mefloquine or chloroquine as prophylaxis, do not use halofantrine to treat an attack of malaria</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Antacids</td>
<td>Absorption of isoniazid reduced</td>
</tr>
<tr>
<td></td>
<td>Antiepileptics</td>
<td>Metabolism of carbamazepine, ethoxusimide and phenytoin inhibited resulting in enhanced effects</td>
</tr>
<tr>
<td></td>
<td>Narcotic analgesics</td>
<td>Prolonged effect of narcotic analgesics</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------</td>
<td>---------</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>Antiepileptics</td>
<td>Antagonism of anticonvulsant effect</td>
</tr>
<tr>
<td></td>
<td>Beta-adrenergic blockers, calcium channel blockers, quinidine, quinine.</td>
<td>Increased risk of bradycardia</td>
</tr>
<tr>
<td></td>
<td>Halofantrine</td>
<td>Increased risk of ventricular arrhythmias</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>Antiepileptics</td>
<td>Metronidazole inhibits metabolism of phenytoin increasing plasma phenytoin concentration. Phenobarbitone increases metabolism of metronidazole</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
<td>Disulfiram like reaction</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>Epileptic like seizures</td>
</tr>
<tr>
<td></td>
<td>Disulfiram</td>
<td>Acute toxic psychosis</td>
</tr>
<tr>
<td></td>
<td>Oral anticoagulants</td>
<td>Effect of warfarin and nicoumalone enhanced</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>Probenecid</td>
<td>Excretion of nitrofurantoin reduced increasing risk of side effects</td>
</tr>
<tr>
<td></td>
<td>Antacids, magnesium salts</td>
<td>Nitrofurantoin may be less effective as it is not well absorbed.</td>
</tr>
<tr>
<td>Penicillins</td>
<td>Antacids</td>
<td>Decreased absorption of oral penicillins</td>
</tr>
<tr>
<td></td>
<td>Cytotoxics</td>
<td>Excretion of methotrexate reduced (therefore risk of toxicity)</td>
</tr>
<tr>
<td>Quinine</td>
<td>Antihistamines</td>
<td>Increased risk of ventricular arrhythmias with astemizole and terfenadine</td>
</tr>
<tr>
<td></td>
<td>Cimetidine</td>
<td>Increased plasma-quinine concentration.</td>
</tr>
<tr>
<td></td>
<td>Cardiac glycosides</td>
<td>Digoxin plasma concentration increased (halve digoxin maintenance dose)</td>
</tr>
<tr>
<td></td>
<td>Mefloquine</td>
<td>Increased risk of arrhythmias</td>
</tr>
<tr>
<td></td>
<td>Oral anticoagulants</td>
<td>Increased prothrombin time</td>
</tr>
<tr>
<td>AFFECTED DRUG</td>
<td>INTERACTS WITH</td>
<td>OUTCOME</td>
</tr>
<tr>
<td>---------------------</td>
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<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4-Quinolones</td>
<td>Anticoagulants</td>
<td>Enhanced effect of warfarin and nicoumalone with ciprofloxacin, nalidixic acid and norfloxacin.</td>
</tr>
<tr>
<td>4-Quinolones (cont.)</td>
<td>Antidiabetics</td>
<td>Effect of sulphonyureas enhanced</td>
</tr>
<tr>
<td></td>
<td>Cyclosporin</td>
<td>Increased risk of nephrotoxicity</td>
</tr>
<tr>
<td></td>
<td>Multivalent metallic cations (Ca, Al, Fe, Mg, Zn) including sucralfate, antacids, multivitamins</td>
<td>Absorption of ciprofloxacin, norfloxacin and ofloxacin reduced (50 - &gt; 90%)</td>
</tr>
<tr>
<td></td>
<td>Probenecid, loop diuretics</td>
<td>Excretion ciprofloxacin, nalidixic acid and norfloxacin reduced.</td>
</tr>
<tr>
<td></td>
<td>Theophyllines</td>
<td>Increased plasma theophylline concentration.</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Antacids</td>
<td>Absorption of rifampicin reduced</td>
</tr>
<tr>
<td></td>
<td>Anticoagulants</td>
<td>Accelerated metabolism of nicoumalone and warfarin resulting in suboptimal coagulation</td>
</tr>
<tr>
<td></td>
<td>Antidiabetics</td>
<td>Increased metabolism of chlorpropamide, tolbutamide and possibly other sulphonylureas resulting in reduced effect</td>
</tr>
<tr>
<td></td>
<td>Antiepileptics</td>
<td>Phenytoin metabolism increased (reduced plasma concentration)</td>
</tr>
<tr>
<td></td>
<td>Antifungals</td>
<td>Metabolism of fluconazole, itraconazole and ketoconazole increased (reduced plasma concentrations)</td>
</tr>
<tr>
<td></td>
<td>Antivirals</td>
<td>Increased metabolism of idinavir possibly saquinavir (reduced plasma concentrations)</td>
</tr>
<tr>
<td></td>
<td>Corticosteroids</td>
<td>Corticosteroid metabolism increased therefore replacement doses need to be increased.</td>
</tr>
<tr>
<td></td>
<td>Oral contraceptives</td>
<td>Contraceptives effect reduced and can result in spotting, pregnancy</td>
</tr>
<tr>
<td></td>
<td>Cyclosporins</td>
<td>Accelerated metabolism of cyclosporin resulting in reduced effect</td>
</tr>
<tr>
<td></td>
<td>Theophyllines,</td>
<td>Metabolism of theophylline increased</td>
</tr>
<tr>
<td>Rifampicin (cont.)</td>
<td>Quinidine</td>
<td>Metabolism of quinidine enhanced (plasma-quinidine concentration reduced)</td>
</tr>
</tbody>
</table>
APPENDIX 3

HAEMATOLOGICAL REFERENCE VALUES FOR NORMAL INFANTS AND CHILDREN

<table>
<thead>
<tr>
<th></th>
<th>At birth (Full term)</th>
<th>Day 3</th>
<th>1 month</th>
<th>2 - 6 months</th>
<th>2 - 6 years</th>
<th>6 - 12 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Red Blood Cell Count</strong></td>
<td>6.0±1.0</td>
<td>5.3±1.3</td>
<td>4.2±1.2</td>
<td>3.0±0.8</td>
<td>4.6±0.7</td>
<td>4.6±0.6</td>
</tr>
<tr>
<td><strong>Haemoglobin (g/L)</strong></td>
<td>165±30</td>
<td>185±40</td>
<td>140±30</td>
<td>115±20</td>
<td>125±15</td>
<td>135±20</td>
</tr>
<tr>
<td><strong>Packed cell volume/haematocrit</strong></td>
<td>0.54±0.10</td>
<td>0.56±0.11</td>
<td>0.43±0.12</td>
<td>0.35±0.07</td>
<td>0.37±0.03</td>
<td>0.40±0.05</td>
</tr>
<tr>
<td><strong>Mean cell volume (MCV) (fL)</strong></td>
<td>110±10</td>
<td>108±13</td>
<td>104±19</td>
<td>91±17</td>
<td>81±6</td>
<td>86±8</td>
</tr>
<tr>
<td><strong>Mean cell haemoglobin MCH (Pg)</strong></td>
<td>34±3</td>
<td>34±3</td>
<td>34±6</td>
<td>30±5</td>
<td>27±3</td>
<td>29±4</td>
</tr>
<tr>
<td><strong>Mean cell haemoglobin concentration (MCHC) (g/L)</strong></td>
<td>330±30</td>
<td>330±40</td>
<td>330±40</td>
<td>330±30</td>
<td>330±30</td>
<td>330±30</td>
</tr>
<tr>
<td><strong>Reticulocytes (%)</strong></td>
<td>2 - 5</td>
<td>1 - 4.5</td>
<td>0.3 - 1</td>
<td>0.4 - 1</td>
<td>0.2 - 2</td>
<td>0.2 - 2</td>
</tr>
<tr>
<td><strong>White blood cell count (x10^9/L)</strong></td>
<td>18±8</td>
<td>15±8</td>
<td>12±7</td>
<td>12±6</td>
<td>10±5</td>
<td>9±4</td>
</tr>
<tr>
<td><strong>Neutrophils (x10^9/L)</strong></td>
<td>3 - 10</td>
<td>2 - 8</td>
<td>3 - 16</td>
<td>4 - 10</td>
<td>6 - 9</td>
<td>1 - 5</td>
</tr>
<tr>
<td><strong>Lymphocytes (x10^9/L)</strong></td>
<td>0.7 - 1.5</td>
<td>0.5 - 1</td>
<td>0.3 - 1</td>
<td>0.1 - 1</td>
<td>0.1 - 1</td>
<td>0.1 - 1</td>
</tr>
<tr>
<td><strong>Monocytes (10^9/L)</strong></td>
<td>0.2 - 1</td>
<td>0.1 - 2.5</td>
<td>0.2 - 1</td>
<td>0.2 - 1</td>
<td>0.2 - 1</td>
<td>0.1 - 1</td>
</tr>
<tr>
<td><strong>Eosinophils (x10^9/L)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Expressed as mean +2 SD or 95% range
## HAEMATOLOGICAL REFERENCE RANGES FOR ADULTS

<table>
<thead>
<tr>
<th>TEST</th>
<th>NORMAL RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1</strong></td>
<td><strong>WBC (TOTAL)</strong></td>
</tr>
<tr>
<td><strong>2</strong></td>
<td><strong>WBC (DIFFERENTIAL)</strong></td>
</tr>
<tr>
<td></td>
<td>NEUTROPHILS</td>
</tr>
<tr>
<td></td>
<td>LYMPHOCYTES</td>
</tr>
<tr>
<td></td>
<td>MONOCYTES</td>
</tr>
<tr>
<td></td>
<td>EOSINOPHILS</td>
</tr>
<tr>
<td></td>
<td>BASOPHIL</td>
</tr>
<tr>
<td><strong>3</strong></td>
<td><strong>RBC</strong></td>
</tr>
<tr>
<td></td>
<td>MEN:</td>
</tr>
<tr>
<td></td>
<td>WOMEN:</td>
</tr>
<tr>
<td><strong>4</strong></td>
<td><strong>Hb</strong></td>
</tr>
<tr>
<td></td>
<td>MEN:</td>
</tr>
<tr>
<td></td>
<td>WOMEN:</td>
</tr>
<tr>
<td><strong>5</strong></td>
<td><strong>Hct (PVC) (Ratio)</strong></td>
</tr>
<tr>
<td></td>
<td>MEN:</td>
</tr>
<tr>
<td></td>
<td>WOMEN:</td>
</tr>
<tr>
<td><strong>6</strong></td>
<td><strong>MCV</strong></td>
</tr>
<tr>
<td><strong>7</strong></td>
<td><strong>MCH</strong></td>
</tr>
<tr>
<td><strong>8</strong></td>
<td><strong>MCHC</strong></td>
</tr>
<tr>
<td><strong>9</strong></td>
<td><strong>PLATELET COUNT</strong></td>
</tr>
<tr>
<td><strong>10</strong></td>
<td><strong>Prothrombin Time (PT)</strong></td>
</tr>
<tr>
<td><strong>11</strong></td>
<td><strong>Activated Partial Thromboplastin Time (APTT)</strong></td>
</tr>
<tr>
<td><strong>12</strong></td>
<td><strong>BLEEDING TIME (IVY’S METHOD)</strong></td>
</tr>
<tr>
<td><strong>13</strong></td>
<td><strong>CLOTTING TIME (TUBE METHOD)</strong></td>
</tr>
<tr>
<td><strong>14</strong></td>
<td><strong>RETICULOCYTE COUNT</strong></td>
</tr>
<tr>
<td><strong>15</strong></td>
<td><strong>ESR</strong></td>
</tr>
<tr>
<td></td>
<td>MEN:</td>
</tr>
<tr>
<td></td>
<td>MEN:</td>
</tr>
<tr>
<td></td>
<td>WOMEN:</td>
</tr>
<tr>
<td></td>
<td>WOMEN:</td>
</tr>
</tbody>
</table>
## HAEMATOLOGICAL REFERENCES RANGES DURING PREGNANCY AND OBSTETRIC DELIVERY

<table>
<thead>
<tr>
<th>TEST</th>
<th>PREGNANCY</th>
<th>DELIVERY</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC (TOTAL)</td>
<td>5.0 - 16.0 (x 10^9/L)</td>
<td>&lt;40.0 (x 10^9/L)</td>
</tr>
<tr>
<td>WBC (DIFFERENTIAL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NEUTROPHILS</td>
<td>2.5-14.0 (x 10^9/L)</td>
<td>&lt;36.0 (x 10^9/L)</td>
</tr>
<tr>
<td>LYMOPHOCYTES</td>
<td>Slightly lower than non-pregnant</td>
<td></td>
</tr>
<tr>
<td>MONOCYTES</td>
<td>&lt;0.1 (x 10^9/L)</td>
<td>Low</td>
</tr>
<tr>
<td>EOSINOPHILIS</td>
<td>&lt;0.02 (x 10^9/L)</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>BASOPHILIS</td>
<td>&lt;1%</td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>120-320 (x 10^9/L)</td>
<td>Raised post-partum</td>
</tr>
<tr>
<td>TEST</td>
<td>LOW LIMIT</td>
<td>HIGH LIMIT</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>Na⁺</td>
<td>134</td>
<td>144</td>
</tr>
<tr>
<td>K⁺</td>
<td>3.5</td>
<td>5.0</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>95</td>
<td>107</td>
</tr>
<tr>
<td>Urea</td>
<td>1.70</td>
<td>8.3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>63</td>
<td>120</td>
</tr>
<tr>
<td>Glucose (fasting)</td>
<td>3.5</td>
<td>5.5</td>
</tr>
<tr>
<td>Glucose (Random)</td>
<td>3.9</td>
<td>6.6</td>
</tr>
<tr>
<td>Uric acid</td>
<td>140</td>
<td>450</td>
</tr>
<tr>
<td>ALT/SGPT</td>
<td>5</td>
<td>37</td>
</tr>
<tr>
<td>AST/SGOT</td>
<td>5</td>
<td>36</td>
</tr>
<tr>
<td>ALP</td>
<td>36</td>
<td>275</td>
</tr>
<tr>
<td>GGT</td>
<td>7</td>
<td>52</td>
</tr>
<tr>
<td>LDH</td>
<td>0.0</td>
<td>460</td>
</tr>
<tr>
<td>ACP</td>
<td>2.5</td>
<td>5.2</td>
</tr>
<tr>
<td>CK/CPK</td>
<td>0.0</td>
<td>170</td>
</tr>
<tr>
<td>CKMB</td>
<td>1.0</td>
<td>25</td>
</tr>
<tr>
<td>a - Amylase</td>
<td>0.0</td>
<td>200</td>
</tr>
<tr>
<td>Total protein</td>
<td>66</td>
<td>87</td>
</tr>
<tr>
<td>Albumin</td>
<td>36</td>
<td>46</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.1</td>
<td>2.5</td>
</tr>
<tr>
<td>Phosphate</td>
<td>0.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Bilirubin: Total</td>
<td>3.4</td>
<td>17</td>
</tr>
<tr>
<td>Bilirubin: Direct</td>
<td>0.8</td>
<td>5.1</td>
</tr>
<tr>
<td>TEST</td>
<td>LOW LIMIT</td>
<td>LIMIT</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>2.8</td>
<td>5.5</td>
</tr>
<tr>
<td>High density lipoprotein</td>
<td>1.0</td>
<td>1.8</td>
</tr>
<tr>
<td>Low density lipoprotein</td>
<td>0.0</td>
<td>5.0</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.0</td>
<td>2.3</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.0</td>
<td>10</td>
</tr>
<tr>
<td>Total iron</td>
<td>9.0</td>
<td>30</td>
</tr>
<tr>
<td>Transferrin</td>
<td>2.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Osmolality</td>
<td>275</td>
<td>295</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>1.5</td>
<td>4.0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.7</td>
<td>2.19</td>
</tr>
<tr>
<td>TEST</td>
<td>LOW LIMIT</td>
<td>HIGH LIMIT</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>Total glycated haemoglobin</td>
<td>4.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Cerebrospinal fluid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>120</td>
<td>130</td>
</tr>
<tr>
<td>Glucose</td>
<td>0.6</td>
<td>2.5</td>
</tr>
<tr>
<td>Protein</td>
<td>0.15</td>
<td>0.45</td>
</tr>
<tr>
<td>Urine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>2.5</td>
<td>8.0</td>
</tr>
<tr>
<td>Creatinine: Female : Male</td>
<td>7100</td>
<td>17700</td>
</tr>
<tr>
<td></td>
<td>5300</td>
<td>15900</td>
</tr>
<tr>
<td>Osmolality</td>
<td>300</td>
<td>1000</td>
</tr>
<tr>
<td>Phosphate</td>
<td>16</td>
<td>48</td>
</tr>
<tr>
<td>K⁺</td>
<td>35</td>
<td>90</td>
</tr>
<tr>
<td>Na⁺</td>
<td>140</td>
<td>260</td>
</tr>
<tr>
<td>TEST</td>
<td>LOW LIMIT</td>
<td>HIGH LIMIT</td>
</tr>
<tr>
<td>Protein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.G</td>
<td>1.016</td>
<td>1.025</td>
</tr>
<tr>
<td>Urea</td>
<td>250</td>
<td>600</td>
</tr>
<tr>
<td>Uric acid</td>
<td>1480</td>
<td>4430</td>
</tr>
<tr>
<td>VMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine clearance: Male : Female</td>
<td>97</td>
<td>137</td>
</tr>
<tr>
<td></td>
<td>88</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>30 (3hrs urine)</td>
</tr>
</tbody>
</table>
## Endocrinology Reference Ranges

### Thyroid Hormones References Ranges (Adults)

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3</td>
<td>1.5 --------------- 3.7 nmol/L</td>
</tr>
<tr>
<td>T4</td>
<td>50.0 --------------- 129.0 nmol/L</td>
</tr>
<tr>
<td>TSH</td>
<td>0.8 --------------- 5.0 mU/L</td>
</tr>
</tbody>
</table>

### Reproductive Hormones

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolactin</td>
<td>110 - 550 mU/L</td>
<td>50 - 500 mU/L</td>
</tr>
<tr>
<td>FSH</td>
<td>Early follicular 2.6 - 6.0 iU/L</td>
<td>1.2 - 5.0 iU/L</td>
</tr>
<tr>
<td></td>
<td>Luteal phase 1.6 - 5.5 iU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post menopause 128-130 iU/L</td>
<td></td>
</tr>
<tr>
<td>LH</td>
<td>Early follicular 3.0-12.0 iU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ovulation peak 25.0-65.0 iU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Luteal phase 2.5-13.0 iU/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post menopause 25.0-120 iU/L</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>Follicular phase 110-440 pmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Luteal phase 367-770 pmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pre-ovulation peak 500-1285 pmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post menopause 36-128 pmol/L</td>
<td></td>
</tr>
<tr>
<td>Progesterone</td>
<td>Follicular phase 0.6-3.2 nmol/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Luteal phase 9.5-79.5 nmol/L</td>
<td></td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.3-3.6 nmol/L</td>
<td>10.4-31.2 nmol/L</td>
</tr>
</tbody>
</table>
APPENDIX 4

ADDITIVES TO I.V. FLUIDS

Guidelines for the direct addition of medicaments to infusion containers.

1. Drugs should only be added to infusion containers when constant plasma concentrations of the drug are required or when there is no alternative.

2. In general, only one drug should be added to any infusion container and the components should be of known compatibility (see table) Drugs must not be added to containers of blood, plasma, parenteral amino acid preparations, mannitol and sodium bicarbonate solution.

3. The giving set should not be used for more than 24 hours and strict asepsis should be maintained throughout.

4. It is good practice to examine intravenous infusion from time to time while they are running to ensure that the rate of flow is satisfactory. If any sign of contamination or any other sign of interaction is observed the infusion should be discontinued.

Problems involving Additives.

- Some drugs including most antibiotics become unstable and deteriorate in a large volume of fluid. Most of these (i.e. antibiotics corticosteroids and parenteral vitamins) are better given intermittently by injection into the intravenous infusion set.

- The accidental entry and subsequent growth of micro-organisms converts the infusion fluid pathway into a vehicle for infection with micro-organisms.

- Dosage may be inaccurate if the rate of infusion changes (e.g. drip blocks).
## APPENDIX 5

### DRUGS INCOMPATIBILITIES IN INTRAVENOUS FLUID

<table>
<thead>
<tr>
<th>DRUG</th>
<th>INCOMPATIBLE WITH</th>
<th>REASON</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Penicillins (Na+ or K+ salts of Benzyl-penicillin and the Semi-synthetic Penicillins) Hydrocortisone Sodium Succinate Tetracyclines</td>
<td>Tetracyclines Gentamicin</td>
<td>Precipitation Inactivation</td>
</tr>
<tr>
<td></td>
<td>Tetracyclines</td>
<td>Precipitation</td>
</tr>
<tr>
<td></td>
<td>Penicillin Suphonamides (Na+ salts) Hydrocortisone Sodium Succinate Calcium salts</td>
<td>Precipitation Precipitation Precipitation</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>Sodium Bicarbonate All Penicillins</td>
<td>Tetracycline Chelate formed Precipitation Reduced activity of Gentamicin</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>All other antibiotics Hydrocortisone Sodium Phosphate</td>
<td>Loss of potency</td>
</tr>
</tbody>
</table>
Drug use in pregnancy

There are many drugs that can disrupt the development of the foetus (especially during the first trimester), or can have effects on maturing babies and new borns through drugs excreted in breast milk. Often the effect of the drugs on the foetus and babies are unknown.

**Generally, drugs should be avoided in pregnancy**
Some drugs are known to be safe ( e.g. penicillin ), others have a slight risk, which is outweighed by the benefit of the treatment ( e.g. malaria is such more dangerous to pregnancy than anti malarial drugs).

The list below contains references to drugs found in this formulary. It is not a comprehensive list for all drugs.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Comment</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ace Inhibitor (1,2,3,)</td>
<td>Avoid, can effect foetal and neonatal blood pressure control and renal function; possible skull defects.</td>
<td>Antipileptics</td>
</tr>
<tr>
<td>Alcohol (1,2,)</td>
<td>Regular alcoholics teratogenic, possible growth retardation.</td>
<td>Benefit of treatment outweighs risks to foetus, risk increases if more than 1 drug used ( see also individual drugs )</td>
</tr>
<tr>
<td>Aminoglycides (2,3,)</td>
<td>Auditory or vestibular nerve damage, greatest risk with streptomycin, less risk gentamycin but avoid unless essential.</td>
<td>Antipsychotics (3)</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>see theophylline</td>
<td>Antihistamines</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>see antidepressants</td>
<td>No evidence of teratogenicity</td>
</tr>
<tr>
<td>Anaesthetics general (3)</td>
<td>Depress neonatal respiration</td>
<td></td>
</tr>
<tr>
<td>Anaesthetics local (3)</td>
<td>Large doses causes neonatal respiratory depression, hypotonia and bradycardia</td>
<td>Aspirin (3)</td>
</tr>
<tr>
<td>Anticoagulants heparin(1,2,3,), osteoporosis after prolonged use</td>
<td>Betablockers</td>
<td>Impaired plate let function, risk of haemorrhage, delayed onset and increased duration of labour. Avoid in last weeks of pregnancy. High doses cause closure of the foetal ductus arteriosus in utero and possible pulmonary hypertension of the new born.</td>
</tr>
<tr>
<td>Anticoagulants oral (1,2,3,)</td>
<td>congenital malformations Foetal and neonatal haemorrhage</td>
<td>See betablockers</td>
</tr>
<tr>
<td>Arthemeter</td>
<td>Insufficient</td>
<td>Calcium Channel blockers</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>See corticosteroids</td>
<td>May cause intra-uterine growth retardation, neonatal hypoglycaemia and bradycardia</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>See corticosteroids</td>
<td>May cause intra-uterine growth retardation, neonatal hypoglycaemia and bradycardia</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>See corticosteroids</td>
<td>May cause intra-uterine growth retardation, neonatal hypoglycaemia and bradycardia</td>
</tr>
<tr>
<td>Bendrofluazide</td>
<td>See diuretics</td>
<td>May inhibit</td>
</tr>
<tr>
<td>Calcium Channel blockers</td>
<td></td>
<td>May inhibit</td>
</tr>
<tr>
<td>Drug</td>
<td>Classification</td>
<td>Notes</td>
</tr>
<tr>
<td>--------------------</td>
<td>---------------------------------------</td>
<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Captopril</td>
<td>See ACE inhibitors</td>
<td>Should not be used to treat hypertension in pregnancy.</td>
</tr>
<tr>
<td>Carbamazepine (1)</td>
<td>Possibly teratogenic</td>
<td>Thiazides cause neonatal thrombocytopenia</td>
</tr>
<tr>
<td>Carbimazole (2,3,)</td>
<td>Neonatal goitre and hypothyroidism</td>
<td>See tetracycline</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Not known to be harmful</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol (3)</td>
<td>Neonatal “grey syndrome”</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>See antimalarials</td>
<td></td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>See antihistamines</td>
<td>avoid, foetotoxicity and teratogenicity</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>See antipsychotics</td>
<td></td>
</tr>
<tr>
<td>Clofibrate</td>
<td>See benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>Clofibrate</td>
<td>See benzodiazepines</td>
<td></td>
</tr>
<tr>
<td>Clozapine</td>
<td>Avoid</td>
<td></td>
</tr>
<tr>
<td>Cogentine</td>
<td>See opioid analgesics</td>
<td></td>
</tr>
<tr>
<td>Cotrimoxazole (1)</td>
<td>Theoretical teratogenic risk</td>
<td></td>
</tr>
<tr>
<td>Danazol (1,2,3,)</td>
<td>Weak androgenic effects</td>
<td></td>
</tr>
<tr>
<td>Dapsone (3)</td>
<td>Neonatal haemolysis and methaemoglobinuria. Adequate folic acid supplements necessary</td>
<td>neonatal goitre and hypothyroidism</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>See corticosteroids</td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>See hypnotics and anxiolytics</td>
<td></td>
</tr>
<tr>
<td>Digoxin</td>
<td>May need dosage adjustment</td>
<td></td>
</tr>
<tr>
<td>Diltiazem</td>
<td>See calcium channel</td>
<td></td>
</tr>
</tbody>
</table>
Lignocaine
See anaesthetic, local
Paracetamol
Not known to be harmful

Lithium (1,)
Dose requirements increased, neonatal goitre and lithium toxicity. Risk of teratogenicity, including cardiac abnormality
Pethidine Analgesics
Phenobarbitone (1,2,)
See opioid analgesics
Congenital malformation, neonatal bleeding tendency

Lorazepam
See hypnotics and anxiolytics
Phenytoin (1,3,)
Congenital malformation - see also anti epileptics

Mebendazole
Possible toxicity
Pilocarpine
Avoid

Mefloquine
Possibly teratogenic
Pindolol
See beta blockers

Metform in
avoid
Podophylline (1,2,3,)
Avoid: neonatal death and teratogenic

Metoclopramide
Not known

Nitrazepam
See hypnotics and anxiolytics
Promethazine
See antihistamines

Nitrofurantoin (3)
May produce neonatal haemolysis
Pyrimethamine + Sulphadoxine (1)
Possibly teratogenic neonatal haemolysis and methaemoglobinemia

Nitrous oxide
See anaesthetics, general

Norethsterone
See contraceptives, oral
Quinine (1)
No adverse effects

NSAIDs (3)
Avoid unless large benefit of treatment. Regular use causes closure of ductus arteriosus in utero and possible persistent pulmonary hypertension of the newborn
Quinolones (1,2,3,)
Rifampicin(1)
High doses teratogenic

Oestrogens
See contraceptives respiration
Tetracyclines (1)
Effects on skeletal development

Opioid analgesics (3)
Depress neonatal respiration
Tetracycline (2,3,)
Dental discoloration
<table>
<thead>
<tr>
<th>Drug</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Theophyllin (3)</td>
<td>Neonatal irritability and apnoea have been reported</td>
</tr>
<tr>
<td>Thiazides (3)</td>
<td>Neonatal thrombocytopenia possible</td>
</tr>
<tr>
<td>Thiopentone</td>
<td>See anaesthetics: General</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>See ntipsychotics</td>
</tr>
<tr>
<td>Timolol</td>
<td>See beta blockers</td>
</tr>
<tr>
<td>Trimethoprim (1)</td>
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</tr>
<tr>
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## APPENDIX 7

### DRUG USE IN BREAST FEEDING

Administration of some drugs to nursing mothers may cause toxicity in the infant (e.g. ergotamine), whereas others may have an effect on the neonate (e.g. digoxin). Toxicity to the infant can occur if the drug enters the milk in pharmacologically significant quantities. Milk concentrations of some drugs might exceed those in maternal plasma so that therapeutic doses in the mother might be toxic to the infant. For many drugs there is insufficient evidence to provide guidance and it is therefore only advisable to administer those drugs that are necessary to the mother during breast feeding.

The following list contains the drugs covered in this formulary that should be used with caution or which should be avoided in breast feeding.

<table>
<thead>
<tr>
<th>Drug</th>
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</tr>
</thead>
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<tr>
<td>Beta blockers</td>
<td>Monitor infant, possible toxicity due to beta blockade, but amount excreted of most beta blockers too small, atenolol has greatest risk</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>See corticosteroids</td>
</tr>
<tr>
<td>Bromocriptine</td>
<td>Suppress lactation</td>
</tr>
<tr>
<td>Captopril</td>
<td>Avoid</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Probably amount too small to be harmful</td>
</tr>
<tr>
<td>Carbinazole</td>
<td>Amounts in milk may be harmful</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>Excreted in low concentrations</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Avoid, may cause neonatal &quot;Grey syndrome&quot;</td>
</tr>
<tr>
<td>Chloridiazepoxide</td>
<td>See benzodiazepines</td>
</tr>
<tr>
<td>Chlorormethiazole</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>Amount probably too small to be harmful</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Drowsiness in infant reported</td>
</tr>
<tr>
<td>Cimetidine</td>
<td>Monitor infant</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>Avoid, high concentration on breast milk</td>
</tr>
<tr>
<td>Codeine</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Contraceptives, oral</td>
<td>Avoid combined oral contraceptives until weaning or 6 months after birth. Adverse effects on lactation</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>See corticosteroids</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug</th>
<th>Caution or Avoid</th>
</tr>
</thead>
<tbody>
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<td>Alcohol</td>
<td>Large amounts may be persistent pulmonary hypertension for the newborn.</td>
</tr>
<tr>
<td>Amiloride</td>
<td>Avoid</td>
</tr>
<tr>
<td>Aminophylline</td>
<td>See theophylline</td>
</tr>
<tr>
<td>Amitriptylline</td>
<td>See antidepressants</td>
</tr>
<tr>
<td>Anticoagulants, oral</td>
<td>Risk of haemorrhage, warfarin appears to be safe</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Small amount of tricycles in breast milk, manufacturers Advise to avoid</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Significant amount of some antihistamines although not known to be harmful</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Avoid, possible effects on development of nervous system</td>
</tr>
<tr>
<td>Acetyl salicylic acid</td>
<td>Avoid</td>
</tr>
<tr>
<td>Atenolol</td>
<td>See beta blockers</td>
</tr>
<tr>
<td>Arthemeter</td>
<td>Insufficient information</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Avoid if possible, large dose may cause drowsiness</td>
</tr>
<tr>
<td>Beclomethasone</td>
<td>See corticosteroids</td>
</tr>
<tr>
<td>Bendrofluazide</td>
<td>See thiazdes</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>Avoid repeated doses, lethargy and weight loss in infant</td>
</tr>
<tr>
<td>Drug</td>
<td>Instructions</td>
</tr>
<tr>
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<td>------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Diazepam</td>
<td>See benzodiazepines</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>Avoid</td>
</tr>
<tr>
<td>Disopyramide</td>
<td>Monitor infant for antimuscarnic effects</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>See tetracyclines</td>
</tr>
<tr>
<td>Enalapril</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Ergotamine</td>
<td>Avoid</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Not known to be harmful</td>
</tr>
<tr>
<td>Ethynloestradiol</td>
<td>See contraceptives, oral</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Avoid</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Avoid</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>避</td>
</tr>
<tr>
<td>Glibenclamide</td>
<td>See Sulphonylureas</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>See antipsychotics</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>See thiazides</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>See corticosteroids</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Amount too small to be harmful Short course is safe in usual dose</td>
</tr>
<tr>
<td>Idoxuridine</td>
<td>May make breast milk taste unpleasant</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Avoid, see also antidepressants</td>
</tr>
<tr>
<td>Insulin</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Maybe harmful</td>
</tr>
<tr>
<td>Iodine</td>
<td>Harmful, if required stop breast feeding, danger of hypothyroidism</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>Monitor possible toxic effects, theoretical risk of convulsion and neuropathy</td>
</tr>
<tr>
<td>Labetolol</td>
<td>See beta blockers</td>
</tr>
<tr>
<td>Levodopa</td>
<td>No information</td>
</tr>
<tr>
<td>Lignocaine</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Substance</td>
<td>Effect</td>
</tr>
<tr>
<td>--------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Progesterones</td>
<td>High doses suppress lactation</td>
</tr>
<tr>
<td>Promethazine</td>
<td>See antihistamines</td>
</tr>
<tr>
<td>Propranolol</td>
<td>See beta blockers</td>
</tr>
<tr>
<td>Pyrmentamine</td>
<td>No adverse effect + Sulfadoxine</td>
</tr>
<tr>
<td>Quinine</td>
<td>High doses are tetratogenic, but malaria may outweigh risk</td>
</tr>
<tr>
<td>4 Quinolones</td>
<td>Possible anthropathy</td>
</tr>
<tr>
<td>Rifampicin</td>
<td>Amount too small to be harmful</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>See aminoglycides</td>
</tr>
<tr>
<td>Sulphonylureas</td>
<td>Neonatal hypoglycaemia, avoid, substitute with insulin</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>Effects on skeletal development. Avoid.</td>
</tr>
<tr>
<td>Theophylline</td>
<td>Neonatal irritability and apnoea have been reported</td>
</tr>
<tr>
<td>Thiazides</td>
<td>Possible suppression of lactation</td>
</tr>
<tr>
<td>Thiopentone</td>
<td>See anaesthetics: General</td>
</tr>
<tr>
<td>Thioridazine</td>
<td>See antipsychotics</td>
</tr>
<tr>
<td>Timolol</td>
<td>See beta blockers</td>
</tr>
<tr>
<td>Trimethprim</td>
<td>Short term use not known to be harmful</td>
</tr>
<tr>
<td>Warfarin</td>
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