Preface

I have the pleasure to put at the disposal of all health professionals the Egyptian National Formulary which has been prepared by a group of prominent professors of Medicine, professors of Pharmacy, and experts of the Ministry of Health and Population (MOHP).

The present work is a continuation of the efforts of MOHP to enhance rational use of drugs through encouraging the use of generic drugs by prescribers and dispensers, which leads to a better utilization of available resources and makes pharmaceutical products more affordable.

We hope that the Egyptian National Formulary will be of usefulness to all.

Minister of Health and Population
Prof. Dr. Hatem El-Gabaly
2007
Foreword

The national health authorities undertake continuous endeavours to enhance the essential drugs concept being the corner pillar in the rational use of drugs. In this framework the national Essential Drugs List (EDL) has been prepared and published a number of years ago.

The present National Drug Formulary has been conceived to complement the national Essential Drugs List. It has been compiled by experts from MOHP, professors of Medicine and professors of Pharmacy.

The present formulary offers the user valuable information on all drugs included in the EDL regarding uses, adverse effects, drug interactions, drugs used during pregnancy and lactation, pharmacogenetics, geriatric and paediatric drug use, and importance of compliance with treatment regimens.

The drugs in the formulary are mentioned in their non-proprietary names (generic names). Of great value for the users is that each therapeutic group is preceded by common disease states.

We hope that the formulary will be a valuable contribution to Rational Use of Drugs.
Formulation Committee

Prof. Dr. Mamdoh Zaky
Prof. Dr. Ez El Deen El Denshary
Prof. Dr. Haidar Ghaleb
Prof. Dr. Manal Nour
Prof. Dr. Mohsen Fathallah
Prof. Dr. Esmat Sheba
Prof. Dr. Roshdy El Badrawy
Prof. Dr. Taha El Shewy
Prof. Dr. Zeinab Ebied

Medical Editor

Dr. Mohamed K. Allam

Revision Committee

Prof. Dr. Ahmed Abdel Salam
Prof. Dr. Abdel Rahman Al-Naggar

Computer Revision:
Eng. Hany Kamal

Coordinator

Prof. Dr. Zeinab Ebied

Under Secretary of State

Prof. Dr. Zeinab Ebied
CONTENTS

Preface i
Foreword iii
Abbreviations vi
Abbreviations vii
1. Teratogenicity and Breast Feeding 2
2. Paediatrics 8
3. Geriatrics 13
4. Patient Compliance 19
5. Drug Interactions 22
6. Pharmacogenetics 26
7. Adverse Drug Reactions (ADR) 30
8. Gastro-Intestinal Tract Drugs 47
9. Cardiovascular System Drugs 62
10. Respiratory System Drugs 90
11. Anti-Allergic Drugs 97
12. Neuro Psychiatric Drugs 109
13. Drugs for Infectious Diseases 125
14. Endocrine Drugs 169
15. Malignant Diseases and Immunosuppressive Drugs 184
16. Nutrition and Blood Restorative Drugs 196
17. Skeletal Muscle Relaxants 207
18. Ophthalmic Preparations 216
19. Ear, Nose and Oropharynx Drugs 222
20. Dermatological Drugs 228
21. Vaccines and Sera 237
22. Anaesthetic Preparations 248
Index 257
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt;</td>
<td>5-Hydroxytryptamine</td>
</tr>
<tr>
<td>ACE</td>
<td>Angiotensin converting enzyme</td>
</tr>
<tr>
<td>ACh</td>
<td>Acetylcholine</td>
</tr>
<tr>
<td>ACTH</td>
<td>Adrenocorticotropic Hormone</td>
</tr>
<tr>
<td>ADR(s)</td>
<td>Adverse drug reactions</td>
</tr>
<tr>
<td>AFP</td>
<td>Alpha fetoprotein</td>
</tr>
<tr>
<td>ALT</td>
<td>Alanine transferase</td>
</tr>
<tr>
<td>ARF</td>
<td>Acute renal failure</td>
</tr>
<tr>
<td>AST</td>
<td>Aspartate transferase</td>
</tr>
<tr>
<td>ATP</td>
<td>Adenosine triphosphate</td>
</tr>
<tr>
<td>AV</td>
<td>Atrio-ventricular</td>
</tr>
<tr>
<td>bid</td>
<td>Bis In Die (Latin: Twice a day)</td>
</tr>
<tr>
<td>BP</td>
<td>Blood pressure</td>
</tr>
<tr>
<td>BSP</td>
<td>Bromosulphalein</td>
</tr>
<tr>
<td>CCB</td>
<td>Calcium channel blockers</td>
</tr>
<tr>
<td>CHF</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>CMV</td>
<td>Cytomegalovirus</td>
</tr>
<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>COP</td>
<td>Cardiac output</td>
</tr>
<tr>
<td>CTZ</td>
<td>Chemoreceptor trigger zone</td>
</tr>
<tr>
<td>CVS</td>
<td>Cardiovascular system</td>
</tr>
<tr>
<td>ECG</td>
<td>Electro cardio gram</td>
</tr>
<tr>
<td>ESR</td>
<td>Erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>GGT</td>
<td>Gama glutaryl transferase</td>
</tr>
<tr>
<td>GIT</td>
<td>Gastrointestinal tract</td>
</tr>
<tr>
<td>HB</td>
<td>Haemoglobin</td>
</tr>
<tr>
<td>HCl</td>
<td>Hydrochloric acid (gastric acid)</td>
</tr>
<tr>
<td>HPF</td>
<td>High power field</td>
</tr>
<tr>
<td>ICP</td>
<td>Intracranial pressure</td>
</tr>
<tr>
<td>IM</td>
<td>Intra muscular</td>
</tr>
<tr>
<td>IV</td>
<td>Intra venous</td>
</tr>
<tr>
<td>LES</td>
<td>Lower oesophageal sphincter</td>
</tr>
<tr>
<td>LTI</td>
<td>Lower urinary tract infection</td>
</tr>
<tr>
<td>LVF</td>
<td>Left ventricular failure</td>
</tr>
<tr>
<td>MAOI(s)</td>
<td>Monoamino oxidase inhibitor(s)</td>
</tr>
<tr>
<td>NB</td>
<td>Nota Bene (Latin: Note Well)</td>
</tr>
</tbody>
</table>
Abbreviations

NSAID (s) - Non steroidal anti-inflammatory drug (s)
OTC - Over the counter
PO - Per Os
qid - Quater In Die (*Latin*: Four times a day)
RAA - Renin angiotensin aldosterone
RBC (s) - Red blood cell (s)
SC - Subcutaneous
sid - Semel In Die (*Latin*: Once a day)
SLE - Systemic lupus erythematosus
STD (s) - Sexually transmitted disease (s)
TCA (s) - Tricyclic antidepressant (s)
TIA (s) - Transient ischemic attack (s)
tid - Ter In Die (*Latin*: Three times a day)
UTI - Upper urinary tract infection
VC - Vomiting centre
VMC - Vasomotor centre
WBC (s) - White blood cell (s)
SECTION I

TERATOGENICITY AND BREAST FEEDING

In this section:

1.1 Drugs in Pregnancy 2
1.2 Placental Transfer 2
1.3 Foetal Development and Drug Effects 3
1.4 Proven Human Teratogens 3
1.5 Drug Excretion in Human Milk 4
1.6 Reducing Risk of Infant Exposure to Drugs in Breast Milk 5
1.7 Drugs Contraindicated During Lactation 5
1. Teratogenicity and Breast Feeding

The use of drugs during pregnancy and lactation is controversial and presents great challenge to clinicians. The use of drugs during pregnancy is of special concern because of medical, social, and legal implications. Congenital anomalies or birth defects are among the leading causes of infant morbidity and mortality.

1.1 Drugs in Pregnancy

Congenital malformation is defined as structural abnormalities of prenatal origin that are present at birth that seriously interfere with viability or physical well being.

Some drug induced defects relate to changes in functions or conditions that are not structural abnormalities e.g. mental or physical growth retardation, CNS depression, deafness, tumours or biochemical changes. Congenital anomalies i.e. birth defects, include both these toxicities and structural changes.

The prevalence of major malformations is 3% and similar rate is discovered in months or years following birth. Anomalies of internal organs e.g. heart, kidneys, reproductive system and GIT may go unrecognized for years or discovered only at autopsy.

Minor malformations are not included in this percentage e.g. umbilical and inguinal hernias, phimosis, external ear, cryptorchidism, hydrocele, and angiomads. The malformations of little medical significance are not included in incidence data even if they have emotional cosmetic effects. Approximately 6 newborn infants in every 100 will be with a major malformation, but only 3 of these will be identified at birth or in the neonatal period. To these, one can add an unknown number of infants with mental and physical growth retardation and those of minor structural anomalies.

Drug consumption during pregnancy

Many drugs are regularly consumed during gestation including some that are potential teratogens. Women consume an average of 5 to 9 medications. Vitamins and iron supplements are the most commonly used followed by anti-infective and analgesic antipyretic anti-inflammatory agents.

1.2 Placental Transfer

Most medications cross the placenta to the foetus. During gestation, the surface area of the placenta increases, while the placental thickness decreases to 1/5 at term. Both processes tend to favour the transfer of chemicals to the foetus.

Mechanism of placental transfer

Drugs, nutrients and other substances cross the placenta by …

- Simple diffusion e.g. most drugs
- Facilitated diffusion e.g. glucose
• Active transfer e.g. vitamins, amino acids
• Pinocytosis e.g. immune antibodies
• Breaks between cells e.g. erythrocytes

The last two are of no practical importance in drugs transfer

**Factors influencing rate of transfer**

• Molecular weight
• Lipid solubility
• Uterine and umbilical blood flow (major factor)
• Maternal diseases e.g. hypertension, diabetes

### 1.3 Foetal Development and Drug Effects

Early in the embryonic period (conception to 56 days), during the pre-implantation and presomite stage (0 to 14 days), exposure to a teratogenic agent usually produces an “all or none” effect on the ovum. The ovum either dies from a lethal dose of a teratogenic drug or it regenerates completely after exposure to a sub-lethal dose. During organogenesis, insult with the same teratogen may produce major morphologic changes.

**Causes of malformation**

These are classified into …

• Genetic defects: monogenic origin and chromosomal abnormalities (25%) e.g. Down syndrome.
• Interaction between hereditary tendencies and non-genetic environmental factors (20% of all defects) e.g. congenital hip dislocation
• Environmental factors: e.g. maternal infections, chemicals and drugs (10% of all defects). Only 2 viruses and a protozoan have been proven to induce malformation. Bacteria tend to release toxins that cause extensive tissue damage and foetal death rather than structural anomalies. The viruses are rubella (cataract, heart disease and deafness) and cytomegalovirus (CMV) infection (deafness, mental retardation, microcephaly, chorioretinitis, seizures, blindness and optic atrophy). The protozoan Toxoplasma gondii (hepatosplenomegaly, jaundice, rash, chorioretinitis, cerebral calcifications and hydrocephalus or microcephalus.
• Maternal infections account for 2% and maternal diseases e.g. diabetes and hyperthermia account for 1-2%.
• Unknown causes: account for 60-65% of cases.

### 1.4 Proven Human Teratogens

Numerous drugs are associated with congenital malformation e.g. **aminopterin/methotrexate**, **ACE-Inhibitors**, **antineoplastics**, **anti-thyroids**, **barbiturates**, **carbamazepine**, **cocaine**, **coumarin derivatives**, **diethylstilbesterol**, **ethanol** (large dose), iodides, radioactive **iodine**, **lithium**, **methadone**, **phenytoin**, **retinoid**, **vitamin A** (>18,000 IU/day), **tetracycline** and **valproic acid**.
FDA categories (teratogenic risks of drugs):

**Category A**

Controlled studies in women fail to demonstrate a risk to the foetus in the first trimester and the foetal harm appears remote.

**Category B**

Animal reproduction studies have not demonstrated a foetal risk, but there are no controlled studies in pregnant women. Or animal reproduction studies have shown an adverse effect that was not confirmed in controlled studies in women in the first trimester.

**Category C**

Studies in animals have revealed adverse effects on foetus and no controlled studies in women are available. Or, studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the foetus.

**Category D**

Evidence of human foetal risk is positive, but the benefits from use in pregnant women may be acceptable despite the risk.

**Category X**

Studies in animals or humans have demonstrated foetal anomalies or there is evidence of foetal risk based on human experience or both and the risk of the drug in pregnant women clearly outweighs any possible benefits. The drug is contraindicated in women who are or may become pregnant.

1.5 Drug Excretion in Human Milk

Breast milk is the optimal source of nutrition for infants. The risk to the infant depends on the amount of drug bioavailable to the mother, the amount reaching breast milk and the actual amount of drug ingested and bioavailable to the nursing infant.

**Mechanism of transfer from blood to milk**

The basic mechanisms are the same as those across other biologic membranes.

- Diffusion of low molecular weight substances through small water-filled pores
- Diffusion of lipid soluble compounds through lipid membranes
- Active transport carrier-mediated

**Factors affecting drug excretion in breast milk**

The drug dose, route and frequency of administration and metabolism are important factors in determining the amount of drug available for excretion into milk.

**Maternal parameters**

- Drug dosage and duration of therapy
Route and frequency of administration
Drug metabolism and renal clearance
Blood flow to the breasts
pH of milk
Milk composition

Drug parameters
- Oral bioavailability (to mother and infant)
- Molecular weight
- Lipid solubility
- Protein binding

Infant parameters
- Infant age
- Feeding pattern
- Amount of breast milk consumed
- Drug absorption, distribution, metabolism and elimination

1.6 Reducing Risk of Infant Exposure to Drugs in Breast Milk
A drug should be used only if medically necessary and treatment cannot be delayed until the infant is ready to be weaned.

Drug selection
- Consider whether the drug can be safely given directly to the infant
- Select the drug that passes poorly into breast milk with the lowest milk-to-plasma ratio
- Avoid long-acting formulations e.g. sustained release
- Determine length of therapy and if possible avoid long-term usage

Feeding pattern
- Avoid nursing during times of peak drug concentration
- If possible, plan breast-feeding before administration of the next dose

Other considerations
- Always observe the infant for unusual signs or symptoms e.g. sedation, irritability, rash, decreased appetite, failure to thrive
- Discontinue breastfeeding during the course of therapy if the risks to the foetus outweigh the benefit of nursing
- Provide adequate patient education to increase the understanding of risk factors.

1.7 Drugs Contraindicated During Lactation
All drugs of abuse are contraindicated during lactation e.g. amphetamine, cocaine, heroin, phencyclidine and marijuana, accumulate in breast milk and cause irritability and poor sleep patterns.

- Antineoplastics: potential for immune suppression
- Bromocriptine: suppresses lactation
- Ergotamine: potential for suppressing lactation, vomiting, diarrhoea and convulsions
- Immunosuppressants: potential for immunosuppression
- Lithium: milk contains 40% of maternal serum concentration
- Misoprostol: produces severe diarrhoea in infants
• **Nicotine** (smoking): decreased milk production
• **Phenindione**: massive scrotal haematoma and wound oozing after herniotomy

**Drugs requiring temporary cessation of breast-feeding**

• **Metronidazole**: diarrhoea and secondary lactose intolerance.
• **Radiopharmaceuticals**: Stop breastfeeding temporarily to allow clearing from milk according to the chemical nature of the isotope.
• **Quinolones**: potential arthropathy in infants.
SECTION II

PAEDIATRICS

In this section:

2.1 Problems of the Newborn 8
2.2 Infant Feeding 9
2.3 Neural Tube Defects 9
2.4 Developmental Screening 10
2.5 Indications for Prenatal Nutrition Support 11
2. Paediatrics

2.1 Problems of the Newborn

Jaundice

Neonatal jaundice presents commonly to the general practitioner as many mothers are discharged home at 48 hours. When bilirubin level is approaching 350 µmol/L, the following is relevant to formulate a plan of action.

- Is the baby mature?
- Is the baby gaining weight or at least not loosing weight?
- Is the baby breast fed?
- Are there physical signs e.g. hepatosplenomegaly?

If the baby is breast fed and there are adequate quantities of milk, hospitalization is not necessary. If jaundice is prolonged more than two weeks, then the jaundice may be obstructive and this must be investigated.

Vomiting

Many babies regurgitate without effort at the end of the feed despite conscientious winding. An anxious mother may describe this as copious or projectile. On the first day of life, altered blood and mucus may be vomited. If vomiting persists and the baby looses weight, a period of hospital observation will be necessary. Other than a saline washout of the stomach, therapy should not be attempted. Infections, partial intestinal obstruction and metabolic problems such as adrenogenital syndrome must be excluded.

Sticky eyes

Gonococcal ophthalmia is a neonatal emergency presenting in the first 48 hours of life. It is important to perform bacteriological examination and the swabs taken for Gram stain and culture. Frequent instillation of antibiotic eye drops and systemic penicillin is still the treatment of choice.

Staphylococcal infection is the other possibility and needs immediate antibiotic therapy. Otherwise, the average sticky eye which is commoner in babies with small orbits needs only local cleaning with cotton-wool and sterile water.

The other important pathogen is chlamydia which is difficult to isolate as conjunctival scrapings are necessary. The best and correct treatment is tetracycline topically.

Rectal bleeding

It is common when a firm stool is passed with blood streak due to anal fissure. If bleeding is severe, coagulation disorders are possible and an extra-dose of vitamin K should be given. Necrosing enterocolitis is common in premature babies with rectal bleeding, abnormal distension, and vomiting. Birth asphyxia with ischemic colitis is a common cause.
2.2 Infant Feeding

Breast or bottle?
Breast feeding is preferred to bottle feeding because it increases the chance of bonding between mother and baby as well as to avoid gastroenteritis which is a major cause of infant mortality. Breast feeding provides immunological advantages in form of lymphocytes and antibiotics particularly against E. coli. Otherwise the humanised demineralised whey formula artificial milks are excellent and bio-chemically suitable for newborns.

Weaning
It is not necessary to introduce solid foods into the diet until the age of four months. Earlier introduction is reasonable in babies with oesophageal reflux or the body is not satisfied. Late weaning is associated with food refusal and beyond six months both breast and artificial feeds are nutritionally lacking in iron and vitamins. Suitable weaning foods are baby rice or purified fruits and vegetables. If the baby is hungry, cereal is an excellent weaning food as the calorie content is higher. Proprietary foods are acceptable, but any food can be given with the help of a home blender, provided it is not too salty.

Possetting (regurgitation, reflux)
It is a very common condition in the first six months of life. It begins in the first week of life and is not projectile despite what the mother says. It is equally common in breast and bottle fed babies. One important factor is weight gain. If the baby is not thriving, treatment should be given. Investigation is rarely necessary and often unhelpful. Mothers should be surprised during a feed for technique, and the size of the tip hole should not be too small. Specific treatment is either to thicken the feeds with gel or use infant Gaviscon putting one measure into each feed. Most important is to explain to the patient that the condition may persist until the age of nine months.

Food refusal
Despite the successful introduction of solid foods in the second year of life a model feeder may become rejected and refused. At best, milk and the occasional pudding are accepted. The situation can possibly be avoided by careful introduction of solids keeping to the rules of giving one new food at a time and then in small quantities. Feedings must be given without hurries, relaxed and without maternal anxiety. The child should be presented with small quantities of attractive food and left to feed itself. Forced feeding and scenes are counterproductive. Paediatric tonics do not exist.

2.3 Neural Tube Defects

Screening
Alpha fetoprotein (AFP) is produced by the foetal liver and in certain circumstances it may leak into amniotic fluid and maternal blood. If there is an open neural tube defect the AFP will
be elevated in liquor and maternal blood.

Congenital nephrotic syndrome and skin lesions e.g. epidermolysis bullose will also leak this protein for the same reason.

More commonly, twins and premature deliveries are important causes of false positive AFP defects. The diagnosis should be confirmed with ultrasound scanning of the foetus.

**Range and prevention**

Neural tube defects vary from very simple spina bifida occulta and small hairy patch on the skin to gross anencephaly which is non-viable. Most lesions fall between the two extremes. Interference depends on the degree of leg paralysis (height and extent), competence of the anal and bladder sphincters and the presence or absence of hydrocephalus at birth. There is possible prevention by vitamins supplementation around the time of conception (before and after).

**2.4 Developmental Screening**

**General principles**

The idea of screening the pre-school child is to pick up any disorder in the developing child, apply medical therapy, counsel the parents and arrange for special education. This procedure is ideally carried out in the home environment where the child is most comfortable.

**Motor development**

The muscle tone is examined e.g. hypertonia or hypotonia. Head lag should have disappeared by four months of age. By six months, the baby should be sitting with a reasonable straight back even if he cannot support himself. Towards the end of the first year, a child gets into his feet but it may be 18 months before he walks alone. The premature babies are retarded and it is important to subtract the number of weeks of pre-term delivery to maturity.

Fine motor movements are assessed at ten months of age with hand/eye coordination. A small cube is offered to the child and at this age the crude palmer grip changes to a pincer grip.

**Sight**

By two months, the eyes should focus and at this age the eyes are examined for squint (with the baby sitting on the mother’s knee and the light reflex being observed in relation to the pupil. If the reflexes are symmetrical with the eyes looking in all directions, then there is no squint. Also if small objects are reached for by the child, this indicates very good visual acuity.

**Hearing**

It must be tested when the baby is at risk e.g. premature delivery, birth asphyxia, hyperbilirubinemia during the first week and those who received gentamycin. The distraction test is performed at 8 – 9 months. The test is done while the baby sits on the
mother’s knee with the assistant (observer) directly in front to provide distraction and to observe the visual response to sound of high and low pitch quality.

2.5 Indications for Prenatal Nutrition Support

- Extremes of pre-term deliveries
- Respiratory distress
- Congenital GIT anomalies (duodenal atresia, jejunal atresia, esophageal atresia, tracheo-esophageal fistula, pyloric stenosis, congenital webs, volvulus)
- Abdominal wall defects: omphalocele, congenital diaphragmatic hernia
- Necrotizing enterocolitis
- Chronic diarrhoea
- Inflammatory bowel disease
- Chylothorax
- Abdominal trauma
- Adverse effects of treating neoplastic disease: nausea, vomiting, glossitis, eosophagitis
- Anorexia nervosa
- Cystic fibrosis
- Chronic renal failure
- Hepatic failure
- Metabolic errors
SECTION III

GERIATRICS

In this section:

3.1 Physiologic Changes of Aging 13
3.2 Common Geriatric Disorders 14
3.3 Strategies for Healthy Prescribing in Older Patients 16
3. Geriatrics

Geriatric medicine focuses primarily on the medical disorders of old age. The clinical implications of distinguishing between age-related changes and age-related diseases are important. A pathologic process may demand an extensive diagnostic evaluation so that appropriate therapeutic and preventive measures can be implemented.

On the other hand, correct diagnosis of changes secondary to the normal process of aging may avoid subjecting the elderly to unnecessary and costly diagnostic procedures which may not improve the patient’s life quality.

3.1 Physiologic Changes of Aging

**Body conformation and composition**

Generally there is decrease in cell mass e.g. brain, liver, kidney, bone and muscle but not heart, lung and prostate.

There is increase in fat and decrease in total body water (6%) and decrease in weight and height. The vertebrae may show kyphosis and scoliosis.

**Neurologic**

There is a decrease in cerebral blood flow and nerve conduction. Altered sleep patterns and decline in memory may show, but learning is intact.

**Cardiovascular**

Arteries: increase in collagen and smooth muscle with elastic tissue loss resulting in decreased compliance and increased peripheral resistance (systolic hypertension).

Veins: loss of elastic tissue, intimal thickness and fibrosis of tunica.

Heart: increases in weight with greater collagen-to-muscle ratio. Cardiac output at rest is unchanged but decreases with exercise or stress.

**Respiration**

Alveolar surface decreases, with decreased vital capacity and respiratory volume.

There is increased residual volume, with abnormal ventilation–perfusion ratio in lung bases with reduced arterial pO$_2$ but normal pCO$_2$.

**Skin**

There is thinning of dermis and subcutaneous tissue, loss of vascular bed, hair and glands, hair greying, decreased sensory perception, thermoregulation and sweating.

**Musculoskeletal**

There is loss of height, osteoporosis (especially in females) and degenerative changes in joint cartilage with loping of joint bones.

There is loss of muscle mass with increase in collagen.
Gastrointestinal tract

There is loss of teeth, enamel (attrition), the dentine becomes more opaque, with decreased dental pulp and content. There is also recession of gum and resorption of alveolar bone.

There is decrease in peristalsis and uncoordinated oesophageal movement, along with decreased gastric secretion and emptying time.

Also, there is decreased colon peristalsis and constipation. A decrease in liver weight but with normal function and altered drug metabolism and likelihood of forming gall-stones may be present.

Genitourinary and reproduction

A decrease in renal weight is observed. Total number of nephrons, renal perfusion, and glomerular filtration, concentrating ability, re-absorption, and secretory transport and bladder capacity are all affected.

In females decreased ovarian follicles before menopause are evident. Atrophy of primary and secondary sex organs occurs.

In males, testicular androgen decreases, with decreased sperm production, erectile dysfunction and enlargement of the prostate.

Special senses

Eyes typically show presbyopia, decreased accommodation, reduced vision field, dark adaptation, colour discrimination, cataract and muscular degeneration.

Ears exhibit loss of tympanic membrane elasticity, decreased sound perception but normal vestibular function.

Taste declines with degeneration of taste buds, and smell declines with decreased detection of common odours.

Immunity

There is a decrease in both cellular and humoural immunity but normal complement.

3.2 Common Geriatric Disorders

Sensory impairment

Visual and auditory disturbances

The most common causes of visual loss are cataract, glaucoma, senile macular degeneration and diabetic retinopathy.

Presbycusis due to exposure to loud noises, ototoxic drugs and disturbed sound localization are not uncommon.
Instability and falls

30% of falls of the elderly that occur every year results in or requires hospitalization. The most common causes of falls include accidents e.g. slip 40% of which are due to stiffness and lack of coordination. Also, syncope, dizziness, vertigo, orthostatic hypotension and drug related are common causes of instability. Other common causes are CVS-related (arrhythmias, carotid sinus syncope) and CNS-related (TIAs, stroke, seizures, and Parkinsonism).

Incontinence

Amounts to 10% among the elderly, and females have a higher incidence. The adverse effects of urine incontinence include social withdrawal, decubitus ulcers, catheter problems and recurrent urinary tract infection.

Geriatric dementia

About 10–20% suffer some kind of impaired intellectual functions that are diagnosed as dementia. In 50% dementia is due to problems with memory function while 5% are due to depression. It is a clinical syndrome in the intellectual function sufficient to compromise social and occupational functions. It occurs in individuals with clear consciousness.

Types

Alzheimer-type dementia (primary degenerative dementia) occurs in the elderly at a 2:1 female to male ratio Vascular dementia has an earlier onset and it occurs in males more than females.

Other types of dementia include multi-infarct dementia, Binwanger’s disease (micro-thrombi). Pick’s disease (simple pre-senile dementia), symptomatic dementia, pseudodementia (50% in depression), Parkinson’s disease dementia, dementia due to disseminated sclerosis, panencephalitis, and drugs and toxins.

Systemic diseases such as pulmonary, hepatic, renal, sepsis, heart failure, thyroid disorders, collagen diseases, trauma, neoplasm and Vitamin B₁₂ – folic acid deficiency may result in dementia.

Delirium

There is impairment in intellectual function and fluctuations in alertness and perception due to systemic disorders and drugs.

Involution depression

It occurs in 5% of persons over 65 years. There are sleep problems, vegetative symptoms, dysphoria, and preoccupation of vague physical complaints, anxiety, anhedonia and delusions.

Infections

Geriatrics presenting with infections suffer from several problems. They are at greater risk for certain infections with higher risks of morbidity and mortality.
The aetiology and pathogenesis differ from adults. Signs and symptoms may be atypical, non specific or totally absent. Anti-infective medicines may result in slower clinical responses, greater side-effects and may require longer courses.

There is significant decline in both cell-mediated and humoural immunity. The presence of an underlying chronic condition (e.g. diabetes, malignancy, inadequate nutrition and higher exposure to nosocomial infections) further complicates the situation.

Infections of geriatric interest include pneumonia, genitourinary tract infection, cholecystitis, tuberculosis, cholangitis, diverticulitis, infective arthritis, meningitis and herpes zoster.

β-lactams and quinolones are preferred in geriatric treatment. In all cases, renal function must be assessed if the antibiotic has potential renal toxicity.

### 3.3 Strategies for Healthy Prescribing in Older Patients

Ensure that a proper indication is established and do not just treat symptoms.

Put the problems in context. Is it affecting the patient’s quality of life or causing functional decline? Balance the risks of medication with its potential benefits.

General condition of the patient is important. What is the overall health status? Is there known hepatic or renal impairment?

What drugs, including non-prescription drugs, social drugs and other self-medication is the patient taking? Who else is prescribing?

Consider non-drug alternatives to therapy e.g. physiotherapy counseling and relaxation techniques.

If drug treatment is necessary, know the drug well including its mechanism of action, route of metabolism and excretion, side-effect profile in the elderly and clinically significant drug interactions.

Dose carefully. The well known rule “start low and go slow” is appropriate. Adjust the dosage according to the patient’s response.

Simplify the regimen as much as possible by minimizing dose frequency, using mono-therapy or at least a minimum number of drugs possible.

Review the need for all prescribed medications periodically with the intent to eliminate unnecessary drugs.

Try to anticipate and minimize adverse drug reactions by considering side effect profiles when selecting a specific drug group.

In general, if an older patient receives a new drug and develops new symptoms e.g. confusion, orthostatic hypo-
tension or fall consider that the symptoms may be drug induced.

Beware of enforced compliance and its potential for adverse drug reaction (ADR) when an elderly is moving from an ambulatory to a long-term care facility or hospital setting.

Minimize the use of potentially inappropriate medications in the elderly with diseases that may be exacerbated e.g. beta-blockers in asthma or severe vascular disease.

Determine whether the patient needs help using the medication. Pharmacists, nurses and other professionals can serve as resources for older patients who are living alone or are functionally impaired. Written instructions, information leaflets, calendars, special containers, special packaging and a variety of other reminder devices can enhance the appropriate use of medications.

Educate the patient about intended therapeutic effects, possible adverse drug reactions and signs of toxicity.

Be sure to schedule regular follow-ups, constantly re-evaluate the older patient's medication regimen and document the outcomes of the interventions based on predetermined therapeutic goals.
SECTION IV

PATIENT COMPLIANCE

In this section:

4.1 Definition 19
4.2 Non-Compliance 19
4.3 Physician’s Role in Improving Patient Compliance 19
4.4 The pharmacists and Nurses Role in Improving Compliance 20
4.5 Role of the Pharmaceutical Industry and Clinical Pharmacist in Improving Compliance 20
4. Patient Compliance

4.1 Definition

The degree to which patients adhere to the treatment plan

Even the most thorough and well-designed therapeutic regimen will fail without patient compliance. Various studies showed that 15% to 95% of patients have been found to be non-compliant. Most probably, 35% to 50% of patients make some error with their medications (incorrect dose, errors in timing, adding non-prescribed medications, or not taking medication). Irregular dosing exposes a patient to the risks of medication without concomitant therapeutic benefit.

4.2 Non-Compliance

It is encountered more when certain factors associated with the therapeutic situations, and the patient characteristics exist. When these factors are recognized, strategies to improve compliance can be developed.

Patient factors in non-compliance

Forgetfulness is the most frequent reason of non-compliance. It may also result from fear of adverse effects of addiction, fear of the state that treatment implies or fear of loss of independence.

Medication factors in non-compliance

Complex regimens with frequent doses or with many medications increase errors in dosage times, scheduling with meals, etc. If drugs look alike, patients may confuse medications, and repeat or omit doses.

Other factors include adverse effects, unpleasant tastes or smells and not following precautions during therapeutic regimen e.g. no alcohol, coffee or cheese, etc.

Disease factors in non-compliance

Certain types of diseases e.g. chronic diseases with day-to-day fluctuation in symptoms (e.g. rheumatoid arthritis) have important compliance problems. A prophylactic therapy may have more symptoms than the disease itself e.g. hypertension will lead to non-compliance.

4.3 Physician’s Role in Improving Patient Compliance

Proper diagnosis and effective therapy are the main and most important roles of the physician. Directions must be clear, precise and accepted and suit the patient’s life and the disease process.

Adherence to a drug regimen and explaining the problems will avoid non-compliance. Education promotes and improves compliance and must not be
induced by hard evidence. Trust in the prescribed therapy is essential and crucial to patient compliance.

Explaining the purpose of the medication regimen, its beneficial effects as well as side effects are essential. Explaining the drug shape, formulation, colour and dosage schedule will create a trusting relationship. Therefore, good communication between the physician and the patient is essential.

4.4 The pharmacists and Nurses Role in Improving Compliance

Information that patients do not discuss with physicians can be delegated to the treating physician by the pharmacist who notices that the patient cannot pay for a full prescription or does not obtain refills. Incorrect prescription should be noted and corrected by consulting with prescribing physician.

Nurses and pharmacists instruct patients on their medications especially before discharge from the hospital. Reviewing the medication features, directions, side effects, interactions, precautions, and medications role with the patient will enhance the patient’s knowledge and leads to promising results.

4.5 Role of the Pharmaceutical Industry and Clinical Pharmacist in Improving Compliance

The mainstay of pharmaceutical industry’s help is through introducing effective medications with few or less side effects with convenient dosing regimens.

Improving drug taste, changing appearance, or colour can help. Introducing sustained release and fixed-dose combination products will help compliance by reducing the dose frequency and number of medicines per day.

Also, introducing medications with specific pharmacokinetic qualities that reduce the effects of missed doses and errors is of great help e.g. large-dose drugs with long half lives given once daily at bed time instead of a 3-4 times of smaller doses per day.

The interlocking roles of different players in healthcare provision definitely enhance patient compliance, achieving the therapeutic goals and avoiding the hazards non-compliance.
SECTION V

DRUG INTERACTIONS

In this section:

5.1 Definition 22
5.2 Classification 22
5.3 Prevention and Management 24
5. Drug Interactions

5.1 Definition
The effects of one drug are altered by prior or concurrent administration of another drug(s).

The altered response may be

- Synergism (greater response)
- Antagonism (lesser response)
- Threatening toxicity

The total incidence of drug side-effects is 10%, of which 22% are due to drug interactions.

Causes
The number of new drugs developed every year is exploding. Polypharmacy occurs either due to improper utilisation of self-medication or iatrogenic by attending at several treating physicians. Both the sheer increase in drug number and polypharmacy add to the drug interactions probability of occurrence.

Hazard or benefit?
Drug interactions may be desired and utilised to increase response and decrease toxicity. Or it can be undesired and harmful with decreased efficacy and increased toxicity.

5.2 Classification

Drug-non drug interactions

Physiologic
- Neonates and premature infants (low hepatic enzymatic activity) e.g. tetracycline toxicity
- Diet: tetracycline and dairy products (Ca++)
- Pregnancy: tetracycline and teeth mottling

Pathologic or disease-drug interactions:
Examples include: GIT malabsorption syndrome, fistulae, heart failure as in β-blockers and Ca++ channel blockers, hepatic cirrhosis with decreased biotransformation, renal disorders and decreased drug clearance, burns associated with hypoproteinemia that decreases plasma protein binding capacity.

Drug-drug interactions

Pharmacokinetic interactions

Alteration in gastro-intestinal absorption: decreased or increased rate and/or amount of intestinal absorption

Alteration in plasma-protein binding and cellular uptake: Only when the drug is highly bound (>90%) and volume of distribution is small will such alteration increase the free fraction of the active drug e.g. pyrazolones, salicylates, sulphonamides, thiazides, valproic acid will displace phenytoin, oral anticoagulants, oral hypoglycemics and glucocorticoids from its albumin binding fraction to free active drug.
**Hepatic biotransformation:** Microsomal enzyme induction (synthesis and/or effect) increases the metabolic degradation of drugs normally metabolized in the liver e.g. oral anticoagulants, oral hypoglycemics, anticonvulsants, and steroids. Therefore, such induction decreases these drugs' half-life time, reduce their effect and bring about a need to increase their therapeutic dose. If the inducing drug is stopped suddenly, it will result in an increase in their half-life and toxicity.

The microsomal enzyme inducing drugs include barbiturates, chloral hydrate, phenytoin, chronic alcoholism, narcotic abuse, rifampicin, griseofulvin and steroid hormones.

**Enzyme inhibition:** They decrease metabolic biotransformation of drugs leading to an increase in their half-life and effect or toxicity. They include the following: valproic acid, MAOIs, metronidazole, cimetidine, chloramphenicol, co-trimoxazole and oral contraceptives.

**Alteration in renal excretion:** Competitive inhibition of tubular transport system by one drug decreases the clearance of another drug e.g. penicillin is affected by probenecid.

On the other hand, urine acidification causes ionization of basic drugs therefore increasing their clearance, while acidic drugs lead to decreasing their clearance e.g. quinidine (basic) and a urine acidifier such as ammonium chloride.

Urine alkalization will decrease basic drug clearance, while acidic drugs increase their clearance e.g. aspirin (acidic) and sodium bicarbonate (urine alkalinizer).

**Pharmacodynamic interactions**

Represent interactions that occur at the reception site. Examples include:

**Synergism** e.g. aspirin and warfarin

**Antagonism**

- Competitive (specific): atropine and parasympathomimetics.
- Physical: heparin and protamine sulphate.
- Chemical: metals and chelating agents.
- Pharmaceutical: gum solution and alcohol.

**Drug interactions of therapeutic importance**

They produce serious complications that need special consideration and precautions during therapy. On the other hand minimal interactions may be neglected.

The most serious interactions include CNS function (vital medullary and higher centres), CVS (cardiac depressants, arrhythmias, hypotensive and hypertensive crisis), Blood coagulation disorders, hormonal (hypoglycemia, glucocorticoids and oral contraceptives), and drug-disease interactions e.g. marked hepatic or renal disorders.
5.3 Prevention and Management

Careful patient’s drug history taking, either for prescribed, or for self-medication, and especially for allergy e.g. urticaria, angioneurotic oedema or swelling in hands, feet or ankles.

Physicians must get familiar with the pharmacologic properties of the prescribed drugs.

Avoiding poly-pharmacy as far as possible or drugs especially known to be:

- Potent
- Incompatible
- Of narrow therapeutic index e.g. aminoglycosides, digoxin, lithium, methotrexate, theophylline, warfarin, oral hypoglycemics, anti-arrhythmic and anti-hypertensive

Make use of the newly introduced drug information services and appropriate literature.

Consult with well trained clinical pharmacists.

Perform serum drug monitoring for drugs of narrow safety margin

Make use of drug-interaction alert chart.
SECTION VI

PHARMACOGENETICS

In this section:

6.1 Approach to the Patient with Genetic Disorder 26
6.2 Management of Genetic Disorders 26
6.3 Treatment of Genetic Disorders 27
6. Pharmacogenetics

With the advent of new investigative tools especially recombinant DNA technology, it is now possible to diagnose genetic disorders at the most fundamental level and demonstrate specific mutations in the DNA molecule. These same techniques offer promise that potentially definitive therapy for some disorders is possible through replacement of defective genes. There are genetic disorders such as inborn errors of metabolism that can be managed diagnostically and therapeutically. It is estimated there are 100,000 genes in the human genome and more than 1300 human diseases have been ascribed to a mutation in one of these genes. A recent map of human genome includes the chromosomal location of more than 350 of these disorders.

6.1 Approach to the Patient with Genetic Disorder

In dealing with inherited disorders, individuals seek medical advice for some symptoms requiring medical attention and also asymptomatic relatives come to physicians because a family member is affected and the individual seeking medical advice is concerned that he or his children, born or unborn, may develop similar problems.

The first step in evaluation for a suspected inherited disorder is a careful and detailed family history with regard to a family tree or pedigree for organizing and recording this information e.g. age, sex, clinical status (alive unaffected, alive affected, stillborn, dead) and relationship of various family members to each other.

The clinical manifestations of genetic disorders may vary in different family members either in expressivity (variations in severity and types of clinical manifestations) or penetration (the extent to which the genetic defect expresses itself clinically in affected members of a pedigree).

Physical examination is performed to define the extent of clinical involvement as well as good biotechnical and cytogenetic tests for genetic disorders.

6.2 Management of Genetic Disorders

Once the diagnosis of a genetic disorder is established, the physician is obliged to advise the patient and relevant family members about the possibility of a similar disorder occurring in other individuals and the likelihood of recurrence in subsequent generations.

Counselling the patient and family can be informative; providing an estimation of the recurrence risk, and supportive; giving an explanation of disease prognosis and providing emotional support and direction to community resources for financial aid.

The general guidelines and indications for referring individuals and
families to genetic counselling services are:

- History of the genetic disease in the family
- Mental retardation of unknown cause
- Dysmorphic physical findings of unknown cause
- Family member with a known or suspected chromosomal abnormality
- Family member with a known or suspected inborn error of metabolism
- More than one family member with similar dysmorphic features
- Child with an unusual facial appearance of unknown cause
- Presence of cleft lip and/or palate
- Child with ambiguous genitalia
- Child with a genetic form of short stature or with undiagnosed short stature
- Individuals considering first cousins
- Family history of a child with Down’s syndrome
- Women over 35 years of age who are pregnant or are considering pregnancy
- Women with multiple spontaneous abortions of unknown aetiology
- A pregnant woman or a woman considering pregnancy at risk of having a child with genetic defect

Once a couple is established to be at risk of having an affected child, the pregnancy can be monitored through amniocentesis. The process is safe to the mother and the abortion rate is less than 1%. The fluid is analysed for increased concentrations of abnormal constituents e.g. alpha-fetoprotein that indicates a foetus with open neural-tube defect. Amniotic cells are analysed directly or placed in culture where metabolic studies, enzyme assays, karyotypes or DNA analysis can be performed. Foetoscopy for obtaining foetal blood or administering drugs and drug products to the foetus have greater risk of abortion (5%).

Prenatal diagnosis makes it possible to initiate intrauterine therapy which is useful to treat metabolic disorders e.g. methylmalonic acidemia with pharmacologic doses of Vitamin B₁₂ administered to the mother.

When no form of effective therapy, either intrauterine or post natal is available and the genetic disorder is clinically devastating, prenatal diagnosis offers the parents the option of a therapeutic abortion.

### 6.3 Treatment of Genetic Disorders

The progress made in defining biochemical derangements in genetic disorders made it possible to design therapy for many disorders.

For several enzyme deficiencies it is possible to prevent the accumulation of toxic intermediates or catabolic products e.g. dietary restriction of phenylalanine in phenylketonuria. In other disorders, it is possible to replace the deficient end product of a pathway e.g. hormone replacement in inherited endocrine deficiency syn-
dromes. The activity of some mutant enzymes can be stimulated by the administration of pharmacologic doses of cofactors e.g. pyridoxine in homocystinuric patients with selective defects in cystathionine synthetase. Mutant or absent proteins can be replaced e.g. insulin in type I diabetes mellitus. Cells containing normal proteins or enzymes can be administered e.g. red blood cell transfusions for sickle cell anaemia or bone marrow transplantation for adenosine deaminase deficiency.

Replacement of defective gene products is less than satisfactory in the long run for many genetic disorders. If the gene product is used, this necessitates repeated administrations. In the case of protein, purified products may be difficult to obtain in sufficient quantities, the exogenous protein may be rapidly cleared by immune mechanisms and for some disorders the protein may not reach the appropriate intracellular site where it is needed.

The ideal therapy is replacement of the defective gene so the patient has a continuous source of the normal gene product. This is done by organ or cell transplantation. This approach has limited usefulness due to lack of suitable donors and the problem of immune rejection and/or immunosuppressive therapy.

To avoid these drawbacks, normal or mutant alleles for a number of human genes have been isolated. These normal genes have been introduced into patient’s cells and the transplanted genes have been shown to produce normal gene products and correct the metabolic errors in these cells e.g. the gene for hypoxanthine-guanine phosphoribosyl transferase has been cloned and introduced into the cells of patients and the defect in purine metabolism was corrected.
SECTION VII

ADVERSE DRUG REACTIONS (ADR)

In this section:

7.1 Aetiology 30
7.2 Diagnosis 30
Special Adverse Drug Reactions 31
7.3 Hepatotoxic Agents 31
7.4 Drug-Induced Renal Failure 38
7.5 Blood Dyscrasias 40
7.6 Dermatitis Medicamentosa (Drug Eruption) 41
7.7 Cardiovascular 43
7.8 Gastrointestinal 44
7.9 Neurologic and Psychiatric 45
7.10 Ocular 45
7. Adverse Drug Reactions (ADR)

The beneficial drug effects are coupled with the risk that they may also cause untoward effects. The morbidity and mortality that result from these side effects often present diagnostic problems, as these drugs can involve every organ and system in the body.

The extremely large number and variety of drugs and drug products available over the counter (OTC) or by prescription from physicians make it impossible for patient or physician to obtain the knowledge necessary to use all these drugs well. The public uses many OTC drugs unwisely and physicians may prescribe the restricted drugs incorrectly.

Physicians must recognize that providing directions with prescriptions doesn’t always guarantee their patient compliance.

Every drug can produce untoward consequences, even when used according to standard or recommended methods of administration. When used incorrectly, the drug’s effect may be reduced or adverse reactions can be expected to occur more frequently. The administration of several drugs during the same period of time also may result in adverse interactions between drugs.

In the hospital, all drugs should be under physician control and patient compliance must be ensured, however, errors may occur or the drug may be given to the wrong patient. Patients receive an average of 10 different drugs while hospitalised. The sicker the patient, the more drugs are given with increase in ADR probability. When less than 6 different drugs are given, the probability is over 40%. In ambulatory patients, the ADR incidence is about 20%.

In general, aspirin, digoxin, anticoagulants, diuretics, antimicrobials, steroids and hypoglycemic agents account for about 90% of all reactions.

7.1 Aetiology

ADRs occur in one of two forms. The most frequent is exaggerated, but predicted, pharmacological action of the drug. The other form is toxic effects that result from mechanisms unrelated to the intended pharmacological action. These are unpredictable, usually severe, and result from a number of recognized as well as unrecognized mechanisms. Some of the mechanisms of extra pharmacological toxicity include direct cytotoxicity, abnormal immune response or genetic enzymatic defects.

7.2 Diagnosis

The manifestations of ADRs frequently resemble those associated with other diseases and may be produced by different and dissimilar drugs.

Illness related to drug’s pharmacologic action might be more easily recognized than illness attributable to
immunologic or other mechanisms e.g. cardiac arrhythmias in patients under digitalis, hypoglycemia in patients given insulin, and bleeding in patients receiving anticoagulants can be more easily recognized and related to the prescribed drug than are symptoms as fever or rash which may be caused by many drugs.

Once ADR is suspected, the discontinuation of the suspected drug followed by disappearance of the reaction indicates a drug-induced illness. Re-appearance of the reaction upon cautious re-administration of the drug provides further confirmation of the relationship.

With concentration dependent adverse reactions, lowering the dose is followed by disappearance of the reaction and increasing the dose may cause it to reappear. When the reaction is allergic re-administration of the drug is hazardous, since anaphylactic shock may develop.

If patient is receiving many different drugs, when ADR is suspected, the drugs most likely to be incriminated can be identified. All drugs may be discontinued at once or if this is not practical, drugs should be discontinued one at a time, starting with the most suspected drug and the patient is observed for improvement of signs and symptoms. The time taken for the disappearance of a concentration dependent adverse reaction will depend on the time taken for the blood concentration to fall below the range associated with the adverse effect.

Serum antibody is demonstrated with drug allergy involving blood elements e.g. agranulocytosis, haemolytic anaemia and thrombocytopenia. In other types of drug allergy, precipitation, haemagglutination or complement-fixation tests with drugs or drug degradation products are rarely related to ADR. Skin tests with drugs or its degradation products are of little value in allergic individual.

Patients' drug history is important for diagnosis. Attention must be directed to the OTC as well as to prescription drugs. Frequently ADRs occur when drugs prescribed or purchased OTC interact via mechanisms such as duplication, addition, counteraction or synergism.

To assist in the identification of ADR, an index of the drugs recognized as producing a number of reactions is included. It includes the well-documented reactions and it suggests the likely causative drug.

Special Adverse Drug Reactions

7.3 Hepatotoxic Agents

- Inorganic

Metals, metalloids (antimony, arsenic, copper, iron, lead, manganese, phosphate), iodides and hydrazine derivatives

- Organic

*Natural*: plant e.g. nutmeg, tannic acid.
*Mycotoxins* e.g. *aflatoxin* and antibiotics.

*Synthetic:* Non-medicinal organic compounds, alkanes, amines and aromatic compounds.

*Medicinal:* over 100 drugs used in diagnosis and treatment.
## Index of drugs with well-documented ADRs

<table>
<thead>
<tr>
<th>Organ/System</th>
<th>Documented ADRs</th>
<th>Implicated Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear</td>
<td>Vestibular disorders</td>
<td>Aminoglycosides, Quinine, Mustine</td>
</tr>
<tr>
<td></td>
<td>Deafness</td>
<td>Aminoglycosides, Ethacrynic acid, Furosemide, Quinine, Bleomycin, Chloroquine, Mustine, Aspirin, Nortriptyline</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Myopathy/Myalgia</td>
<td>Corticosteroids, Chloroquine, Chlofibrate, Oral contraceptive, Amphotericin, Carbinoxolone</td>
</tr>
<tr>
<td>Bone disorders</td>
<td>Osteoporosis</td>
<td>Corticosteroids, Heparin</td>
</tr>
<tr>
<td></td>
<td>Osteomalacia</td>
<td>Anti-convulsants, Glutethemide, Aluminum hydroxide</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Schizophrenia like/paranoid-reactions</td>
<td>Amphetamines, Lesergic acid, Levodopa, Tricyclic antidepressants, MAOIs, Bromides, Corticosteroids</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
<td>Centrally acting anti hypertensive (reserpine, methyl-dopa, clonidine), Propranolol, Corticosteroids, Amphetamine withdrawal, Levodopa</td>
</tr>
<tr>
<td></td>
<td>Hypomania, mania or excited reactions</td>
<td>Levodopa, Sympathomimetics, Corticosteroids, MAOIs, Tricyclic antidepressants</td>
</tr>
<tr>
<td></td>
<td>Hallucinatory states</td>
<td>Amantadine, Narcotics, Pentazocine, Propranolol</td>
</tr>
</tbody>
</table>
Index of drugs with well-documented ADRs (continued)

<table>
<thead>
<tr>
<th>Organ/System</th>
<th>Documented ADRs</th>
<th>Implicated Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric</td>
<td>Hallucinatory states</td>
<td>Levodopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Meperidine</td>
</tr>
<tr>
<td>Delirious /</td>
<td>Confusion states</td>
<td>Digitalis</td>
</tr>
<tr>
<td>confusion states</td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Bromides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sedatives and hypnotics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phenothiazines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antidepressants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Corticosteroids</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Isoniazid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levodopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Amantadine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Penicillins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aminophylline</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylprednisol</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td></td>
<td>Anorexiant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Levodopa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MAOIs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sympathomimetics</td>
</tr>
<tr>
<td>Drowsiness</td>
<td></td>
<td>Anxiolytics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anti-psychotic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tricyclic antidepressants</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Antihistamines</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Methylprednisol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clonidine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reserpin</td>
</tr>
</tbody>
</table>

**Hepatotoxic drug classification and pathological features**

1. **Predictable (intrinsic) hepatotoxins**

All recipients are susceptible, they are dose-dependent and of high incidence.

*Direct*: act via direct biochemical attack of cell membrane or protein denaturation. They produce zonal necrosis e.g. *carbon tetrachlorides* and *phosphorus*. They induce acute toxicity.

*Indirect*: act via inhibition of the essential metabolites for cell integrity. Liver injury develops within several days (delayed) following ingestion.

They are either:

*Cytotoxic hepatotoxins*: produce necrosis or steatosis e.g. **6-mercaptopurine**.

*Steatosis*: results from interference with apoprotein synthesis of the lipoprotein-complex required for lipid
transport from the liver and from other defects in lipid metabolism.]

Cholestatic hepatotoxins: produce jaundice or hepatic dysfunction by selective interference with mechanisms or structures involved in bile excretion or uptake of its constituents from the blood. The canalicular endothelium and liver cells swell and compress bile ducts forming thick bile casts and plugs, with bile droplets inside the hepatocyte. If it progresses, it leads to cellular damage. They are of two types.

*Canalicular type:* mild portal inflammation e.g. 17-anabolic steroids.

*Hepatocanalicular:* slight hepatic injury e.g. phenothiazines, chlorpropamide, chlorthiazide, erythromycin, and thiouracil.

2. Nonpredictable (Idiosyncratic) hepatotoxins

It occurs due to hepatic susceptibility rather than intrinsic toxicity. It is non-dose dependent with low incidence. It is mediated via a drug allergy mechanism.

*Hypersensitivity:* It is of minor incidence (1%) and represents one stage of this type of toxicity. It is accompanied with fever, rash, eosinophilia and usually develops after a sensitization period of 1–5 weeks. There is necrosis or cholestasis e.g. phenytoin, and sulphonamides.

*Metabolic:* Hepatotoxic metabolites produce necrosis or cholestasis e.g. isoniazide. It occurs after weeks to months of drug administration.

**Clinical aspects and presentation**

Hepatic injury may be acute or chronic and may be solitary or with other systemic manifestations. Examples:

*Allergic reactions* (fever, rash, eosinophilia, mononucleosis, lymphadenopathy) e.g. anticonvulsants, oxyphenacetin

*Haemolytic anaemia* e.g. phenylbutazone, and anticonvulsants

*Bone-marrow injury* e.g. phenylbutazone, and anticonvulsants

*Renal injury* e.g. anticonvulsants, methoxyflurane

*GIT ulceration and pancreatitis* e.g. tetracycline, and phenylbutazone

These reactions occur at any time during therapy and usually clear within few weeks after discontinuation, but excessive damage leads to fatal results.

1. Acute hepatic injury (ALT, AST)

It resembles viral hepatitis e.g. elevated enzymes, anorexia, nausea and fatigue. In severe cases there may be
deep jaundice, purpura, bleeding, coma and even death.

The fatality rate is 10-50% and survivals enjoy complete recovery.

Acute steatosis resembles acute fatty liver of pregnancy or Reye’s syndrome with slight jaundice and moderate elevation of enzymes but it is more serious e.g. tetracycline injection.

The cholestatic type resembles obstructive jaundice with pruritis and elevated enzymes (γ-glutamyl transpeptidase provides a highly sensitive index).

2. Chronic hepatic injury (chronic necro-inflammatory disorder)

Chronic active hepatitis: It resembles the auto-immune type of active hepatitis. Implicated drugs include phenacetin, iproniazid, isoniazid, methyl-dopa, sulphamides, nitrofurantoin, and propylthiouracil.

Steatosis: implicated drugs include ethanol, methotrexate, cytotoxics, glucocorticoids.

Phospholipidosis: It is accumulation of phospholipids in the lysosomes with the development of cirrhosis.

Cirrhosis: types and implicated drugs include:

- Macronodular e.g. ethanol, methotrexate
- Primary biliary e.g. chlorpromazine, phenothiazine, organic arsenic, tolbutamide, and thiobendazole.
- Congestive cirrhosis e.g. oral contraceptive, thioguanine, urethan.

Vascular lesions: include sinusoidal dilatation e.g. anabolics, oxazepam, contraceptives, and hepatic vein thrombosis e.g. contraceptives.

Neoplasms: Adenoma e.g. anabolics, contraceptives. Carcinoma (Hepatocellular) e.g. anabolics, contraceptives (Cholangiocellular). Angiosarcoma e.g. vinyl chlorides, arsenicals

Granulomas: e.g. allopurinol, hydrazine, penicillins, phenylbutazone, quinidine, sulphonamides, sulphonylureas

Management of drug-induced hepatotoxicity

Stop drug administration, in severe cases administer prednisone 100 mg/d, Supportive and symptomatic measures (acute hepatitis) include:

- Bed rest until acute symptoms subside
- Avoid physical exertion and unnecessary transportation
- Avoid drugs and elective surgery under general anaesthesia
- Palatable, soft and bland diet mainly consisting of carbohydrates, proteins and minimal fat
- In impending hepatic coma apply protein restriction down to 40 gm/d that can be increased as improvement progresses
- In severe vomiting administer glucose 10% IV and suction (nasogastric tube)

**Altered drug pharmacokinetics in hepatic disorders**

Alteration of pharmacokinetic characteristics of various drugs has been associated with liver disease. The most dramatic alteration is cumulative changes of drug disposition especially in chronic hepatitis, degeneration and cirrhosis.

Increase in the bioavailability of drugs that have high first-pass effect is due to reduction in the initial metabolism prior to reaching the systemic circulation as well as due to bypassing of blood around the liver as a result of intra- and extra- hepatic shunts.

Alteration in drug distribution due to hypoalbuminemia in cirrhosis results from a decrease in protein binding capacity with increase in the unbound fraction of the drug in the serum. This is very significant for drugs that are highly protein-bound (over 90%), leading to an increase in their volume of distribution.

Also the changes in drug clearance is due to changes in liver blood flow especially for drugs with high excretion ratio e.g. propranolol and lidocaine.

**Precautions of drug administration in hepatic injury**

The prescribed drugs and their doses must be adjusted and based on the patient’s response as well as on drugs elimination and their pharmacokinetic properties. The documented hepatotoxic drugs should be avoided. Examples of drugs with affected pharmacokinetic parameters include:

- **Increased bioavailability**: (drugs highly affected by first-pass metabolism): meperidine, pentazocine, propranolol, salicylamide
- **Increased volume of drug distribution** (highly protein-bound): benzodiazepine, lidocaine, pancuronium, valproic acid, theophylline, propranolol
- **Decreased elimination** (increased half-life): chloramphenicol, acetyaminophen, diazepam, isoniazid, meperidine, prednisone, meprobamate, carbencillin, clindamycin, lidocaine, hexobarbital, phenobarbitone, theophylline.

**Drugs to be avoided or used cautiously in hepatic cirrhosis**

They include drugs that induce encephalopathy or variceal bleeding. Drug-induced encephalopathy is the result of altered pharmacokinetics with accumulation and increased CNS sensitivity to these drugs. They include sedatives, hypnotics, antianxiety, anti–psychotics, anaesthetics, alcohol and narcotics.
Diuretic therapy induces electrolyte imbalance that results in hepatic coma i.e. hypokalaemia and hypovol–aemia (hepato-renal failure).

Drug-induced variceal bleeding may result from direct esophageal irritation and erosion, or form increased gastric acidity with regurgitation leading to esophageal erosion and haemorrhage e.g. potassium chloride, analgesic, anti-inflammatory, anti-rheumatics, quinidine, ferrous sulphate and ascorbic acid.

**Hepatotoxic drugs (alphabetical listing)**

They produce changes in liver function or lead to jaundice or hepatitis. They should be kept in mind for the possibility of altering the following laboratory tests e.g. Urine: increased bilirubin (false positive). Serum: AST, ALT, GGT, alkaline phosphatase, bilirubin (icterus index), bromo-sulphalein (BSP). Antibody retention and flocculation and thymol turbidity are increased (false positive). Cholesterol and blood glucose are decreased (false negative).

The list include: acetohexamide, allopurinol, acetylsalicylic acid, amodiaquin, amphotericin B, anabolic, androgens, antimony, organic arsenical compounds, bisth-muth, carbamazepine, chlorpropamide, cyclophosphamide, desipramine, erythromycin estolate, ethambutol, ethionamide, gold compounds, haloperidol, hydrazine compounds, ibufenac, imipramine, indandiones, isoniazid, loncomycin, MAOIs, mercaptopurine, methoxalen, methimazole, methyl dopa, methy luracil, methylbutazone, oral contraceptives, propylthiouracil, protriptyline, pyrazinamide, tetracyclines (in large doses or prolonged use), thioguanine, tolazamide, triacylholleandomycin, and trimethadone.

**7.4 Drug-Induced Renal Failure**

Acute and chronic renal damage are classified morphologically into glomerular, tubular, interstitial, vascular and urinary outflow derangement (obstructive uropathy). Glomerular lesions may be diffuse (all glomeruli are uniformly involved), focal (some glomeruli are affected), or segmental (only part of the glomerular tufts is involved).

Chronic renal failure is irreversible with reduction in GFR to less than 30% of normal. In ARF, 20% of cases are drug-induced.

**1. Glomerular damage**

Clinically there are heavy albuminuria, oedema, casts (red cells and HB) and RBCs. Implicated drugs include: penicillamine, probenecid, procarbamid, hydralazine, captopril, NSAID, allopurinol, and serum sickness.
2. Acute tubular necrosis (toxic nephropathy)

It is due to direct toxic injury. Clinically there are haematuria, tubular cells and casts (granular and tubular cells), tubular acidosis (due to proximal tubular decreased re-absorption of \( \text{HCO}_3^- \) or distal tubular decreased \( \text{H}_2^+ \) secretion.

Implicated drugs include antimicrobials (sulphonamides, tetracyclines, cephalosporins, aminoglycosides, colistin, polymyxin, amphotericin B, rifampin and grisofolvin), heavy metals (mercury, lead, arsenic, gold and barium), and miscellaneous (radio-iodinated contrast agent, cisplatin, doxorubicin, streptozocin, methramycin, halothane, methoxyflurane and ethylene glycol).

3. Medullary-papillary necrosis

Occurs in the following cases:

- Increase in some drug concentration and decreased blood supply (hypoxia) leading to papillary necrosis e.g. analgesic nephropathy (phenacetin abuse).
- Impaired concentration ability leading to nephrogenic diabetes insipidus with diluted urine, polyuria, polydypsia and nocturia.
- Decreased sodium chloride re-absorption leading to salt wasting e.g. lithium, demeclocycline, vitamin D and methoxyflurane.

4. Tubulo-interstitial nephropathy

In 60% of cases it is due to direct toxins and in 40% it is allergic. The acute type leads to acute renal failure with tubular dysfunction. It is allergic and is not dose-related and it appears after 2 to 40 days of therapy. Clinically there are fever, mild haematuria (painless), proteinuria (tubular origin), pyuria and casts (granular, tubular cells and WBCs), skin rash and eosinophilia.

Implicated drugs include antimicrobials (penicillin particularly methicillin, carbinicillin, cephalosporin, erythromycin, nafcillin, oxacillin and sulphonamides, rifampin and ethambutol), diuretics (furosemide, ethacrynic acid, thiazide, diamox, spironolactone and mercurials), and NSAIDs, allopurinol, probenecid, cimetedine, captopril, interferon, phenobarbitone, phentoin, phenindione.

The chronic type has undulant course and renal involvement may go undetected unless laboratory and biopsy results are done.

5. Obstructive uropathy

In 15% of cases it is a post-renal failure. It should be ruled out initially, as it is reversible. Signs and symptoms include flank pain due to capsular stretch, crystalluria (irritation) or stone and obstruction (partial obstruction results in oliguria and complete obstruction leads to anuria).
If the acute condition is not corrected it will go into chronicity with a resulting distal tubular defect. The later manifest with decreased hydrogen ion excretion leading to distal tubular acidosis with decreased potassium ion excretion (hyperkalemia), inability to concentrate urine due to lack of sodium ions in the interstitium and decreased sodium re-absorption leading to salt wasting. The increased pressure in the proximal tubules activates the RAA system with vasoconstriction and decrease in renal blood flow and glomerular filtration rate which leads to the mentioned distal tubular defects.

In renal pelvis, ureters and bladder there are crystalluria (uric acid due to cytotoxics), stone, blood clots and papillary necrosis.

7.5 Blood Dyscrasias

Aetiology may be due to a dose-related myelosuppression e.g. cytotoxics, idiosyncrasy (allergic, enzymatic deficiency e.g. G-6-D deficiency, or haemoglobin abnormality) or exposure to excessive ionizing irradiation.

1. Haemolytic anaemia

Signs and symptoms include chills, fever, nausea, vomiting, abdominal and back pain, pallor, slight jaundice, red urine and acute renal failure.

Management (emergency): stop medications, steroids and administer packed RBCs. In G-6-D deficiency stop medication, administer packed RBCs and perform renal function profile.

Implicated drugs: G-6-D deficiency (antimalarials e.g. primaquine, chloramphenicol, sulphonamides, co-trimoxazole, nalidixic acid, nitrofurantoin, salicylates, phenacetin, procainamide, vitamin C and vitamin K), idiosyncrasy: (NSAIDs, antimalarials, methyldopa, levodopa, chlorpromazine, antituberculous, chloramphenicol, sulphonamides, penicillin and cephalosporin.

2. Lymphadenopathy

Implicated drugs include phenytoin and primidone.

3. Leucocytosis

Implicated drugs include corticosteroids and lithium.

4. Eosinophilia

Implicated drugs include imipramine, chlorpropamide, sulphonamides, nitrofurantoin and methotrexate.

5. Pancytopenia and aplastic anaemia

Implicated drugs include anti-rheumatics (pyrazolones and gold salts), antibacterials (sulphonamides, chloramphenicol and streptomycin), anti-malarials, cytotoxics, oral hypoglycoemics, antiepileptics and insecticides.
Management is with androgens, anabolic steroids and fresh packed RBCs.

6. Agranulocytosis (with relative lymphocytosis)

Implicated drugs include anti-rheumatics (pyrazolones, gold salts), antiepileptics, CNS depressants (phenothiazines and TCA), sulphonylurea, anti-thyroid, antibacterial (sulphonamides, chloramphenicol, streptomycin) and antimalarials.

7. Thrombocytopenia

Signs and symptoms include subcutaneous petechiae, GIT and urinary bleeding (haematuria).

Implicated drugs include those that produce myelo-suppression or platelet dysfunction e.g. anti-rheumatics (pyrazolones, indomethacin and gold), sulphonylureas, antiepileptics, antihypertensives (methyldopa, thiazides), antibacterials (sulphonamides, chloramphenicol, tetracycline), antimalarials and insecticides.

Management: avoid trauma, sport, elective surgery or dental procedure, stop the implicated medications, and perform platelet transfusion.

7.6 Dermatitis Medicamentosa (Drug Eruption)

A wide variety of drugs, in susceptible individuals, act systematically and cause a wide variety of acute or chronic inflammatory skin reactions. Improvement follows drug withdrawal after few days or longer. A provocation by re-exposure for diagnostic purposes should never be attempted as it is of no value.

Management: Discontinuation of all medications, if possible. Increase drug elimination by increasing fluid intake. Give specific antidote (if available), e.g. dimercaprol in heavy metals and sodium chloride for iodides and bromides. Treat the different stages of dermatitis; acute: local cold compresses and soothing wet-lotion dressings. For infections give antibiotics combined with topical anti-infective agent.

Precautions

Prescribe drugs that are really indicated and do not exceed 3 at a time. Never prescribe a topical drug which will be given later systemically e.g. antihistaminic. It is preferable to give drugs orally than: SC, IM or IV Use drug cautiously in patients with history of allergy e.g. urticaria or asthma.

1. Photo-dermatitis

Signs and symptoms: Acute inflammatory reaction following solar or UV-exposure, varies from simple erythema to severe exfoliation with systemic manifestations.

Implicated drugs: Hypnotic-antipsychotics (barbiturates, benzodiazepines and phenothiazines), oral contraceptives, cytotoxics, antibacterials (sulphonamides, griseofulvin, tetracyclines), weak antiseptic soap and cream e.g. hexachlorophen

Ministry of health and population
and halogenated salicylanilides), gold salts, thiazides and sulphonylureas.

2. Acniform eruptions
Signs and symptoms: Inflammatory pleomorphic lesions e.g. pustules, black heads, white heads, enlarged pores, cysts and scarring, localized on face, neck, chest, back and shoulders.

Implicated drugs: Hormones (steroids, androgens, oral contraceptives), antituberculoses (isoniazid, ethionamide).

3. Erythema multiforme (Stevens-Johnson syndrome)
Signs and symptoms: Acute inflammatory polymorphic lesions, which occur on dorsum of hands, forearms, feet, necks, oral mucosa and genitalia. It is self-limited.

Implicated drugs: CNS depressants (barbiturates, phenothiazines, phenytoin, codeine), antibacterials (sulphonamides, penicillin, tetracycline, griseofulvin), oral hypoglycemics and diuretics.

4. Exfoliative dermatitis
It is itching and weeping red patches which spread with desquamation, accompanied with fever and systemic symptoms and may be fatal.

Implicated drugs: CNS depressants (barbiturates, phenytoin, phenothiazines), antibacterials (sulphonamides, penicillin, streptomycin, griseofulvin), pyrazolones and gold salts.

5. Erythema nodosum (fixed dermatitis)
It is tender, nodular and erythematous dermatitis occurring on extensor surface of legs, less often forearms and male genitalia.

Implicated drugs: CNS depressants (barbiturates, phenothiazines, morphine), antipyretics, antirheumatics, antibacterial (sulphonamides, penicillin, streptomycin), antimalarial and CVS (digitalis, quinidine and hydralazine).

6. Urticaria (hives) and angioneurotic oedema (giant hives)
It is acute or chronic inflammatory reactions with polymorphic pruritic wheal reactions. Acute attacks are self-limited (few minutes to weeks) and have a tendency to recur. If larynx is affected, it may result in respiratory obstruction.

Implicated drugs: CNS (barbiturates, phenytoin, narcotics), antirheumatic (aspirin, pyrazolones, gold), antibacterial (sulphonamides, penicillin, streptomycin, chloramphenicol, tetracycline, griseofulvin), vaccines, saccharin.
7. Lupus erythematosus-like syndrome
It is acute or chronic dermatitis consisting of mild local eruptions over the nose and cheeks. Diagnosis is by direct immunofluorescent test of frozen skin biopsy.

Implicated drugs: antibacterials (sulphonamides, penicillin, griseofulvin, isoniazid, tetracycline, streptomycin), antiepileptics, pyrazolones, oral contraceptives, hydralazine, chlorpromazine, steroid withdrawal

8. Hyperpigmentation
Implicated drugs: phenothiazines, oral contraceptives, gold salts, ACTH, cytotoxics and antimalarial.

9. Alopecia
Implicated drugs: heparin, cytotoxics, oral contraceptives, phenothiazines, methyl dopa, ethionamide.

10. Contact dermatitis (by local use) Eczema
Implicated drugs: anti-histaminic, antimicrobials, anaesthetics and lotion or cream preservatives

11. Anaphylaxis
Implicated drugs: antibacterials (penicillin, cephalosporin, streptomycin), iron, dextran, procaine, insulin, demeclocycline, lidocaine, iodinated drugs (contrast media).

12. Fever
Implicated drugs: antibacterial (penicillin, novobiocin, amphotrecin B, cephalosporin, sulphonamides), anti-histamines, barbiturates, phenyltoin, iodides, thiouracil, methyldopa, quinidine and procainamide.

7.7 Cardiovascular
1. Cardiomyopathy
Failure, arrhythmia, etc. cytotoxics (daunorubicin, adriamycin), emetine, lithium, phenothiazines, sympathomimetics.

2. Pericarditis
Procaainamide, hydralazine, emetine.

3. Exacerbation of angina (myocardial ischemia)
Vasopressin, oxytocin, ergometrine, β-blocker withdrawal, α-blockers, hydralazine, nefidipine, excess thyroxin.

4. Congestive heart failure or fluid retention
Oestrogen, steroids, phenylbutazone, indomethacin, β-blockers, mannitol, diazoxide.

5. Hypertension
Oral contraceptives, sympathomimetics, TCA or MAOIs with sympathomimetics, corticosteroids, phenylbutazone, clonidine and α-methyldopa.
6. Arrhythmias
Sympathomimetics, thyroid, digitalis, quinidine, aerosol propellants, TCA, thioridazine, lithium, papaverin, lincomycin IV, adriamycin, daunomycin, anticholinesterases.

7. Hypertension
Nitroglycerine, phenothiazine, morphin, diuretics, levodopa and citrated blood.

7.8 Gastrointestinal
1. Dental discolouration and mottling (pitting)
Implicated drugs: tetracycline

2. Gingival hyperplasia
Implicated drugs: phenytoin

3. Oral ulceration
Implicated drugs: aspirin, cytotoxics, and gentian violet

4. Taste disturbances
Implicated drugs: penicillamine, metronidazol, griseofulvin, lithium, biguanides, and rifampicin

5. Dry mouth
Implicated drugs: anticholinergics, levodopa, TCA, clonidine, and methyldopa

6. Salivary glands swelling
Implicated drugs: phenylbutazone, guanethidine, clonidine, and iodides.

7. Peptic ulcer or haemorrhage
Implicated drugs: aspirin, phenylbutazone, indomethacin, ethacrynic acid, and potassium chloride tablets

8. Nausea and vomiting
Implicated drugs: digitalis, opiates, oestrogen, levodopa, bromocryptine, potassium chloride, aminophylline and tetracycline

9. Diarrhoea or colitis
Implicated drugs: macrolides (clindamycin), broadspectrum antibiotics, methyldopa, digitalis, colchicines, purgatives, and lactose excipients

10. Constipation or ileus
Implicated drugs: TCA, phenothiazines, opiates, aluminium hydroxide, calcium carbonate, ion exchange resins, and ferrous sulphate

11. Pancreatitis
Implicated drugs: corticosteroids, thi-azides, azathioprine, oral contraceptives, sulphonamides, opiates, furosemide.
7.9 Neurologic and Psychiatric

1. Peripheral neuropathy (paraesthesias, muscle cramps)

Implicated drugs: cytotoxics (vincristine, mustine, procarbazine), TCA, antibacterial (isoniazide, nitrofurantoin, streptomycin, chloramphenicol, ethambutol, demeclocycline, nalidixic acid) tolbutamide, chloropropamide, and phenytoin

2. Extrapyramidal effects (tremors, hypertonia, dyskinesia)

Implicated drugs: butyrophenones, phenothiazines, TCA, methyldopa, levodopa, and metoclopramide

3. Seizures

Implicated drugs: amphetamines, analeptics, phenothiazines, lidocaine, theophylline, nalidixic acid, physostegmine, TCA, lithium, and vincristine

4. Depression

Implicated drugs: β-blockers, corticosteroids, centrally acting antihypertensives, levodopa, and amphetamine withdrawal

5. Psychotic symptoms (delusion, illusion, hallucination)

Implicated drugs: amphetamines, levodopa, TCA, MAOIs, corticosteroids, and bromocryptine

7.10 Ocular

1. Corneal opacities

Implicated drugs: vitamin D, chloroquine, indomethacin, and amiodarone

2. Cataract

Implicated drugs: phenothiazines, corticosteroids, busulphan, and chlorambucil

3. Retinopathy

Implicated drugs: chloroquine, and phenothiazine

4. Optic neuritis

Implicated drugs: chloramphenicol, streptomycin, isoniazide, ethambutol, phenothiazines, penicillamine, and phenylbutazone
SECTION VIII

GASTRO-INTESTINAL TRACT DRUGS

In this section:

8.1 Anti-Emetics and Anti-Nausea (Gastro-prokinetics) 47
8.2 Anti-Emetics During Cytotoxic Therapy (Serotonin Antagonists) 48
Topic: Peptic ulcer 49
8.3 Peptic Ulcer Drugs 50
8.4 Antacids 52
8.5 Antidiarrhoeal Drugs 53
8.6 Intestinal Evacuants, Laxatives, Purgatives 55
8.7 Anti haemorrhoids 56
8.8 Antiflatulents 57
8.9 Intestinal Antiseptics 58
8.10 Enema 58
8.11 Liver Support 58
8.12 Cholagogues 59
8.13 Antispasmodics 59
8. Gastro-Intestinal Tract Drugs

8.1 Anti-Emetics and Anti-Nausea (Gastroprokinetics)

Nausea and vomiting can follow the administration of many drugs, particularly cancer chemotherapeutic agents. These symptoms may occur upon emergency from general anaesthesia and often accompany infectious and non-infectious gastrointestinal disorders. They are also encountered all too frequently during early pregnancy or as a result of motion sickness.

Vomiting is under the control of two medullary centres; the vomiting centre (VC) and the chemoreceptor trigger zone (CTZ).

The VC receives afferent stimuli from the GIT via the vagus nerve, e.g. in inflammatory conditions and due to drug effects (e.g. copper sulphate, mustard, tetracycline, cytotoxic drugs as cisplatin, and hypertonic salts). It also receives impulses from the labyrinth (motion sickness). The activation of the CTZ results in efferent impulses to VC as well as in cases of increased ICP. It also receives impulses from higher cortical centres and pain stimuli.

The CTZ is stimulated by drugs such as cardiac glycolsides, morphine, codeine, levodopa, ergot alkaloids, and cytotoxics. It is also stimulated in diseases such as uraemia, and motion sickness.

Metoclopramide

Pharmacological action

Central antiemetic: It is a dopaminergic (D_2) receptor blocker. In high doses it blocks 5-HT_3 receptors. It also has cholinergic effects (sensitizes the gut to ACh and release ACh from GIT cholinergic neurons).

Peripheral: It increases gastric motility with increased tone of lower oesophageal sphincter (LES) and rapid gastric emptying. It increases intestinal peristalsis and shortens transit time. These properties are due to the blocking of the inhibitory action of dopamine on GIT and the direct cholinergic effects.

Dose

Oral, IM or IV, ADULT: 10 mg (5 mg for 15-19 years adolescents) tid. CHILD: up to 1 year 1 mg bid; 1-3 years 1 mg tid/bid; 5-9 years 2.5 mg tid; 9-14 years 5 mg tid. Before radiological examination, a single IM dose of 10-20 mg (10 mg in young adults); CHILD: under 3 years 1 mg, 5-9 years 2.5 mg, 9-14 years 5 mg by continuous IV infusion. Before starting chemotherapy, 2-4 mg/kg over 15-30 minutes, then 3-5 mg/kg over 8-12 hours (maximum 10 mg/kg/day).

Indications

Nausea and vomiting
Contraindications

GIT haemorrhage, obstruction, perforation or immediately after surgery, and pheochromocytoma

Precautions

Renal and hepatic impairment; in elderly and under 20 years, pregnancy and lactation, patients with hypertension, parkinsonism, history of depression and after gut anastomosis in patients with diabetic gastroparesis, insulin dosage or timing might require adjustment.

Adverse effects

Diarrhoea, galactorrhoea and gynaecomastia can occur. May induce extrapyramidal manifestations (facial and skeletal muscle spasm and oculogyric crisis) in young patients

Drug interactions

Aspirin, paracetamol, opioid analgesics, reserpine, antimuscarinics, antipsychotics, lithium, tetrabenazine, levodopa and bromocryptine

Patient instructions

Take each dose 30 minutes before meals and at bedtime. Use caution when performing other tasks requiring mental alertness. Report any involuntary movements especially in children and elderly.

Domperidone

Pharmacological action

Gastric prokinetic (increase gastric tone without diarrhoea) by its dopamine antagonism (D₂-receptor)

Dose

Tablets 10 mg, suspension 1 mg/ml and suppository 10 mg (infantile), 30 mg (paediatric) and 60 mg (adult)

Adverse effects

Gynaecomastia and galactorrhoea (stimulates prolactin release)

8.2 Anti-Emetics During Cytotoxic Therapy (Serotonin Antagonists)

Ondansetron

Pharmacological action

Anti-nausea and anti-emetic by antagonizing serotonin (5- HT₃); more effective than metoclopramide

Dose

Tablets 4 and 8 mg, 4 and 8 mg IV ampoules, (0.15 mg/kg/dose paediatric, 24 mg PO and 8 mg IV adults)

Indications

Severe nausea and vomiting during cytotoxic therapy. Hyperemesis gravidarum.

NB: Serotonin released from enterochromaffin cells stimulates afferent
vagus nerve to produce nausea and blocks those receptors that have anti-nausea and anti-emetic actions.

**Tropisetron**

**Dose**

5 mg capsules and 2.5 mg ampoules

**Indications**

see ondansetron

**Topic: Peptic ulcer**

Incidence: total 10%; Site: duodenal 20-50% gastric 50%; Sex: duodenal: male to female 3:1 and equal in gastric

Sites: Duodenal bulb, prepyloric antrum along the lesser curvature, lower oesophagus, jejunum (Zollinger syndrome) and ileum (Meckel’s diverticulum). Shape and character: round, oval, elliptical or elongated, with smooth margin, deep and penetrating to muscularis mucosa; occurring in areas bathed by acid and pepsin. The role of *Helicobacter pylori* is particularly important by diminishing mucosal defences through inflammation and is the main cause of high recurrence.

Diagnosis: Clinical: asymptomatic; mainly in elderly patients. Pain in the epigastric region that radiates to the back. The pain may be substernal, lower abdominal or periumbilical. It is characterised with periodic remissions and exacerbation. Epigastric tenderness with minimal rigidity.

Nausea and vomiting suggest pyloric obstruction.

Radiology: By standard technique and double (air) contrast technique.

Endoscopy: definitive, combined with brush cytology (biopsy) to exclude malignancy

Gastric juice analysis: achlorhydria (gastric cancer) and Zollinger syndrome (basal acid secretion more than 15 mmol/hour).

Complications: bleeding, pyloric obstruction, penetration and perforation (peritonitis).

Differential diagnosis: peptic oesophagitis, pancreatitis, cholelithiasis, cholecystitis, irritable bowel syndrome, non-ulcer dyspepsia and malignant gastric ulcer.

Peptic ulcer occurs in the presence of acid and pepsin although not necessarily in excess amount. Gastric ulcer is associated with normal acid secretion while duodenal ulcer with excess secretion.

Lines of treatment: General: rest and sedation. They can heal gastric ulcer and symptomatically improve duodenal ulcer. Smoking lowers the rate of ulcer healing and tends to increase its relapse. Diet: patients should avoid spices. Duodenal ulcer patients are advised to take meals at regular intervals to buffer intragastric acidity. Patients should avoid gastric and duode-
nal irritants such as caffeine, alcohol, aspirin, and indomethacin.

Peptic ulcer drugs include: histamine (H₂ receptor) antagonists (cimetidine, ranitidine, oxmetidine, and famotidine), proton pump (H⁺-K⁺, ATPase) inhibitors (omeprazole); anticholinergic drugs (pirenzepine); mucosal protective agents, sucralfate, colloidal bismuth compounds, prostaglandin analogues (misprostol); and antacids.

8.3 Peptic Ulcer Drugs

8.3.1 Proton pump inhibitors

Omeprazole

Pharmacological action

Decrease gastric HCl secretion by irreversible non-competitive inhibition of H⁺-K⁺-ATPase in gastric parietal cells.

Dose

20 mg capsules and 40 mg vials. 20-40 mg at bed time to decrease HCl for 24 hours

Indications

Peptic ulcer, (NSAIDs) dyspepsia to prevent duodenal ulcers and bleeding; ulcer healing rate is 90% within two weeks.

Adverse effects

Nausea, diarrhoea, abdominal pain, CNS (dizziness, headache), rash, gynaecomastia, increased liver transaminases and hypergastrinaemia with hyperplasia of enterochromaffin like cells and carcinoid tumours of the stomach (after several years of large doses). Enzyme inhibition decreases metabolism of diazepam, phenytoin, warfarin and tolbutamide.

8.3.2 H₂ receptor antagonist

Cimetidine

Pharmacological action

It reduces both day time and nocturnal gastric acid secretion. It competitively inhibits the action of histamine at the histamine H₂ receptors of parietal cells, also it blocks acid secretion induced by histamine, gastrin, cholinergic drugs and vagal stimulation.

Dose

By IM injection, 200 mg every 4-6 hours, maximum 2.4 g/day. Slow IV injection of 200 mg over at least 2 minutes, repeated after 4-6 hours. When larger doses are given or there is cardiovascular impairment, the dose should be diluted and given over 10 minutes, maximum 2.4 g/day. By IV infusion, 400 mg in 100 ml of normal saline (0.9% sodium chloride) infused over ½-1 hour (may be repeated every 4-6 hours) or by continuous IV infusion at a rate of 50-100 mg/hour, maximum 2.4 g/day. CHILD by IM or slow IV injection or IV infusion, 20-30 mg/kg/day in divided doses.

Indications

In benign duodenal, gastric or stomach ulcers, Zollinger-Ellison syndrome, reflux oesophagitis, prophy-
laxis of GIT haemorrhage as a result of stress ulcer and in patients at risk of acid aspiration during general anaesthesia.

**Precautions**

Exclude the possibility of malignancy before starting treatment, reduce dose in renal and hepatic impairment. IV injections should be given very slowly. Should be avoided in patients stabilized on phenytoin, warfarin, theophylline (or aminophylline) and cyclosporin.

**Adverse effects**

Altered bowel habits, dizziness, rash, tiredness, rarely gynaecomastia, reversible liver damage, rarely bradycardia and AV block.

**Drug interactions**

Phenytoin, warfarin, theophylline, aminophylline, cyclosporin, opioid analgesics, amiodarone, flecaïnine, lignocaine, procainamidine, propafenone, quinidine, rifampicin, metronidazole, nicoumalone, amitryptiline, desipramine, doxepin, imipramine, nortriptyline, metformin, carbamazepine, ketoconazole, chloroquine, quinine, chlorpromazine, benzodiazepines, some β-blockers, some calcium channel blockers, fluorouracil and sucralfate.

**Patient instructions**

Take after meals and again at bedtime. Should not be crushed or chewed. If you are taking antacids; at least 1 hour should separate doses of the two medications.

**Ranitidine**

**Pharmacological action**

A more potent and more selective H₂ antagonist with longer duration of action than cimetidine.

**Dose**

150 mg twice daily (morning and at night), or for patients with gastric and duodenal ulceration 300 mg as a single daily dose at night for 4-8 weeks. For Zollinger-Ellison syndrome 150 mg tid increased if necessary up to 6 g/day in divided doses. Maintenance: 150 mg at night. CHILD 8-18 years 150 mg at night. Prophylaxis of acid aspiration, 150 mg by mouth then every 6 hours IM injection of 50 mg every 6-8 hours. Slow IV injection, 50 mg diluted to 20 ml and given over at least 2 minutes (could be repeated every 6-8 hours).

**Indications**

To inhibit gastric secretion in duodenal and gastric ulcers, Zollinger-Ellison syndrome, reflux oesophagitis, in the prophylaxis of GIT haemorrhage as a result of stress ulcer and in patients at risk of acid aspiration during general anaesthesia.

**Contraindications**

Porphyria
Precautions
Exclude the possibility of malignancy before starting treatment. Reduce dose in renal and hepatic impairment. IV injections should be given very slowly.

Adverse effects
Altered bowel habits. Rare reports of breast swelling, bradycardia and AV block.

Drug interactions
Glipizide, warfarin, and procainamidine.

Patient instructions
Take on an empty stomach or with food or milk. One hour should separate doses of ranitidine and antacids.

8.4 Antacids
They neutralize gastric acidity by increasing the pH of the stomach and inhibiting proteolytic activity of pepsin. Antacids are classified as systemic (absorbable) that can produce systemic alkalosis, and non-systemic as aluminium, calcium, and magnesium salts (not absorbed to a significant extent so has no systemic effect).

Aluminum hydroxide
Pharmacological action
It is a non-systemic buffer antacid that neutralizes acid and binds to bile acid, pepsin and phosphates.

Dose
Suspension 5-10 ml, tablets 1-2 chewed qid between meals and at bedtime. CHILD 6-12 year up to 5 ml tid

Indications
For use in dyspepsia and in hyperphosphataemia

Contraindications
Hypophosphataemia, porphyria, undiagnosed GIT or rectal bleeding.

Precautions
Impaired renal function, renal dialysis, constipation, dehydration, fluid restriction

Adverse effects
Constipation, intestinal obstruction (large doses), hypercalciuria and risk of osteomalacia

Patient instructions
Do not take for longer than 2 weeks. Taking too much can cause stomach to secrete excess stomach acid. Reduce acidity for about 30 minutes when taken on an empty stomach and for about 3 hours when taken 1 hour after meals.

Magnesium trisilicate
Pharmacological action
Non systemic buffer antacid, reacts slowly with Hcl, stimulates gut motility.

Ministry of health and population
**Dose**

10 ml tid in water, 2 g by mouth

**Indications**

Dyspepsia.

**Contraindications**

Hypophosphataemia

**Precautions**

Liquid preparations are more effective than solid; impair absorption of simultaneously administered drugs; may damage enteric coating of other drugs

**Adverse effects**

Diarrhoea (magnesium)

**Drug interactions**

Aspirin, diflunisal, flecainide, mexiletine, quinidine, ciprofloxacin, rifampicin, pivampicillin, most tetracyclines, itraconazole, ketoconazole, chloroquine, hydroxychloroquine, phenothiazines, iron, penicillamine, and sucralfate

**Patient instructions**

May cause diarrhoea; chew before swallowing with a glass of water.

8.5 Antidiarrhoeal Drugs

Diarrhoea is characterized by excessive faecal loss of fluid and electrolytes. It occurs due to infectious and non-infectious GIT disorders. Although acute onset diarrhoea is most often of infectious origin, it is usually self-limited, and specific chemotherapy is seldom warranted or effective unless there is evidence of GIT erosion or systemic disease. Hence, the treatment is generally non-specific and is usually aimed at reducing the discomfort and inconvenience of frequent bowel movement. In some instances the oral or parenteral replenishment of fluid and electrolytes may be necessary and life saving.

8.5.1 Electrolytes of body fluid (restoratives)

**Oral rehydration solution**

**Pharmacological action**

It contains glucose, salt, and amino acids. Acute diarrhoea in children should always be treated with oral rehydration solution according to plans A, B, and C as follows.

*Plan A:* No dehydration, nutritional advice and increased fluid intake are sufficient (soup, rice, water, yoghurt).

*Plan B:* Moderate dehydration, a large amount of solution can be given if the child continues to have frequent stools.

*Plan C:* Severe dehydration, hospitalisation is necessary, but the most urgent priority is to start rehydration

**Dose**

According to fluid loss: 200-400 ml solution after every loose motion; INFANT (1-11 months) tid usual
feeding volume; CHILD 200 ml after every loose motion.

**Indications**

Fluid and electrolyte loss in diarrhoea

**Precautions**

For those who cannot retain the solution orally, IV treatment should be considered. Overdose may cause hypernatraemia and hyperkalaemia.

8.5.2 Intestinal adsorbants

**Kaolin, Pectin**

**Pharmacological action**

These increase the viscosity of gut content and act as a coat for the bowel and adsorb toxins.

**Dose**

Up to 24 g (usually in combination with other anti-diarrhoeal drugs

**Indications**

Symptomatic treatment of diarrhoea

**Drug interactions**

Absorption of other drugs may be reduced if administered concomitantly

8.5.3 Antipropulsives

**Loperamide**

**Dose**

Acute diarrhoea: initial 4 mg followed by 2 mg for each stool. The usual daily dose is 6-8 mg and 16 mg should not be exceeded daily. CHILD 13-20 kg, initial 3 mg/day in divided dose. Subsequent doses: 1 mg/kg/day in divided dose. Total dose should not exceed that given on first day. Chronic diarrhoea; 4-8 mg/day in divided dose; maximum 16 mg/day

**Indications**

Management of acute and chronic diarrhoea

**Contraindications**

Children are more prone to its CNS depressive action, so its use is not recommended for children below 2 years.

**Precautions**

Should be used cautiously in patients with hepatic dysfunction, dysentery, inflammatory bowel disease or pseudomembranous colitis

**Adverse effects**

Abdominal pain, toxic megacolon hypersensitivity reactions and CNS depression

**Drug interactions**

Opioid analgesics

**Patient instructions**

Use caution when performing tasks that requires mental alertness. Drink plenty of fluids.
8.6 Intestinal Evacuants, Laxatives, Purgatives

Glycerine and Gelatin

Pharmacological action

Soften faecal impaction and stimulate rectal peristalsis by increasing faecal bulk.

Dose

Infantile and adult suppositories

Indications

Constipation to evacuate the distal intestinal content and avoid straining at stools.

Lactulose

Pharmacological action

A synthetic non-absorbable disaccharide (galactose plus fructose); it is metabolized by colonic bacteria into low molecular weight acids that acidify the colonic contents, trap ammonia, and inhibit ammonia-producing bacteria. The laxative actions of these metabolites expel the trapped ammonium ion from the colon.

Dose

Constipation, initial 10-20 g (15-30 ml)/day in single or 2 divided dose; then dose is reduced gradually to 7-10 g (10-15 ml)/day. CHILD less than 1 year 2.5 ml bid; 1-5 years 5 ml bid; 5-10 years 10 ml bid. Hepatic encephalopathy, initially, 20-30 g may be given every hour; then the dose is adjusted every 1-2 days to produce 2-3 soft stools/day.

Indications

Constipation and hepatic encephalopathy

Contraindications

Intestinal obstruction and galactosaemia

Precautions

Diabetes mellitus

Adverse effects

GIT disturbances (flatulence, cramps, nausea and vomiting); prolonged use may lead to excessive water and electrolyte loss.

Drug interactions

Neomycin, non-absorbable antacids

Patient instructions

Can be mixed with fruit juice, water or milk to make it more palatable. Do not take other laxatives while receiving lactulose, increase dietary fibre and fluid intake and participate in regular exercise.

Senna Extract

Pharmacological action

Contains anthraquinone glycosides that stimulate the Auerbach’s plexus with purgation
**Dose**

15-30 mg of total sennosides given as a single dose at bedtime. CHILD over 6 years, give half the adult dose. Bowel evacuation, 1 mg/kg on the day before examination

**Indications**

Constipation and in evacuation of bowel before investigational procedures or surgery

**Contraindications**

Nausea, vomiting, and other symptoms of appendicitis

**Precautions**

Inflammatory bowel disease; prolonged use should be avoided

**Adverse effects**

Colic or cramps and discoloration of urine; prolonged use may lead to diarrhoea with excessive water and electrolyte loss (especially potassium) and the possibility of melanosina coli in colon

**Drug interactions**

Antacids and milk

**Patient instructions**

Do not use longer than 1 week; take with a full glass of water or juice; contact your doctor if rectal bleeding; adequate fluid intake 4-6 glasses of water daily

---

**Bisacodyl**

**Pharmacological action**

Contact irritant laxative (a stimulant). It is a synthetic congener of phenolphthalein. It directly stimulates sensory nerve endings in the colon increasing peristalsis.

**Dose**

Oral and suppository laxative; 5 mg tablets and 5-10 mg suppository

**Indications**

Acute constipation, clearing GIT before surgery or x-ray, after intestinal anthelminthic therapy to expel worms, to prevent straining at stool (piles, cardiac disorders, glaucoma, anal fissure, proctitis)

**8.7 Anti haemorrhoids**

**8.7.1 Products containing corticosteroids**

**Fluocortolone**

**Dose**

Ointment, apply bid for 5-7 days (tid-qid on the first day if necessary), then once daily for few days after symptoms have cleared. Suppository, use one/day after a bowel movement; In severe cases, start with bid-tid, then 1 suppository on alternate days for 1 week.
Indications
For occasional short-term therapy of haemorrhoids after exclusion of infections

[Contraindications, precautions, adverse effects, drug interactions, patient instructions, see corticosteroids]

Hydrocortisone

Dose
Ointment, apply night and morning and after a bowel movement (not to exceed 7 days). Suppository, insert one suppository night and day after a bowel movement (not to exceed 7 days)

Indications
For occasional short-term therapy of haemorrhoids after exclusion of infections.

[Contraindications, precautions, adverse effects, drug interactions, patient instructions, see corticosteroids]

8.8 Antiflatulents

Simethicone combinations and Dimethicone

Pharmacological action
Simethicone reduces surface tension of gas bubbles fuse them and helps in eliminating gas or air from GIT.

Dose
Plain dimethicone 10 mg, 30 mg chewable tablets, 100 mg/5 ml emulsion and 40 mg/ml drops

Indications
Meteorism, flatulence, dyspepsia and distension; combined with antacids, digestive enzymes, antispasmodics, gastroprokinetics, and antidiarrhoeals.
8.9 Intestinal Antiseptics

Neomycin

Dose
Tablets 500 mg and suspension 125 mg/ml. Orally: 1 g qid to decrease ammonia production in hepatic encephalopathy, and 2-6 g/day pre-operative to sterilize GIT for intestinal surgery. Topical: For external ear and conjunctiva and with chlorhexidine for staphylococcus nasal carriers

Adverse effects
Poorly absorbed, 13% of malabsorption is due to atrophic action on mucosa (diarrhoea), steatorrhea, azotorrhoea, vitamins, sugars and minerals loss.

Nifuroxazide

Pharmacological action
It has wide range of bactericidal activity against gram positive and gram negative enteropathogenic bacteria (Staph., Strept., Campylobacter jejuni, Shigella, Salmonella, E. coli and Yersinia). It is not absorbed and act locally. It doesn’t disturb intestinal flora.

Dose
200 mg capsules and 200 mg/5 ml suspension. 200 mg qid or tid.

Indications
Acute and chronic bacterial diarrhoea, gastroenteritis, acute and chronic colitis and intestinal antiseptic. It is safe during pregnancy, lactation, and infancy.

[Chloramphenicol and streptomycin: see anti-infectious drugs]

8.10 Enema

Sodium phosphate (cleansing enema)

Pharmacological action
Break hard faecal impaction in rectal and pelvic colon.

Dose
120 ml enema

Indications
Acute constipation to avoid straining at stools. Avoid rectal and anal prolapse, piles, and anal fissure

8.11 Liver Support

Silymarin

Pharmacological action
Lipotropic

Dose
35 mg tablet, 70 mg capsule, and 140 mg sachet; tid

Indications
Fatty degeneration of liver from any cause e.g. hepatitis, and chronic congestion
8.12 Cholagogues

Cynara extract

Pharmacological action

Choleretic

Dose

5 ml ampoules

Indications

Hepatic dysfunction, stimulates liver cells to secrete bile of normal composition in maldigestion

Magnesium sulphate

Pharmacological action

It is a soluble inorganic salt that retains water by osmotic effect leading to distension and purgation and so it should be given with plenty of water. When combined with cynara in capsules it is cholekinetic stimulating the evacuation of gall bladder by relaxing the sphincter of Oddi

Indications

Chronic cholecystitis to drain gall bladder inflammatory exudates

8.13 Antispasmodics

Atropine sulphate

Dose

Pre-medicated, IV injection, 300-600 µg immediately before induction and in incremental doses of 100 µg for the treatment of bradycardia; with neostigmine, 0.6-1.2 mg.

Indications

Adjust to the treatment of gastric and duodenal ulcers to facilitate radiological examination of the gut, treatment of irritable bowel syndrome, with opiate analgesics in biliary and ureteric colics, in parkinsonism, in the treatment of some arrhythmias (sinus bradycardia and heart block), in the treatment of irreversible anticholinesterase poisoning, mushroom poisoning, as a pre-medication in anaesthesia, with neostigmine to control its adverse effects in reversal of competitive neuromuscular blockers, and in ophthalmology (refraction, iridocyclitis and convergent squint).

Contraindications

Glaucoma, prostatic enlargement, pyloric stenosis, ulcerative colitis, hepatic and renal disease, tachycardia, myocardial ischemia, myasthenia gravis, unstable cardiovascular status, and in acute haemorrhage

Precautions

Extremes of age, infants below 3 month, fever, thyrotoxicosis, cardiac insufficiency, hypertension, Down's syndrome.

Adverse effects

Dry mouth, constipation, mydriasis and cycloplegia, increased intraocular pressure, flushing, rashes, dry skin, palpitations and arrhythmia and difficulty in micturition
Drug interactions
Disopyramide, mexiletine, TCA, MAOIs, ketoconazole, antihistamines, phenothiazines, cisapride, domperidone, metoclopramide, amantadine and sublingual nitrates.

Patient instructions
Adequate oral fibre intake, Not to drive (Dilated pupils, mydriasis)

Hyoscine butylbromide
Pharmacological action
synthetic anticholinergic anti-spasmodic drug, with anti-secretory actions on GIT and anti-parkinsonism, antiemetic and amnestic actions on CNS

Dose
10 and 20 mg tablets, 5 mg/5 ml syrup, 20 mg ampoules, and 7.5, 10 and 15 mg suppository

Indications
Intestinal colic, nausea and vomiting, and pre-anaesthetic medication

Contraindications
Glaucoma, and prostatic hypertrophy

Adverse effects
Urinary retention, blurred vision, xerostoma, and sedation

Mebeverine
Pharmacological action
Antispasmodic, direct smooth muscle relaxant; it is more specific on the colon and has fewer adverse effects.

Dose
100 and 135 mg tablets and 10 mg/ml suspension

Indications
Intestinal, ureteric and biliary colic

Pipenzolate plus Phenobarbitone
Pharmacological action
Antispasmodic.

Dose
15 mg paediatric drops; 3-5 drops.

Indications
Intestinal colic, diarrhoea, and dyspepsia in children
SECTION IX

CARDIOVASCULAR SYSTEM DRUGS

In this section:

Topic: Hypertension 62
  9.1 Antihypertensive Drugs 62
  9.2 Antihypotensives 73
Topic: Coronary Artery Disease 73
  9.3 Anti-Angina Drugs 74
Topic: Congestive Heart Failure (CHF) 75
  9.4 Cardiac Stimulants 76
Topic: Cardiac Arrhythmias 79
  9.5 Antiarrhythmic 79
Topic: Myocardial Infarction 81
  9.6 Thrombolytics (fibrinolytics) 82
  9.7 Anti-platelets (anti-aggregants) 83
  9.8 Hyperlipidaemias 83
  9.9 Anticoagulants 85
  9.10 Haemostatics 87
9. Cardiovascular System Drugs

Topic: Hypertension

Hypertension is defined as an elevation of systolic and/or diastolic blood pressure to more than 140/90 mmHg.

Incidence is about 26% of the population. Types:

- Essential or primary hypertension
  It represents 90% of cases. The cause is unknown but the following may play a role: increased adrenergic responses, high RAA system activity, rapid degradation of vasodilators, prostacyclin, and bradykinin, and decreased release of the endothelial-relaxation factor (nitric oxide).

- Secondary hypertension
  It represents 10% of cases. Aetiology includes:

  Renal: parenchymal renal diseases (e.g. glomerulonephritis, collagen diseases) and renovascular disorders (e.g. arteriosclerotic, thrombotic or embolic). Supra-renal: cortical (e.g. hyperaldosteronism and Cushing's syndrome) or medullary (e.g. pheochromocytoma). Neurogenic: increased sympathetic outflows e.g. brain tumours, and increased intracranial pressure, hyperparathyroidism, myxoedema and hyperthyroidism, toxæmia of pregnancy (eclampsia), drug induced: oral contraceptives, oestrogen, NSAIDs, sympathomimetics, MAOIs, cocaine and liquorice.

Complications: cardiac (LVF, CHF, coronary artery disease and myocardial fibrosis), optic (fundus changes), vascular (atherosclerosis, arteriosclerosis, necrotizing arteriolitis), brain (TIAs, encephalopathy, cerebral thrombosis, intracranial haemorrhage and subarachnoid haemorrhage), renal (nephrosclerosis, and renal insufficiency).

Severity classifications:

- Borderline: occasional BP more than 140/90
- Stage I (Mild): without target-organ damage and BP 140-159/90-104.
- Stage II (moderate): target organ damage and BP 160-179/105-114.
- Stage III (accelerated malignant): target organ damage and BP more than 180 mmHg or more than 115 mmHg.

Hypertensive crises:

Encephalopathy, epistaxis, acute LVF, pulmonary oedema, dissecting aneurysm, acute glomerulonephritis, and toxæmia of pregnancy

9.1 Antihypertensive Drugs

Strategy of treatment:

- Diuretics
- Sympatholytic and vasodilator drugs
- ACE inhibitors
• Ca++ channel blocker
• Beta blockers

9.1.1 Diuretics
Potassium-sparing diuretics
Spironolactone
Dose
100-200 mg/day increased to 400 mg if required. CHILD 3 mg/kg/day in divided doses

Indications
Oedema associated with liver cirrhosis and heart failure, nephrotic syndrome and in primary hyperaldosteronism

Contraindications
Hyperkalaemia, pregnancy, breastfeeding, porphyria, Addison's disease and renal failure

Precautions
Diabetes mellitus, patients predisposed to acidosis, serum electrolytes and kidney functions should be assessed regularly.

Adverse effects
GIT disturbances, headache, muscle cramps and hormonal disturbances (Gynaecomastia, hirsutism, menstrual irregularities and impotence).

Drug interactions
NSAIDs, anti-diabetics, ACE Inhibitors, prazosin, terazosin, cardiac glycosides, corticosteroids, cyclosporin, trilostane, potassium salts, oral contraceptives and carbenoxolone

Patient instructions
Avoid large quantities of potassium rich food or potassium salt substitutes.
Be careful while performing other tasks requiring mental alertness.

Thiazides
Hydrochlorothiazide
Dose
Oedema, initially 25-50 mg/day. In the elderly, an initial dose of 12.5 mg/day may be sufficient. Maintenance 25-50 mg on alternate days. Hypertension, 25 mg/day, up to 50-100 mg/day if necessary.

Indications
Oedema associated with congestive heart failure, renal or hepatic disorders, and in hypertension

Contraindications
Severe hepatic or renal dysfunction, Addison's disease, pre-existing hypercalcaemia

Precautions
Hepatic or renal dysfunction, elderly monitor blood glucose

Adverse effects
Fluid and electrolyte disturbances (hyponatraemia, hypokalaemia, hy-
pochloremic alkalosis, hypomagnesaemia and hyperuricaemia) which manifest by dry mouth, thirst, weakness, muscle pain, cramps and GIT upsets, hypersensitivity reactions and blood disorders

**Drug interactions**

NSAIDs, cholestryamine, amiodarone, disopyramide, flecainide, quinidine, lingocaine, mexiletine, tocainide, antidiabetics, ACE inhibitors, prazosin, terazosin, indapamine, β-blockers, calcium salts, cardiac glycosides, corticosteroids, other diuretics, lithium, oral contraceptives and carbenoxolone

**Patient instructions**

Drink 2-3 litre/day of water. Frequent assessment of blood pressure while taking drug. Avoid aspirin. May increase blood glucose level.

**Osmotic diuretics**

**Mannitol**

**Dose**

The usual adult dose is 50-200 mg by IV infusion of 5-25% solution, adjusted to maintain a urine flow of 30-50 ml/hour. In raised intracranial and intraocular pressure, a 15-25% solution is administered in a dose of 1-2 g/kg over 30-60 minutes.

**Indications**

To increase urine flow in acute renal failure, to reduce raised intracranial and intraocular pressure and to promote the excretion of toxic substances by forced diuresis

**Contraindications**

Pulmonary oedema, intracranial haemorrhage (except during craniotomy), congestive heart failure, metabolic oedema with capillary fragility, in patients with renal failure unless a test dose produced a diuretic response, and administration with whole blood

**Precautions**

Careful monitoring of fluid and electrolyte balance, renal functions and vital signs are necessary during infusion.

**Adverse effects**

Fluid and electrolyte imbalance with circulatory overload and acidosis at higher doses, nausea, vomiting, thirst, headache, dehydration, chest pain, blurred vision and fever may occur

**Loop diuretics**

**Furosemide**

**Dose**

Oedema, initially, 40 mg/day or on alternate days up to 80 mg/day adjusted according to response, which may reach 600 mg/day in severe cases. In emergency treatment IM or slow IV injection of 20-50 mg at a rate less than 4 mg/minute, CHILD 0.5-1.5 mg/kg to a maximum daily dose of 20 mg. IV infusion, initially, 250 mg over 1 hour, if no satisfactory
urine response, 500 mg over 2 hours, then 1 g over 4 hours and if still no urine response, dialysis is recommended.

**Indications**

Treatment of oedema associated with congestive heart failure, pulmonary, renal or hepatic disorders and in some patients unresponsive to thiazide diuretics.

**Contraindications**

Renal failure secondary to nephrotoxic or hepatotoxic drugs or associated with hepatic failure, precomatose states associated with hepatic cirrhosis and porphyria.

**Precautions**

Prostatic hypertrophy or impairment of micturition.

**Adverse effects**

Fluid and electrolyte imbalance hyponatraemia, hypokalaemia, hypochloraemic alkalosis, hyperurecamia, nephrocalcinosis, and hyperglycaemia, GIT, visual disturbances, headache, hypersensitivity reactions, pancreatitis, deafness specially if other ototoxic drugs are co-administered.

**Drug interactions**

NSAIDs, amiodarone, disopyramide, flecaainide, quinidine, tocainide, aminoglycosides, cephalothin, polymyxin, vancomycin, antidiabetics, ACE inhibitors, prazosin, terazosin, indapamide, β-blockers, cardiac glycosides, corticosteroids, metolazone, other diuretics, lithium, oral contraceptives, and carbenoxolone, lignocaine, mexiletine.

**Patient instructions**

Take with food and milk, do not use if discoloured, take it early in day as it may cause disruption of sleep, diet high in potassium, do not take OTC medications, may feel fatigue during first few weeks.

**9.1.2 Sympatholytics and vasodilators**

**Alpha Methylldopa**

**Dose**

Initial 250 mg bid-tid for 2 days, then adjusted by small increments every 2 days. Usual maintenance dose 0.5-2 g/day. CHILD initial 10 mg/kg/day in 2-4 divided doses increased up to a maximum of 65 mg/kg/day.

**Indications**

Moderate to severe hypertension used in conjunction with diuretics, and in hypertensive crisis. It is the safest drug during pregnancy.

**Contraindications**

Active liver disease, mental depression and porphyria.

**Precautions**

Impaired liver or kidney functions, history of haemolytic anaemia or
parkinsonism. Not recommended in phoeochromocytoma. Periodic blood counts and liver function tests are advised every 6-12 weeks of treatment.

**Adverse effects**

Drowsiness, dizziness, weakness, fatigue, and loss of libido, impotence, mental changes, fluid retention and oedema, CVS disorders; bradycardia, postural hypotension, syncope, aggravate angina, GIT disorders; nausea, vomiting, diarrhoea, and dry mouth. If thrombocytopenia or leucopenia occurs discontinue treatment

**Drug interactions**

Alcohol, NSAIDs, anaesthetics, anxiolytics, hypnotics, calcium channel blockers, beta-blockers, antipsychotics, dopaminergics, contraceptive pills, corticosteroids, lithium, nitrates, and diuretics carbenoxolone

**Patient instructions**

Do not to take OTC medications, avoid exposure to sunlight, use care while driving, avoid alcoholic beverage, avoid sudden position changes to avoid orthostatic hypotension, report fever, muscle aches, jaundice and flu-like symptoms, urine may darken when exposed to air, hot baths or showers may aggravate dizziness, cessation of smoking and weight reduction.

**Clonidine**

**Pharmacological action**

Stimulates the nucleus tractus solitarius in medulla oblongata that inhibits the VMC and sympathetic outflow to heart, kidney and periphery i.e. it has central alpha-2 agonist action and suppresses the RAA-axis

**Dose**

50-100 µg tid increased every every second or third day. Max. daily dose 1.2 mg

**Indications**

In mild to moderate hypertension in geriatrics, adolescents, renal impairment, diabetes, myocardial ischemia and CHF.

**Adverse effects**

Sedation, dizziness, dry mouth and post-treatment syndrome (sweating, anxiety, palpitation, arrhythmia and increased blood pressure).

**Reserpine**

(in a fixed dose combination with dihydroergocristine, and clopamid)

**Dose**

Initial up to 50 µg/day for 2 weeks, then tapered to the lowest possible dose necessary to maintain the response. A maintenance dose of 250 µg/day is usually adequate. The full effect is only reached after several or continual use and persists for up to 6
weeks after its discontinuation. To minimize Adverse effects and tolerance, smaller doses of reserpine could be given in conjunction with thiazide diuretics.

**Indications**

Mild to moderate hypertension unresponsive to other agents.

**Contraindications**

Active peptic ulcer, ulcerative colitis, Parkinsonism and history of mental disease.

**Precautions**

Debilitated and elderly patients, cardiac arrhythmia, myocardial infarction, renal insufficiency, gallstones or bronchial asthma. If used in patients requiring electroconvulsive therapy, an interval of at least 7-14 days should be allowed to elapse between the last doses and the commencement of therapy.

**Adverse effects**

Nasal congestion, CNS disorders (headache, depression, drowsiness, nightmares, GIT disorders (diarrhoea, cramps, and increased gastric acidity), CVS disorders (bradycardia and postural hypotension), breast enlargement, gynaecomastia, decreased libido and impotence.

**Drug interactions**

Alcohol, anesthetics, NSAIDs, calcium channel blockers, beta blockers, anti-hypertensives, anti-depressants, domperidone, metoclopramide, nitrates, levodopa, antipsycotics, anxio-lytics, hypnotics, contraceptives, corticosteroids, diuretics and carbene-xolone.

**Patient instructions**

Tell your doctor about any allergic reactions especially to reserpine or rauwolfia alkaloids, tell your doctor if you have arrhythmia, epilepsy, gallstones, kidney disease and peptic ulcers, tell your doctor if you are pregnant or breast-feeding.

**Sodium Nitroprusside**

It is inorganic nitrate, most rapidly acting powerful direct vasodilator due to accumulation of cyclic GMP and relaxation of arterioles and venules.

It decreases both preload and afterload with decreased myocardial O2 consumption.

**Dose**

3-5 microgram/kg/min. (vial 50 mg) diluted in 5% glucose. 1/2 life 3-4 min, action within seconds and effect ceases after discontinuation. Target serum level 10 mg%.

**Contraindications**

Cerebral ischemia (cerebro-vascular insufficiency), coarctation of aorta, compensatory hypertension e.g. shunts, dissecting aneurysm, liver and renal dysfunction, severe myocardial ischemia.
Adverse effects
Nausea, colic, sweating, retching, headache, restlessness, dizziness, fatigue, chills, palpitation, premature beats, cramps, confusion, nasal stuffiness.

Large doses: Cyanide poisoning and goitrogenic.

Prazosin
Pharmacological action
Blocks peripheral post-synaptic alpha sympathetic receptors with lowering of blood pressure (Selective alpha-1 blocker), decreases in plasma renin activity and renal blood flow. It decreases after load and preload with relief of pulmonary congestion.

Dose
Initial 1 mg/12 hour and increase gradually to 5-10 mg/day (cap. 1,2.5 mg)

Indications
Mild to moderate hypertension, refractory CHF, Raynaud vasospasm.

Adverse effects
Syncope (first-dose phenomena), dizziness, headache, weakness, palpitation, nausea, red sclera, impotence and aggravates myocardial ischemia.

9.1.3 Angiotensin converting enzyme inhibitors (ACE-I)
They inhibit the protease enzyme blocking conversion of angiotensin-I to angiotensin-II, which is potent vasocostrctor and leads to decreased aldosterone level (decreased Na+-water retention) and increased bradykinin which is vasodilator.

Captopril
Dose
Hypertension, initial 12.5 mg twice daily increases at intervals of 2-4 weeks according to response (6.5 mg twice daily in elderly and in renal impairment). Usual maintenance daily dose 25-50 mg twice daily and should not exceed 50 mg thrice daily. In congestive heart failure, initial 6.25-12 mg (given under close medical supervision), maintenance daily dose 25 mg 2-3 times daily (Should not exceed 50 mg thrice daily).

Indications
Used alone or in combination in the treatment of mild to moderate hypertension, in severe hypertension resistance to other medications, and in the treatment of severe congestive heart failure (adjunct), following myocardial infarction.

Contraindications
Pregnancy, breast-feeding, prophyria, and aortic stenosis or outflow tract obstruction.
Precautions
Renal functions should be assessed prior to administration. Monitor proteinuria and WBC counts. Initial doses should be given at bedtime. Used cautiously in patients with impaired renal functions, reno-vascular hypertension or collagen vascular disease.

Adverse effects
Skin rash with pruritis, fever or eosinophilia, dry cough, taste disturbances, hyperkalemia, deterioration of renal functions in patients with pre-existing renal disease and hematological disorders.

Drug interactions
Alcohol, anaesthesia, NSAIDs, anxiolytics, hypnotics, calcium channel blockers, beta-blockers, antipsychotics, dopaminergics, contraceptive pills, corticosteroids, lithium, nitrates, potassium salts, diuretics, probenecid, cyclosporin and carbadoxolone.

Patient instructions
Monitor and record blood pressure daily, weight self-daily at consistent time, if overweight, supervised weight management program, low sodium diet, expect increased urine output, not to discontinue taking drug and not take OTC medication without consulting physician.

Lisinopril
Pharmacological action
It is an ACE-I with uses similar to captopril in the treatment of hypertension and congestive heart failure.

Dose
In the treatment of hypertension initial dose 2.5 or 5 mg daily. The dose should be given according to the response; the usual maintenance dose is 10 to 20 mg once daily up to 40 mg daily. In the treatment of congestive heart failure an initial dose of 2.5 mg daily.

Adverse effects and precaution: As for captopril. Life threatening hyperkalemia developed in patients given lisinopril whilst taking a very low calorie diet with protein supplement which supply a high daily potassium intake.

Selective angiotensin II inhibitor (receptors blocker)
Losartan, Valsartan
Pharmacological action
They are angiotensin II blockers block vascular, renal and suprarenal receptors.

Dose
Losartan: Tablets 50 mg/day. Valsartan: Tablets 80-160 mg/day.
**Indications**

Severe malignant, high-renin hypertension.

**Adverse effects**

Sweating, headache, dizziness, fatigue, premature beats and risk of hypotension in hyponatremia, hypovolemia, renal impairment and biliary cirrhosis. (No cough or angio-oedema like ACE I).

**Contraindications**

Pregnancy and lactation

**9.1.4 Calcium channel blockers**

These block $\text{Ca}^{2+}$ influx to muscle cells and so decrease muscle contraction.

**Nifedipine**

**Dose**

Angina, initially 10 mg 3 times/day, increase to 20 mg 3 times/day if necessary. In elderly initially 5 mg 3 times/day (for immediate effect bite capsule and retain liquid in mouth). Raynaud disease 10 mg 3 times/day (maximum 20 mg 3 times/day). Hypertension and angina prophylaxis 20 mg twice daily after food, increased to 40 mg twice daily if necessary.

**Indications**

Angina pectoris (classic and vasospastic), hypertension and Raynaud disease.

**Contraindications**

Cardiogenic shock, pregnancy, porphyria, who experience ischemic pain on its administration.

**Precautions**

Hypotension, patients with poor cardiac reserve and breast-feeding. Reduce dose in hepatic impairment. Adjustment of anti-diabetic dose may be required.

**Adverse effects**

Vasodilatation (flushing, headache, hypotension, dizziness, peripheral oedema), paradoxical increase in ischaemic pain, GIT disturbance, gum hyperplasia and depression.

**Drug interactions**

Antidiabetic, carbamazepine, phenytoin, phenobarbitone, primidone, antihypertensives, antipsychotics, $\beta$-blockers and cimetidine.

**Patient instructions**

Visit dentist on routine basis because gum swelling may occur, there may be increased chest pain at short medication and with dose changes but this effect is transient, use caution while performing tasks requiring mental alertness, sustained release capsules must be swallowed whole not chewed, divided or crushed.
Diltiazem

Dose

Angina, initially 60 mg three time daily, thereafter, dosage may increase up to 360 mg/day. Hypertension, initially 60-120 mg twice daily increased at 14-day intervals as required to a maximum of 350 mg/day.

Indications

Management of classic and vasospastic angina and hypertension.

Contraindications

Sick sinus syndrome, second and third degree heart block and marked bradycardia, pregnancy, porphyria, acute myocardial infarction and pulmonary congestion.

Precautions

Reduce dose in elderly, hepatic and renal impairment. Use cautiously in patients with first degree heart block, bradycardia, and impaired left ventricular function.

Adverse effects

Headache, peripheral oedema, and dizziness and GIT disturbances.

Drug interactions

β-blocker, amiodarone, carbamazepine, antihypertensives, antipsychotics, cyclosporin, lithium, theophylline and cimetidine.

Patient instructions

Take pulse so regularly while taking medication, swallow whole sustained release capsule, notify if irregular heart beat, shortness of breath.

Verapamil

Dose

Oral, supraventricular tachycardia, 40-120 mg three times/day. Angina, 80-120 mg three times/day. Hypertension, 240-480 mg/day in 2-3 divided doses by slow IV injection (over 2 minutes) 5-10 mg (preferably with ECG monitoring), further 5 mg may be required after 5-10 minutes in paroxysmal tachycardia.

Indications

Angina pectoris (classic and vasospastic), hypertension, supraventricular tachyarrhythmias (class iv antiarrhythmic).

Contraindications

Patients with second and third degrees heart block, Wolf-Parkinson-White syndrome, hypotension, cardiogenic shock, marked bradycardia, uncompensated heart failure, patients treated with beta blockers, in sick sinus syndrome and porphyria.

Precautions

Pregnancy and breast-feeding, arrhythmia in children, first-degree heart block, and acute myocardial infarction. Reduce dose in hepatic impairment.
Adverse effects
Constipation may precipitate heart failure, hypotension and heart block.

Drug interactions
β-blockers, digoxin, general anesthetics, amiodarone, quinidine, rifampicin, carbamazepine, antihypertensives, antipsychotics, cyclosporin, lithium, tubocurarine, theophylline and cimetidine.

Patient instructions
Administer with milk or meals, give IV slowly over two minutes, no double dose, no sudden arrest of taking medication, report any irregular heartbeats, swelling of hand and feet, avoid use of alcohol and limit caffeine, stress the importance of compliance in all areas of treatment regimen, diet, exercise, stress, reduction drug therapy.

Amlodipine
Pharmacological action
Calcium channel blocker with more prolonged duration of action, used in treatment of malignant hypertension and treatment of stable angina pectoris.

Dose
5 mg daily, as a single dose may be increased if necessary to 10 mg daily.

Adverse effect and precautions: as nifedpine

9.1.5 Beta Blockers
Non-selective β1 blocker
Propranolol
Dose
Gradually build up the dose. In hypertension initially 40 - 80 mg twice daily increased to 60 - 320 mg/day. Angina initial 40 mg 2 - 3 times daily increased at weekly intervals to 120 - 240 mg/day. Myocardial infarction administer within 5 - 21 days of infarction 40 mg 4 times/day for 2 - 3 days then 80 mg twice daily. Arrhythmia 30 - 160 mg/day. Thyrotoxicosis and hypertrophic subaortic stenosis, 10 - 40 mg 3 - 4 times daily. Pheochromocytoma, 60 mg/day on 3 preoperative days (with alpha blocker). Migraine prophylaxis and essential tremor, initial 40 mg 2-3 times daily increased weekly up to 160 mg/day. Anxiety states 40 mg/day. Child hypertension 1 mg/kg/day in divided doses increase to 2 - 4 mg/kg/day in divided doses. Arrhythmia, thyrotoxicosis and pheochromocytoma 250 - 500 mg/kg 3 - 4 times/day.

Indications
Treatment of hypertension and improvement of exercise tolerance in angina. Arrhythmia thyrotoxicosis and pheochromocytoma (in conjunction with alpha-blocker), myocardial infarction, portal hypertension, hypertrophic subaortic stenosis, migraine prophylaxis and essential tremors.
**Contraindications**

Obstructive airway disease, heart failure, second and third degree heart block, cardiogenic shock, metabolic acidosis and sinus bradycardia.

**Precautions**

Abrupt withdrawal may precipitate angina. Decrease dose in renal impairment (Atenolol) and in hepatic impairment (propranolol). Use cautiously in late pregnancy, breastfeeding, diabetes mellitus, and myasthenia gravis and in pheochromocytoma (add alpha-blocker).

**Adverse effects**

CVS effects (bradycardia, hypotension, heart block and heart failure), bronchospasm (More with propranolol), fatigue, cold extremities, CNS effects (nausea, vomiting and diarrhoea).

**Drug interactions**

Alcohol, anesthetics, amiodarone, lidocaine, rifampicin, fluoxetine, anti-diabetics, hypnotics, calcium channel blockers, cardiac glycosides, cholinergics, anti-psychotics, ergotamine, sympathomimetics, theophylline, thyroidine, cimetidine, diuretics and carbinoxolone.

**Patient instructions**

Sudden discontinuation can cause chest pain or heart attack, not to take drug if pulse is less than usual rate, not to take OTC medications.

**Selective β1 blocker**

**Atenolol**

**Dose**

In hypertension 50-100 mg/day as a single dose. Full effect is evident after 1-2 weeks. Angina, 100 mg/day in single or divided dose.

**Indications**

In hypertension, angina pectoris and cardiac arrhythmia (injection).

All other items same as propranolol

**9.2 Antihypotensives**

**Midodrine**

**Pharmacological action**

It has cardiac stimulant action and is a peripheral vasoprotective.

**Dose**

Drops 1% and tablets 2.5 mg 3-4 times/day

**Indications**

Hypotension states and circulatory collapse to improve blood flow at rest (cerebral and peripheral).

**Topic: Coronary Artery Disease**

Types of myocardial ischemia

Angina Pectoris
Angina Pectoris is the principal symptom of ischemic heart disease which is manifested by sudden, severe, pressing substernal pain that often radiates to the left shoulder.

Types of angina:

Stable (typical) angina (angina of effort): Where atherosclerosis restricts blood flow in the coronary vessels, attacks are usually caused by exertion and relieved by rest.

Unstable angina (acute coronary insufficiency).

Prinzmetal angina (variant angina); caused by coronary vasospasm, in which attacks occur at rest.

Pain: chiefly retrosternal and radiates to left arm, neck, back and lower jaw. Character: constricting or crushing. Duration: less than 15 min.

Sweating, nausea, vomiting, collapse, shock.

ECG changes: ST-segment displacement: depressed in effort induced angina and elevated in Prinzmetal variant angina. T-wave inversion.

Precipitating factors:

- Increased oxygen supply: hyperthyroidism, increased sympathoadrenal discharge, hypertension, stress and exertion.
- Decreased oxygen supply: coronary atherosclerosis, coronary spasm, anatomical kinks or narrowing, anemia, shock, asphyxia, pneumopathy, cocaine abuse.

9.3 Anti-Angina Drugs

Nitrates

Isosorbide dinitrate

Dose

Initially, 20 mg 2-3 times/day or 40 mg twice/day up to 120 mg/day in divided doses (10 mg twice/day in those who have not received nitrates before).

Indications

Prophylaxis and treatment of angina and in left ventricular failure.

Contraindications

Severe hypotension, hypovolaemia, marked anemia, constrictive pericarditis or raised intracranial pressure.

Precautions

Used cautiously in patients with closed angle glaucoma, early myocardial infarction, severe renal or hepatic impairment, hypothyroidism, malnutrition or hypothermia. Tolerance to the effect of nitrates may develop.
**Adverse effects**
Flushing of face, throbbing headache, and tachycardia. Larger doses may lead to vomiting, hypotension and syncope, methemoglobinemia.

**Drug interactions**
Alcohol, anesthetics, calcium channel blockers, anti-hypertensives, disopyramide, antidepressants, antimuscarinics, antipsychotics, dopaminergics, contraceptive pills, corticosteroids, diuretics and carbinoxolone.

**Patient instructions**
Report these symptoms; dizziness, retching, nausea, abdominal pain, chest pain, tinnitus, caution to avoid sudden position changes to prevent orthostatic hypotension.

**Glyceryl trinitrate**
**Dose**
Sublingually, 0.3 -1 mg repeated as required. Orally 2.6 - 6.4 mg as sustained release tablets 2-3 times/day. IV infusion, 10-20 mg/minute.

[β-blockers: see under anti-hypertension.]

**Calcium channel blockers: see under anti-hypertension.**

**Topic: Congestive Heart Failure (CHF)**
**Classification**
Low output failure
Systolic dysfunction (dilated cardiomyopathy)
There is hypofunction of the left ventricle and dilated, elevated left ventricular end diastolic volume, ejection fraction < 40%, decreased stroke volume, decreased COP and S3 gallop.
Aetiology: ischemic: coronary artery diseases.
Non-ischemic: anomalies, valvular disease (stenosis or regurgitation), hypertension, carditis, arrhythmias, volume overload, Ca++ and K+ depletion, nutritional deficiency.
First line therapy: vasodilator therapy and digitalis.

**Diastolic dysfunction**
There is normal left ventricular contraction, normal heart size, impaired left ventricular relaxation, impaired left ventricular filling, decreased left ventricular end-diastolic volume, normal ejection fraction, decreased stroke volume and decreased COP.
Aetiology: coronary ischemia, pericarditis, idiopathic hypertrophic subaortic stenosis, aortic regurgitation, sodium and water retension, amyloidosis and sarcoidosis.

Drugs of choice: negative inotropics to slow heart rate (β-blockers and cal-
Cium channel blockers). Digitalis is contraindicated.

High output failure

Normal or increased contractility, normal heart size and left ventricular end-diastolic volume, increased ejection fraction and COP.

Aetiology: anaemia, Thyrotoxicosis, arterio-venous shunts, pulmonary disease, infections, toxaemia, pheochromocytoma and Beri-Beri.

Risk factors

Male, elderly, hypertension, coronary artery disease, dislipidaemia, diabetes, smoking, rheumatic heart disease, mechanical problems and cardiomyopathy

Site

Left ventricular failure.

Right ventricular failure (corpulmonale).

Congestive heart failure (CHF).

Onset: Acute or chronic.

Precipitating causes

Acute infection, fever, pregnancy, severe physical stress, bacterial endocarditis, environmental heat and humidity, emotional crisis and excess Na+ intake.

Drug-induced

Antifibrillatory, β-blockers, calcium channel blockers, daunomycin, doxorubicin, diazoxide, oral contraceptives, lithium, NSAIDs, steroids, TCA, androgens and volume expanders

Major signs and symptoms

Dyspnea, cough on exertion, orthopnea, cardiac asthma, pulmonary oedema and rales, neck vein distension, gallop, hydrothorax, cardiomegaly, fatigue, confusion, nocturia, gravitational oedema and ECG changes (ST-segment and T-wave abnormalities and atrial enlargement, high voltage precardial leads).

9.4 Cardiac Stimulants

Treatment of heart failure aims to relieve symptoms, improve exercise tolerance reduce incidence of acute exacerbation, and reduce mortality.

Cardiac stimulant drugs have inotropic effect (increase myocardiac contraction) and chronotropic effect (increase heart rate).

Drugs used in treatment of heart failure:

- Cardiac glycosides
- Sympathomimetics
- ACE inhibitors
- Diuretics
9.4.1 Cardiac Glycosides

Digoxin

Pharmacological action

Direct inhibition of membrane-bound (Na⁺-K⁺-ATPase) which leads to an increase in the intracellular conc. of Ca²⁺.

Dose

Rapid digitalization 1-1.5 mg in divided doses/24 hours. Moderate digitalization 250-500 mcg/day (higher dose divided). Maintenance 62.5-500 mcg/day (higher dose divided) usual range 125-250 mcg/day according to renal function and heart response in atrial fibrillation.

Indications

Heart failure and supraventricular arrhythmias.

Contraindications

Ventricular fibrillation, hypertrophic obstructive cardiomyopathy, Wolff-Parkinson-White syndrome, partial heart block.

Precautions

Cases of acute myocarditis, severe pulmonary disease, myocardial infarction, Cases that previously received cardiac glycosides or undergoing cardioversion. Reduce dose in elderly and in renal impairment.

Adverse effects

Nausea, vomiting, anorexia, diarrhoea, abdominal pain, mental and visual disturbance and gynaecomastia. Any type of arrhythmia. Chronic toxicity may lead to hypokalemia.

Drug interactions

NSAIDs, anion exchange resin, quinidine, amiodarone, propafenone, erythromycin, rifampicin, anti-epileptics, beta-blockers, calcium salts, verapamil, diuretics, aminoglutethimide, suxamethonium and carbeneoxolone.

Patient instructions

Take digoxin at same time each day, avoid OTC medications without consulting e.g. antacids, antidiarrheals.

Treatment of toxicity

Stop digitalis, stop K⁺ depleting diuretics, slow IV infusion of k⁺, give antiarrhythmic drug, atropine can be used to control sinus arrest and AV block, Fab fragment of digitalis specific antibodies.

Ouabain (Strophanthin-G)

Pharmacological action

Cardiac glycoside derived from strophanthus gratus seeds. It is poorly absorbed orally, no protein bound, most potent for rapid actions parenterally. Its actions are primarily inotropic with little slowing effect, renal excretion. It has very rapid onset of
action (5 min), peak (45 min) and short duration (24 hours).

Dose
Ampoule 0.25 mg/ml.

Indications
When cardiac glycoside with rapid elimination is needed e.g. atrial flutter to convert it to fibrillation and after elimination normal rate is restored or atrial fibrillation persists that needs a longer cardiac glycoside e.g. digoxin.

9.4.2 Sympathomimetics (β1-receptor stimulants)

Dopamine
Dose
IV infusion, initially 2-5 mg/kg/min gradually increases to 5-10 mg/kg/min.

Indications
Correction of hemodynamic disturbances associated with cardiogenic shock in myocardial infarction, endotoxic septicemia, renal failure or cardiac surgery.

Contraindications
Should never be given simultaneously with epinephrine.

Precautions
Ischaemic heart disease, hyperthyroidism and diabetes mellitus.

Adverse effects
Tachycardia, arrhythmia, hypotension and headache.

Drug interactions
Halogenated anesthetics, doxapram, epinephrine, beta-blockers, and theophylline.

Dobutamine
Pharmacological action
Inotropic action by stimulation of B1 sympathetic cardiac receptors, peripheral vasodilator action and increase COP.

Dose
IV infusion 10 microgram/kg min. (vial 250 mg). Half-life 2 min. 3-day infusion lasts effect for 4 weeks.

Indications
Heart failure and acute pulmonary oedema in myocardial infarction, shock, cardiac surgery when arrhythmia is a problem (less arrhythmogenic than dopamine) when the blood pressure is below 100 mmhg.

Adverse effects
Nausea, headache, palpitation and anginal pains.
Isoprenaline
Pharmacological action
Strong β-sympathetic receptor stimulant, rapidly metabolized by liver, onset 5 min. Duration one hour.

Dose
Amp. 0.2 and 1 mg. Linguits 10-15 mg and Atomizer 1-3 %.

Indications
Carotid sinus stimulation and heart block 1: 5000 solutions Injection or linguits 30 mg/4-6 hours.
Bronchial asthma (acute attack), chronic emphysema and Bronchospasm during anaesthesia (atomizer is more effective).

Adverse effects
Palpitation, ventricular arrhythmia, tremors, nausea, excitement, slight increase in systolic pressure and decrease diastolic B.P.

Topic: Cardiac Arrhythmias
Aetiology
Augmented automaticity in His-Purkinje system (disturbed impulse formation):
Coronary artery disease, myocarditis, acidosis, hypoxia, hypercapnea, sympato-adrenal discharge electrolyte disturbance e.g. hypokalemia, hypercalcemia, infection, toxaemia, shock, hyperparathyroidism and drugs (digitalis, sympathetic agonists, alcohol, benzodiazepines, tobacco). They produce atrial and ventricular arrhythmias (premature beats, flutter, tachycardia and fibrillation).

Disturbed impulse conduction:
Coronary artery disease, rheumatic fever, myocarditis, diphtheria, drugs (digitalis and antifibrillatory drugs, ... etc).
They produce SA-block and AV-block (first, second and complete heart block), bundle branch block and hemiblock.

Signs and symptoms
They depend on type and nature of arrhythmia, ventricular rate, duration of arrhythmia and underlying condition of the heart.
Cerebral ischemia: dizziness and syncope.
CHF.
Anginal pain.
General weakness and fatigue.
Asymptomatic.

9.5 Antiarrhythmic
An arrhythmia is an abnormality of rate, regularity, or site of origin of the
cardiac impulse or a disturbance in conduction that causes an alteration in the normal sequence of activation of the atria and ventricles.

Causes of arrhythmia:

- Altered normal automaticity.
- Abnormal generation of impulse.
- Rentrant arrhythmia.

Classification of antiarrhythmic drugs:

- Sodium channel blockers:
  Quinidine, procainamide, disopyramide, lidocaine, mexiletine, propafenone, flecainide

- β-blockers:
  Propranolol, esmolol

- Potassium channel blockers:
  Amiodrone, sotalol

- Calcium channel blockers:
  Verapamil, diltiazem

9.5.1 Sodium channel blockers

Quinidine sulphate

Pharmacological action

It blocks fast sodium influx during depolarization (sodium channel blocker). It is classified as class I (A) antifibrillatory drug (moderate phase - depression, slows conduction and prolongs repolarization by increasing the effective refractory period.

Dose

Loading dose 12 mg/kg PO and maintenance dose 6 mg/kg every 4-6 hours. Target serum level 2-7 ng/ml.

ECG changes: Short ST- interval, reduce amplitude of delayed after depolarization and PR and QRS- intervals are unchanged.

Indications

Atrial and ventricular premature contractions, paroxymal supraventricular tachycardia, ventricular tachycardia and prophylaxis of atrial fibrillation.

Adverse effects

GIT (nausea and vomiting), thrombocytopenia, rash, hypotension, idiosyncrasy, respiratory diseases, heart block and tachyarrhythmia (secondary to therapy).

Lidocaine

See under local anaesthesia

Beta-Blockers

See under hypertension
9.5.2 Potassium channel blockers

**Amiodarone**

**Dose**

IV infusion 5 mg/kg in 250 ml glucose as a 5% injection infused over 20 minutes to 2 hours and repeated bid or tid up to a maximum of 1.2 g in up to 500 ml of glucose injection/day (Monitor ECG). Maintenance dose 200 mg/day orally.

**Indications**

Class III anti-arrhythmic drug used in the management of ventricular and supraventricular arrhythmias where other drugs can not be used including Wolf - Parkinson - White syndrome.

**Contraindications**

Bradycardia, heart block, severe hypotension or severe respiratory depression, porphyria and breastfeeding.

**Precautions**

Used with caution in-patient with heart failure, iodine sensitivity or history of thyroid dysfunction. Electrolyte disturbances should be corrected before starting treatment. Patients advised to use wide spectrum sunscreens. If prolonged or repeated infusions, a central venous catheter should be considered.

**Adverse effects**

Thyroid dysfunction, reversible corneal deposits, photosensitivity, GIT disturbances, diffuse pulmonary alveolitis, hepatitis and blood disorders.

**Drug interactions**

Digoxin, anticoagulants, beta-blockers, diltiazem, verapamil, diuretics, phenytoin, cimetidine.

**Patient instructions**

Regular ophthalmic examinations are recommended, eat small frequent meals or dividing daily dose and taking 2 or 3 doses with meals, heart rate < 60, blood pressures should be reported, avoid exposure to sunlight.

**Calcium channel blockers, verapamil: See under anti-hypertension**

### Topic: Myocardial Infarction

**Aetiology**

Coronary atheromatous luminal narrowing or spasm with superimposed coronary thrombosis.

Affected regions: anterior (worse prognosis), lateral and inferior.

**Precipitating factors**

Non in most cases, severe emotions, exertion, trauma, respiratory infection, pulmonary embolism, hypoxia, hypoglycemia, anaphylaxis.
Signs, symptoms and diagnosis

ECG: T-wave inversion, ST-segment elevation, pathological Q-wave and new left bundle branch block.

Pain: Sudden, more severe than angina and prolonged more than 15 minutes.

Accompanying symptoms: shock, profound weakness, dyspnea, nausea, vomiting.

Cardiac enzymes elevation: CPK, AST and LDH.

Radionucleotide Scanning: technetium 99 which is Ca$^{++}$ seeking (hot-spot) or Thallium 201 which is taken similar to K$^{+}$ (cold-spot).

Complications


9.6 Thrombolytics (fibrinolytics)

Once the blood pressure is controlled in patients suffering from myocardial infarction or other thrombolic complications, patients should receive thrombolytics within first 2-5 hours, which accelerates clot lysis.

Streptokinase

Pharmacological action

It is a polypeptide that binds to plasminogen to form active plasminogen-streptokinase complex that cleaves other molecules of plasminogen to form active plasmin. It acts on fibrin clot leading to its dissolution. It is antigenic and minimal fibrin specificity.

Dose

1.5 million U over 1 hour by IV infusion.

Precautions

Inability to open 100% of the artery occlusions. The complications of bleeding and haemorrhagic stroke especially in old patients more than 75 years. Inconsistency to maintain good blood flow in the infarct-related artery after it is successfully opened.

Contraindications

Recent head trauma or intracranial tumour. Aortic dissecting aneurysm. Previous haemorrhagic stroke. Non-haemorrhagic stroke or cerebrovascular events within one year. Active internal bleeding (excluding menses). Major surgery within 2 weeks.

Relative contraindications

Uncontrolled hypertension > 180/110 mmHg and safe level is < 180/110
mHg. Remote thrombotic stroke and recent transient ischemic attack. Cardiopulmonary resuscitation for more than 10 min. Recent trauma or major surgery less than 2-4 weeks. Active peptic ulcer. Pregnancy. Diabetic retinopathy.

9.7 Anti-platelets (anti-aggregants)

Inhibition of platelet aggregation. The platelets contribute to haemostasis by forming platelet plug and by promoting thrombin production, platelet plug occurs through:

- Platelet adhesion.
- Release reaction.
- Platelet aggregation.

Acetyl Salicylic Acid

Pharmacological action

Inhibits arachidonate pathway via inhibition of cyclooxygenase enzyme.

Dose

300-900 mg every 4-6 hours, when necessary, maximum 4 g daily. As antiplatelet 150-300 mg sid.

Indications

Used for mild to moderate pain, fever, inflammation and the prevention of myocardial infarction and stroke.

Contraindications

GIT ulcer, gout, bleeding tendencies and allergy. Children under 12 years and with breast-feeding, pregnancy, asthma and nasal polyps.

Precautions

Asthma, allergic diseases, impaired liver and kidney functions. Prolonged medication with salicylates requires medical supervision.

Adverse effects

GIT disturbances, increased bleeding time, Raye syndrome, and precipitation of allergic attacks. Chronic over dosage leads to salicilism.

Drug interactions

Antacids, anticoagulants, antiepileptics, cytotoxics, diuretics, uricosuric, metoclopramide, domperidone and alcohol.

Patient instructions

Take with food or after meals. Do not crush or chew. Take with a full glass of water. Do not use if it has strong vinegar like odour. Do not place or dissolve on an oral lesion.

9.8 Hyperlipidaemias

Hyperlipoproteinaemia is a condition in which the concentration of cholesterol-or triglyceride carrying lipoproteins in plasma is elevated. This can accelerate the development of atherosclerosis and myocardial infarction.
Bezafibrate

Pharmacological action
Fibrate derivatives stimulate lipoprotein lipase, enhance ULDL catabolism, and decrease triglycerides.

Dose
200 mg 3 times/day taken with or after food. 200 mg twice daily may be adequate for maintenance.

Indications
In conjunction with dietary modifications in the treatment of type IIa, IIb, III, IV and V hyperlipoproteinaemia.

Contraindications
Severe liver or kidney dysfunction, primary biliary cirrhosis, gall bladder disorders, pregnancy, hypoalbuninaemia and nephritic syndrome.

Precautions
In patients taking anticoagulant therapy, the dose of anticoagulant should be reduced to 50% initially and then adjusted as necessary.

Adverse effects
GIT disturbances (nausea, vomiting, diarrhoea and dyspepsia), weight gain, headache and myositis-like syndrome.

Drug interactions
Anticoagulants and anti-diabetics

Patient instructions
Avoid alcohol and prolonged exposure to sunlight. Strict birth control procedures. Notify your doctor if chest pain, shortness of breath, swelling of feet and weight gain.

Gemfibrozil

Pharmacological action
Fibrate derivative, stimulates lipoprotein lipase, enhances VLDL catabolism and decreases cholesterol synthesis at mevalonic acid stage, decreases triglycerides by 30-60%, increases HDL-C by 10-15% by upregulating ApoAI genes and decreases liver lipogenesis.

Dose
Capsule 300 mg TDS and tablets 600 mg twice/day.

Indications
Dyslipidemia mainly hypertriglyceridemia, hypercholesterolemia and atherosclerosis.

Adverse effects
Rash, gastro-intestinal upset, headache, gallstones and myopathy.

Atorvastatin

Pharmacological action
Statin derivative, it is hydroxymethylglutaric acid reductase inhibitor. Decrease cholesterol synthesis and lipoprotein levels by increasing the hepatic LDL receptors enhancing uptake
and catabolism of LDL (40%) i.e. up-regulating LDL receptor proteins. Also, it has triglyceride-lowering effect.

**Dose**

Tablets 10, 20 mg 1-2 times/day. Response is after 2-4 weeks.

**Indications**

Dyslipidemia, hypercholesterolaemia (mainly LDL-C).

**Adverse effects**

Headache, insomnia, myositis (aches, fatigue and cramps), increase serum enzymes (CPK, transaminases and alkaline phosphatase), rhabdomyolysis, increase myopathy with niacin, cyclosporin, erythromycin.

9.9 Anticoagulants

These are drugs that modify unwanted coagulation and are used in prevention or treatment of blood clotting.

They are classified into:

Injectable anticoagulants e.g. Heparin.

Oral anticoagulants e.g. Coumarine and indendion.

**Heparin salts**

**Dose**

5000 U. IV followed by IV infusion of 1000 –2000 U/hour or 5000-10,000 U IV every 4 hours By SC prophylaxis of DVT 5000 u/2 hours before surgery, then every 8 – 12 hours until patient is ambulant, in pregnancy 10,000 U/12 hours. Treatment of DVT 10,000-20,000 U/12 hours. Ampoules 12500 I.U., 20000 U, 5000 U, 12000 U, 5000 I.U. (1 mg = 130 U)

**Indications**

Initiation of anticoagulant therapy in deep venous thrombosis (DVT), disseminated intravascular coagulopathy and prophylaxis of postoperative thrombosis.

**Contraindications**

Hypersensitivity to heparin, severe liver or kidney damage, peptic ulcer infective endocarditis, haemorrhagic, blood disorders, severe trauma, administration by IM route and cerebral aneurysm and severe hypertension.

**Precautions**

When treatment is prolonged monitor activated partial thromoplastin time and platelet count.

**Adverse effects**

Haemorrhage, thrombocytopenia, hypersensitivity reactions and osteoporosis after prolonged use.

**Drug interactions**

NSAIDs, dipyridamole, sulphinpyrazone, spinal and epidural anesthetics.

**Patient instructions**

See warfarin
Antidote
Protamine sulphate (Dose; 50 mg given over 10 min. by IVI slowly to avoid collapse.

Phenindione
Dose
200 mg on first day, 100 mg on second and maintenance dose of 50-150/day according to coagulation tests.

Indications
Prophylaxis of embolisation in rheumatic heart disease and atrial fibrillation, prophylaxis after prosthetic heart valve; prophylaxis and treatment of deep venous thrombosis and pulmonary embolism and transient ischaemic attacks.

Contraindications
Pregnancy and breast-feeding, active peptic ulcer, in active endocarditis, haemorrhagic blood disorders, severe wounds including surgical, cerebrovascular disorders and severe hypertension.

Precautions
Monitor treatment with prothrombin time.

Adverse effects
Haemorrhage, hypersensitivity reactions, skin rash, pyrexia diarrhoea, or orange coloration of urine.

Drug interactions
Anabolic steroids, NSAIDS, anion-exchange resin, dipyridamole, oral contraceptives, vitamin k and thyroxin.

Patient instructions
Consult your physician or pharmacist when considering use of other medications in particular aspirin containing products or herbal products.

Warfarin
Dose
10 mg/day for 2 days, then maintain by 3 mg/day. Gradually withdraw treatment.

Indications
Prophylaxis of embolisation in heart disease and atrial fibrillation, prophylaxis after prosthetic heart valve, prophylaxis and treatment of venous thrombosis and pulmonary embolism and ischaemic attack.

Contraindications
Pregnancy and bleeding, active peptic ulcer, infective endocarditis, haemorrhagic blood disorders, severe wounds (including surgical), cerebrovascular disorders and severe hypertension.

Precautions
Monitor treatment with time.
**Adverse effects**

Haemorrhage, alopecia, fever, diarrhoea, vomiting and skin reactions.

**Drug interactions**

Alcohol, NSAIDS, anabolic steroids, co-trimoxazole, erythromycin, cephamandole, rifampicin, sulphonlureas, anti-epileptics, anti-fungals, allopurinol, sulphinpyrazone, dipyridamole, chloral, vitamin K.

**Patient instructions**

See phenindione.

**Enoxaparin sodium**

**Pharmacological action**

It is a low molecular weight heparin that binds to anti-thrombin III, changes its conformation and accelerates its inactivation of factors, IX, XII, XI, X, II and plasmin prolongation of coagulation time but bleeding time is little affected.

**Dose**

20 and 40 mg ampoule, 0.5-2 mg/kg controlled by 3 fold coagulation time. SC onset 1.5 hour, peak 3 hours and duration 18 hour.

**Indications**

Uses as prophylaxis and treatment of pulmonary embolism and thrombophlebitis, acute coronary thrombosis, arterial occlusion, vascular disease (thromboangitis obliterans,) exchange transfusion, haemodialysis and prolonged immobilization (surgical or medical).

**Adverse effects**

Haemorrhage, sensitization, alopecia, osteoporosis, thrombocytopenia, and diarrhoea.

**Contraindications**

Haemorrhagic tendencies and blood dyscrasias, GIT ulceration, bacterial endocarditis, CNS surgery, hepatic and renal disorders and heparin sensitivity and shock.

**Toxicity**

Haemorrhage from mucous membranes, skin and internal organs.

**9.10 Haemostatics**

**Ethamsylate**

**Dose**

Oral, 500 mg 4 times/day. IM or IV injection of 1 g, maintenance 500 mg every 4-6 hours.

**Indications**

Haemorrhage from small blood vessels and in menorrhagia.

**Contraindications**

Porphyria.

**Precautions**

Transient hypotension has been reported following IV injection.
Adverse effects
Nausea, headache and skin rashes.

Patient instructions
Avoid using aspirin and herbs interfering with clotting such as garlic and ginko.

[Vitamin K (Phytomenadione): see under vitamins]
SECTION X

RESPIRATORY SYSTEM DRUGS

In this section:

Topic: Chronic Obstructive Pulmonary Disease 90
Topic: Chronic Bronchitis 90
Topic: Emphysema 90
Topic: Bronchial Asthma 90
10.1 Bronchodilators 91
10.2 Anti-Tussives 94
10.3 Mucolytics 95
10. Respiratory System Drugs

**Topic: Chronic Obstructive Pulmonary Disease**

COPD is productive cough occurring for most days of the week for 3 consecutive months for 2 successive years. Only patients present when they start to get dyspnoea due to the onset of significant chronic obstructive airways disease (COAD) or chronic obstructive pulmonary disease (COPD). Bronchial asthma and bronchiectasis are not included. It is the fourth leading cause of death and its incidence of 2-6% of adult population.

**Pathophysiology**

It is primarily a disease of the small airways and adjacent alveoli. The obstruction is fixed and irreversible from inflammatory and structural changes in the small airways (chronic bronchitis) and/or loss of the lung elastic recoil as well as alveolar wall destruction (emphysema).

**Complications**

Increased obstruction, recurrent respiratory infection, increased sputum production, pulmonary hyperinflation, and altered pulmonary gas exchange. The end result include: Respiratory muscle fatigue, ventricular disorders, pulmonary hypertension and cor pulmonale.

**Topic: Chronic Bronchitis**

The typical patient is a 45-65 years old smoker with chronic productive cough, moderate dyspnoea and recurrent respiratory infections with hypoxia and cyanosis. The end-stage is complicated by polycythaemia and cor pulmonale.

**Topic: Emphysema**

The typical patient is 55-75 years old smoker with severe dyspnoea as primary complaint. Symptoms appear earlier in patient with α1-antitrypsin deficiency. Cough may be absent with scanty sputum. Patient is often thin, barrel-chested and breath through pursed lips with prolonged expiratory phase with pinkish discoloration due to maintenance of adequate oxygenation through increased work of breathing.

**Topic: Bronchial Asthma**

It is chronic inflammatory disorder of the airways in which in susceptible patients many cells and cellular episodes of bronchospasm and bronchial responsiveness to a variety of stimuli occur.

**Pathogenesis**

Inflammatory hyper-reactivity induced by immunologic stimuli in 20% of cases, and non-immunologic stimuli in 80% of cases (intrinsic asthma) due to physical, chemical and psychogenic factors.
Pathologic changes
Hypertrophy and hyperplasia of bronchial smooth muscles. Mucous gland hypertrophy and excessive mucus secretion. Mucosal oedema due to exudative inflammatory reaction and exudates. There is chronic inflammatory response.

Symptoms
Episodes of expiratory wheezing, dyspnoea and cough. Chronic cough with wheezing. It is influenced by environmental factors.

10.1 Bronchodilators
10.1.1 Xanthines
They relax smooth muscle notably bronchial muscle, stimulate nervous system, stimulate cardiac muscle, and act on the kidney to produce diuresis.

Theophylline
Dose
Over 70 kg 500 mg every 12 hours. Under 70 kg and elderly 350 mg every 12 hours.

Indications
Relief of bronchospasm in asthma, bronchitis and emphysema.

Contraindications
Porphyria, hypersensitivity to xanthines, peptic ulcer, seizures disorders, and suppositories contraindicated in presence of irritation or infection of rectum or lower colon.

Precautions
Liver disease, epilepsy, pregnancy, breast feeding, cardiac disease, elderly patients and fever. Serum drug concentration monitoring is necessary. Patients should not change from one sustained release theophylline to the other without clinical assessment.

Adverse effects
GIT irritation (nausea, vomiting, diarrhoea, abdominal pain) and CNS stimulation (insomnia, anxiety, dizziness). High doses lead to tachycardia, tachypnoea and convulsions.

Drug interactions
Ciprofloxacin, enoxacin, erythromycin, rifampicin, viloxazine, carbamazepine, primidone, phenytoin, phenobarbitone, beta-blockers, diltiazem, verapamil, aminoglutethimide, interferon, lithium, contraceptive pills, beta 2 agonists, cimetidine and sulphinpyrazone.

Patient instructions
Do not smoke. Avoid food or beverages containing caffeine. Elderly patients take safety precautions. (Rise slowly and request assistance if dizziness occurs). Do not take OTC cough, cold or breathing medication.
Aminophylline

Dose
Slow IV injection (over 20 minutes) 250-500 mg or child 5 mg/kg. Maintenance if required in patients not previously treated with theophylline in adults 500 mg/kg/hour by slow IV infusion.

Indications
Relief of bronchospasm in asthma, bronchitis and emphysema.

All other items are similar to theophylline.

10.1.2 Beta-Stimulants

Salbutamol (Selective B₂ agonist)

Dose
Oral, 4 mg, tid or qid. Child, under 2 years, 100 µg/kg qid; 2-6 years 1-2 mg tid or qid. SC or IM injection, 500 µg repeated every 4 hours if necessary. Aerosol inhalation, in acute and intermittent episodes and in prophylaxis of exercise-induced asthma 100-200 µg (1-2 puffs), child, 100 µg (1 puff) 200 µg (2 puffs). Chronic maintenance therapy 200 µg (2 puffs) tid or qid, child 100 µg (1 puff) tid or qid.

Indications
Chronic management or prophylactic therapy of bronchial asthma.

Contraindications
Hyperthyroidism and ischaemic heart disease.

Adverse effects
Fine tremors, nervous tension, headache, tachycardia and hypokalaemia after high dose, palpitations, insomnia, urticaria and angioedema.

Drug interactions
Cardiac glycosides, quinidine, monoamine oxidase inhibitors, TCA, halogenated anaesthetics, corticosteroids, and beta-blockers.

Terbutaline (Selective B₂ agonist)

Dose
2.5 mg Tablets, 1.5 mg/5 ml syrup. Inhaler 0.25 mg/mist.

Indications
Prophylactic and management of bronchial (acute exacerbation, intermittent symptoms and protective in exercise-induced asthma). In productive cough and antitussive to produce bronchial dilation inhibiting cough reflex and expulsion of bronchial exudates.

Adverse effects
Palpitations, fine tremors, tolerance dose-duration effect (least adverse effects after inhalation).
10.1.3 Other Inhalants

Sodium Cromoglycate

Pharmacological action
Inhibit degranulation of the pulmonary mast cell by a variety of stimuli.

Dose
Inhalation of dry powder, 20 mg qid (up to 6-8 times/day) Adult, child 10 mg 4 times daily when stabilized 5 mg 4 times daily.

Indications
Prophylactic control of asthma, seasonal and perennial allergic rhinitis and allergic conditions of the eye including acute and chronic conjunctivitis and viral keratoconjunctivitis.

Precautions
Has no role in the acute attacks. Gradual drug withdrawal. Pregnancy and breast-feeding.

Adverse effects
Inhalation of dry powder may lead to bronchospasm, cough and throat irritation, transient bronchospasm.

10.1.4 Inhaled Corticosteroids

Beclomethasone Dipropionate

Dose
Aerosol inhalation, 200 mcg (4 puffs) twice daily, or 100 mcg (2 puffs) 3-4 times daily. Child, 50-100 mcg (1-2 puffs) 2-4 times/day.

Indications
Prophylaxis of asthma not fully controlled by bronchodilators or cromoglycate.

Contraindications
Primary treatment of status asthmatics or acute episodes of asthma, systemic fungal infections, untreated localized infections of nasal mucosa.

Precautions
Transferring patients from oral corticosteroids to inhalation type should be done gradually. High doses of inhaled steroids may lead to adrenal suppression. Patients may have to change to oral corticosteroids during periods of stress.

Adverse effects
Hoarseness, candidiasis of mouth or throat, acne, fever, neck pain, headache, fatigue, migraine, weakness, muscle or joint pain.

Drug interactions
Ketoconazole, dietary supplements

Patient instructions
Benefit requires daily use as instructed. Not to continue intranasal therapy beyond 3 weeks. Not to exceed prescribed dose. Wash inhaler daily with warm water and dry thoroughly. Not to use for acute severe
asthma attack requiring rapid relief. Use with caution if sores or injuries in nasal passages are present.

10.2 Anti-Tussives

Cough is an important protective mechanism but may also occur as a symptom of an underlying disorder. Cough suppressants such as dextromethorphan may provide the patient with relief, although they control cough rather than eliminate it, cough suppressants must not be used to treat productive cough and should not be combined with expectorants in the treatment of cough.

Clobutinol
Pharmacological action
Depresses cough reflex in useless cough and dyspnea.

Dose
40 mg tablets, 20 mg/5 ml syrup, 60 mg/ml drops and 20 mg ampoule.

Indications
Anti-tussive in bronchial irritation and early stages of bronchitis or bronchial irritation.

Dextromethorphan
Dose
10-20 mg every 4 hours, to a usual maximum of 120 mg/day. Child, 2-6 years, 2.5-5 mg every 4-8 hours (with a maximum of 30 mg/day) 6-12 years, 5-15 mg every 4 hours, (maximum 60 mg/day).

Indications
Dry or painful cough.

Contraindications
Patients at risk of developing respiratory failure, liver disease, porphyria and with MAOI.

Precautions
Asthma, history of drug abuse, headache, CNS stimulants, hepatic or renal Impairment.

Adverse effects
Dizziness and constipation. Excitation and respiratory depression may occur after over-dosage.

Drug interactions
Mexiletine, MAOI, anxiolytics, hypnotics, cisapride, domperidone, metoclopramide, alcohol, anaesthetics, buprenorphine, butorphenol, nalbuphine and pentazocine and drugs that inhibit CYP2D6 can inhibit drug metabolism.

Patient instructions
Do not use this drug to suppress productive cough or chronic cough that occurs with smoking, asthma or emphysema. Report if your cough persists.
10.3 Mucolytics

**Carbocysteine**

**Pharmacological action**
Mucolytic, dissolves viscid bronchial secretion to be easily expectorated.

**Dose**
375 mg capsules and 125 mg and 250 mg/5 ml syrup.

**Indications**
Expectorant in productive cough to expell bronchial secretion.

**Ambroxol**

**Dose**
30 mg tablets, 75 mg capsules, 15, 30 mg/5 ml syrup and 7.5 mg drops.

Indications similar to carbocysteine.

**Bromhexine**

**Dose**
4-16 mg tid

**Indications**
In respiratory disorders associated with viscid or excessive mucus.

**Precautions**
Peptic ulcer.

**Adverse effects**
GIT upsets.

**Guaiphenesin**

**Dose**
200-400 every 4 hours. Child, 2-6 years, 50-100 mg every 4 hours, 6-12 years, 100-200 mg every 4 hours.

**Indications**
Expectorant.

**Contraindications**
Porphyria.

**Precautions**
Cough with excessive secretions, 7 to 10 days in duration with fever. Diabetes, heart disease, kidney disease.

**Adverse effects**
GIT discomfort. Nausea and vomiting with very large doses, rash, urticaria.

**Drug interactions**
ACE inhibitors, antithyroid agents, MAOIs, potassium products.

**Patient instructions**
Don’t take for persistent or chronic cough such as with smoking, asthma. If cough persists more than 1 week, inform your doctor. Drink a glass of water or other fluid with each dose of expectorant.
SECTION XI

ANTI - ALLERGIC DRUGS

In this section:

Topic: Allergy (Immunology) 97
Topic: Allergy Involving External Agents 98
Topic: Atopy 98
Topic: Major Allergens 101
Topic: Occupational Allergy 102
Topic: Drug Reactions 102
Topic: Atopic Food Hypersensitivity 102
Topic: Insects Stings 103
  11.1 Antihistaminics 103
  11.2 Beta-Stimulants 105
  11.3 Glucocorticoids 106
11. Anti-Allergic Drugs

They are mainly three groups

- Antihistaminic
- Sympathomimetic
- Corticosteroids

Topic: Allergy (Immunology)

It is the most misused term in medicine to seek external causes for their symptoms. It describes an acquired specific alteration of the individual’s state of reactivity to a chemical substance or organism occurring after the first exposure to it. The alteration may be favourable or unfavourable and the definition implies what we now call an “immunological” mechanism.

A substance against which the immune system directs such a specific response is an “allergen” and the allergens may be strictly either external or constituents of the body itself. The term “auto-allergy” is used for what is more commonly called “auto-immunity”.

Classification of allergic reactions

It was proposed by Gell and Coombs (1963), but it was not complete, because additional reaction types have been proposed and new mechanisms emerge with further research. The 4 types of reaction are not exclusive and may occur together.

Type I: Immunoglobulin E (Reagin) mediated

Specific IgE antibody is produced and becomes bound to the surface of tissue mast cells and blood basophils. The subsequent reaction of allergen with cell-bound IgE results in extrusion of the basophilic granules of these cells liberating pharmacologically active substances particularly histamine and leucotrienes [SRS (A) slow reacting substance of anaphylaxis]. These mediators produce vasodilatation, broncho-constriction, mucus secretion and irritation. The reaction starts within 10 minutes. Complement is not involved and corticosteroids have little direct suppressive action on it. Occasionally, subclasses of IgG may act in a similar way to produce a modified type I response.

Type II: Cytotoxic Antibody Mediated

IgG or IgM antibodies are directed against allergens on cell surfaces, complement is activated and tissue damage results. This is a feature of autoimmune disease but external agents may become bound to cell proteins and act as hapten in the production of an allergen e.g. thrombocytopenic purpura, penicillin-induced haemolytic anaemia. Some drugs induce auto-antibodies without becoming bound to the cell membrane e.g. methyldopa haemolytic anaemia.
**Type III: Immune complex mediated**

This also involves IgG or IgM antibodies to a specific allergen complexes of antigen, antibody and complement are formed. The complement is activated and adjacent tissues are not directly involved (innocent bystanders) are damaged. There are localised types in which the reaction is confined to one organ e.g. extrinsic allergic alveolitis (Farmer’s lung).

If the complexes are disseminated widely by the circulation, generalised disease with fever, urticaria, arthropathy and involvement of many systems results. The classical condition is serum sickness and many drugs reaction are of this type. The drug possibly forms a hapten with serum protein.

**Type IV: Cell mediated**

The tissue damage is produced not by antibody but by specifically sensitized T-lymphocytes e.g. tuberculin reaction and of graft rejection, allergic contact eczema, the allergen being bound as a hapten to epithelial cell protein.

**Topic: Allergy Involving External Agents**

History is important, even exceeding that in other branches of medicine.

Clinical tests: Prick testing is a simple procedure of great value in the diagnosis of atopic disease and relatively few test substances will suffice in most cases. The manufacturer’s instructions should be followed and minimal skin trauma is required. False negative results may be seen in young children under about 5 years old but otherwise it is very reliable. The results must be positive skin reactions are not associated with clinical symptoms. Intradermal testing may be needed with less satisfactory test preparations or when delayed Type III or IV reactions are suspected. It is potentially dangerous, false positive reactions are often seen and it is better left to the specialist. Patch testing should be carried out only by a practitioner with considerable dermatological experience.

Laboratory tests: add little to allergic diagnosis. A raised total IgE can help in atopic disease when prick tests with available allergens are negative, but it is usually less sensitive. IgG antibody should be measured in cases of suspected extrinsic allergic alveolitis. Eosinophilia is usual in atopic disease but occurs in intrinsic asthma also.

**Topic: Atopy**

It describes a state peculiar to man, subject to hereditary influence and manifesting itself by asthma, rhinorrhea and atopic eczema. IgE levels are raised and skin tests against the allergens involved are positive at 10-15 minutes (the immediate response), owing to a local Type I reaction.

The tendency is present from conception but the clinical manifestations
occur at varying times after birth in response to allergens or other factors.

Atopy should be considered a variable condition ranging from the full syndrome of infantile eczema, asthma, rhinorrhoea, immediate food reaction and a wide spectrum of skin reactivity.

The symptoms of atopy usually occur in infancy or early in childhood and often regress in adolescence. This may be due to mal adaptation to environmental allergens. Strict avoidance of potential allergens particularly foods other than breast milk will improve atopy. Sometimes, infants exposed to food allergens ingested by the lactating mother or even from maternal circulation in utero.

Atopy does not include increased susceptibility to most drug reaction, nasal polypi, insect sting anaphylaxis extrinsic allergic alveolitis or chronic urticaria. Incidence of atopy exceeds 20%.

**Atopic disease of the upper respiratory tract**

This is the commonest site for atopic disease due to accessibility of the mucous membranes to allergens in inspired air. The symptoms are these of a type I reaction in the membranes of the nose, sinuses, pharynx and Eustachian tubes.

Irritability and itching are prominent, rubbing of the nose or eyes, grimacing, irritation of soft palate (odd noises), sneezing and rhinorrhoea.

The mucous membranes appear pale with a bluish tinge, swelling of turbinate and obstruction. Epistaxis may occur and chronic nasal obstruction in childhood produce narrowing of the nostrils and high arched palate.

Pain is absent and its presence suggests secondary infection. Nasal polypi and otitis media are not due to this atopic disease.

**Atopic asthma in children and young adults**

Grass pollen grains are not usually inhaled below the larynx. The allergen is probably carried in the circulation but reflex factors may be involved. There is hyperaemia, mucus secretion and oedema broncho-spasm. The reaction is prolonged and may recur many hours after a single exposure to allergen.

Probably immune reaction other than Type I also occur in young children. Cough (particularly nocturnal) is more obvious than wheezing due to Type I reaction. When cough and wheezing occur together in childhood, infection is presumed and symptoms are more severe and prolonged than those produced by the infection alone.

Anti allergic management will control the condition whereas repeated antibiotic courses will not. The condition tends to improve as the child’s immunity to endemic viruses develops.
Non-atopic allergic respiratory disease

Extrinsic allergic alveolitis occurs in individuals who are non-atopic and are heavily exposed to aero-allergens small enough (less than 5 microns) to reach the alveoli. It is associated with Type III reaction but other immune mechanisms may be involved. Ig antibodies are present in serum and produce late 3-6 hours complement mediated reaction on intradermal skin testing with allergens. Organic dusts are the causal factors often of occupational origin e.g. Farmer’s lung and bird fancier’s lung.

The lesion is basically an allergic pneumonia in the acute state and with pulmonary fibrosis as it becomes chronic.

Intrinsic (cryptogenic, Non-allergic) asthma: Asthma or rhinorrhoea occurs in middle or late adult life without an extrinsic allergic cause. Auto-immune factors may be present. Extrinsic occupational or domestic factors occur in this age group. A hamster or other rodent pet will sometimes cause severe asthma. Grass pollen and moulds are more likely than mites to produce asthma in an adult. There is marked eosinophilia but serum IgE levels are normal.

Atopic (immediate) urticaria angio-oedema

They may occur after specific foods e.g. eggs, nuts and fish, cheese, peas, beans, cereals and same fruits. These reactions occur in full atopics with a history of eczema. They are accompanied by immediate burning sensation within the mouth and often vomiting. Type I skin test is positive.

Drug urticaria and angio-oedema

Aspirin is the commonest cause of acute urticaria in non-atopic individuals. It is pharmacological idiosyncrasy and not immunological. Similarly, some food dyes, morphine derivatives, muscle relaxants, vasodilators and atropine will cause non-specific liberation of histamine with urticarial reactions. Any drug can cause urticaria by allergic mechanisms as often Type III as type I.

Atopic eczema

It is the comment infantile eczema of brief duration without other symptoms of atopy, while persistent atopic eczema is accompanied by syndrome including reactions to food. When food hypersensitivity is present, it causes either gastro-intestinal symptoms or urticaria.

Allergic contact eczema

It is entirely different condition from Atopic eczema and is due to type IV reactions to substances combined as haptens with epithelial cell protein. It occurs at the site of contact with characteristic patterns of distribution e.g. hands, under metal fasteners where cosmetics deodorants are applied. The eye-lid skin is very sensitive. The appropriate investigation is the patch
test read at 48 to 72 hours. It is strongly suppressed by corticosteroids.

**GIT atopy**

Atopic allergens may produce angioedema at any site in GIT. There is swelling in mouth or pharynx, dysphagia, abdominal pain, vomiting, diarrhoea and symptoms of sub acute intestinal obstruction.

In infants, cow’s milk hypersensitivity may mimic congenital hypertrophic pyloric due to angio-oedema of the pylorus.

**Non-atopic GIT allergy**

It is not yet certain whether gluten entropathy is an allergic condition or due to chemical idiosyncrasy. Aphthous ulcers may be partially due to allergic aetiology.

**CVS allergy and anaphylaxis**

There is giddiness, syncope and anxiety with tachycardia and hypotension. It is due to disseminated Type I reaction after ingestion, inhalation or more usually parenteral administration of antigen by a drug or vaccine or an insect sting. Arrhythmias, laryngeal angio-oedema or asthma may occur. Myocarditis and pericarditis may occur as a part of serum sickness Type III reactions.

**Genito-urinary tract allergy**

Some drug nephropathies have an allergic basis and the kidneys are involved in serum sickness. Also nephrotic syndrome complicates atopic disease in which the allergen may be foods or respiratory allergens e.g. grass pollen. Sometimes, allergy to semen in women. IgE antibodies are responsible with acute post-coital vulvo-vagnitis but generalized urticaria or anaphylaxis may occur.

**Allergy and CNS**

Anxiety and syncope occur as CNS symptoms of histamine release in anaphylaxis and CNS manifestations of immune complex deposition in serum sickness. Also migraine, epilepsy and behaviour disorders in children are due to allergy.

**Allergies of the eye**

The conjunctiva is affected by hay fever with echemosis particularly in children mainly due to pollen. The skin of the eye lids may be affected by contact eczema. Abuse of topical therapy, drops or eye washes may be responsible for chronic allergic conjunctivitis.

**Topic: Major Allergens**

**House dust mite**

Dermatophagoides mites are the major allergen of house dust. 20% of population has atopic skin reactivity to them. Mite faeces are the most important particles as their size is equivalent to grass pollen grains and they are suspended in the air after being disturbed. They feed on skin scales and are most numerous in beds and also on other epithelial products.
e.g. feathers. They are most numerous in early autumn and in humid conditions. Bedrooms should be kept dry and regular vacuum cleaning of bedding will reduce their number but eggs persist.

**Pollens**

Grass pollens is a major aero-allergen and travel in clouds and is at maximum on dry afternoons with a wind. Asthma may occur up to 12 hours after exposure.

**Domestic animals**

The important allergens are usually saliva, urine and dander rather than in hair of cats, dogs, birds and horse dander.

**Moulds**

They cause asthma rather than rhinorhoea as spores are small to reach the lower respiratory tract affecting agricultural workers and other occupational activities.

**Topic: Occupational Allergy**

It is the most important cause of allergic disease occurring for the first time in adult. The constant introduction of new chemicals and new techniques ensures new allergens will appear in the future.

Atopic occupational allergens e.g. many mammals particularly laboratory rodents may cause asthma. The rat is most important and allergens are a primary factor. Specific mould asthma in agricultural and horticultural workers and farmers may develop “Bran asthma” due to storage mites. Platinum salts are among the inorganic chemicals in causing Type I reactions. Also allergic alveolitis may occur in malt workers, and mushroom growers. Other examples are epoxy resin activators, fumes from heated PVC (meat wrappers asthma, drugs in manufacture, saw dusts of certain woods, synthetic dyes in cosmetics and clothing, many plants, rubbers, drugs of topical medications (contact allergens).

**Topic: Drug Reactions**

Probably all drugs are capable of producing adverse reactions in a few individuals.

Idiosyncrasy is a biochemical abnormality of the patient leading to qualitative difference from the normal drug response e.g. haemolytic anaemia due to 8-aminoquinolones in glucose-6-phosphate dehydrogenase deficiency and acute porphyria due to sulphonamides or barbiturates. Allergic hypersensitivity is impossible to distinguish from the idiosyncrasy response.

**Topic: Atopic Food Hypersensitivity**

This can occur with any food but is common with eggs, milk, nuts, fish, and shellfish, slightly less common with cereals, fruits and legumes and rather rare with other foods. It occurs mainly in full atopics who have ec-
Chemicals are added to the diet as preservatives, stabilizers, colourings and flavouring. They are considered as drugs in their ability to produce adverse reactions e.g. sulphur dioxide (as sodium metabisulphite) a preservative that may aggravate asthma by direct irritant effect. Benzoate preservatives and artificial dyes of which tartrazine cause asthma and urticaria in susceptible individuals. The flavouring agent monosodium glutamate causes acute neurological symptoms.

**Topic: Insects Stings**

Wasp and bee stings may cause severe and sometimes fatal anaphylaxis in few individuals due to an IgE reaction to venom and Type III responses. There is no evidence that desensitization is of benefit.

### 11.1 Antihistaminics

They relieve symptoms of allergic reaction, such as urticaria, allergic rhinitis, and allergic conjunctivitis; they also control pruritis in skin disorders such as eczema, food allergies, insect sting and some symptoms of anaphylaxis.

**Chlorpheniramine maleate**

H₁-receptor antagonist

**Dose**

4 mg every 4-6 hours (maximum 24 mg/day). Child 1-2 years 1 mg twice daily, 2-5 years 1 mg every 4-6 hours (maximum 6 mg/day) and 6-12 years 2 mg every 4-6 hours. (Maximum 12 mg/day).

**Indications**

For the control of allergy (hay fever, allergic rhinitis and conjunctivitis, atopic dermatitis) and in common cold preparation.

**Contraindications**

Premature infants, neonates and pregnancy, asthmatic attack, stenosing peptic ulcer.

**Precautions**

May affect performance of skilled tasks. Should be used cautiously in patients with glaucoma, prostatic hypertrophy, intestinal obstruction, epilepsy and severe cardiovascular disorders, bladder neck obstruction and pregnancy (do not use in 3rd trimester or in nursing mother).

**Adverse effects**

Sedation, CNS stimulation may occur in children, dry mouth blurred vision, thickened respiratory secretions, retention of urine and decreased GIT motility.
Drug interactions
Alcohol, tricyclic anti-depressants, anti-muscarinics, anxiolytics, hypnotics and betahistine, MAO therapy.

Patient instructions
Advise patient to take sips of water frequently; suck ice chips, sugarless hard candy or gum if dry mouth occurs. Avoid exposure to sunlight.

Astemizole
H1-receptor antagonist

Dose
10 mg/day (must not be exceeded). Child 6-12 years 5 mg/day (must not be exceeded).

Indications
For the control of allergic reactions such as hay fever or hives.

Contraindications
Porphyria, pregnancy, patients with pre-existing prolongation of QT-interval.

Precautions
Although drowsiness is rare, patients should be advised that it might occur.

Adverse effects
Increased appetite and weight gain, ventricular arrhythmia, cardiotoxicity with overdose, nervousness, dry mouth, shortness of breath, rash.

Drug interactions
Alcohol, erythromycin, ketoconazole, itraconazole, tricyclic anti-depressants, antimuscarinics, anxiolytics, hypnotics and betahistine.

Patient instructions
To relieve mouth dryness, chew sugarless or suck ice chips or hard candy. Be cautious in performing tasks that require alertness.

Loratadine
H1-receptor antagonist

Pharmacological action
It is antihistaminic (H1 blocker) for systemic use. Long duration of action without sedative effect.

Dose
10 mg tablets/day, syrup 5 mg/5 ml. Combined preparation with pseudoephedrine mainly in running nose, allergic rhinitis and common cold.

Indications
Antiallergic in: urticaria, angioneurotic oedema, serum sickness, allergic drug reaction, allergic rhinitis, hay fever and common cold.

Promethazine
Pharmacological action
It is a phenothiazine derivative with antihistaminic action and antiseroter-
tonin on smooth muscles. Central sedative action.

**Dose**
Syrup 5, 6 mg/5 ml. And amp. 25 mg/2 ml.

**Indications**
Antiallergic and mild sedative-hypnotic action. Combined therapy in cold and cough preparation.

**Precautions**
Avoided in driving and professions which need alertness e.g. machinery, … etc.

**Cetirizine**

**Pharmacological action**
Antihistaminic for systemic use.

**Dose**
10 mg tablet/12 hours.

**Indications**
Allergic disorders.

---

11.2 Beta-Stimulants

**Epinephrine (Adrenaline)**

**Dose**
Acute bronchial asthma: SC or IM 1 mg = 1: 1000 solution) repeated every 15-30 minutes. Acute anaphylaxis, IM of 1 mg/ml, under 1 year 0.05 ml. year 0.1 ml, 2 years 0.2 ml, 3-4 years 0.3 ml, 5 years 0.4 ml, 6-12 years 0.5 ml, adult 0.5-1 ml.

**Indications**
Acute reversible airway obstruction and acute anaphylaxis.

**Contraindications**
Hyperthyroidism, cardiovascular disease (hypertension, ischaemic heart disease, arrhythmia or tachycardia).

**Precautions**
Care should be taken in patients with closed angle glaucoma and diabetes mellitus.

**Adverse effects**
Central stimulation (anxiety, tremors, insomnia) CVS disorders (hypertension, tachycardia, arrhythmia, anginal pains).

**Drug interactions**
Cardiac glycosides, quinidine, monoamine oxidase inhibitors, tricyclic
antidepressants, halogenated anaesthetics, corticosteroids and beta-blockers.

**Patient instructions**

Periodically familiarize yourself with use so you maintain an adequate comfort level. Obtain new kit by expiration date or colour change or sooner if precipitate is noted in solution.

### 11.3 Glucocorticoids

**Hydrocortisone sodium succinate**

**Dose**

By IM or slow IV or infusion 100-500 mg, 3-4 times daily (as required). Child, slow IV injection, up to 1 year 25 mg, 1-5 years 50 mg, 6-12 years 100 mg.

**Indications**

Emergency treatment of adrenal insufficiency, status asthmatics and anaphylactic shock (with epinephrine).

**Contraindications, precautions, adverse effects, drug interactions**, and patient instructions: similar to dexamethasone

**Fludrocortisone**

**Pharmacological action**

Oral corticosteroid 10-fold active as cortisol.

**Dose**

0.1 mg Tablets.

**Betamethasone**

**Pharmacological action**

Corticosteroid 30 fold active as cortisol. Potent anti-inflammatory

**Dose**

Tablets 0.5 mg (3 mg/d) amp. 7 mg/2 ml.

**Triamcinolone**

**Pharmacological action**

Corticosteroid 5 fold active as cortisol. Produces severe muscle wasting.

**Dose**

Tablet 4 mg (20 mg/d). Vials 40 mg.

**Indications**

Collagen diseases to control oedematous, degenerative and fibrotic process e.g. SLE, scleroderma, dermatomyositis, sarcoidosis, nephrotic syndrome, polyarteritis nodosa, etc. Blood dyscrasias e.g. hemolytic anemia, thrombocytopenic purpura. Miscellaneous: acute polyneuritis, toxic encephalitis. Antiallergic in hypersensitivity reactions, status asthmaticus, skin diseases e.g. eczema, exfoliative dermatitis.

**Adverse effects**

Cushing-like syndrome, psychosis, steroid diabetes, osteoporosis, hir-
sufism, oedema, potassium loss, myopathy, and indigestion.

**Contraindications**

Epilepsy, diabetes, T.B., hypertension, peptic ulcer infectious diseases, fungal and viral infections.

[Dexamethasone: see under endocrine, supra renal cortical hormone.

Prednisolone: see under endocrine, supra renal cortical hormone.]
SECTION XII

NEURO- PSYCHIATRIC DRUGS

In this section:

Topic: Neuroses 109
Topic: Psychosis (Affective Disorders) 111
Topic: Parkinson's Disease 112
Topic: Epilepsy and Seizure Disorders 112
12.1 Hypnotics, Sedatives and Anxiolytics 113
12.2 Antipsychotics 115
12.3 Antidepressants 117
12.4 Antiparkinsonian Drugs 118
12.5 Antiepileptics 120
12. Neuro Psychiatric Drugs

Neuro-Psychiatric Disorders

Topic: Neuroses

They are defined as the minor mental illnesses in which the patient has at least some degree of insight into the fact that he or she is ill which is concerned with reality. They are classified into: anxiety, phobic, hysterical, depressive and obsessional.

Anxiety neurosis

The main symptoms are related to increased activity of the autonomic nervous system both the sympathetic and parasympathetic. The patient experiences tachycardia, pallor, sweating, dry mouth, tremors, etc. When these symptoms are experienced and are not attached to any particular situation or object, this is called “free floating anxiety” which is associated with conditions such as depersonalisation and derealisation. There are associated organic conditions which have similar presentation e.g. thyrotoxicosis, pheochromocytoma and hypertension.

Genetic factors play a part. It is extremely common in childhood, adolescence and old age. They are associated with menopause, head injury, acute infection, epilepsy and thyrotoxicosis. Conditions are controlled by anxiolytics and beta-blockers (when predominantly physiological).

Phobic states

These are classified as:

- Animal phobias
- Agoraphobia
- Social phobias
- Miscellaneous phobias

Animal phobias

These are relatively rare and 95% occur in women. They begin in early childhood and consist of the monosymptomatic phobia of a single animal species and with little generalisation. The patient has little general anxiety and few associated symptoms. The condition needs only behaviour therapy by direct exposure to the feared stimulus with modelling of fearless behaviour by the therapist.

Agoraphobic syndrome

It is very common and occurs in women between the ages of 15-35. It consists of multiple symptoms which include fear of going out alone, fear of shopping, fear of travelling, fear of closed spaces or fear of open spaces. There are many associated symptoms such as general anxiety, panic attacks, dizziness, depression and depersonalisation. The condition shows partial remissions and relapses for several years. The condition needs behaviour therapy, anxiolytics or TCA in low doses.

Social phobias

These are almost equally common in men and women and occur after puberty in the age range 15-30 years.
The main symptoms consist of fear of being in public places e.g. eating in restaurants or drinking or writing when in company. Once it starts, the condition is continuous without treatment. Drugs have a very small part to play but small doses of imipramine or diazepam may be useful to facilitate the effects of behaviour therapy.

**Miscellaneous phobias**

They occur at anytime of life. The symptoms are restricted to very specific situations e.g. fear of heights, fear of thunder, fear of lightening, fear of darkness, fear of driving, aeroplanes and lights. There are no associated symptoms and very little generalised anxiety.

**Hysterical neurosis**

It starts early in life which occurs mainly in females and is demonstrated by recurring episodes of different symptoms. The patient behaves in a manner which shows attention-seeking self petty and self concern.

There are various associations of hysteria that include organic brain damage, multiple sclerosis, cerebral atherosclerosis, cerebral tumours, encephalopathies, mental deficiency, severe concussion, depression, schizophrenia and anxiety states. The important clinical features are disturbances of sensations with anaesthesia, parasthesia, disturbed motility, ataxia, paralysis and tremors.

**Depressive neurosis**

It is due to exogenous understandable response to an environmental stress that is different from psychotic endogenous depression. In neurotic depression, the depressed mood is similar to normal unhappiness and tends to fluctuate from time to time. There is no diurnal variation in mood and anxiety is a common accompaniment. Delusions and hallucinations are completely absent, common complaints are lack of energy, poor concentration and preoccupied with unpleasant thoughts.

**Obsessional disorders**

They have two different components:

- The obsessional idea (rumination)
- The compulsive behaviour (ritual)

The obsessional idea is sometimes called a rumination and consists of unwanted, intrusive thought which the patient recognises but cannot eradicate from his mind.

The compulsive behaviour is a motor act which a patient feel compelled to perform despite recognizing the ridiculousness of his action.

Common themes include ritual hand washing (to cope with harmful contamination), elaborate checking and the patient can be totally preoccupied with cleanliness and tidiness. The patient may keep his experience secret for years and present normal life style.
The condition may be associated with encephalitis lethargia and post-encephalitic states.

Management needs behaviour therapy mainly and clomipramine is the most useful for the compulsive ritualisers with depressed mood and must be continued for over a year.

**Topic: Psychosis (Affective Disorders)**

**Major depression (mood disorders)**

It is divided into unipolar (only depression) and bipolar (alternating depression and mania or hypomania).

**Vegetative and somatic complaints**

In depression: There are symptoms of: anhedonia, fatigability, insomnia, social withdrawal, psychomotor retardation, agitation, hypochondrial complaints and decreased personal hygiene and crying spells.

In mania: There are symptoms of: hyperactivity, pressured speech, hypersexuality, easily angered and dangerous behaviour.

**Intellectual disturbances**

In depression: Disorientation, delirium, amnesia and indecisive.

In mania: Flight of ideas, speed thinking, poor judgement and impulsive action and decisions.

**Emotional disturbances**

In depression: Hopelessness helplessness syndrome, dysphonia, despair, anguish and gloomy thoughts.

In mania: Elevated mood, euphoria, grandiosity, irritability and hostility.

**Iatrogenic depression**

Steroids, oral contraceptives, anti-hypertensive, digitalis, cytotoxics, indomethacin, ethambutol, stimulant withdrawal

**Symptomatic depression**

CNS (cerebral tumours, head injury, epilepsy, Parkinsonism, disseminated sclerosis), CVS (myocardial infarction, CHF and cardiac surgery), Hormonal (Addison’s, hyperthyroidism, Cushing’s), Chronic illness (pernicious anaemia, pellagra, rheumatoid arthritis, SLE and porphyria), Malignancy and surgical e.g. amputation.

**Schizophrenia (thinking disorders)**

It is a delusional-hallucinatory syndrome, hereditary long-life disease in adolescence of acute or gradual onset with recurrent course and males and females are equally affected. It is characterized by disturbed perception (illusion, delusion and hallucination, delirium and disorientation), disturbed mood and emotions (blunting emotions, apathy, worried and incongruity between mood and emotions), disturbed conation (hesitation, depersonalisation, poorly motivated, excite-
ment, apathy, catatonia and stereotyped). To be diagnosed continuous signs persist for at least 6 months and mood disorders are ruled out.

**Topic: Parkinson's Disease**

**Aetiology**

Idiopathic, post-encephalitic (viral), Neurotoxins, Drug-induced e.g. neuroleptics

**Classic features**

Tremors (pill-rolling type), hypertonia (cogwheel or ratchet) and impaired swallowing, bradykinesia (lack of spontaneous movements), postural disturbances (stooped posture and impaired postural reflexes), autonomic dysfunction (sialorrhoea, seborrhoea, increased sweating, orthostosis, constipation and erectile dysfunction, cognitive decline, dementia, depression, apathy and bradyphrenia

**Stages**

Stage I: only unilateral and minimal functional impairment. Stage II: Bilateral involvement without balance impairment. Stage III: Postural imbalance, mild to moderate disability. Stage IV: Severe disability, cannot walk or stand unassisted. Stage V: bed restriction and do not respond to therapy.

Stages I and II require minimal or no treatment.

**Topic: Epilepsy and Seizure Disorders**

It is a clinical manifestation consists of sudden and transient abnormal phenomena that may include alteration of consciousness, motor, sensory, autonomic and psychic events unprovoked by any immediate identified cause.

**Aetiology**

Metabolic: hypoglycaemia, hypoxia, hyponatraemia, hypocalcaemia, acid-base disturbances, hepatic and renal failure, drug-withdrawal and drug intoxication; Focal cortical damage e.g. infarction, tumour, contusion, abscess, meningitis, encephalitis; Perinatal injury and mal development; Febrile; Idiopathic (grandmal and petitmal).

**Clinical patterns**

**Partial (focal) seizures:** They are localized and restricted in single hemisphere or portion of hemisphere that leads to a wide variety of focal signs and symptoms.

a. Simple partial seizures (auras) are:

- Without impairment of consciousness
- Focal motor or sensory symptoms
- Autonomic symptoms
- Psychic symptoms

b. Complex partial psychomotor seizures occur with impairment of consciousness.
There are organized high level activity in diverse forms e.g. inappropriate behaviour (automatism), psychiatric disorders (illusion, hallucination and stereotype sequence), emotions (anxiety and phobias), complicated memories (dream like status). The drugs of choice for treatment are carbamazepine, phenytoin, and valproic acid.

c. Partial seizures that evolve to generalized seizures

**Generalized seizures:**

Primary convulsive seizures: They are related to generalized involvement of both hemispheres.

Grandmal (generalized tonic-clonic) seizures: Drugs of choice include valproate, phenytoin, carbamazepine and new antiepileptic drugs.

Non-convulsive seizures: lack of convulsions means petitmal seizures. In children there are brief episodes of loss of consciousness. Drugs of choice include ethosuximide, and valproate.

Miscellaneous seizures: primarily in infants and children. Myoclonic seizures (juvenile myoclonic epilepsy), clonic seizures, tonic seizures, akinetic (atonic) seizures, and infantile spasms. Drugs of choice include valproate, and clonazepam.

**12.1 Hypnotics, Sedatives and Anxiolytics**

A sedative drug decreases activity, moderates excitement, and calms the subject. A hypnotic drug produces drowsiness and facilitates the onset and maintenance of sleep from which the patient can be easily aroused.

Sedative-hypnotic cause graded dose-dependent depression of the CNS. Most sedative-hypnotic, when used in high doses, may depress respiratory and vasomotor centres leading to coma and death.

**Phenobarbitone**

**Dose**

Oral, 60-180 mg by night. CHILD 5-8 mg/kg/day. By IM or IV 100-200 mg repeated after 6 hours if necessary, maximum 600 mg/day

**Indications**

For the control of tonic-clonic (grand mal) and partial (focal) seizures and status epilepticus. Prophylaxis of febrile convulsions in children.

**Contraindications**

Severe hepatic, renal or respiratory dysfunction and porphyria.

**Precautions**

In extremes of age, in acute pain, mental depression, hepatic, renal or respiratory impairment. May cause drowsiness, so tasks needing mental
Alertness should be avoided and withdraw drug gradually.

**Adverse effects**

Sedation (less marked with prolonged use), mood changes, folate deficiency and hypocalcaemia (after prolonged administration). High doses lead to nystagmus and ataxia and toxicity lead to severe cardiovascular and respiratory depression.

**Drug interactions**

Disopyramide, quinidine, chloramphenicol, doxycycline, metronidazole, oral anticoagulants, tricyclic antidepressants, griseofulvin, antipsychotics, digitoxin, corticosteroids, cyclosporin, oral contraceptives, theophylline, thyroxine, isradipine and other antiepileptics.

**Patient instructions**

Use with caution when driving or performing other tasks requiring mental alertness. Avoid concurrent use of alcohol. Do not stop suddenly, it can increase seizures.

**Diazepam**

**Dose**

In anxiety, orally, 2 mg tid increased if necessary to 15-30 mg/day in divided doses; elderly should receive half the dose. Insomnia, 5-15 mg at bedtime in acute anxiety and acute alcohol withdrawal symptoms, IM or slow IV, 10 mg. In status epilepticus, slow IV, as a 0.5 % solution, 10-20 mg at a rate of 0.5 ml/30 seconds repeated if necessary after 30-60 minutes.

**Indications**

In the treatment of severe anxiety states, as a hypnotic in the short treatment of insomnia, as a sedative, premedicant in anaesthesia, in the management of status epilepticus and febrile convulsions, in the control of muscle spasms and in the management of alcohol withdrawal symptoms.

**Contraindications**

Patients with pre-existing CNS depression, arteriosclerosis or coma alone in the treatment of depression, porphyria, acute pulmonary insufficiency or sleep apnoea.

**Precautions**

Elderly, debilitated, chronic pulmonary disease, personality disorders, pregnancy and breast-feeding, impaired hepatic or renal function. Skills that need alertness should be avoided. Withdraw drug gradually. In case of IV injection, facility resuscitation should be at hand.

**Adverse effects**

Drowsiness, sedation and ataxia (commonest). Vertigo, headache, confusion, slurred speech, urinary incontinence or retention, loss of libido and amnesia. Respiratory depression and hypotension may occur with high doses. Rebound anxiety occurs with tolerance.
Drug interactions
Anaesthetics, alcohol, opioid analgesics, antidepressants antihistamines, antihypertensives, antipsychotics, disulfiram, levodopa and cimetidine.

[Patient instructions
see phenobarbitone]

12.2 Antipsychotics
Antipsychotic drugs or neuroleptic drugs are those used to treat very severe psychiatric illness, the psychosis, they have beneficial effects on mood, but carry the risk of producing characteristic adverse effects that mimic neurological disease. Antipsychotic drugs share many pharmacological effects and therapeutic applications. Chlorpromazine and haloperidol are commonly taken as prototypes for the group. Many antipsychotic drugs, and especially chlorpromazine and other agents of low potency, have sedative effects. These are especially conspicuous early in treatment, although tolerance to this effect is typical, sedation may not be noticeable when very agitated psychotic patients are treated. They also have anti-anxiety effects. However, this class of agents is not generally used for such a purpose, because of their autonomic and neurological adverse effects, which paradoxically can include severe anxiety and restlessness.

Mechanism of action
Antipsychotic action: They are dopamine antagonists blocking postsynaptic dopamine receptors (D₂) in mesolimbic and hypothalamic systems. Atypical neuroleptics also block presynaptic D₁-receptors.

Chlorpromazine
Dose
In psychosis, orally, initially 25 mg 3 times/day adjusted to usual maintenance dose of 75-300 mg/day. Elderly, 1/3 to 1/2 adult dose. Child, 1-5 years 0.5 mg/kg every 4-6 hours, 6-12 years 1/3 to 1/2 adult dose. In intractable cough 25-50 mg 3-4 times/day. For the relief of acute symptoms, IM 25-50 mg every 6-8 hours. Child as oral dose.

Indications
In chronic and acute schizophrenia, control of manic phase in manic-depressive disorder, control of severe anxiety status in other psychiatric illnesses. To control nausea and vomiting induced by disease, drugs or postoperatively, alleviation of intractable cough, to control acute intermittent porphyria and to induce hypothermia.

Contraindications
Patients with pre-existing CNS depression, coma, bone-marrow suppression or phaeochromocytoma, closed angle glaucoma, parkinsonism, diabetes mellitus, hypothyroidism, myasthenia gravis and prostatic hypertrophy and untreated epileptics.

Precautions
Epilepsy, pregnancy and breast-feeding. Skills which need alertness
should be avoided in first days of drug administration. Regular ophthalmological and haematological examinations are recommended. Avoid abrupt drug withdrawal.

**Adverse effects**

Sedation (tolerance develops to this effect). Antimuscarinic action (dry mouth, constipation, difficulty with micturition, blurred vision, mydriasis. CVS, (tachycardia and ECG changes and postural hypotension is common). Hypersensitivity reactions (urticaria, systemic lupus like syndrome), blood disorders, extra pyramidal manifestations (parkinsonism like syndrome), endocrine and metabolic changes (amenorrhoea, galactorrhoea, gynaecomastia, and hyperglycaemia).

**Drug interactions**

Alcohol, anesthetics, antacids, TCA, antiepileptics, ACE-Is, reserpine, metyldopa, metirosine, anxiolytics, hypnotics, antimuscarinics, propranolol, calcium channel blockers, desferrioxamine, domperidone, metoclopramide, dopaminergics, lithium, and cimetidine

**Patient instructions**

Not to stop taking medication abruptly. Avoid intake of alcoholic beverages and OTC medications. Dry mouth may be relieved by rinsing mouth with warm water, sucking on sugarless hard candy or gum. Dizziness or light needless may be experienced when rising to a sitting or standing position.

**Haloperidol**

**Dose**

In schizophrenia and psychosis. As short term adjunctive therapy in severe anxiety, psychomotor excitement and agitation.

**Indications**

In schizophrenia and other psychoses. As short term adjunctive therapy in severe anxiety, psychomotor excitement and agitation. In the management of nausea, vomiting, intractable hick-up and motor tics.

**Contraindications**

Extra-pyramidal diseases

**Precautions**

In depression

**Adverse effects**

Extra pyramidal manifestations especially in thyrotoxicosis. Less sedating, hypotensive and antimuscarinic actions than chlorpromazine. Rarely liver function disturbances, GIT upsets and weight loss may occur.

**Drug interactions**

Alcohol, anaesthetics, calcium channel blockers, ACE-I methyldopa, metirosine, reserpine, anxiolytics, hypnotics, carbamazepin, indomethacin, metoclopramide, lithium, rifampicin and dopaminergics
Patient instructions
Avoid exposure to sunlight. Use mouth rinses, good oral hygiene. Use caution while performing other tasks that require mental alertness.

12.3 Antidepressants
Tricyclic and related antidepressants are the most widely used drugs in the treatment of depressive disorders. The response to antidepressant therapy is usually delayed with a lag-period of up to two weeks and at least six weeks before maximum improvement.

Imipramine
Pharmacological action
Antidepressant by central noradrenaline reuptake inhibitor.

Dose
10 and 25 mg tablets. 75-200 mg/d and maintenance 50-150 mg/d.

Indications
Endogenous depression, nocturnal enuresis

Adverse effects
Cholinergic blocking action, cardiac arrhythmias, tremors (mild extra pyramidal symptoms), sweating, fatigue, and excitement.

Contraindications
Glaucoma, enlarged prostate and drugs (MAOIs, alcohol, and barbiturates (potentiation) and antagonizes guanethidine.

Amitriptyline
Dose
Oral initially 50-75 mg, in elderly and adolescents 25-50 mg/day in divided doses or a single dose at bedtime. Increased gradually to a maintenance of 50-100 mg/day (maximum period of treatment should not exceed 3 months)

Indications
Treatment of endogenous depression particularly where sedation is required. Nocturnal enuresis in children.

Contraindications
Heart block, arrhythmias, immediately following myocardial infarction, liver failure, mania and porphyria

Precautions
Patients with prostatic hypertrophy, glaucoma, heart diseases, epilepsy, liver dysfunction, constipation and hyperthyroidism. Reduce dose in elderly. Avoid during performance of tasks requiring alertness. Should not be used within 14 days of MAOI discontinuation.
Adverse effects
Antimuscarinic effects, sedation but less than clomipramine, dry mouth, constipation, retention of urine, blurred vision, CVS (hypotension, bradycardia, arrhythmia, syncope), sweating, tremor and personality changes and less common are blood disorders.

Drug interactions
Alcohol, MAOI, antiepileptics, adrenergic neuro-blockers, clonidine, antihypertensives, antihistamines, antimuscarinics, antipsychotics, anxiolytics, hypnotics, disulfiram, sublingual nitrates, sympathomimetics, oral contraceptives and cimetidine.

Patient instructions
Do not stop it suddenly. Do not take part in any activity. Tell your doctor if pregnancy or breast-feeding.

Clomipramine
Dose
Oral, initially, 10 mg/day increased to a usual maintenance dose of 30-50 mg/day. Maximum 30-150 mg/day, elderly 75 mg).

Indications
Depressive illness, in obsessive and phobic states and in cataplexy associated narcolepsy.

Contraindications
Recent myocardial infarction, arrhythmias, severe liver disease and porphyrias.

Precautions
Cardiac disease, history of epilepsy, pregnancy, and breast feeding and thyroid disease.

Adverse effects
Sedation, dry mouth, blurred vision, constipation, nausea, postural hypotension, tachycardia, sweating, tremor, rash, hypersensitivity reactions, behavioural disturbances, increase appetite and weight gain and movement disorders.

Patient instructions
The drug may impair ability to perform skilled tasks e.g. operating machinery, driving.

12.4 Antiparkinsonian Drugs
12.4.1 Antimuscarinic drugs
Anticholinergic agents are useful for patients with minimal symptoms, for those unable to tolerate levodopa because of adverse effects or contraindication.

These drugs are also useful to alleviate the parkinsonian syndrome induced by antipsychotic drugs.
The deficiency of dopamine in the striatum of patients with parkinsonism intensifies the excitatory effects of the cholinergic system within the striatum.

**Benztropine mesylate**

**Dose**

Oral, 0.5-1 mg/day usually at bedtime gradually increased to a usual maintenance dose of 1-4 mg/day as a single or divided doses (maximum 6 mg/day).

**Indications**

First line drug in mild Parkinsonism, or as an adjunct to levodopa in more severe cases, in the management of drug-induced extra-pyramidal symptoms (but not tardive dyskinesia).

**Contraindications**

Children less than 3 years, narrow angle glaucoma, pyloric or duodenal obstruction, bladder neck obstructions.

**Precautions**

Given cautiously in patients at risk of urinary retention, glaucoma and CVS disease. Avoid abrupt discontinuation of the drug. Patients should not drive or operate machinery.

**Adverse effects**

GIT disturbances, dry mouth, blurred vision, tachycardia and sedation, urinary retention, impairment of recent memory.

**Drug interactions**

Disopyramide, tricyclic antidepressants, and MAOI, ketoconazole, antihistamines, cisapride, domperidone, metoclopramide, amantadine and sublingual nitrates.

**Patient instructions**

Take with food. Maintaining good dental hygiene can relieve the dry mouth. Avoid excess sun or exercise that may cause excessive sweating.

**12.4.2 Dopaminergic drugs**

In parkinson’s disease there is marked deficiency in the dopaminergic innervation of the basal ganglia. Concurrent administration of levodopa with an inhibitor of aromatic L-amino acid (dopa) decarboxylase that is unable to penetrate into the CNS greatly diminishes the decarboxylation of levodopa in peripheral tissues. Such reduction allows a greater proportion of levodopa to reach the desired receptor sites in the neostriatum.

**Levodopa plus Carbidopa**

**Dose**

Expressed as levodopa, initially 100-125 mg tid-qid, gradually increased by small increments to 0.75-1.5 g/day in divided doses after meals.

**Indications**

The treatment of choice in patients with idiopathic Parkinson’s disease.
Contraindications
Closed angle glaucoma

Precautions
Pulmonary diseases, peptic ulceration, CVS and endocrine disorders, psychiatric disturbance. And history of malignant melanoma. Periodic evaluations of hepatic, hematological, cardiovascular and renal functions are advised.

Adverse effects
GIT disturbances (anorexia and nausea), postural hypotension, dizziness, reddish discoloration of body fluids, abnormal involuntary movements and psychiatric symptoms

Drug interactions
Volatile anesthetic, MAOI, antihypertensives, reserpine antipsychiatric, anxiolytics, metoclopramide.

Patient instructions
Avoid activities that require alertness. Notify your doctor if you start to experience any uncontrolled movements of limbs and face. Diabetic patients should not change their medication dosage. Avoid taking vitamins and foods rich in pyridoxine.

12.5 Antiepileptics
Treatment should be started with a single drug, but the choice of an anticonvulsant can only be made on an individual basis and will depend on the efficacy of the drug and the patient’s tolerance of treatment. All antiepileptic drugs commonly produce neurological adverse effects at too high a dose.

Treatment is normally continued for a minimum of two years after the last seizure. Withdrawal should be extended over a period of several months since abrupt withdrawal can lead to complications such as status epilepticus.

Choice of antiepileptic in management of convulsive disorders:
Carbamazepine, phenobarbital, phenytoin and valproate are widely used in the treatment of generalized tonic-clonic, simple partial and complex partial seizures.

Valproates are widely used in the treatment of absence seizures.

Phenobarbital or phenytoin are widely used for tonic seizures.

Valproate or clonazepam are used for atonic seizures.

Clonazepam is used for atypical absence seizures.

Valproate is widely used and most effective for juvenile myoclonic seizures.
Mechanism of action of antiepileptic agents

Antiepileptic drugs act either by inhibiting the discharge of the abnormal focus, or by inhibiting the spread of the discharge to normal brain tissues by reducing post-tetanic potentiation. These effects may be produced by reduction of cell membrane permeability to sodium or calcium e.g. phenytoin. Alternatively, by modifying neurotransmitters e.g. enhancing GABA-mediated synaptic inhibition through potentiation of postsynaptic action of GABA e.g. benzodiazepines, and phenobarbitone, or by inhibiting GABA-transaminase e.g. valproate

Carbamazepine

Dose

Epilepsy, initially, 100-200 mg 1-2 times/day increased slowly to 0.8 - 1.2 g/day in divided doses. Child, daily in divided doses, up to 1 year: 100-200 mg, 1-5 years; 200-400 mg, 5-10 years; 400-600 mg, 10-15 years; 0.6-1 g. Trigeminal neuralgia, initially 100 mg 1-2 times/day increased to reach 400-800 mg/day in 2 divided doses.

Indications

To control tonic clonic (grand mal) and partial (focal) seizures. Treatment of trigeminal neuralgia. Prophylaxis in manic-depressive disorders

Contraindications

Atrioventricular conduction defects (unless paced), patients on MAOI or within 14 days of their administration.

Precautions

Blood disorders, raised intra-ocular pressure, pregnancy, hepatic, renal, cardiac dysfunction. Avoid sudden withdrawal. Periodic eye examination.

Adverse effects

Dizziness, drowsiness and ataxia (occur initially). Nystagmus and diplopia are symptoms of high plasma levels. GIT upsets (dry mouth, constipation, pain, nausea and vomiting) are less common. Hypersensitivity reactions may manifest as: rash, blood disorders, photosensitivity, and lymphadenopathy.

Drug interactions

MAOIs, dextropropoxyphene, doxycycline, erythromycin, isoniazid, oral anticoagulants, anxiolytics, hypnotics, verapamil, diltiazem, isradipine, viloxazine, other antiepileptics, digitoxin, corticosteroids, cyclosporin, lithium, oral contraceptives, theophylline, thyroxidine and cimetidine.

Phenytoin

Dose

Oral, 150-300 mg/day increased gradually as necessary, usually to 300-400 mg/day, maximum 600 mg/day. CHILD, 5-8 mg/kg/day. In status epilepticus, slow IV of 10-15
mg/kg maintenance doses of about 100 mg should be given thereafter at 6 hourly intervals (monitor ECG and blood pressure). In arrhythmia, 305-5 mg/kg by slow IV (monitor ECG and blood pressure).

**Indications**

Control of tonic-clonic (grand mal) and partial (focal) seizures and status epilepticus. In prophylaxis control of seizures developing during or after neurosurgery or following head injuries. Class Ib anti-arrhythmic drug to treat arrhythmia associated with digitalis toxicity.

**Contraindications**

IV administration in sinus bradycardia, heart block Adams-stokes syndrome and porphyria.

**Precautions**

Impaired renal or hepatic function, diabetes mellitus, hypotension, pregnancy and breast-feeding. In case of IV administration, it should be done slowly with ECG and blood pressure monitoring. Gradually withdraw the drug.

**Adverse effects**

Anorexia, headache, dizziness, insomnia, GIT upsets (nausea, vomiting and constipation), gum hyperplasia, hirsutism, rickets, osteomalacia and mild hypersensitivity reactions. Rapid IV administration may lead to CNS depression and hypotension. Toxicity manifests by nystagmus, diplopia and ataxia.

**Drug interactions**

Aspirin, azapropazone, phenylbutazone, amiodarone, quinidine, mexiletine, disopyramide, chloramphenicol, isoniazid, metronidazole, co-trimoxazole, rifampicin, doxycycline, oral anticoagulants, TCA, fluconazole, ketoconazole, miconazole, antipsychotics, isradipine, digitoxin, corticosteroids, cyclosporin, methotrexate, disulfiram, lithium, oral contraceptives, theophylline, thyroxin, cimetidine, sucralfate, sulphinpyrazone, influenza vaccine, folic acid and other antiepileptics

**Valproic acid (valproate)**

**Dose**

Oral, initially, 600 mg/day in divided doses (preferably after meals) increased by 200 mg/day at 3 day intervals to a maximum of 2.5 g/day in divided doses. Child up to 4 years. Initially, 20 mg/kg/day in divided doses increased to a maximum of 40 mg/kg/day. Over 4 years, initially, 400 mg/day in divided doses increased to a maximum of 20-30 mg/kg/day.

**Indications**

Control of primary generalized, absence seizures (petit mal) and myoclonic seizures.
**Contraindications**
Pre-existing liver diseases and pregnancy

**Precautions**
Congenital metabolic disorders, organic brain diseases, mental retardation have an increased risk of hepatotoxicity. Monitor platelet and pancreatic function. Withdraw drug gradually.

**Adverse effects**
GIT upsets (commonest), increased appetite, weight gain, drowsiness, ataxia, blood disorders, impaired liver enzymes and hyper ammonaemia. Liver dysfunction, which necessitates drug withdrawal.

**Drug interactions**
Aspirin, antidepressants, other antitieptics and anti psychotics.

**Clonazepam**

**Dose**
Initially, 0.5 mg. The dose is gradually built up until an optimum response is obtained. Child, initially, 250 mcg for children below 5 years, and 500 mcg till 12 years, maintenance doses: infants 0.5-1 mg, children 1-5 years; 1-3 mg; children 5-12 years; 16 mg, adults; 4-8 mg.

**Indications**
In the treatment of all types of epilepsy and seizures, in status epilepticus and in the management of panic disorders

**Contraindications**
Respiratory depression, acute pulmonary insufficiency and porphyria

**Precautions**
Respiratory disease, renal or hepatic dysfunction, pregnancy and breastfeeding, elderly and debilitated. Avoid sudden withdrawal.

**Adverse effects**
Drowsiness (commonest), excessive bronchial secretion, dizziness, muscle hypotonia, mental changes and dependence.

**Drug interactions**
Carbamazepine, phenobarbitone and phenytoin accelerate metabolism of clonazepam. Drugs interacting with all other benzodiazepines: anaesthetics, alcohol, opioid analgesics, antidepressants, antihistamines, antihypertensives, antipsychotics, disulfiram, levodopa and cimetidine

Patient instructions

see phenobarbitone.
SECTION XIII
DRUGS FOR INFECTIOUS DISEASES

In this section:

Topic: Acute Rheumatic Fever 125
Topic: Infective (Bacterial) Endocarditis 125
Topic: Meningitis 127
Topic: Pneumonia 128
Topic: Tuberculosis 132
Topic: Infection Diarrhoea 134
Topic: Urinary Tract Infection 135
Topic: Sexually Transmitted Disease (STDs) 137
Topic: Antibacterials Classification: 140
A. Antibacterial Drugs 141
13.1 Pencillins 141
13.2 Cephalosphorins 143
13.3 Aminoglycosides 144
13.4 Macrolides 145
13.5 Tetracyclines 147
13.6 Choloramphenicol 148
13.7 Other Antibiotics 149
13.8 Sulphonamides 149
13.9 Fluoroquinolones 150
13.10 Urinary Antiseptics 152
13.11 Antituberculous Drugs 152
13.12 Anti-Leprotic Drugs 154
B. Antiviral 155
C. Antifungal Drugs 156
D. Anti-protozoal Drugs 159
13.13 Antiamebiasis and Antigiardiasis 159
13.14 Antimalarial Drugs 161
E. Anthelmintic Drugs 162
F. Antiseptics and Disinfectants 164
13. Drugs for Infectious Diseases

Selected infectious diseases

**Topic: Acute Rheumatic Fever**

It occurs as a complication of group AB-haemolytic streptococci pharyngeal infection.

Complication of this infection:

Scarlet fever in 15% of cases. Acute rheumatic fever and rheumatic heart disease by the highly rheumatic strains (M-1, M-3 and M-18). These complications have high morbidity but anti microbial therapy can prevent them. Post-streptococcal glomerulonephritis (immunologic complication) in which antibiotics do not reduce its development but decrease its incidence.

Diagnosis: (Modified Jones criteria)

Manifestation: Carditis: valvulitis (systolic and diastolic murmurs), myocarditis and pericarditis. Migrating (leaping ) polyarthritis: in large joints that respond to salicylates within 48 hours. chorea: delayed-appearance, involuntary-movement. Erythema marginatum: non-pruritic round with pale centre on trunk. Subcutaneous nodules: firm, painless nodules over bony surfaces e.g. elbow and knee. Arthralgia without inflammation. Fever more than 39°C early in the disease. Elevated ESR and C-reactive protein (more specific). Anti-streptolycin O titre more than 320 Todd unit (recent infection). Prolonged PR-interval suggesting carditis.

**Topic: Infective (Bacterial) Endocarditis**

Definition: It produces life threatening haemodynamic disturbances and embolic episodes. Without antimicrobial therapy and surgical procedures, condition is 100% fatal. When the valve is traumatized or damaged, it promotes small sterile thrombi (vegetations) of platelets and fibrin deposition forming non bacterial thrombotic endocarditis. They serve as a nevus for bacterial colonization during bacteraemia or systemic mycosis (fungi).

Infective organisms: streptococcus viridians (35%). staphylococcus aureus (30%) staphylococcus epidermidis (10%), pseudomonas aeruginosa (less than 10%), enterococci, Candida albicans e.g. IV drug abusers. They possess adherence factors that facilitate their colonization. The organism is rapidly covered with fibrin and platelets sheath. This is a vascular encasement which provides protection from host defence and help further bacterial replication and vegetative growth.

Involved sites: Mitral valve (55%): mainly due to streptococcus viridians in right heart disease in more than 85% of cases. Aortic valve (45%). Tricuspid valve and pulmonary valve (1%) by staphylococci. Mainly in IV drug abuse. Less on the endocardium or extra cardiac endothelium producing endarteritis.


Symptoms signs, laboratory data, and complications: Bacteraemia, sepsis, syndrome. Fever, chills, night sweats, malaise, fatigue, tachycardia, hypotension, ill-appearing. May be: acute, sub acute or chronic. Laboratory data: positive blood cultures, leucocytosis, elevated ESR and increased rheumatoid factor.

CNS: Cerebral emboli, mycotic aneurysm, vertebral osteomyelitis, epidural abscess. Headache, back pain, focal weakness, paraesthesia, papilloedema, focal vertebral tenderness, focal neurological signs: weakness, exaggerated reflexes, positive Babinski’s sign. Laboratory data: head CT scan, spinal MRI, cerebral arteriogram, increased ESR.

Cardiovascular (with left-sided endocarditis): Mitral regurgitation, aortic regurgitation, CHF, aortic ring abscess, valve rupture with hemodynamic collapse. Dyspnoea, orthopnoea, hepatojugular reflux, pedal oedema, increased venous pressure, cardiac murmurs, rales, waterhammer pulse. Laboratory data: ECG, Echocardiography, chest X-ray.


Renal: Immune-complex glomerulonephritis, renal artery emboli, internal and perinephric abscess. Oliguria, flank pain, flank tenderness. Laboratory data: oliguria, pyuria, increased serum creatinine and BUN and renal sonography.

GIT: Liver abscess, splenic abscess, intestinal emboli with ischemia. Abdominal pain, focal abdominal tenderness, hepatomegaly splenomegaly. Laboratory data: abdominal CT and sonography.

Skin and Eye: Septic emboli, Immune complex vasculitis. Rash, focal painful lesions, visual complaints, painful macules and nodules, nail bed splinter haemorrhage, petechiae, fundal Roth spots, clubbing of fingers. Laboratory data: skin biopsy.

Classification: It is classified according to severity and onset or according to the current system which is based on the causative organism because it provides information about the disease course, underlying cardiac disease and the antimicrobial regimens to adopt.
According to onset and severity:
Acute bacterial endocarditis (ABE): it is caused by staphylococcus aureus and staphylococcus epidermidis, streptococcus pyogens streptococcus pneumonia, and Nisseria gonorrhoea.

Signs and symptoms: high fever, septic appearance, echymosed emboli, splinter haemorrhage in nail bed, systemic toxicity and leucocytosis. Progression of untreated cases is fulminating and fatal within few days to 6 weeks.

Sub acute bacterial endocarditis (SBE): It is due to streptococcus viridians, anorexia, weight loss, clubbing of fingers, Osler’s nodes on tip of index finger. Signs and symptoms: insidious onset, weakness, fatigue, low grade fever, night sweats, If untreated it is fatal within 6 weeks to 3 months.

Fungal endocarditis (candida albicans) (less than 10%). This occurs primarily in: IV drug abusers. Prosthetic valves. Immunocompromised patients. IV Catheters Patients receiving broad spectrum antibiotics.

Viral meningitis: It has self–limited course with lymphocytic pleocytosis.

Sub acute and chronic illness: Tuberculous, Syphilitic, Fungal: Coccidioides and Cryptococcus (in HIV-infected patient).

Non-infective (aseptic) meningitis: chemical irritants, drugs: trimethoprim-sulphamethoxazole, azathioprine, anti-rejection monoclonal antibody muromonab (OKT3) and NSAIDs (ibuprofen, naproxen and sulindac). Signs and symptoms: Antecedent upper respiratory tract infection. Rapid onset of fever, headache lethargy, confusion or more slowly progress of meningeal symptoms with prolonged respiratory or ear symptoms, and nuchal rigidity. 50% of patients have neck stiffness. Altered mental state (lethargy and confusion), photophobia, stiff neck, Kerning’s sign (Pain upon extension of the hamstrings when lying supine with thighs perpendicular to trunk) and Brudzinki’s sign (reflex flexion of hips and knee produced upon flexor of neck when lying in recumbent position). Petaechial or purpuric rash on extremities (meningococcal) and requires immediate therapy (advances rapidly). Cranial nerves dysfunction (15%), seizures (35%) and focal neu-
rlogic signs (15%). Cerebral oedema and brain herniation which is fatal.

Investigation: CSF: pH 7.3, electrolyte low in serum except chloride and WBCs less than 5,000,000/mm$^3$. Immediate lumbar puncture for gram stain, culture and antibiotic therapy (sensitivity). In meningitis, protein increases (less than 50 mg%) and glucose decreases (less than 60% of plasma).


**CSF penetration of Antimicrobials**

Very good: chloramphenicol, metronidazole, rifampicin, trimethoprim-sulphamethoxazole. Good (adequate penetration in meningitis): penicillin, other β-lactams (clavulanic acid, sulbactam, imipenem), cephalosporin (cefotaxime), fluoroquinolones (ciprofloxacin). Inadequate and poor (even with meningitis): aminoglycosides, erythromycin, clindamycin and vancomycin.

**Topic: Pneumonia**

It is inflammation of the lung parenchyma caused by infection. It remains a common cause of death in the elderly and most often due to streptococcus pneumonia (pneumococcus). Rapid onset of chest pain with fever or rigor may be accompanied by blood streaked sputum. Unilateral chest wall movement can be the only sign of presentation but labial herpes occurs in 10% of cases. Nearly all cases respond to penicillin and resistant strains have rarely been described. Sero-type 3 is classically the most serious infection and can cause a very prolonged illness with slow response to antibiotics.

Other causes of sudden pleuretic pain include pulmonary infarction when fever is rarely prominent initially and spontaneous pneumothorax where breath sounds are absent on the affected side. Fever and rigors can also occur in septicaemia particularly urinary tract infection.

Clinical presentation: cough, fever, expectoration, tachycardia, dyspnoea, tachypnoea, spread to pleura: pleurisy and pain on inspiration and if infected empyema. Decreased breath sound, crepitations, dullness and egophony
(vocal tone changes). Chest infiltrates (X-ray) and leucocytosis.

Pathophysiology: There is alveolitis, inflammatory exudates, spread to interstitium and consolidation in one lobe (labour pneumonia) or around bronchi (bronchopneumonia) with impaired gas exchange.

Complications: Pulmonary: atelectasis during acute phase or resolution and usually clears with coughing and deep breathing exercise. Lung abscess: especially in aspiration pneumonia due to gram negative anaerobes or gram positive anaerobes. Treated with: Metronidazole or clindamycin, high penicillin dose IV or β-lactamase inhibitor combination. Pleural effusion: requires needle aspiration and if complicated needs drainage. Infiltration with fibrin and leukocytes with empyema that needs surgical chest tube for drainage. Extra pulmonary: Bacteraemia with metastatic infections (25% of cases).

**Pneumonia in immune compromised host**

Immuno-suppression with steroids and for cytotoxic therapy, cough, mild dyspnoea and fever may be the only clues to pneumonia, and diagnosis depends on suspicion and suggestive infiltrate on a chest X-ray. Such shadows may be due to opportunistic infection e.g. pneumocystitis carinii (in leukaemia patients), aspergillus fumigates (with haemorrhagic pulmonary infarction), cryptococcus neoformans, candida albicans or commoner bacteria e.g. Klebsiella, Escherichia coli and Mycobacterium tuberculosis. Chest X-ray change may be due to toxic action of drugs on the lungs or reaction to radiotherapy. Opportunistic infections may be treatable e.g. pneumocystitis responds to high doses of co-trimoxazole, invasive aspergillosis to amphotericin B and tuberculosis by appropriate chemotherapy. Diagnosis is confirmed by chest radiograph, blood count and sputum examination.

**Indications for hospitalization**

Probably 50% of cases of pneumonia are due to pneumococci and rapidly respond to penicillin or co-trimoxazole for 10 days. Fever persisting for more than 48 hours suggests an alternative diagnosis which needs chest radiograph, sputum and blood culture and serology that require hospitalization.

Pneumonia in a patient with previously known chest disease e.g. chronic bronchitis and emphysema leads to the possibility of respiratory failure for which oxygen therapy or ventilator management may require hospitalization. Marked central cyanosis with blue tongue discoloration indicating an oxygen saturation of less than 90% implies that continuous oxygen therapy may be needed which is best given by nasal prongs at a flow rate of 2-3 litres/min as patients tolerate this much better than any mask. Severe persistent chest pain needs narcotic analgesics which may exacerbate lethal respiratory failure if there is carbon dioxide that is only proven by arterial blood gas analysis.
Slowly resolving pneumonia

With persistent chest signs, cough or dyspnoea or haemoptysis over one week, always suggest in adults the possibility of carcinoma. The patient requires chest radiograph, bronchoscopy and sputum cytology.

Pneumonia in previously healthy patients

The possible organisms are: streptococcus pneumonia, mycoplasma pneumonia, viruses: influenza, parainfluenza, respiratory syncytial virus (RSV), adenovirus and corona virus (SARS). Rare causes include: coxiella burnetti (Q fever), psittacosis and legionella.

In bacterial pneumonia pleuritic chest pain is common, sputum purulent from onset and signs and symptoms of consolidation. The white count is high. In viral or mycoplasma pneumonia sputum is mucoid at least initially, pleurisy is less common, the chest and signs and symptoms may be few or absent and the white count is normal or low. Viral infections may be super infected by bacteria.

Mycoplasma infections often give rise to difficulties in diagnosis. There is often a cyclical incidence with a peak every 4 to 5 years, so epidemiological knowledge may be helpful.

Patients are usually respond promptly to erythromycin or tetracycline.

Viral pneumonia is usually mild and many cases remain undiagnosed. In few cases, influenza may progress to a fulminant pneumonia due to the virus itself and sometimes to secondary bacterial infection (often by staphylococci).

Initial antibiotic therapy for these previously well patients, before an organism is isolated should reflect the causes. Pneumococcal pneumonia will respond to penicillin and mycoplasma, Q fever and psittacosis all respond to tetracycline or erythromycin.

Pneumonia in patients with pre-existing disease

These patients will usually have long-standing chest disease, probably chronic bronchitis. They will have several adverse factors including mucus hyper secretion, decreased mucociliary clearance and bronchospasm. Other problems include bronchial obstruction due to tumour or foreign body and lung damage by fibrosis and pollution. The organisms are those associated with chronic bronchitis: Haemophilus influenza and streptococcus pneumonia together with influenza viruses. Staphylococcus aureus may be implicated in damaged lung tissue and pseudomonas aeruginosa colonises the bronchi of some patients with bronchiectasis and cystic fibrosis. Eradication in the latter patients is difficult and without value. Antibiotics useful in this group in-
clude penicillin and co-trimoxazole. Amoxicillin with clavulanic acid is useful in infections due to haemophilus influenza resistant to amoxicillin. Those patients cause anxiety not from infection but from the complications of sputum retention, dyspnoea and hypoxia.

Pulmonary antimicrobial defence mechanisms

Aerodynamic filtration, cough reflex, mucociliary transport system (each cell has 200 cilia that beat upwards 500 times/min) and mucus layer contains lysozyme and secretory IgA antibodies. Alveolar macrophages and neutrophils, humoral and cellular immune responses and pulmonary secretions of surfactants, lysosomes, IgG plus complement (opsonins).

Clinical types

Pathogens for community-acquired pneumonia. Typical agents incidence percent:

- **Streptococcus pneumonia** (pneumococcus) 25-60
- **Haemophilus influenza** (β-lactamase producing) 3-10
- **Staphylococcus aureus** (30% fatal) 3-5
- **Gram-negative bacilli**, (in nursing facilities) 3-10

The latter include klebsiella pneumonia (35% fatal) and pseudomonas aeruginosa (60% fatal)

- **Legionella species** (pneumophilia) in elderly and COPD 2-8
- **Chlamydia pneumonia** 4-6
- **Mycoplasma pneumonia** (walking pneumonia) 1-6
- **Viral** 10

The latter include: influenza A and B, rhinovirus, corona virus (SARS), parainfluenza.

Fungal: In immune compromised patient and opportunistic infection. In community acquired pneumonia the infection is treated on an out patient basis and it is difficult to determine its true incidence and morbidity, 25% require hospitalization with mortality rate 10%. The organism is identified in only 40% of cases. Atypical pathogens account for 10-20% of cases and are associated with atypical signs and symptoms (sub acute onset nonproductive cough with extra pulmonary manifestation and worse chest X-ray).

Aspiration pneumonia

Predisposing factors: alteration of consciousness (alcoholism, seizure, general anaesthesia, cerebrovascular accidents, drug intoxication, head injury and severe illness), impaired swallowing mechanism (neurologic disorder, oesophageal dysfunction), nasogastric feeding, tracheostomy, endotracheal intubation and periodontal disease.
Clinical types

Shock (25% of cases and 25% fatal): fever, tachypnoea, cough, rales, wheezing, cyanosis and apnoea.

Pneumonia: resolves over few days or weeks without complication.

Bacterial pneumonia: it follows an initial period of improvement. There is fever, dyspnoea, pulmonary infiltration and leucocytosis. Most cases are due to wide spectrum of Gram positive and Gram negative anaerobes (60-90%) and aerobes (50%) from oropharynx and GIT (poly microbial). They are mainly anaerobes (60%) in community-acquired aspiration pneumonia and aerobics (40%) in hospital acquired aspiration pneumonia.

Pneumonia in cystic fibrosis

It is a genetically linked disease affecting exocrine gland secretion in the body. Progressive pulmonary Disease is the major cause of morbidity and mortality. The presence of airway mucus plugging leads to respiratory dysfunction and infection with chronic pulmonary disease.

Infection leads to increased frequency and duration of cough, dyspnoea, increased expectoration, decreased exercise tolerance and anorexia.

Microbiology: early, staphylococcus aureus is important pathogen and later pseudomonas aeruginosa develops with others that need in vitro sensitivity tests.

Nosocomial (hospital-acquired) pneumonia

Aetiology: intubation or tracheostomy, age more than 70 years, chronic lung disease, malnutrition, depressed consciousness, thoracic or abdominal surgery and immunosuppressive therapy.

Microbiology: gram negative bacilli (60%): pseudomonas aeruginosa and enterobacter, staphylococcus aureus (25%), anaerobes (15%), streptococcus pneumonia (15%), haemophilus influenza (15%), viral (15%) and fungi (aspergillus) less than 1%.

Topic: Tuberculosis

Phthisis or "wasting", in 1882 Koch isolated Mycobacterium tuberculosis (aerobic acid-fast bacilli). Modern era of medical therapy started in 1944 with the discovery of streptomycin and para-aminosalicylic acid (PAS), followed by isoniazid (INH) in 1952 and Rifampicin in 1960. Mycobacteria replicate slowly every 24 hours, while other bacteria every 20-40 min.

Mycobacterium tuberculosis thrives in high O₂ tension e.g. in lung apex, growing ends of bone, brain and renal parenchyma.

Transmission: It is transmitted by airborne droplets (less than 10 micron) and not through clothes, bedding or
dishes. It is not deposited on intact skin or mucosa to invade tissues. Transmission can occur through GIT e.g. infected milk. The primary lesions occur in the lung or intestine and produce the primary complex. Through abraded skin, the primary complex also occurs. Clinical disease development following infection occurs in 10% within lifetime and 5% within one year from infection of these sites.

Risk factor: diabetes, silicosis, gastrectomy, chronic renal failure, blood disorders, HIV, children less than 2 years, adolescents, elderly, corticosteroids, IV drug abuse.

Signs and symptoms: active TB is misdiagnosed or unsuspected in community hospital in 50% of cases. Fever (in 50% of cases), cough (in 80% of cases), haemoptysis (in 25% of cases) and abnormal pulmonary signs (in 30%) in form of apical dullness and post-tussive rales.

Diagnosis: Mantoux method (purified-protein derivative, PDD) skin test. Intradermal 0.1 ml of 5 TU (Tuberculin unit) is injected into forearm. Positive test is diagnosed when there is palpable induration more than 5 mm 48-72 hour after injection (10 mm is cutoff for positive in persons with risk of HIV). Microscopic examination or tissue biopsy depending on the site of injection. Bacteria take Ziehl-Neelsen stain (not gram stain). It is positive when there are 10,000 organisms/ml. Positive bacterial culture for viable organisms is a strong evidence but as the bacilli grow slowly (once/24h), it takes from 2 to 8 Weeks to become positive.

Immunization: BCG vaccination (Bacillus of chalmette and Guerin) is derived from strain of bovine mycobacterium. It is only used in infants and children (tuberculin negative) and persons exposed to highly infectious untreated patients with active TB.

Extra pulmonary TB and Tuberculous meningitis

Miliary TB, bone/joint TB, renal TB and TB meningitis need more than 6 to 9 months treatment regimen and children and infants may require 12 months therapy.

Tuberculous meningitis is the most common site of extra pulmonary complications. Signs and symptoms: Headache, fever, restlessness irritability, nausea, vomiting, positive Brudzinski’s sign and neck rigidity. Isoniazid readily penetrates into CSF and reaches 100% as in serum. Rifampicin: CSF concentration is only 6 to 30% of serum. Ethambutal: must be used in higher doses to achieve bactericidal concentration in CSF 10 to 55% as in serum. Streptomycin: penetrates poorly even with inflamed meninges. Dexamethasone: 10 mg/day for 6-8 weeks then tapered slowly after symptoms subside in moderate to severe meningitis, prolongs survival and reduces intracranial pressure.
**Topic: Infection Diarrhoea**

It generally has symptoms of anorexia, vomiting, fever, and abdominal discomfort. Diarrhoea of less than 2 weeks is defined as acute and if it lasts more than 14 days, it is persistent or chronic.

Persistent symptoms: Upper GIT symptoms: nausea, vomiting, epigastris pain. Small intestine symptoms: profuse watery diarrhoea (adults if adequately hydrated excrete up to 1 L of fluid/hour), non-inflammatory and non-bloody due to enteroxin. Large intestine symptoms (dysentery): tenesmus, fecal urgency, less profuse diarrhoea, lower abdominal pain and stools contain mucus blood with longer incubation period.

Severity: Mild: diarrhoea does not limit activity or less than 3 stools/day without abdominal or systemic symptoms. Moderate: There is change in activity or with more than 4 loose stools/day and usually with abdominal symptoms: nausea, vomiting, colic and tenesmus. Severe: It does not allow usual activity with symptoms of fever, malaise and dehydration.

Predisposing or exacerbating factors: Increase gastric pH (antacids, H₂-Blockers, proton-pump inhibitors) predisposes to salmonellosis, antibiotic therapy predisposes to clostridium difficile due disruption of bowel flora and immunosuppressives e.g. steroids.

Sources of infection: Bacterial (20-30%): faecal-oral (person-to-person) e.g. shigella, haemorrhagic Escherichia coli in child care centres. Water-born: e.g. vibrio cholera, cryptosporidium (HIV-patients). Food-born: e.g. salmonella, Staphylococcus aureus (restaurant), clostridium perfringes. Overgrowth after antibiotic therapy: e.g. clostridium difficile. Zoonotic: in farms e.g. campylobacter.

The entero pathogens initially adhere to mucosal surface that is followed by mucosal integrity disruption by microvilli dissolution and cellular invasion. This facilitates the toxin to reach target epithelial cells.

**Pathogenic mechanism**

Bacterial: The enterotoxin in small intestine leads to profuse explosive watery diarrhoea (site of major intestinal electrolyte transport) with dehydration. It may be heat labile (cholera-like) or heat stable. The enteroinvasive and entero haemorrhagic type (bacteria) invade and affect small and large intestine with non-inflammatory necrosis, inflammation, entero invasive, bleeding, haemolytic-uraemic syndrome, and systemic symptom (entero haemorrhagic). Cytotoxin production damages the intestinal mucosa leading to sever inflammatory reactions.

Viral (30-40%): rotavirus (in infants and children) and Norwalk virus. They are self-limited as the humoral immunity responds rapidly and life-
time of mature enterocytosis is short (3-5 days).

Parasitic (protozoal and fungal): Giardia lamblia (small intestine), Entamoeba histolytica (colon), moniliasis

Unknown (40%).

**GIT defence mechanisms**

Gastric acidity (shigella survive acid pH), peristalsis, mucus, mucosal tissue integrity, intestinal immunity and normal bacterial flora (compete for space and nutrients and produce inhibitory substances to the enteropathogens).


**Selected infective diarrhoea**

Salmonella (typhoid fever): ingestion of contaminated poultry, colic, fever, tensmus, distension and skin rash.

Shigella: Contaminated food (10-100 organisms) incubation period (12-24h.) fever, dysentery, colic, tenesmus.

Campylobacter: day-care centres, contaminated eggs, raw milk, travel. Mild to severe diarrhoea, fever, malaise.

Clostridium difficile: with antibiotic and antineoplastics. Mild to severe diarrhoea and colic.

Staphylococcal food poisoning: contaminated meat, milk, exposed food. (incubation period 2-4 hours) and resolves in 48 hours. Nausea, diarrhoea.

Travellers diarrhoea (Escherichia coli): contaminated food (vegetables and cheese), water, travels (incubation period 16-48 hours) Nausea, vomiting, mild to severe diarrhoea and colic.

Entrohaemorrhagic (Escherichia coli): beef, raw milk, water, (incubation period 48-96 hours) diarrhoea, headache bloody stools.

Cryptosporidiosis: immunosuppression, day-care centres, water, animal handlers. Mild to sever diarrhoea (chronic or self-limited) large fluid.

Viral gastro-enteritis: community-wide outbreaks, contaminated food (incubation period 16-48 hours) Nausea, diarrhoea (self-limited), colic.

**Topic: Urinary Tract Infection**

It is the most common bacterial infections in man, ranging in severity from asymptomatic bacteruria to acute pyelonephritis with septicaemia. After
one year of age until age 50 years, it is a disease of females, due to their anatomic and physiologic differences e.g. urethral length and antibacterial factors secreted from prostate. After age of 50, it is a problem in male due to prostatic changes, urethral instrumentation and surgery that tend to rise with increasing age.

Pathogenic and predisposing factors: most common is by ascending spread via urethra, vesico-ureteral reflux, ureters or decreased ureteric peristalsis. The low urine pH and high osmotic urea have antibacterial effect. Extremes of age, female gender (30 times more), pregnancy (twice as non pregnant), instrumentation (65%), urinary tract obstruction (stenosis, prostate, stones, tumours), neurologic dysfunction (spinal card injury, stroke, diabetes, prolonged immobilization), renal disorder and previous antibacterial therapy altering normal flora of urogenital tract (5-folds in females). Frequent sexual intercourse in women is added risk factors.

Signs and symptoms: Lower UTIs, (cystitis): dysuria, frequency, urgency, suprapubic pain, pyuria, haematuria. Upper UTIs (pyelonephritis): Loin pain, costovertebral angle tenderness, fever, chills, nausea, vomiting, haematuria.

Upper urinary tract infections include all renal disorders in which localized or generalized changes in the tubulo-intestinal area are predominant over glomerular or vascular lesions. They are classified into:

Tubulointerstitial nephritis: acute toxic diffuse nephritis: develops during infectious disease due to toxæmia e.g. typhoid, diphtheria. It receives high portion of COP and has largest endotheliovascular surface.

Focal suppurative interstitial nephritis: This occurs in pyemia.

Pyonephrosis: There is marked dilation of renal pelvis due to distal obstruction with secondary bacterial infection. Perinephritis, perinephric abscess and adhesions complicate the condition.

Specific infection: e.g. TB, bilharziasis, hydatid disease.

Pyelonephritis: Routes of infection: direct, ascending urogenous and descending haematogenous or lymphatic. Type: Acute: kidney enlarges, cortex shows tiny abscesses, medulla shows yellow streaks and pelvis distended with pus. Chronic: lesion may be focal or diffuse with cortical scarring with irregular surface. Renal pelvis is thickened, dilated and contains pus. Interstitial tissue is infiltrated and thickened with chronic inflammatory cells. Condition is complicated with hypertension (20%) and chronic renal failure depending on the severity, recurrence and nature of urinary obstruction.

Laboratory diagnosis

Urinalysis: UTIs reveals bacterial count of more than 20/HPF or 105 bacteria/ml, pyuria more than 8
WBCs/mm³ of non-spun urine or 2-5 WBCs/HPF of centrifuged urine and WBC (pus) casts.

Dipstick to detect nitrite formation from the reduction of nitrates by bacteria (needs at least 105 bacteria/ml).

Leukocyte esterase test to detect esterase activity of leukocytes in urine.

Urine culture (major criterion): mid-stream (clean catch) spearmen is essential in fameless after local cleaning. Suprapubic bladder aspiration is indicated in questionable results or patients with voiding problems. Urine is plated within 20 min of collection or refrigerated after this duration. First-voided morning sample contains higher bacteria than later one.

**Complicated (hospital-acquired) UTI**

It is due to polymicrobial infection abnormalities or catheterization

**Gonorrhoea**

An acute infectious disease of the epithelium of the urethra, cervix, rectum and pharynx that may spread resulting in metastatic complications e.g. sepsis. If untreated, spontaneous resolution after several weeks and more than 95% within 6 months.

Causative organism: Neisseria gonorrhoea.

Signs and symptom: In males incubation period 1-7 days, uretheritis, purulent discharge, frequency, urgency with swollen red meatus. In females incubation period 7-21 days and signs and symptoms are trivial in from of cervicitis and vaginal discharge (mucopurulent cervicitis), endometritis and salpingitis (15%) with menorrhagia, lower pelvic pain and tenderness.

Diagnosis: Gram-stain smear and culture and sensitivity. Fermentation reactions and in endocervical culture.

Complication: In males: post-gonococcal non-specific urethritis, prostatitis, epididymitis, and if bilateral sterility. In females: bartholinitis, salpingitis (sterility), endometritis. In both: septicemia and arthritis, Reiter’s syndrome (urethritis, polyarthritis, conjunctivitis or uveitis) and pelvic inflammatory disease (acute or chronic in due to ascending, surgical or traumatic related infection with abscess, and adhesions with sterility). Conjunctivitis neonatrom.
**Trichomoniasis**

It is due to flagellate protozoan Trichomonas vaginalis. It occurs more common in females with vaginitis, urethritis and cystitis (20% in reproductive period) in males: urethritis, prostatitis, cystitis. Most infected males are asymptomatic carriers.

Signs and symptoms: In females: copious greenish-yellow, frothy vaginal discharge with inflammation of the perineum, vagina and cervix with strawberry red spots. In males: usually asymptomatic with transient urethral discharge in early morning (Bonne jour drop), dysuria and frequency.

**Genital candidiasis**

It is due to yeast infection Candida albicans. Predisposing factors include diabetes, pregnancy and prolonged antibiotic therapy.

Signs and symptoms: In females: vulval irritation and vaginal discharge. Vagina is covered with white cheesy material. In patients receiving gestogenic contraceptive, corticosteroids and immunosuppressive. In males: glans irritation with slight urethral discharge and there may be erosions or vesicles.

**Genital herpes**

Infection is due to type 2 herpes virus hominis. Incubation period 4-7 days and condition tends to relapse. Relationships exist between herpes and carcinoma of cervix.

Signs and symptoms: itching and soreness with small erythematous patch or small vesicles. Their erosion produce superficial circular ulcers with a red areola within 1 day. Ulcers become crusted and heal within 15 days with scarring. Inguinal lymph nodes are slightly enlarged and tender. Viral shedding correlates from onset of vesicles to the appearance of crust stage. Usually duration of first episode is 7-10 days and recurrent 5 days.

**Genital warts (Condyloma Acuminata)**

It is due to the human papilloma virus (Types 6 and 11). Incubation period 1-6 months

Signs and symptoms: soft, moist, pink or red minute swellings that grow rapidly and become pedunculated producing cauliflower appearance. In males: on penis and urethral meatus. In females: on vulva, vaginal wall, cervix and perineum. During pregnancy they grow rapidly.


**Granuloma inguinal**

It is chronic granulomatous condition caused by gram negative bacillus (Donovania granulomatis) found in mononuclear cells. incubation period 1-12 weeks.
Signs and symptoms: initial painless, beefy-red nodule and slowly produce granulomatous velvety mass. It erodes producing an ulcer with rolled edges. Lymph nodes are not affected although the groin swells. In males: penis, scrotum, groin and thigh hours. In females: vulva, vagina and perineum.

**Lymphogranuloma venereum**

It is caused by chlamydia trachomatis (serotype L1, L2, L3). Incubation period 7-28 days.

Stage I: Small vesicular lesion that ulcerates and heals rapidly passed unnoticed. Stage II: Unilateral tender inguinal lymphadenitis to form large tender eurent and covered with red skin (Bubo formation). Multiple sinuses develop discharging purulent pus and heal by scaring. Stage III: perirectal abscesses, rectovaginal Fistulas, rectal structures and genital elephantiasis. Treatment prevents this stage. Diagnosis: free intradermal test.

**Chancroid (soft chancre)**

It is caused by gram negative bacillus Haemophilus ducreyi. Incubation period 3-10 days starts as small painful papule rapidly breaks to form shallow ulcer with ragged undermined edges, shallow painful and non-indurated with reddish border. Inguinal lymph nodes are tender, enlarged and matted forming abscess (bubic) in the groin.

**Syphilis**

It is caused by Treponema palladium (spirochete). It is classified into:

Congenital: Early: infants up to age 2. Late: Stigmas occur in later life.

Acquired: Primary: lesion in form of chancre. Secondary: various skin and mucosal lesions.

Latent: Early (infection less than 2 years duration). Late (infection more severe than 2 years duration).

Tertiary or late: Benign in skin, bone and viscera (cardiovascular and neurosyphilis).

**Diagnosis**

Signs and symptoms: Dark field examination of fluids from lesion. Serologic tests (repeated every 2 weeks for 6 months and then monthly for 2 months).

Specific tests:

- Fluorescent Treponemal Antibody (FTA-ABS).
- Treponema Pallidum Immobilization (TPI).
- Treponema pallidum Hemagglutination (TPHA).

Non-specific (screening tests)

- Venereal disease Research Laboratory (VDRL).
- Rapid Plasma Reagin (RPR).
Acquired Immunodeficiency Syndrome (AIDS)

It is due to Retrovirus (presence of reverse transcriptase enzyme) that enables it to make a copy DNA of its RNA genome. It infects helper T-lymphocytes, Monocyte/macrophage, CNS, endothelial and epithelial cells.

Source of infection: Highest concentration in blood and semen. Lower concentration in cervicovaginal secretions.

Transmitted by: Sexual contact (75%). IV drug abuse (15%). Blood and its products transfusion. It is not transmitted during normal social contact e.g. shaking hands, hugging, eating utensils. Bathrooms and aerosol coughing.

Incubation period 6 months to 10 years. 55% are carrier and show positive ELISA test. 35% pass to AIDS prodrome (onset from 6 months to 10 years). 10% pass to AIDS syndrome.

Signs and symptoms: AIDS-prodrome: non-specific complaints (for 3 months or more): malaise/fatigue, fever more than 38 °C (continuous or intermittent), night sweat, oral thrush, lymphadenopathy and hepatomegally. Altered immunity: herpes zoster, herpes simplex. Non-Hodgkin’s lymphoma, cutaneous fungal recurrent infections, recurrent non-typhoid salmonellosis and oral leukoplakia.

AIDS Syndrome

Kaposi’s sarcoma: lymphoreticular and endothelial cell proliferation starts on feet or ankles as dark blue or purple-brown nodules or plaques (1 cm in diameter) and in oral cavity and anorectal region (2 years prognosis).

Opportunistic-disseminated infection (6 months prognosis): by protozoa, fungi, bacteria and viruses.

CNS (50%): headache, encephalitis, meningitis, convulsions, blindness and dementia.

Pulmonary: Pneumocystis carinii pneumonia (cough, dyspnoea and respiratory insufficiency).

GIT: anorexia, dysphagia (herpes and candida), malabsorption and diarrhoea and marked weight loss.

Acute abdomen: infection and perforation and lymphoma lymphadenopathy.

Lympho-reticular malignancy

Topic: Antibacterials

Classification:

According to their antimicrobial activity:

Drugs effective against gram-positive organisms: Penicillins, macrolides.

Drugs effective against gram negative organisms: Aminoglycosides, polymixins.
Broad spectrum affecting both gram-positive and gram-negative organisms: Some penicillins, cephalosporins, tetracyclines, chloramphenicol.

According to activity:

Drugs effective against gram-positive organisms: Penicillins, macrolides.

Drugs effective against gram negative organisms: Aminoglycosides, polymixins.

Broad spectrum affecting both gram-positive and gram-negative organisms: Some penicillins, cephalosporins, tetracyclines, chloramphenicol

Resistance to antimicrobial drugs

Biochemical mechanisms: production of inactivating enzymes. Reduced bacterial permeability to antibiotics. Modification of the receptor site.

Genetic basis of acquired resistance: bacterial resistance results from a stable genetic change that may be chromosomal or extrachromosomal.

Cross resistance: micro-organisms resistant to a certain drug may also be resistant to others having a similar mechanism, e.g. polymyxin-B and colistin.

Emergence of resistance may be minimized by: maintaining sufficiently high levels of the drug in tissues. Combination therapy, e.g. Isoniazid and rifampicin for tuberculosis. Avoid exposure of micro-organisms to a particularly valuable drug by restricting its use, e.g. rifampicin for tuberculosis.

A. Antibacterial Drugs

13.1 Pencillins

13.1.1 Long acting penicillin

Penicillins are bactericidal. They inhibit the synthesis of bacterial cell walls. They bind to cell receptors (Penicillin binding proteins: PBPs essential for cell wall synthesis).

Penicillin G Benzathine

Dose

When reconstituted with 10 ml water for injection, 10 ml 3-4 times/day, child 5 ml 3-4 times/day. It is long acting repository form, duration 1-3 weeks depending on dose 600,000-1,200,000 u. injected deep IM

Indications

Penicillin sensitive infections.

Contraindications

Patients allergic to penicillin or beta lactam antibiotics.

Precautions

Use caution in patients with a history of penicillin or cephalosporine hypersensitivity reactions. Impaired renal...
function, pre-existing seizure disorders.

**Adverse effects**

Nausea or diarrhoea, CNS toxicity with massive IV dosages. More serious hypersensitivity reactions followed injection rather than oral administration.

Patient Instructions: It is only given by injection deep IM and not orally.

**Penicillin Procaine**

**Dose**

When reconstituted with 4-6 ml water for injection 1 ml every 12-24 hours by IM injection. For early syphilis: 3 ml/day for 10 days. Long acting, peak 4 hours and duration 24 hours.

**Indications**


Contraindications, precautions, adverse effects, and patient instructions: As penicillin G sodium.

**13.1.2 Short acting penicillin**

**Penicillin G sodium (Benzyl Penicillin)**

**Dose**

By IM or slow IV or IV infusion: 0.6-1.2 g/day in 2-4 divided doses (1 mg= 1679 u.) (Maximum 2.4 g/day), neonate, 30 mg/kg/day (in 2 divided doses in the first few days of life then in 3-4 divided doses), child 1 month-12 years, 10-20 mg/kg/day in 4 divided doses. Bacterial endocarditis; slow IV or IV infusion, child 1 month-12 year, 180-300 mg/kg/day in 4-6 divided doses.

**Indications**

In tonsillitis, otitis media, erysipelas, streptococcal endocarditis, meninigo-coccal, pneumococcal meningitis and prophylaxis in limb amputation.

Contraindications, precautions, adverse effects, and patient instructions: As penicillin Benzathine.

**13.1.3. Oral penicillin:**

**Penicillin V (Phenoxy-methyl):**

**Dose**

250-500 mg every 6 hours at least 30 minutes before food, child up to 1 year 62.5 mg. 6-12 years 250 mg every 6 hours. Acid –Resistant and active orally.

**Indications**

Tonsillitis, erysipelas, otitis media and prophylaxis of rheumatic fever.

Contraindications, precautions, adverse effects, patient instructions: As penicillin G Sodium.
13.1.4 Broad spectrum semi synthetic penicillin

Amoxycillin

Dose
Oral, 250 mg every 8 hours doubled in severe infections, child up to 10 years 125 mg every 8 hours doubled in severe infections, severe or recurrent purulent respiratory infections. Urinary tract infection, 3 g repeated after 10-12 hours. Gonorrhoea, single dose of 3 g with probenecid. Otitis media, 3-10 years, 750 mg twice/day for 2 days. By IM injection, 500 every 8 hours child 50-100 mg/kg/day in divided doses. By IV Injection or infusion, 500 mg every 8 hours increased to 1 g every 6 hours child 50-100 mg/kg/day in divided doses.

Indications
Urinary tract infections, otitis media, chronic bronchitis, typhoid fever, gonorrhoea.

Contraindications
Penicillin hypersensitivity.

Piperacillin

Dose
By IM or slow IV infusion: 100-150 mg/kg/day in divided doses and increased in severe infections to 200-300 mg/kg/day in life threatening infections.

Indications
Broad spectrum and against pseudomonas aeruginosa.

Precautions
History of allergy, renal impairment, Diabetics taking amoxicillin should know that this drug might cause false positive sugar reaction with a urine glucose test.

Adverse effects
Nausea, diarrhoea, and rarely pseudomembranous colitis. Rashes are common with patients with glandular fever and chronic lymphatic leukemia.

Drug interactions
Probenecid and oral contraceptives.

Patient instructions
Tell your doctor if you have kidney disease, asthma, or allergies. This medication for your current infection only. You should not give it to other people or use is for other infections.

13.2 Cephalosporins

Cephalosporins mechanism is the same as mechanism of penicillin.

Cephadroxil

Dose
Orally active, capsules 250 mg, 500 mg, tablets 1 g, suspension 125 mg,
250 mg and 500 mg/5 ml given twice daily.

**Indications**

First generation against β-lactam susceptible and against more gram positive organisms (in patient Sensitive to penicillin) in meningitis, endocarditis, respiratory, urinary, soft tissue infection, septicemia, bone and joint infections, septicemia and pyoderma.

**Adverse effects**

Bleeding (antiagregant), allergic rash, fever, neutropenia, eusinophilia diarrhoea, phlebitis, opportunistic infection (pseudomonas and fatal) and increase hepatic transaminases.

**Cephoperazone**

**Dose**

Vials 0.5 and 1 g, injection IM and IV/12 hour, third generation.

**Indications**

In serious mixed infection and traverse blood brain barrier (CNS and meninges).

**Adverse effects**

Bleeding, allergy, fever, phlebitis fever, rash and increase hepatic transaminases.

**Cefotaxime:**

**Dose**

By IM or IV 1 g every 12 hours in moderate to severe infections, 1 g every 8 hours in life threatening conditions, up to 12 g daily. Gonorrhoea 1 g as a single dose. In severe renal impairment, doses to be halved after the initial dose. Neonate 50 mg/kg/day in 2-4 divided doses, up to 200 mg/kg/day in severe infections. Child, 100-150 mg/kg/day in 2-4 divided up to 200 mg/kg/day in severe infections. By IV infusion, 1-2 g over 20-60 minutes.

**Indications**

Infections due to susceptible gram positive and negative bacteria (more against gram negative): Brain abscess, gonorrhoea, meningitis, pneumonia, typhoid fever and septicemia.

**Ceftazidime**

**Dose**

Parental administration IM and IV vials of 250 mg, 500 mg, and 1 g and 2 g, dose every 12 hours, third generation.

**Uses And Adverse effects**

Similar to cephoperazone.

13.3 Aminoglycosides

The aminoglycosides are used primarily to treat infections caused by aerobic gram-negative bacteria: they act to interfere with protein synthesis in susceptible microorganisms. Although most inhibitors of microbial protein synthesis are bacteriostatic, the aminoglycosides are bactericidal.
Serious toxicity is a major limitation to the usefulness of the aminoglycosides, and the same spectrum of toxicity is shared by all members of the group. Most notable are ototoxicity, which can involve both the auditory and vestibular functions of the eighth cranial nerve, and nephrotoxicity.

**Gentamycin**

Gentamycin is an important agent for the treatment of many serious gram-negative bacillary infections. However, emergence of resistant microorganisms in some hospitals has become a serious problem and may limit the future use of this agent.

**Dose**

By IM or slow IV infusion: 2-5 mg/kg/day in 3 divided doses. In renal impairment the interval between doses should be 12 hours when creatinine clearance is 30-70 ml/minute, 24 hours for 10-30 ml/minute, and 48 hours for 5-10 and 3-4 days after dialysis for less than 5 ml/minute.

Child up to 2 weeks, 3 mg/kg every 12 hours; 2 weeks to 12 years 2 mg/kg every 8 hours. By intrathecal injection, 1 mg daily (maximum 5 mg/day), with 2-4-mg/kg daily by IM in divided doses every 8 hours.

**Indications**

Septicaemia and neonatal sepsis, meningitis and other CNS infections, biliary tract infections, acute pyelonephritis or prostatitis or endocarditis.

**Contraindications**

Allergy to any amino glycosides patients with myasthenia gravis, parkinsonism, or other conditions with muscle weakness, and pregnancy.

**Precautions**

Monitoring of serum drug level is recommended with prolonged or high doses specially in elderly, infants and patients with hepatic or renal impairment.

**Adverse effects**

Ototoxicity (cochlear and vestibular), nephrotoxicity, respiratory depression, allergy and neuromuscular block.

**Drug interactions**

Cephalosporines, vancomycin, cholinergics, loop diuretics, cytotoxics, amphotericin, and cyclosporin and muscle relaxants.

**Patient instructions**

Report any dizziness or sensation of ringing or fullness in the ears.

**13.4 Macrolides**

**Erythromycin**

Erythromycin and other macrolide antibiotics inhibit protein synthesis by binding reversibly to 50 S ribosomal subunits of sensitive microorganisms.
Dose

250-500 mg every 6 hours or 0.5-1 g every 12 hours up to 4 g/day in severe infections. Child up to 2 years 125 mg every 6 hours, 2-8 years 250 mg every 6 hours doses doubled for severe infections. Early syphilis, 500 mg 4 times daily for 14 days.

Indications

Patients hypersensitive to penicillin, sinusitis, diphtheria and whooping cough prophylaxis, legionnaires diseases, chronic prostatitis and acne vulgaris.

Contraindications

Hypersensitive to erythromycin, porphyria, estolate in liver impairment.

Precautions

Patients with history of arrhythmias.

Adverse effects

Nausea, vomiting and diarrhoea after large doses.

Drug interactions

Alfentanil, astemizole, bromocriptine, carbamazepine, corticosteroids, digoxin, disopyramide, ergotamine, levostatin, phenytoin, terfenadine, theophylline, triazolam, warfarin and cyclosporin.

Patient instructions

Discuss with pharmacist, which forms of erythromycin are chemically equivalent. Some types can cause allergic reactions.

Clarithromycin

Pharmacological action

It is a semi-synthetic derivative of erythromycin A. Its antibacterial action is by binding to the 50 S ribosomal subunit of susceptible bacteria and suppresses protein synthesis. It is potent against a wide variety of aerobic and anaerobic gram-positive and gram-negative organisms. It is active against following organisms:

Gram-positive bacteria: staphylococcus aureus, staphylococcus viridans, pneumococci and listeria monocytogenes.

Gram-negative bacteria: Haemophilus influenza, parainfluenza, moraxella catarrhalis, neisseria gonorrhoea, bordetella pertussis.

Mycoplasma, pneumonia, chlamydia tracomatis, Mycobacterium Leprae, chlamydia Pneumonia.

Anaerobes: Clostridium perfringens, peptococcus species.

Pharmacokinetics: Absolute bioavailability oral is 50% and protein binding 70%.
Dose

500 mg tablet/day with food and in severe infections, dose is increased to 500 mg/12 hours. Duration of therapy 7-14 days. Supplied in modified-release tablet-XL

Indications

Infections caused by susceptible organisms: Lower respiratory tract infection e.g. acute and chronic bronchitis and pneumonia. Upper respiratory tract infection e.g. pharyngitis and sinusitis. Skin and soft tissue infections e.g. folliculitis, cellulitis and erysipelas.

Contraindications

Hypersensitivity to macrolides. Renal insufficiency (creatinine clearance less than 30 ml per minute). Pregnancy and Lactation unless the benefit is considered to outweigh the risk.

Drug interactions

It inhibits hepatic cytochrome P450 enzyme system and may be associated with elevation in serum level of warfarin, ergot alkaloids, triazolam, midazolam, disopyramide, lovastatin, phenytoin, cyclosporin and thiophylline and digoxin.

Adverse effect: Nausea, dyspepsia, diarrhoea, vomiting, abdominal pain, stomatitis, glossitis and oral monilia. Headache, arthralgia, myalgia and allergic reactions Dizziness, vertigo, psychosis, increased liver enzymes. Prolongation of Qt internal and ventricular tachycardia.

13.5 Tetracyclines

The tetracyclines possess a wide range of antimicrobial activity against gram-positive and gram-negative bacteria, which overlaps that of many other antimicrobial drugs. They are also effective against some microorganisms that are resistant to agents that exert their effects on the bacterial cell wall, such as Rickettsia, Mycoplasma, Chlamydia.

Tetracycline

Dose

250 mg every 6 hours up to 500 mg every 6-8 hours. Early syphilis, 500 mg 4 times daily for 15 days. Non-gonococcal urthritis, 500 mg 4 times daily for 7-21 days.

Indications

Exacerbation of chronic bronchitis, infections due to brucella, clamydia, mycoplasma, rickettsia, some spirochetes and in acne vulgaris.

Contraindications

Hypersensitivity to any of the tetracycline’s, systemic lupus erythematosis, pregnancy, breast feeding and children below 8 years, renal impairment (not doxycycline) porphyria (doxycyclin).
Precautions
Avoided in liver and severe renal impairment.

Adverse effects
Nausea, vomiting and diarrhoea pseudo-membranous enterocolitis, deposition in growing bone and teeth enamel, hepatic renal toxicity (with outdated preparations) photosensitivity and vestibular reactions.

Drug interactions
Antacids, anti-epileptics, diuretics, retinoids, lithium, oral anticoagulants, ergot alkaloids, methotrexate and oral contraceptives.

Patient instructions
Take by a full glass of water on an empty stomach. Take with food or milk if stomach upsets. Do not take antacids or iron products.

Doxycycline
Dose
Orally available in 50 mg and 100 mg capsules every 12–24 hours.

Indications
Broad-spectrum antibiotics against mycoplasma, rickettsia, spirochetes and chlamydia. It has longer duration than other tetracyclines.

Precautions and contraindications
It should not be prescribed during pregnancy, lactating women or children below 12 years of age to avoid skeletal deformities and dental hypoplasia and staining.

13.6 Choloramphenicol
Dose
For salmonella infections or severe rickettsial diseases: adult dose 2-3 g daily for 2-3 weeks. Children 30-50 mg/kg/day for 2 to 3 weeks. Haemophilus influenza, 50-100 mg/kg/day for 8-14 days. Meningitis 50 mg/kg/day in 4 divided doses.

Indications
Broad-spectrum antibiotic, potentially toxic and is used for Haemophilus influenza and typhoid fever and severe CNS infections.

Contraindications
Pregnancy, breast-feeding and porphyria.

Precautions
Avoid prolonged and repeated doses, blood counts should be monitored.

Adverse effects
Nausea, vomiting, diarrhoea, bone marrow disturbances, gray baby syndrome.
13.7 Other Antibiotics

**Vancomycin HCL**

**Dose**

500 mg IV in 20 minutes every 6-8 hours. Child 20-40 mg/kg/day.

**Indications**

Sepsis or endocarditis caused staphylococci resistant to other drugs.

**Contraindications**

Renal impairment or history of deafness.

**Precautions**

Rapid infusion can lead to flushing prevented by slow infusion and pre-treatment with antihistamines. Blood counts, liver and kidney functions are required, reduce dose in elderly.

**Adverse effects**

Phlebitis at the site of injection, chills and fever.

**Drug interactions**

Anion exchange resins, aminoglycosides, cephalosporins and loop diuretics.

**Patient instructions**

Report pain at infusion site, dizziness or fullness or ringing in ears with IV use. Nausea or vomiting with oral use.

---

13.8 Sulphonamides

Sulphonamides have a wide range of antimicrobial activity against both gram-positive and gram-negative bacteria. In general, the sulphonamides exert only a bacteriostatic effect, and cellular and humoural defence mechanisms of the host are essential for the final eradication of the infection.

**Co-Trimoxazole**

The introduction of trimethoprim with sulphamethoxazole constitutes an important advance in the development of clinically effective antimicrobial agent. The antimicrobial activity of the combination results from its action on two steps of the enzymatic pathway for the synthesis of tetrahydrofolic acid. Sulphonamide inhibits the incorporation of PABA into folic acid, and trimethoprim prevents the reduction of dihydrofolate to tetrahydrofolate.

**Dose**

960 mg every 12 hours (up to 1.44 g), 480 mg every 12 hours if course for more than 14 days Child, 6 weeks to 5 months, 120 mg every 12 hours, 6 months to 5 years 240 mg every 12 hours, 6-12 years 480 mg every 12 hours. Prophylaxis of recurrent UT
infections, 480 mg at night, child 6-12 mg/kg at night.

**Indications**
Acute uncomplicated urinary tract infections, in otitis media, chlamedial infection and prophylaxis of meningococcal meningitis, typhoid fever, sinusitis, Haemophilus influenza, pneumocystis carinii pneumonia.

**Contraindications**
Hypersensitivity to sulphonamides, pregnancy near term, during breast feeding, infants 1-2 months, porphyria patients, glucose-6-phosphate dehydrogenase deficiency, severe renal, hepatic or blood disease.

**Precautions**

**Adverse effects**
Crystalluria, hematuria, skin rash, fever, photosensitivity haemolytic anaemia, megaloblastic anaemia, and kernicterus in newborn.

**Drug interactions**
Methenamine compounds, sulphonylureas, phenytoin, oral anti coagulants, methotrexate.

**Patient instructions**
Take with full glass of water on an empty stomach. Drink several additional glasses of water daily.

### 13.9 Fluoroquinolones
Non fluorinated quinolones are relatively of minor significance because of their limited therapeutic utility and the rapid development of bacterial resistance. The more recent introduction of fluorinated 4-quinolones such as norfloxacin and ciprofloxacin represents a particularly important therapeutic advance, since these agents have broad antimicrobial activity and are effective after oral administration for the treatment of a wide variety of infectious diseases. Relatively few Adverse effects appear to accompany the use of these fluoroquinolones.

**Norfloxacin**

**Dose**
Tablets 400 mg and 800 mg/12 hours.

**Indications**
Bactericidal against pseudomonas and in urinary tract and GIT infections.

Adverse effects and drug interactions: Similar to ciprofloxacin.

**Ciprofloxacin**

**Dose**
Tablets 250 mg, 500 mg, 750mg and ampoule 100 mg, vial 200 mg.tables
every 12 hours and ampoule and vials IM or IV/12 hours.

**Indications**

Used in various infections affecting respiratory tract, GIT, bone, surgery, meningitis (H-influenza) and typhoid.

Adverse effects and drug interactions: Similar to levofloxacin.

**Ofloxacin**

**Dose**

Urinary tract infections 200-400 mg/day up to 400 mg (twice daily). Lower respiratory tract infection; 400 mg daily up to 800 mg (400 mg tid). Uncomplicated gonorrhoea, non-gonococcal utheritis and cervicitis 400 mg as single dose.

**Indications**

Urinary tract infection, lower respiratory tract infection, gonorrhoea and non-gonococcal utheritis and cervicitis.

**Contraindications**

Pregnancy, breast-feeding, patients below 18 hours. History of epilepsy or CNS disorders.

**Precautions**

May affect performance of skilled tasks.

**Adverse effects**

Nausea, vomiting, diarrhoea, headache, dizziness and insomnia.

**Drug interactions**

Theophylline.

**Patient instructions**

Take with food. Avoid antacid use. Avoid excessive exposure to sunlight. Report any tendon pain or inflammation.

**Levofloxacin**

**Dose**

Orally, 500 mg/day. Bactericidal by inhibiting DNA synthesis.

**Indications**

Respiratory infection, against Staphylococcus aureus, Escherichia coli, Pseudomonas enterobacter, klebsiella.

**Adverse effects**

Uncommon, arthropathy (cartilage damage), hepatotoxic, blood dyscrasias and photosensitization (pigmentation).

**Drug interactions**

Antacids interfere their absorption and xanthenes increase seizures.
13.10 Urinary Antiseptics

Nitrofurantoin

It is bactericidal to most Gram positive and Gram negative urinary tract pathogens. Used for acute and recurrent infection and also used prophylactically.

Dose

Oral capsules 50 mg and 100 mg/4-6 hours, 50% excreted rapidly in urine, soluble in acid urine. Less toxic and safer than sulphonides for prolonged use.

Indications

Urinary tract infection (Escherichia coli, streptococcus, staphylococcus Pyrogens and proteus.)

Adverse effects

GIT (nausea, vomiting, dyspepsia), rash, alopecia, asthma and jaundice.

13.11 Antituberculous Drugs

Tuberculosis is a chronic infectious disease caused primarily by Mycobacterium tuberculosis or sometimes M. bovis. Infection is usually due to inhalation of infected droplet nuclei with the lung generally being the first organ affected, but the primary infection is usually asymptomatic. Surviving bacteria may become dormant or in susceptible patients, progress to active primary disease; dormant organisms may produce disease and this often occurs if immune status is altered.

Isoniazid

Dose

300 mg/day. Child, 6mg/kg/day. T.B meningitis, 10mg/kg/day.

Indications

Treatment of tuberculosis.

Contraindications

Porphyria, acute or chronic liver disease, previous INH-associated hepatitis.

Precautions

It should be administered with caution to patient with convulsive disorder, chronic liver disease, and renal dysfunction. Periodic liver function tests and eye examination should be done. Pyridoxine 10mg/day is given to avoid peripheral neuropathy.

Adverse effects

Nausea, vomiting, hypersensitivity reactions, peripheral neuritis, convulsions, hepatitis, and systemic lupus erythematosus-like syndrome.

Drug interactions

 Carbamazepine, ethosuximide, and phenytoin.
Patient instructions
Avoid tasks that require alertness. Avoid eating tuna, yeast, extracts, sausages, certain cheeses. Changing test tape urine tests.

Rifampicin
Dose
In tuberculosis (or other atypical mycobacterium) 600 mg/day in combination with other drugs. In elimination of meningococcal carriers, 600 mg twice daily for 2 days.

Indications
In the treatment of tuberculosis (with other anti-tuberculosis drugs), leprosy (with a sulphone) and prophylaxis of meningococcal meningitis.

Contraindications
Jaundice and porphyria.

Precautions
The indiscriminate use of rifampicin for minor infections may lead to development of resistant mycobacterium.

Adverse effects
Nausea, vomiting, diarrhoea, influenza syndrome, allergic reactions, acute renal failure, impaired liver enzymes, orange discoloration of body secretions.

Drug interactions
Oral anti-coaguants, oral contraceptives, ketoconazole, cyclosporin, chloramphenicol and methadone.

Patient instructions
Take this medication with a full glass of water on empty stomach (1 hour before or 2 hour after meals) for best absorption. It is important to take this medication regularly as directed because inconsistent use might increase its toxicity.

Ethambutol
Dose
Adult and child above 6 years 15mg/kg/day.

Indications
Treatment of tuberculosis

Contraindications
Elderly patients, children below 6 years, patient with impaired renal functions, low vision or optic neuritis.

Precautions
Periodic ocular examination is needed.

Adverse effects
Visual disturbances (loss of acuity, colour blindness, restrictions of visual fields) necessitates discontinuations of ethambutol, peripheral neuritis, hallucinations, joint pain, elevated blood
uric acid, liver impairment, abnormal lung x-rays.

**Drug interactions**
Administrations of alcohol.

**Patient instructions**
Physical exams should include ophthalmoscope fingerprint, testing of colour discrimination. Changes in colour perception are the first signs of toxicity.

**Pyrazinamide**
It is related to isoniazide (pyrazinoic acid amide, adrenamide).

**Pharmacological action**
Tuberculocidal.

**Dose**
Antituberculous, orally 500 mg tablets. 25 mg/kg/day maximum 3 g/day divided into 3-4 doses.

**Adverse effects**
Hepatotoxic (15%), G.I. disturbance, fever, hyperuricemia, uncontrolled diabetes and hemoptysis.

**Streptomycin**

**Pharmacological action**
Bactericidal, inhibits protein synthesis, half-life 2 hours, protein bound 30% with low renal excretion.

**Dose**
Aminoglycoside for IM injection 1 g vial for systemic use in gram-negative bacteria. 1 g/day.

**Indications**
In gram-negative infections, limited in tuberculosis, plague, tularemia and brucellosis (with tetracycline).

**Precautions and Adverse effects**
Ototoxicity, nephrotoxicity, neuromuscular blocker with narrow safety margin.

**Contraindications**
Myasthenia gravis.

**13.12 Anti-Leprotic Drugs**

**Clofazimine**

**Dose**
In Lepromatous lepra reactions, dose is increased to 300 mg daily for maximum of 3 months.

**Indications**
Leprosy.

**Contraindications**
Liver and kidney impairment, pregnancy and breast-feeding.

**Precautions**
Hepatic and renal impairment.
Adverse effects
Nausea, giddiness, headache and diarrhoea in high doses, skin and urine are colored red.

Patient instructions
Red discoloration of skin and urine occurs.

Dapsone
Dose
By mouth adult 100 mg daily, child 10-14 years 50 mg daily.

Indications
Paucibacillary (pb) and multibacillary leprosy.

Contraindications
Hypersensitivity to sulphones, severe anemia.

Precautions
Anemia, G6PD deficiency, pregnancy and breast-feeding, porphyria.

Adverse effects
Haemolysis and methaemoglobinemia, allergic dermatitis, Stevens Johnson syndrome, Dapsone syndrome resembling mononucleosis, rash, fever, jaundice and eosinophilia, GIT irritations, headache, nervousness, insomnia, blurred visions.

B. Antiviral

Acyclovir
Dose
Herpes simplex treatment Adult: 200 mg-400mg (in the immunocompromised) 5 times daily for 5 days. Children 2 years: 1/2 adult dose, above 2 years, adult dose. Herpes simplex prophylaxis: Adult dose: 200 mg qid. Children under 2 years; 1/2 adult dose and above 2 years, adult dose. Herpes zoster: adult dose: 800 mg 5 times daily for 7 days.

Indications
Prophylaxis and treatment of herpes and varicella virus.

Contraindications
Patients allergic to acyclovir.

Precautions
Maintain adequate hydration; doses should be adjusted according to creatinine clearance.

Adverse effects
Rashes, GIT upsets, disturbance in liver, kidney and hematological indices.

Drug interactions
Nephrotoxic drugs, zidovudine and probenicid.
**Patient instructions**

Use a finger coat or latex glove when applying ointments.

**Ribaverin**

**Pharmacological action**

It is guanine analogue against broad spectrum DNA and RNA viruses.

**Dose**

Orally 200 mg capsules in divided doses: 400 mg and 600 mg 12 hours apart in patients less than 75 kg, or 600 mg tid in patients more than 75 kg. It is combined with interferon for 6-12 months to reduce virus relapse. Its target end point is the disappearance of virus from serum (serum conversion).

**Adverse effects**

Hemoglobin reduction, dyspnoea, pharyngitis, pruritus, rash, nausea, insomnia, anorexia and depression.

**Interferon**

**Indications**

Used as prophylaxis against rhinoviruses, cytomegalovirus infections in transplant patients and in the treatment of herpetic keratosis. Interferons are also used in management of some neoplasms (Kaposi sarcoma, hairy cell leukemia, chronic granulocytic leukemia, multiple myeloma and renal cell carcinoma).

**Contraindications**

Hypersensitivity to interferons, severe cardiac, renal, hepatic or CNS disorders, or in patients taking drugs that may lead to these conditions.

**Precautions**

Antibodies may develop to exogenous interferons and diminish their activity.

**Adverse effects**

Influenza-like symptoms (fever, chills, headache), anorexia, weight loss bone marrow depression, renal, cardiovascular and CNS abnormalities.

**Drug interactions**

Vidarabine, theophylline, zidovudine, melphalan and paracetamol.

**Patient instructions**

Instruct in proper method of aseptic preparation of vials and syringes in subcutaneous use. Acetaminophen is recommended to reduce frequent Flu-like symptoms. Rotate subcutaneous injection sites.

**C. Antifungal Drugs**

**Nystatin**

**Dose**

For intestinal candidiasis, 500000 U qid, doubled in severe infections. Children, 100000 U qid.
Indications
Candidiasis.

Precautions
Pregnancy and breast-feeding.

Adverse effects
Nausea, vomiting and diarrhoea.

Patient instructions
If you are using this drug to treat a vaginal infection, avoid sexual intercourse. Use vaginal tablets continuously, even during menstrual period. Do not douche during treatment. If symptoms do not begin to improve 2 or 3 days after starting nystatin, contact your doctor.

Fluconazole
It is triazole derivative, anti-mycotic for systemic use.

Dose
Capsule 50 mg, 150 mg, syrup 5 mg/ml and infusion IV 2 mg/ml 50 ml.

Indications
For systemic fungal infections in immunocompromised patients.

Contraindications
Liver disorders (hepatotoxic).

Amphotericin B
Dose
Slow IV Infusion, 250 microgram/kg/day gradually increases if tolerated 1 mg/kg/day maximum 1.5 mg/kg/day on alternate days.

Indications
Systemic fungal infections.

Contraindications
Patients allergic to amphotericin.

Precautions
Reduce dose in renal impairment. Monitor kidney and liver functions, electrolyte and blood indices. Control reactions with anti-histamines, aspirin or phenothiazine.

Adverse effects
Chills, fever, vomiting, headache, impair renal and hepatic functions, anaemia, hypotension, and hypokalemia.

Drug interactions
Aminoglycosides, cephalosporins, cyclosporin, miconazole.

Patient instructions
Shake container well before use. Take mineral supplements by mouth. Hold the product in your mouth for 1 minute then swallow. This preparation can stain clothing.
Griseofulvin

Pharmacological action
Fungistatic by binding to cell lipids. Absorbed orally.

Dose
1 g/day (adult) and 0.5 g/day (children) for 1-2 months or longer. Dose is divided every 6 hours. 125 mg Cap. 125, 250 mg Tablets, oral suspension 250 mg/5 ml.

Indications
Treatment of tinea capitis, barbe, cruris, cerporis, pedis and onychomycosis.

Adverse effects
(15%) nausea, gastric discomfort, heartburn, diarrhoea, paresthesia, photosensitivity, headache, fatigue, lethargy, insomnia, incoordination, rash, leucopenia (2-3 % discontinue due to Adverse effects).

Itraconazole

Dose
200 mg -600 mg/day depending on site and severity of infection. Give dosage over 200 mg/day in 2-3 divided doses.

Indications
Treatment of blastomycosis, aspergillosis and histoplasmosis fungal infections. Treatment of dermatophytosis, candidiasis, cryptococcus.

Contraindications
Co-administration with terfenadine, astemizole, cisapride, triazolam or oral midazolam.

Precautions
Pregnancy (category C), lactation (excreted in milk). Absorption may be decreased in HIV-infected individuals with hypochlorhydria.

Adverse effects
Rash, pruritus and other skin irritations.

Drug interactions
astemizole, cisapride, terfenadine co-administration. Do not use together with phenytoin, sulphonylurea, tacrolimus, and warfarin.

Patient instructions
Tell patient to report these symptoms to physician; rash, swelling, itching, yellow skin.

Econazole

Dose
Topical, apply sufficient quantity to cover the affected areas once daily for 2 weeks to 1 month.

Indications
Treatment of tinea pedis, tinea cruris, tinea corporis, cutaneous candidiasis, tinea versicolor (Against dermatophytes and Candida).
**Contraindications**

Allergic reactions to econazole.

**Precautions**

Use with cautions in blistered, raw, or oozing area of skin, worsening skin irritation during drug therapy. Consult your doctor before you begin breastfeeding.

Preparation: Cream 1% Topical powder and topical spray.

**Adverse effects**

Burning, Itching, stinging and erythema.

**Patient instructions**

Teach patient to wash and dry skin before applications. Advise patient to report signs of hypersensitivity such as rash, burning or redness.

**D. Anti-protozoal Drugs**

**13.13 Antiamoebiasis and Antigiardiasis**

Drugs used to treat amoebiasis can be categorized as luminal, systemic, or mixed. Luminal amoebicides, exemplified by diloxanide furoate and other dichloroacetamide derivatives, are active only against intestinal forms of amoeba. These compounds can be used successfully by themselves to treat asymptomatic or mild intestinal forms of amoebiasis or, in conjunction with a systemic or mixed amebicide, to eradicate the infection. Systemic amoebicides are effective only in invasive forms of amebiasis. These agents have been employed primarily to treat severe amebic dysentery (dehydrometine) or hepatic abscesses (dehydrometine or chloroquine), but they are rarely used now unless other drugs fail or cause unacceptable adverse effects. Mixed amoebicides are active against both intestinal and systemic forms of amoebiasis. Metronidazole, a nitroimidazole derivative, is the prototypical mixed amebicide, and its use has revolutionized the treatment of this protozoal infection. Because it is well absorbed and therefore may fail to reach the large intestine in therapeutic concentrations, this compound is likely to be more effective against systemic than intestinal amebiasis. Antibiotics such as the amebicidal aminoglycoside paromomycin or tetracycline can be used in conjunction with metronidazole to treat severe forms of intestinal amebiasis. Treatment with metronidazole is often followed by a luminal amoebicide to effect a cure.

**Metronidazole**

**Dose**

For anaerobic infections, oral, 400 mg every 8 hours for 3 days then 1 g every 12 hours, IV infusion: 500 mg every 8 hours for up to 7 days. Child: 7.5 mg/kg (any route) Bacterial vaginosis, oral, 400 mg twice daily for 7 days, or 2 g as a single dose. Trichominiasis, oral, 200 mg every 8 hours or 400 mg every 12 hours for 7 days, or 2 g as a single dose. Amoebiasis: 800 mg every 8 hours for 5 days, Gardiasis: 2 g daily for 3 days. Acute
ulcerative gingivitis: 200 mg daily for 3 days.

**Indications**
Against anaerobic bacteria and protozoa (Bacteroids fragilis, Entamoeba histolytica, Trichomonas vaginalis and giardia lamblia) and in the management of pseudo-membranous colitis.

Contra indications: Porphyria.

**Precautions**
High doses should be avoided in pregnancy and breast-feeding. Dose should be reduced in hepatic impairment and should be given with great care to patients with blood dyscrasias or active disease of the CNS.

**Adverse effects**
Nausea, vomiting metallic taste and GIT upsets, drowsiness, headache, peripheral neuropathy with prolonged treatment and seizures with high doses.

**Drug interactions**
Alcohol, antiepileptics, anticoagulants, cimetedine, disulfiram.

**Patient instructions**
When metronidazole is used to treat vaginal infection, sexual partners should receive concurrent therapy in order to prevent reinfection.

### Diloxanide furoate

**Dose**
500 mg daily for 10 days Child: 20 mg/kg daily in divided doses for 10 days course could be repeated if necessary.

**Indications**
Active against intestinal amoebiasis and used alone in asymptomatic patients (intestinal or hepatic amoebiasis).

**Precautions**
Pregnancy and lactation.

Adverse effect: Flatulence, vomiting, pruritis and urticaria.

Patient Instructions: Do not stop taking the drug before completing the course.

### Tinidazole

**Dose**
For anaerobic infections: 2 g initially followed by 1 g daily or 500 mg twice daily for 5-6 days. Bacterial vaginosis, trichomoniasis, giardiasis and acute ulcerative gingivitis: a single 2 g dose. Child: single dose of 50-75 mg/kg. Intestinal amoebiasis: 2 g daily for 2-3 days. Child: 50-60 mg/kg daily for 5 days. Abdominal surgical prophylaxis: single 2 g dose 12 hours before surgery.
Indications
Active against a range anaerobic and protozoal infections (it differs from metronidazole in having a longer life allowing its administration in single daily doses).

Contra indications: Porphyria.

Precautions, Adverse effects, Drug interactions, Patient instructions
As for metronidazole.

13.14 Antimalarials
Chloroquine Phosphate
Dose
Treatment of benign malaria, oral, initial dose 600mg, then 300 mg after 6-8 hours, then 300 mg/day as a single for 2 days. Child, initial dose 10mg/kg then 5 mg/kg after 6-8 hours then 5 mg/kg day as a dose for 2 days. Treatment of malignant. Malaria: IV infusion, 10 mg/kg infused over 8 hours followed by 3-8 hours infusions of 5 mg/kg. Child, oral, as the child oral doses of benign malaria. Parenteral, as for adults.

Indications
Chemoprophylaxis and treatment of malaria. In rheumatoid arthritis and lupus erythematosus

Contraindications
Porphyria, psoriasis.

Precautions
Large IM doses or rapid infusions may cause severe cardio-respiratory depression. Used cautiously in patients with retinal abnormalities, liver damage, alcoholism, and neurological or hematological disorders. Ocular examination in long-term treatment, severe G.I disorders elderly, G-6-PD deficiency, porphyria, and myasthenia gravis.

Adverse effects
Headache, GIT upsets, pruritis and visual disturbances (with large doses).

Drug interactions
Antacids, anti diarrheals, cholinergics and cimetidine.

Patient instructions
Take with food. Store at controlled room temperature. Protect from light. Irreversible damage to the retina of eye so periodic eye examination Exams should be performed. Do not change the dose or stop taking unless advised.

Pyrimethamine
Pharmacological action
It is Diamenopyrimidine of high potency, slow onset (not used in acute malarial attack) and more prolonged action against malaria. It attacks the primary tissue schizonts before entering RBCs (Exo-erythrocytic stage) specially plasmodium falciparum. It prevents the PABA uptake in the syn-
thesis of folic acid. Therefore, sulphadoxine potentiates its action (Fansidar).

Pharmacokinetics: It is greatly concentrated in tissues and 20% excreted unchanged in urine.

**Dose**

25 mg tablet/week for 10 week and children 12.5 mg.

**Adverse effects**

stomatitis, vomiting, abdominal pain, colitis, diarrhoea, leucopenia, megaloblastic anemia, thrombocytopenia and haemolytic anaemia.

**Indications**

Causal prophylaxis antimalarial.

**E. Anthelmintic Drugs**

**Praziquantel**

**Dose**

60 mg/kg in 3 divided doses, 6 hours apart.

**Indications**

Effective against all human schistosomes, trematodes and cestodes, fluke infections.

**Contraindications**

Pregnancy, ocular cysticercosis.

**Precautions**

Breast-feeding should be stopped 72 hours after drug administration. In cases of cerebral cysticerosis, coadministration of corticosteroids is advised.

**Adverse effects**

GIT upsets, drowsiness and lethargy, headache, rarely hypersensitivity reactions.

**Drug interactions**

Dexamethasone.

**Patient instructions**

Administer tablets during meals with liquids and not to chew tablets. Drug may cause drowsiness so use caution while driving or performing other tasks requiring mental alertness.

**Flubendazole**

**Dose**

It is an analogue of mebendazole. For the treatment of Entrobiasis: 100 mg single dose repeated after 2-3 weeks. For ascariasis, hookworms and trichuriasis: 100 mg twice daily for 3 days.

**Indications**

Threadworm, hookworm, roundworm and whipworm infestations.

**Contraindications, Adverse effects, drug interactions and patient instructions:** Similar to mebendazole.
Levamisole

Dose

In case of ascariasis: 120-150 mg as a single oral dose, children: 3 mg/kg. For hookworm or mixed infections: 300 mg is given over 1-2 days.

Indications

Against roundworm and hookworm infestations. It is also used as an immune-stimulant and as adjunct in patients with malignant diseases.

Contraindications

Levamisole should not be given to patients with pre-existing blood disease or sjogren syndrome. Breast-feeding.

Adverse effects

GIT upsets and dizziness. After long-term use as immuno-stimulant hypersensitivity reactions, CNS disturbances and hematologic disorders are reported.

Precautions

Pregnancy.

Mebendazole

Dose

For threadworm: 100 mg single dose, if re-infection occurs a second dose may be needed after 2-3 weeks. For Ascariasis: 100 mg twice daily for 3 days.

Indication: Threadworm, hookworm, roundworm and whipworm infestations.

Contraindications

Pregnancy especially first trimester and children under 2 years.

Precautions

Allergic to the medicine.

Adverse effects

Abdominal pain and diarrhoea.

Drug interactions

Carbamazepine, cimetidine, hydantoins (phenytoin).

Patient instructions

Doses vary according to type of parasite. Tablets may be chewed, swallowed or crushed and mixed with food. Laxative therapy and fasting are not necessary. If one family member has a pinworm infection, treat all family members in close contact with the patient. Strict hygiene is essential.

Niclosamide

Dose

Taenia solium: 2 g as a single dose after a light breakfast followed by a purgative after 2 hours, child up to 2 years: 500 mg, 2-6 years: 1 g. For the treatment of T. saginata and Diphyllobothrium Latum as before, but half the dose may be taken after breakfast and the remainder one hour later fol-
allowed by a purgative after a further 2 hours. Hymenolepis nana: 2 g on first day, then 1 g daily for next 6 days: child up to 2 years: 1/4 adult dose; 2-6 years 1/2 adult dose.

**Indications**

For all types of tapeworms.

**Precautions**

The tablets should be chewed thoroughly. Anti-emetic should be given before treatment.

**Contraindications**

Pregnancy.

**Adverse effects**

GIT upsets, light-headness and pruritus.

**Patient instructions**

Tablets should be chewed or crushed thoroughly before washing down with water.

**F. Antiseptics and Disinfectants**

They are used to kill microorganisms on surfaces but they are too toxic for systemic adminstration.

They include phenols, cresols and resorcinols; alcohol; acids; halogens and halogen containing compounds; oxidizing agents; heavy metals and their salts and surface acting agents (dertergents).

I. Disinfection of inanimate environment: Table tops, instruments: Lisle (5%), formaldehyde (1-10%), aqueous glutaraldehyde (2%), mercury bichlorite (0.1%). Bandages, bed pans: Sodium hypochlorite (1%), Lisle (5%). Air: Propylene glycol mist or aerosol, formaldehyde vapor. Heat-sensitive instruments: Ethylene oxide gas.

II. Disinfection of skin or wounds: Washing with soap and water, hexachlorophene (2%), tincture iodine (25), ethyl alcohol (70%), povidone-iodine, nitrofurazone (0.2%), cetrimide (Savlon).

III. Topical application of drugs to skin or mucous membranes: Candidasis: gentian violet (1/2000), nystatin cream (100,000 units/g), candicidin ointment (0.6 mg/g), miconazole cream (2%). Burns: Silver nitrate (0.5%), mafenide acetate, silver sulphadiazine 1% (Flamazine). Dermatophytoses: Undeclinic acid (5-10%), tolnaftate (1%). Pyoderma: Ammoniated mercury ointment (2-5%), potassium permanganate (1/10000), bacitracin-neomycin-polymyxin ointment.

**Cetrimide**

**Pharmacological action**

It is cationic detergent (surfactant), quaternary germicide. It is bactericidal affecting cell wall (cytolysis), denature and precipitate proteins. It acts against Gram positive and negative organisms but not active against spores, viruses or fungi. Activity increases in alkaline PH and decreases
in plasma and organic matter. Keratolytic action and emulsifying agent. It has low toxicity and non-irritant with rapid onset of action.

Preparations and Dose (for external use): 0.1 % for minor wounds and Napkin rash. 0.5 % in 70% alcohol for skin sterilization pre-operative. 1% for instruments.

**Chlorhexidine gluconate**

**Dose**
Rinse mouth with 10 ml for 1 minute 2 times/day.

**Indications**
Oral hygiene and inhibition of plaque formation.

**Precautions**
It is not used if the patient is allergic to the drug or any ingredient.

**Adverse effects**
Idiosyncratic mucosal irritation and reversible brown staining of teeth.

**Patient instructions**
Avoid contact with middle ear, eyes, brain, and meninges. Not for use in body cavities.

**Hydrogen Peroxide**

**Dose**
Rinse mouth for 2-3 minutes with 15 ml in water 2-3 times/day.

**Indications**
Oral hygiene.

**Chloroxylenol**

**Pharmacological action**
Similar to cetrimide and non-irritant.

**Dose**
5% is potent.

**Povidone Iodine**

Povidone Iodine 10%: To be applied undiluted in pre-and post-operative skin disinfections.

Povidone Iodine 7.5%: For infected skin conditions. Retain on scalp for 5 minutes before rinsing.

Tincture Iodine 2.5%: To be used undiluted in minor skin wounds.

**Precautions**
Pregnancy and breast-feeding.

**Adverse effects**
Rarely sensitivity may interfere with thyroid function tests.

**Gentian violet (crystal violet)**

**Dose**
Apply 2 or 3 times daily for 2-3 days.

**Indications**
Antiseptic dye against some gram-positive bacteria and candida (less
active against gram negative bacteria and ineffective against acid fast bacteria and spores).

**Contraindications**
Ulcerative lesions, broken skin, mucous membranes.

**Precautions**
Avoid contact with eyes, mucous membranes and broken skin. Animal carcinogenicity has restricted its use.

**Adverse effects**
Can produce irritation and ulceration of skin, stains skin and clothing.

**Patient instructions**
Avoid contact with eyes, nose or mouth. Wear well-fitting and ventilated shoes, change socks at least once a day.

**Castellani paint (Magenta Paint)**

**Indications**
Antiseptic dye effective against some gram positive bacteria and fungi, used in the treatment of some superficial dermatophytosis specially when moist eczematous dermatitis is present.

**Precautions**
Possible carcinogenicity has restricted its use.

**Silver Sulphadiazine**

**Pharmacological action**
Against gram positive bacteria (Staphylococcus, streptococcus. and Cl. welchii) and gram negative bacteria (neisseria and enterobacteria). It is non-irritant with high penetration.

**Dose**
In burns apply daily with a sterile applicator. In leg ulcers, apply at least three times/week. Topical cream 1%.

**Indications**
Skin infections particularly gram-negative infections e.g. pseudomonal infections in second and third degree burns, in infected leg ulcers and pressure sores.

**Contraindications**
Sensitivity to sulphonamides, pregnancy, neonates.

**Precautions**
Hepatic and renal insufficiency, G6PD deficiency, breast-feeding.

**Adverse effects**
Rarely hypersensitivity reactions, argyria and sulphonamide-induced systemic toxicity.

**Drug interactions**
Tell your doctor if you are taking over-the-counter drugs. Proteolytic enzymes interact with silver sulphadiazine.
 SECTION XIV

 ENDOCRINE DRUGS

In this section:

14.1 Anti-Diabetics 169
14.2 Posterior Pituitary Hormones 172
14.3 Suprarenal Cortical Hormones 173
14.4 Female Sex Hormones 175
14.5 Contraceptives 175
14.6 Ovulatory Stimulants 177
14.7 Thyroid Hormones 178
14.8 Drugs for Hyperthyroidism 179
14.9 Hypothalamic Hormones 180
14.10 Anterior Pituitary Hormones 180
14.11 Anti-Parathormone 181
14.12 Drugs Acting on the Uterus 181
14. Endocrine Drugs

14.1 Anti-Diabetics

Diabetes mellitus occurs as a result of a deficiency in insulin synthesis and secretion. It is characterized by hyperglycaemia and disturbances of carbohydrates, fat, and protein metabolism. The aim of treatment is to achieve the best possible control of plasma glucose concentration and to prevent or minimize complications including microvascular ones (retinopathy, albuminuria, neuropathy). Diabetes mellitus is also a strong risk factor for cardiovascular disease.

14.1.1 Insulin

Insulin is the mainstay for treatment of virtually all Type-I and many Type-II diabetic patients. It is a polypeptide hormone of complex structure. It is inactivated by GIT enzymes and must be given by injection. When necessary, insulin may be administered intravenously or intramuscularly; however, long-term treatment relies on subcutaneous injection. In subcutaneous administration the kinetics of absorption are relatively slow and thus do not mimic the normal rapid rise and decline of insulin secretion in response to ingestion of nutrients. Insulin diffuses into the peripheral circulation instead of being released into the portal circulation; hence the preferential effect on hepatic metabolic processes is eliminated.

Human Insulin Dose

Short acting (SC, IM, IV, or infusion), when injected SC it has an onset of action within 30-60 minutes and a peak action between 2-4 hours and a duration of 8 hours. Intermediate and long acting insulins, SC only, have an onset of action of about 1-2 hours with a peak effect after 4-12 hours and duration lasting 16-35 hours.

Indications

In insulin dependent diabetes mellitus and in diabetic ketoacidosis. In some patients with non-insulin dependent diabetes mellitus (during periods of severe infections, stress or trauma, during surgery). In all types of diabetes mellitus during pregnancy.

Contraindications

Hypoglycaemia.

Precautions

Increased dosage requirements are necessary during infection, accidental or surgical trauma, stress puberty, the latter two trimesters of pregnancy, and liver or renal impairment. Changing of Insulin from one species to another or during excessive exercise may also require dosage adjustments. Frequent monitoring of blood and urine for glucose and ketones is essential.
Adverse effects

Hypoglycaemia lipotrophy or lipodystrophy at the site of injection, and local or systemic hypersensitivity reactions.

Drug interactions

Alcohol, monoamine oxidase inhibitors, diazoxide, beta-blockers, nifedipine, clofibrate, corticosteroids, loop diuretics and thiazide diuretics, octreotide, lithium, and oral contraceptives.

Patient instructions

If your physician prescribes 2 types of insulin and recommends mixing, always draw the regular insulin (clear) into syringe first. Some insulin react quickly and require immediate injection. Always have insulin and syringes available. Do not store insulin in your car glove compartment. You should eat on a regular schedule.

Bovine Insulin

Pharmacological action

Secreted from langerhans cells of pancreas. It has important metabolic actions mainly regulate blood glucose level: glucosides, glycogenesis, gluconeogenesis and lipogenesis .It antagonizes the metabolic effects of the other hormones (growth hormone, thyroxine and glucocorticoids).

Dose

Short acting 20 IU, Intermediate acting 40 IU, Neutral 20 IU/ml.

Indications

Mainly for treatment of patients with insulin-dependent type 1 diabetes mellitus and occasionally in type 2 non-insulin dependent and with complications e.g. pregnancy, ketoadosis, infection and stress.

Contraindications

Hypoglycaemia, allergy, anti-body formation (decreased action), skin lipo-atrophy, necrosis and ulceration (intradermal).

14.1.2 Biguanides

Pharmacologic action

They decrease the absorption of glucose from the gut. They decrease mitochondrial oxidative phosphorylation and stimulate anaerobic metabolism of glucose to lactate. They increase glucose uptake by the muscles. They decrease hepatic gluconeogenesis and plasma glucagon level. They increase insulin receptors or receptor responsiveness.

Metformin

Dose

Initial dose 500 mg tid or 850 mg bid with or after food, gradually increased if necessary to a maximum 3 g/day, though most physicians limit this to 2 g/day due to concerns of GIT side effects.

Indications

Non-insulin dependent diabetes mellitus especially in obese patients who
have gained weight under sulphonylurea despite adequate dietary modifications.

**Contraindications**

In conditions of heart, hepatic or renal failure, dehydration, acute or chronic alcoholism, insulin dependent diabetes mellitus breast feeding, pregnancy, porphyria, ketoacidosis, surgery, severe infections and stress.

**Precautions**

Requirement may vary during periods of excessive exercise.

**Adverse effects**

GIT upsets (anorexia, nausea, metallic taste), weight loss, impaired vitamin B12 absorption and lactic acidosis.

**Drug interactions**

Alcohol, mono-amine oxidase inhibitors, diazoxide, beta-blockers, nifedipine, clofibrate, corticosteroids, loop and thiazide diuretics, octreotide, lithium, oral contraceptives and cimetidine.

**Patient instructions**

Take it just before meals. Don’t take if you have stroke, myocardial infarction, hyperventilation, serious infections, require surgery. Contact your physician if gastrointestinal Adverse effects persist.

### 14.1.3 Sulphonylureas

**Pharmacologic action**

**Pancreatic**

They stimulate insulin release from β-cells by blocking ATP-sensitive potassium channels. They also increase glucose transporters and decrease glucagon secretion from α-cells either directly or by release of insulin and somatostatin.

**Extrapancreatic**

They increase tissue sensitivity to insulin and increase number of insulin receptors (upregulation) and also reduce glucose output from the liver and inhibit hepatic gluconeogenesis.

**Glibenclamide**

**Dose**

Initially 5 mg/day (2.5 mg in elderly adjusted according to response (maximum 15 mg) taken at breakfast.

**Indications**

Non-insulin dependent diabetes mellitus (to supplement treatment by diet modification).

**Contraindications**

Insulin dependent diabetes mellitus breast-feeding, pregnancy, porphyria, ketoacidosis, surgery, severe infections and stress.

**Precautions**

Elderly, renal failure and periods of excessive exercise.
Adverse effects

GIT upsets and headache. Rarely sensitivity reactions or blood disorders may occur.

Drug interactions

Alcohol, azapropazone, phenylbutazone, Co-trimoxazole, sulphonamides, rifampicin, miconazole, mono-amine oxidase inhibitors diazoxide, beta-blockers, nifedipine, clofibrate, corticosteroids, loop diuretics and thiazide diuretics, octreotide, lithium, oral contraceptives and sulphinpyrazone.

Patient instructions

Follow the special diet that your doctor gave you. Avoid drinking alcoholic beverages. Eat or drink something containing sugar if you have any symptoms of low blood sugar.

14.2 Posterior Pituitary Hormones

Oxytocin

Dose

Slow IV infusion, as a solution containing 1 unit/l, 1-3 minute adjusted according to response.

Indications

In induction and augmentation of labour, to control postpartum haemorrhage and uterine hypotonicity in the second stage of labour, and to promote lactation in case of defective milk ejection.

Contraindications

Women with severe toxaemia, hypertonic uterine dysfunction, predisposed to uterine tear (high parity, uterine scar). Placenta praevia, mechanical obstruction of delivery and obvious fetal distress.

Precautions

Should be given in induction before head engagement. Hypertension and pressor drugs (reduce rate of infusion).

Adverse effects

Severe uterine contractions leading to uterine tear and foetal asphyxia, maternal hypertension, and arrhythmia.

Drug interactions

Pressor drugs and oxytocics.

Patient Instructions

Application as nasal spray: first sit, clear nasal passages, do not lie down or tilt head back, hold bottle upright into vertical position.

Intravenous injection: early contractions will feel like strong menstrual cramps.

Desmopressin Acetate

Dose

Tablets 0.1, 0.2 mg, drops, spray 0.1 mg/ml (nasal) and ampoule 0.4 mg. Transnasal 40 microgram at bedtime or tablets 400-600 mg/day for 6
weeks as trial and therapy should be continued for 2-4 months (enuresis).

**Indications**

- Diabetes insipidus. Mild to moderate hemophilia to increase factor VIII Concentration. Variceal bleeding due to portal hypertension. Enuresis.

**Adverse effects**

- Transnasal: epistaxis and nasal stuffiness. Nasal congestion (allergic rhinitis and upper respiratory infection) decreases absorption.

---

14.3 Suprarenal Cortical Hormones

14.3.1 Glucocorticoids

Glucocorticoids can improve the prognosis in conditions such as systemic lupus erythematosus, temporal arteritis and polyarteritis nodosa; in such disorders the effects of the disease process may be suppressed and symptoms relieved but the underlying condition is not cured.

They are used both topically and systemically. In emergency situations, hydrocortisone may be given intravenously; in the treatment of asthma, inhalation therapy with beclometasone may be used. Whenever possible, local treatment with creams, inhalations, eye-drops or enemas should be used in preference to systemic therapy.

The rate of withdrawal of systemic glucocorticoids is dependent upon several factors including size of dose, duration of treatment, individual patient’s response and likelihood of relapse of the underlying disease. If there is uncertainty about suppression of the HPA axis, withdrawal should be gradual to enable the adrenal gland to recover. Patients should be advised not to stop taking glucocorticoids abruptly unless permitted by their doctor.

Abrupt withdrawal may be considered in those whose disease is unlikely to relapse and who have treatment for 3 weeks or less.

**Dexamethasone**

**Dose**

- Oral, 0.5-9 mg/day. By IM or slow IV or infusion, 0.50-20 mg. In shock by IV injection or infusion 2-6 mg/kg, repeated if necessary after 2-6 hours. Cerebral oedema by IV injection 10 mg then 4 mg by IM every 6 hours for 2-10 days. Intra-articular 0.8-4 mg, injections to be repeated every 3-5 days to every 2-3 weeks. Eye drops, apply 4-6 times/day or in severe conditions every hour until controlled then reduce frequency.

**Indications**

- Cerebral oedema, congenital adrenal hyperplasia, prevention of nausea and vomiting of cancer chemotherapeutics, intra-articular and topically in eye inflammations (uveitis, scleritis and to reduce post-operative inflammation) or intra-lesional.
Contraindications
Systemic fungal infections, administration of live virus vaccines to patients receiving an immunosuppressive dosage of dexamethasone.

Drug interactions
Alcohol, aspirin, anti-inflammatory medications, warfarin, insulin, Thiazide diuretics, Phenobarbitone, rifampin, ephedrine, oral contraceptives, cholestyramine, colestipol.

Patient instructions
Do not stop taking it suddenly, if you have been taking this drug for more than 1 or 2 weeks. Never increase the dosage or take the drug for longer than prescribed. You should not be vaccinated or immunized. Blood sugar should be monitored. An ophthalmologist should examine your eyes in case of long-term treatment.

Prednisolone

Dose
Initial: 10-20 mg, up to 60 mg/day, maintenance 2.5-15 mg/day. Cushingtonoid adverse effects increase with maintenance doses above 7.5 mg/day.

Indications
In physiological doses for replacement therapy in adrenal insufficiency. In pharmacological doses to induce palliative anti-inflammatory or immunosuppressant effects.

Contraindications
Unless life saving, corticosteroid therapy should be contraindicated in peptic ulcer, psychoses and osteoporosis. Corticosteroids should be used with great caution in severe hypertension, congestive heart failure, diabetes mellitus, infectious disease, glaucoma, undiagnosed red eye, ocular herpes simplex, chronic renal failure, elderly or active tuberculosis.

Precautions
Rapid withdrawal may precipitate adrenal insufficiency, hypotension and death. During long courses of corticosteroid therapy monitor: blood pressure, blood glucose, potassium and ask for symptoms of gastric discomfort or back-pain.

Adverse effects
Diabetes mellitus, osteoporosis (especially in elderly), mental disturbances, spread of infection, peptic ulceration, Cushings syndrome, suppression of growth in children, affect fetal adrenal development and steroid cataract (daily oral prednisolone for years). Joint damage after repeated intra-articular injection and glaucoma after topical dexamethasone or prednisolone for weeks). Sodium and water retention, potassium depletion and hypertension (highest incidence with hydrocortisone, less with prednisolone and least with dexamethasone).

Drug interactions
Barbiturates, carbamazepine, phenytoin, primidone, rifampicin, thiazide
furosemide, NSAIDs, anticoagulants, antidiabetics, antihypertensives and antimuscarinics.

Patient instructions
Similar to Dexamethasone.

14.3.2 Mineralocorticoids
The major mineralocorticoid in human is aldosterone which is controlled by: Renin-angiotensin system, K+ ion directly stimulate aldosterone secretion and ACTH increases aldosterone.

Aldosterone
Dose
500 microgram have been given by slow intravenous injection or by intramuscular injection

Uses and administration: It has no anti-inflammatory effect; it is used with a glucocorticoid in the treatment of adrenocortical insufficiency.

Adverse effect: As for corticosteroid in general

14.4 Female Sex Hormones
Norethisterone
Dose
5 mg tablet bid for 3 weeks.

Indications
Metropathia haemorrhagic (dysfunctional uterine bleeding) as uterine haemostatic agent. Deficient endometrial luteal phase of the cycle e.g. premenstrual syndrome. Dysmenorrhea and endometriosis (to suppress ovulation).

Adverse effects
Oedema, nausea, headache, and cholestatic jaundice.

14.5 Contraceptives
Hormonal contraceptive is one of the most effective method of reversible fertility control, oestrogen plus progestogen combination are the most widely used, they produce a contraceptive effect mainly by suppressing hypothalamic-pituitary system resulting in prevention of ovulation, changes in endometrium make it unreceptive to implantation and changes in the cervical mucus may prevent sperm penetration.

Medroxy progesterone acetate
Dose
In dysfunctional uterine bleeding and amenorrhoea 2.5-10 mg/day for 5-10 days starting on the assumed 16th or 21st day of the cycle. In mild and moderate endometriosis 10 mg 3 times/day or 100 mg every 2 weeks by IM injection for 90 consecutive days. In breast carcinoma, 0.4-1.5 g/day, in renal, endometrial and prostatic carcinoma 100-500 mg/day.
Indications
In dysfunctional uterine bleeding, amenorrhoea, endometriosis, palliative treatment of some neoplasms and progesterone only contraceptives.

Ethinyl Oestradiol

Dose
In replacement therapy, 10-50 micro gram/day on a cyclical basis and in conjunction with a progesterone for part of the cycle (in females with uterus). In primary amenorrhoea 50 micro gram 3 times/day for 14 days every 4 weeks followed by progesterone for the next 14 days. In prostatic cancer 0.15-2mg/day, in breast cancer 1 mg 3 times/day.

Indications
Menopausal and post amenorrhea, oestrogenic component in some contraceptives, palliative treatment of some malignant neoplasms of prostate and breast in postmenopausal females and with norethisterone for disorders of menses.

Oestradiol

Dose
As oily solution to provide a depot for IM injection every 3-4 weeks.

Indications
Menopausal, postmenopausal and menstrual symptoms arising from oestrogen deficiency. Also used in the prophylaxis of post-menopausal osteoporosis.

Contraindications
Pregnancy, oestrogen-dependent carcinoma, history of thromboembolism, Dubin-johnson and Rotor syndromes, porphyria, sickle cell anemia, undiagnosed vaginal bleeding, and deterioration of otosclerosis.

Precautions
Prolonged exposure to unopposed oestrogen may predispose to endometrial carcinoma in post-menopausal females. Breast-feeding, diabetes, epilepsy, asthma, hypertension, vascular headache, cardiac or renal diseases, and history of jaundice.

Adverse effects
Nausea, vomiting, weight gain, breast enlargement, withdrawal bleeding, sodium and water retention with oedema and hypertension (minimal with replacement therapy), in liver disorders, Jaundice, thrombosis, rashes, chloasma, depression, headache and endometrial carcinoma in postmenopausal females.

Drug interactions
Cyclosporin, rifampicin, ampicillin, tetracyclines, oral anticoagulants, tricyclic antidepressants, antidiabetics, griseofulvin, antihypertensives, car-
bamazepine, phenytoin, primidone, phenobarbitone, diuretics and theophylline.

**Patient instructions**

Report if severe or persistent headache or vomiting, speech impairment, chest or abdominal pain occur. Rotate sites of injection with an interval of at least 1 week between applications to particular sites.

**Progesterone**

**Dose**

In dysfunctional uterine bleeding 5-10 mg/day IM injection for 5-10 days before the anticipated onset of menses. Habitual and in vitro fertilization 25-100 mg twice/week increased to daily if necessary from about the fifteenth day of pregnancy or embryo transfer. In pre-menstrual syndrome or puerpural depression 200-400 mg (sid or bid) on the fourteenth day of the cycle and continued till onset of menses.

**Indications**

Dysfunctional uterine bleeding, habitual abortion, in vitro fertilization (IVF) procedures, Pre-menstrual syndrome, puerpural depression and incorporated in intrauterine contraceptive devices.

**Contraindications**

Undiagnosed vaginal bleeding, missed or incomplete abortion, breast carcinoma, disturbances in lipid profile and porphyria (progesterone).

**Precautions**

Breast feeding, diabetes, hypertension, renal, hepatic or cardiac disease.

**Adverse effects**

Acne, urticaria, oedema, weight gain, GIT upsets, premenstrual symptoms, irregular menses.

**Drug interactions**

Cyclosporin, rifampicin, ampicillin, tetracyclines, oral anticoagulants, tricyclic antidepressants, antidiabetics, griseofulvin, antihypertensives, carbamazepine, phenytoin, primidone, phenobarbitone, diuretics and theophylline.

**Patient instructions**

see medroxy progesterone.

14.6 Ovulatory Stimulants

The anti-oestrogen, clomiphen citrate is used in the treatment of female infertility due to disturbances in ovulation. It includes gonadotrophin release by occupying estrogen receptors in the hypothalamus, thereby interfering with feedback mechanisms. Patients should be carefully counselled and should be fully aware of the potential adverse effects, including a risk of multiple pregnancy.

**Clomiphen**

**Dose**

50 mg/day for 5 days starting on the 5th day of the menstrual cycle. In ab-
sence of ovulation a second course of 100 mg/day for 5 days may be given. Long-term cyclical therapy is not recommended.

**Indications**

Treatment of anovulatory infertility, in conjunction with gonadotrophine invitro fertilization programmes.

**Contraindications**

Patients with liver disease or a history of liver dysfunction, endometrial carcinoma, ovarian cysts, undiagnosed uterine bleeding and during pregnancy.

**Precautions**

Patient should be warned of the possibility of multiple pregnancies. Pain may indicate the development of cystic ovaries. Visual disturbances necessitate drug withdrawal.

**Adverse effects**

Reversible ovarian enlargement, flushing, breast engorgement, pelvic discomfort, nausea and vomiting.

**Drug interactions**

Not well documented.

**Patient instructions**

This medication must not be taken during pregnancy or when pregnancy is possible. Use reliable form of birth control while taking this drug. While balanced diet, mild exercise and avoid pregnancy, caffeine, and alcohol. Report any symptoms like yellow skin or eyes, blurred vision. Careful while driving or carrying heavy equipment as blurred vision.

**14.7 Thyroid Hormones**

Thyroid gland is responsible for synthesis and secretion of thyroxine T4 and triiodothyronine T3 hormones that are essential for growth and development and regulation of energy metabolism, TSH stimulate thyroid hormone synthesis and secretion.

Thyroid hormones are used in hypothyroidism (myxoedema) and also in diffuse non-toxic goiter, Hashimoto thyroiditis (lymphadenoid goiter) and thyroid carcinoma. Neonatal hypothyroidism requires prompt treatment for normal development.

Thyroxine sodium is the treatment of choice for maintenance therapy. It is almost completely absorbed from the gastrointestinal tract but the full effects are not seen for up to 1 to 3 weeks after beginning therapy; there is a slow response to dose change and effects may persist for several weeks after withdrawal.

**Thyroxin**

**Dose**

Tablets 0.05 and 0.1 mg. Initial 0.1 mg before breakfast and maintenance 0.025-0.05 mg/day. (Slow onset 48 hours 9 days and duration 2-3 weeks with half life 7 days).
**Indications**

Hypothyroidism (medical or surgical), cretinism, myxedema, panhypopituitarism as replacement therapy. Endemic goiter to inhibit TSH production. Sterility, habitual abortion, psoriasis.

**Precautions**

In elderly and cardiac disorders (angina, heart failure).

**Adverse effects**

Signs and symptoms of hyperthyroidism minus exophthalmos e.g. dyspnoea, tachycardia, anxiety. Atrial fibrillation in old age.

**Levothyroxine sodium**

**Dose**

Initially 100 micrograms/day preferably on empty stomach (25-50 micrograms in elderly and in cardiac patients) increased by 25-50 micrograms at intervals of 2-4 weeks, reaching a usual maintenance dose of 100-200 micrograms/day.

**Indications**

Hypothyroidism, diffuse non-toxic goiter, Hashimoto's thyroiditis and thyroid carcinoma.

**Contraindications**

acute myocardial infarction, thyrotoxicosis uncomplicated by hypothyroidism.

**Precautions**

cardiovascular disorders, prolonged myxoedema and and adrenal insufficiency.

**Adverse effects**

Symptoms of hyperthyroidism, arrhythmia, anginal pain, tachycardia, excitability, flushing, diarrhoea and loss of weight.

**Drug interactions**

phenylbutazone, cholestyramine, rifampicin, oral anticoagulants, phenytoin, phenobarbitone, carbamazepine and propranolol, digitalis glycoside, iron salts, theophylline.

**Patient instructions**

medication needs to be taken for life. Take at same time each day in morning before breakfast. Not to take for weight control. Partial hair loss in child in first few months of therapy.

14.8 Drugs for Hyperthyroidism

**Carbamazole**

**Dose**

Initially 30-60 mg/day and maintained until plasma thyroxin level is normalized. Therefore, the dose is gradually tapered to a usual maintenance of 5-15 mg/day. Child, 15mg/day and adjusted according to response.
Indications

Hyperthyroidism in hope to induce life-long remission, as an adjunct to radioiodine treatment, prior to partial thyroidectomy or in hyperthyroid crisis.

Precautions

Large goiter, pregnancy and breastfeeding. Patient should be instructed to report any sore throat or rash.

Adverse effects

Rash, nausea, and vomiting and mild leucopenia. Agranulocytosis is the most serious adverse effect.

Propyl Thiouracil

Pharmacological action

Inhibits peroxidase enzyme blocking active iodine formation or by blocking iodine incorporation into organic precursors by combination with active iodine.

Dose

Initial (2 months) 200-600 mg/day and maintenance 50-200 mg/day (tablets 50 mg). Therapy is controlled by increase weight, decreased pulse rate and ankle reflex time.

Adverse effects

Failure (10%), GIT disturbance (3%) nausea, colic, diarrhoea and hypersensitivity (Rash, agranulocytosis (0.5%), lymphadenopathy, jaundice, anemia), goitrogenic effect.

Precautions

Pregnancy and lactation, fetal goiter may occur if the drug is given during pregnancy.

14.9 Hypothalamic Hormones

Octreotide

Pharmacological action

Anti-growth hormones.

Dose

Parenteral, (amp. 0.1 mg and 0.2 mg vial).

Indications

Prevention and treatment of acromegally and gigantism due to increase somatotropic hormone.

14.10 Anterior Pituitary Hormones

Tetracosatrin (synthetic ACTH)

Dose

Parenteral, (1 mg ampoule) every 3-7 days.

Indications

stimulates suprarenal cortex to secrete glucocorticoid cortisone uses: replacement therapy with prolonged glucocorticoid therapy to avoid suprarenal depression after drug withdrawal. Inflammatory or allergic
cases. To test adrenocortical function to differentiate between Cushing’s disease due to hyperplasia (Increase stimulation) and carcinoma (no effect).

14.11 Anti-Parathormone

Anti-Parathormone increased by: Reduced Ca++ and increased phosphate. Decreased by: elevate Ca++ or calcitriol and decreased phosphate.

Calcitonin
Pharmacological action
Maintains calcium blood level, homeostasis by inhibiting the bone eroding osteoclasts and bone resorption.

Dose
Amp. 50 and 100 IU and nasal spray 50,100 and 200 IU, IM or SC 100 u/day with adequate Ca and vit D. Intranasal spray 200 u in alternating nares.

Indications
In hypercalcemic state (hyperparathyroidism, vitamin D intoxication and idiopathic hypercalcemia in infancy) and osteolytic bone metastasis. To prevent or retard osteoporosis due to old age, immobilization and chronic corticosteroid therapy.

Adverse effects
spray: Rhinitis, epistaxis, arthralgia, headache and back pain. Injection: Flushing (hands and face) nausea, vomiting and local irritation (10%).

14.12 Drugs Acting on the Uterus

Ergot derivatives
Dose
1-2 mg repeated half an hour later if necessary (max.6 mg/day and 12 mg/week) co-administration of caffeine (100 mg) enhances the effect of ergotamine.

Indications
Treatment of migraine and cluster headache.

Contra indications: Severe hypertension, sepsis, peripheral vascular disease, pregnant, ischaemic heart disease, porphyria.

Precautions
Should be administered with care in severe hyperthyroidism and anemia and should not be used for prophylaxis. Discontinue in cases of numbness or tingling of extremities.

Adverse effects
Nausea and vomiting, weakness and muscle pain, symptoms of peripheral vasoconstriction and CVS disturbances, drug dependence.

Drug interactions
Caffeine, beta-blockers and macrolide antibiotics.
Patient instructions

Avoid any food to which you are allergic, and make your headache worse. Avoid exposure to cold. Elderly patients are more sensitive.

Oxytocin

see under posterior pitutray hormones.
SECTION XV

MALIGNANT DISEASES AND IMMUNOSUPPRESSIVE DRUGS

In this section:

15.1 Alkylating Agents 184
15.2 Vinca Alkaloids and Etoposide 187
15.3 Anti-Metabolites 189
15.4 Cytotoxic Antibiotics 190
15.5 Taxanes 192
15.6 Hormone and Hormone Inhibitors 192
15.7 Immunosuppressants 193
15. Malignant Diseases and Immunosuppressive Drugs

In view of their severe toxicity, the prescription of these agents should be restricted to lifethreatning conditions and their use and administration confined to experienced staff in specialized centres.

General precautions: These agents should not be administered during acute infections, with live vaccines, pregnancy or breast-feeding.

Common adverse effects: Nausea and vomiting, depression of normal cell division in bone marrow, GIT mucosa, skin, gonads, fetus. Hyperurecaemia (leading to renal failure), hypercalcaemia and alopecia. Severe pain and tissue necrosis my follow extravasations, locally.

15.1 Alkylating Agents

It is nitrogen mustard derivative. Alkylating agent forms reactive intermediates that cross-link DNA and therefore interfere with cell replication.

Cyclophosphamide

Dose

Low dose regimen: 2-6 mg/kg week in a single IV dose or in divided oral doses. Moderate dose regimen: 10-15 mg/kg/week in a single IV dose and a high dose regimen 20-40 mg/kg/week in a single IV dose every 10-20 days. Child is given initial doses of 2-8 mg/kg/day, IV oral, maintenance doses of 2-5 mg/kg twice weekly oral. For bone marrow transplantation, 60 mg/kg/day may be given for 2-4 days.

Indications

Malignant tumours including lymphoma, myeloma and several solid tumours. As an immuno-suppressant agent in polymyositis, vasculitis, systemic lupus erythrematosus, nephritic syndrome and in bone marrow and organ transplantation.

Contraindications

Haemorrhagic cystitis, acute systemic or urinary infections drug or radiation-induced urothelial toxicity, porphyria, pregnancy, breast-feeding and use of live vaccines.

Precautions

Adequate hydration and the addition of mesna is recommended to protect against haemorrhagic cystitis. Used cautiously in diabetic. Dose is reduced in elderly, debilitated, in liver or renal dysfunction or adrenalectomy. Frequent blood counts are recommended.

Adverse effect: Leucopoenia, severe and haemorrhagic cystitis, alopecia, hyperpigmentation, and GIT disturbance and hepatotoxicity.
Drug interactions
Allopurinol and suxamethonium.

Patient instructions
Drink 2-3 quarts of fluids daily and urinate frequently. Do not take oral doses at bedtime. Report any blood in the urine.

Ifosfamide
Dose
8-10 g/m2 body-surface divided over 5 days. Courses may be repeated at intervals of 2-4 weeks depending on blood counts.

Indications
In the treatments of several solid tumours, sarcoma and lymphoma.

Contraindications
Haemorrhagic cystitis, acute systemic or urinary infections, drug or radiations-induced urothelial toxicity, porphyria, pregnancy, breast-feeding and use of live vaccines.

Precautions
Adequate hydration and the addition of mesna is advised to prevent haemorrhagic cystitis. Reduce dose in renal impairment.

Adverse effects
Myelosuppression, haemorrhagic cystitis (may involve the kidneys), alopecia, hyperpigmentation and GIT disturbance, CNS Adverse effects (confusion and lethargy) and hepatotoxicity.

Drug interactions
Allopurinol and suxamethonium.

Patient instructions
Similar to cyclophosphamide.

Chlorambucil
Pharmacological action
It is nitrogen mustard derivative. Alkylating agent forms reactive intermediates that cross-link DNA.

Dose
Tablets 2 mg and 5 mg, 3-4 mg/day orally.

Indications

Adverse effects
Transient myelosuppression, dermatosis, vomiting and cholinergic stimulation (Quaternary nitrogen) and pulmonary fibrosis.
**Carboplatin**

**Pharmacological action**
Cross-link DNA and intrastrand adducts.

**Dose**
Parenteral, 50, 150 and 450 mg vial (lyophilized and non-lyophilized). Targeted by calvert equation to AUC 5-7.5 IV

**Indications**
Cancer esophagus, lung, ovary, testes and bladder.

Major toxicity: Myelosuppression (especially thrombocytopenia), nausea and vomiting.

**Precautions**
Maintain adequate hydration of the patient during drug infusion. Renal, hematological, auditory and neurological functions should be monitored during therapy and dose adjusted accordingly.

**Adverse effects**
Severe nausea, vomiting and nephrotoxicity (less with carboplatin), bone marrow depression, hypomagnesaeemia, ototoxicity (severe in children) and neuropathies.

**Drug interactions**
Nephrotoxic and ototoxic drugs.

**Patient Instructions**
See mitomycin

**Asparaginase**

**Pharmacological action**
Some tumor cells cannot synthesize asparagine, which is essential for protein synthesis. Asperginase hydrolyse Asparagine depriving tumors of exogenous protein.

**Dose**
IV infusion of 1000 units/kg/day for 10 days in a solution of saline or glucose 5% given over 30 minutes.

**Indications**
Induction of remission in childhood acute lymphoblastic leukemia in combination with other drugs.
Contraindications
Pancreatitis.

Precautions
A test dose of 50 units is recommended to test for allergy. Pretreatment with asparginase may be associated with increased risk of allergic reactions. Administered cautiously in patient with liver dysfunction.

Adverse effects
Anaphylaxis, liver, renal or pancreatic dysfunctions, GIT upsets and acute leucopenia.

Drug interactions
Methotrexate and vincristine.

Patient instructions
Similar to cisplatin.

15.2 Vinca Alkaloids and Etoposide
Vincristine
Pharmacological action
Block mitosis and produse metaphase arrest.

Dose
IV injection of solution containing 0.1-1 mg/ml saline. In acute Leukemia, for induction of remission in children, 50 mg/kg/week, increasing by weekly increments of 25 mg/kg to a maximum of 150 mg/kg. In adults, 25-75 mg/kg/weekly.

Indications
Acute leukemia and lymphomas (Hodgkin’s and Burkitt’s) and some solid tumours.

Contraindications
Patients with the demyeling form of Charcot – Marie – Tooth syndrome and the intrathecal route.

Precautions
Add laxatives or enema to avoid constipation. Given cautiously in elderly or patients with re-existing neuromuscular disorder. Reduce dose in hepatic disease. Avoid extravasations. Blood counts are needed before each course.

Adverse effects
Myelo-suppression (less than vinblastine). Neurological and neuromuscular affects are more severe and are dose – limiting (impaired walking, convulsions), hypertension, constipation, abdominal pain, alopecia, and urinary disturbances.

Drug interactions
Asparaginase.

Patient instructions
Similar to cyclophosphamide.
Vinblastine

Dose

IV solution containing 1mg/ml in saline. Weekly injections of 100 mg/kg raised by increments of 50 mg/kg to a maximum weekly dose of 500 mg/kg. A maintenance dose is then given of 10 mg once or twice/month. CHILD, initially, 2.5mg/m2 body-surface increased by 1.25mg/m2/week to a maximum of 7.5 mg/m2.

Indications

In the treatment of testicular cancer and lymphomas (Hodgkin’s disease and mycosis fungoides) and in some inoperable solid tumours.

Contraindications

In elderly patients with cachexia or skin ulceration or by intrathecal route.

Precautions

Should not be injected in extremities with poor circulation to minimize risk of thrombosis. Avoid extravasations. Blood counts are needed before each course. Reduce dose in hepatic impairment.

Adverse effects

Myelo-suppression (leucopenia), GIT toxicity (stomatitis, bleeding, nausea and vomiting), CNS toxicity (central and peripheral neuropathy) and inappropriate secretion of anti-diuretic hormone.

Drug interactions

Mitomycin, paracetamol.

Patient instructions

Similar to cyclophosphamide.

Etoposide

Dose

Slow IV infusion in saline or 5% glucose of 50-120-mg/m2 body surface/day for 5 days. Courses may be repeated after 3-4 weeks.

Interactions: Usually with other antineoplastics in refractory tumours of the testis and cancers of lungs. Also tried in other solid tumours, some childhood neoplasms, lymphomas and acute non-lymphocytic leukemia.

Contraindications

Not given to patients with hepatic dysfunction or by intrathecal route.

Precautions

Should be given by infusion over at least 30 minutes to avoid hypotension. Avoid extravasations.

Adverse effects

Myelo-suppression (mainly leucopenia), GIT disturbances (after oral administrations), peripheral and central neuropathies, alopecia, disturbance of liver function and cardiotoxicity.
Drug interactions

With vincristine possible synergistic neuropathy. With Anthracyclines possible cardiomyopathy. Also interact with cyclosporin, phenytoin, Phenobarbital.

Patient instructions

Report any signs of infection such as fever, shaking Chills. Avoid use of aspirin-containing products and alcohol. Hair loss can occur. Dose should never be doubled or extradoses taken.

15.3 Anti-Metabolites

Fluorouracil

{pyrimidine analogue}

Dose

12mg/kg/day IV for 3-4 days. With no evidence of toxicity, this may be followed by 6 mg/kg on alternative days for 3-4 other Nate days for 3-4 other doses. IV infusion, 15mg/kg/day infused in 500 ml saline or glucose 5%, infused over 4 hours and repeated on successive days until toxicity occurs or a total of 12-15 g has been given.

Indications

Solid tumours (breast and colon) and applied topically in solar keratoses and superficial neoplasm's of the skin.

Precautions

Slow infusion decreases hematological toxicity. Frequent blood counts are necessary. Doses should be halved in patients with a poor nutritional state, hepatic or renal dysfunction or after major surgery.

Adverse effects

Myelo-suppression, GIT toxicity, cerebral ataxia and ocular irritation.

Drug interactions

Cimetidine.

Patient instructions

Similar to cyclophosphamide.

Methotrexate

Pharmacological action

It is folic acid analouge.

Dose

Leukemia in children, 15 mg/m2 weekly in combination with other drugs. Psoriasis, 10-25 mg/week.

Indications

Choriocarcinoma, some solid tumours, non-Hodgkin lymphomas and as a maintenance therapy in childhood acute lymphoblastic leukemia. Intrathecal methotrexate is used in the CNS prophylaxis of childhood lymphoblastic leukemia and as a therapy for established meningal carcinoma or lymphoma. Also used in severe psoriasis and rheumatoid arthritis.
Contraindications
Severe renal impairment, significant pleural effusion or ascites, porphyria.

Precautions
Frequent blood counts are necessary. Folic acid supplementation decreases Adverse effects. Reduce dose in renal impairment. Maintain adequate flow of alkaline bomb.

Adverse effects
Myelosuppression (leucopenia, thrombocytopenia and anemia), GIT disturbances, stomatitis and diarrhoea are early signs of toxicity and treatment should be interrupted.

Drug interactions
NSAIDs, trimethoprim, co-trimoxazole, pyrimethamine, probenecid, and etretinate (anti-psoriasis).

Patient instructions
Similar to cyclophosphamide.

15.4 Cytotoxic Antibiotics
They interfere with replication of cells by DNA damage; they form one group of cytotoxic drugs. They intercalate DNA causing strand cession. (Anti-neoplastic).

Doxorubicin
Dose
Given as a single agent in doses of 60-75 mg/m² body-surface as a single dose through a running IV infusion of saline or glucose 5 % repeated every 3 weeks. The maximum total dose should not exceed 550 mg/m². Doses decreased if given with other anti-neoplastic drugs.

Indications
In the treatment of acute leukemia, lymphomas, sarcomas, neuroblastoma and some solid tumours.

Contraindications
Previously serious allergy to the drug or any component of the formulation.

Precautions
Pregnancy and lactation.

Adverse effects
Emetic potential, acute back pain, flushing, chest tightness, mild anemia, diarrhoea, opportunistic infections, myelosuppression (Neutropenia).

Drug interactions
Not all studied.

Patient instructions
Similar to etoposide.
Mitomycin

Dose
Initially, 10-20 mg/m² body surface given as a single dose through a running IV infusion and repeated every 6-8 weeks. Subsequent doses are adjusted according to the effect on bone marrow.

Indications
In the palliative treatment of GIT, bladder tumours.

Contraindications
Impaired renal functions or coagulation disorders.

Precautions
The simultaneous use of radiotherapy should be avoided. Frequent blood counts are necessary. Avoid extravasations.

Adverse effects
Delayed bone marrow depression, renal and pulmonary damage.

Patient instructions
Similar to idorubicin.

Epirubicin

Dose
Given in doses of 75-90 mg/m² body surface as a single dose through a running IV infusion of saline or glucose 5% over 3-5 minutes repeated every 3 weeks. A total cumulative dose of 0.9-1 g/ml should not be exceeded.

Indications
Tried alone or in combination with other drugs in the treatment of acute leukemia, lymphomas and some solid tumours.

Contraindications
Previously serious allergy to the drug or any component of the formulation.

Precautions
Pregnancy and lactation.

Adverse effects
Emetic potential, acute back pain, flushing, chest tightness, mild anemia, diarrhoea, opportunistic infections, myelosuppression (neutropenia).

Drug interactions
Not all studied.

Patient instructions
Similar to doxorubicin.

Idarubicin

Dose
Given in doses of 12 mg/m² body surface daily for 3 days through a running IV infusion of saline or glucose 5% over 5-15 minutes repeated.
**Indications**

Used alone or in combination to induce remission in patients with acute non-lymphoblastic leukemia and in the management of some solid tumours.

**Contraindications**

Patients with heart disease.

**Precautions**

The simultaneous use of radiotherapy should be avoided. Patient who already received irradiation or elderly should be treated cautiously. Dose should be halved in patient with moderate liver dysfunction and those with severe impairment given a quarter of the dose. Frequent blood counts and assessment of cardiac functions are necessary. Avoid extravasations.

Adverse effect: Nausea, vomiting, myelosuppression, cardiomyopathy (more with doxorubicin), alopecia and mucositis

**Drug interactions**

Clindamycin, daunorubicin, cyclophosphamide, methotrexate and streptozocin.

**Patient instructions**

Similar to epirubicin.

**15.5 Taxanes**

**Paclitaxel**

**Dose**

Parenteral, (30mg vial). 135 mg/m² IV over 3 or 24 hours every 3 weeks.

**Pharmacological action**

Promotes microtubule assembly and arrests cell cycle in G2 and M phases.

Major Toxicity: Hypersensitivity reactions, cardiac disturbances, sensory neuropathy, myalgia and arthralgia.

**Indications**

Cancer ovary, bladder, lung and breast.

**15.6 Hormone and Hormone Inhibitors**

**Tamoxifen**

**Pharmacological action**

It is anti estrogen that competes with estrogen for Estrogen receptors, protein of estrogen sensitive tissue and tumer.

**Dose**

In the treatment of breast cancer, 20-40 mg/day. In infertility, 10 mg twice/day on day 2, 3, 4 and 5 of the menstrual cycle (increase to 40 mg on the next cycle if necessary).
Indications
As an adjuvant endocrine therapy in early breast cancer and for palliation in late cases. It is also used to stimulate ovulation in women with anovulatory infertility.

Contraindications
Pregnancy, porphyria.

Precautions
In women with functioning ovaries.

Adverse effects
Hot flushes, vaginal bleeding, amenorrhea, GIT upsets, exacerbations of bony pains and hypercalcemia in patients with bone metastasis, visual disturbances and increased tendency to thrombo-embolism.

Drug interactions
Oral anticoagulants.

Patient instructions
Similar to asparginase.

15.7 Immunosuppressants
Used in organ transplant to suppress rejection, they are used as second line drugs in chronic inflammatory condition. Blood count is required and the dose should be adjusted to prevent bone marrow toxicity.

Cyclosporin

Dose
Organ transplantation; 14-17.5 mg/kg/day as a single dose by mouth form day before transplantation followed by 14-17.5 mg/kg/day for 1-2 weeks post-operatively, then tailed off at intervals of 1 month in steps of 2 mg/kg/day to 6-8 mg/kg/day for maintenance. Lower doses are given if corticosteroids are given concomitantly. In prevention of graft-versus-host disease; 3-5 mg/kg/day by IV infusion over 2-6 hours from day before transplantation to 2 weeks post-operatively, then 12.5 mg/kg/day by mouth for 3-6 months and then tailed off.

Indications
It is used in organ and tissue transplantation for the prophylaxis of graft rejection or in the management of rejection in patients previously treated with other immuno-suppressants. It is also used in some autoimmune disorders (Behcet disease and aplastic anaemia).

Contraindications
Porphyria, pregnancy and breastfeeding.

Precautions
Monitoring of drug concentration is mandatory in all patients. Dosage reduction in renal impairment.
Adverse effects

Nephrotoxicity, hypertensions, electrolyte disturbances, GIT disorders, hepatotoxicity, neurotoxicity and tremor, parasthesias in extremities and convulsions. Increased incidence of the development of lymphoma.

Drug interactions

Amino glycosides, ciprofloxacin, cotrimoxazole, rifampicin, erythromycin, phenobarbitone, phenytoin, primidone, amphotericin, fluconazole, ketoconazole, ACE inhibitors, calcium channel blockers, potassium sparing diuretics, danazol, potassium salt and progesterone.

Patient instructions

Similar to tamoxifen.
SECTION XVI

NUTRITION AND BLOOD RESTORATIVE DRUGS

In this section:

16.1 Vitamins 196
16.2 Minerals 200
16.3 Blood Restorative 202
16.4 Plasma Proteins and Plasma Expanders 204
16. Nutrition and Blood
Restorative Drugs

16.1 Vitamins

Vitamins are divided according to solubility into water soluble which includes vitamin C and vitamin B complex. And, fat soluble which includes: A, E, D and K vitamins. Vitamins are used for the prevention and treatment of specific deficiency states or when the diet is known to be inadequate. It has often been suggested but never convincingly proved, that subclinical vitamin deficiencies cause much chronic ill-health and liability to infections. This has led to enormous consumption of vitamin preparations, which have no more than placebo value. Most vitamins are comparatively non-toxic but prolonged administration of high doses of retinol (vitamin A), ergocalciferol (vitamin D$_2$) and pyridoxine may have severe adverse effects.

**Beta-carotene**

It is in form of fibres included in different formulations given before meals in treatment of obesity or given with other vitamins and herbs as antioxidant and tonic. It is converted to vitamin A in intestinal wall and yields 2 molecules.

**Folic Acid**

Folic acid is essential for the synthesis of DNA and certain proteins. Deficiency of folic acid or vitamin B$_{12}$ is associated with megaloblastic anemia unless vitamin B$_{12}$ is administered concurrently, otherwise neuropathy may be precipitated.

**Dose**

Folate-deficient megaloblastic anemia 5mg/day for 4 months, up to 15 mg/day in malabsorption states. In prophylaxis, 5mg/day or even weekly. In pregnancy 200-500 micrograms/day.

**Indications**

Folate-deficient megaloblastic anemia occurring with poor nutrition, malabsorption syndromes, antiepileptic drugs, and in pregnancy. Prophylaxis of folic acid deficiency in chronic haemolytic states, renal dialysis and pregnancy.

**Contraindications**

Undiagnosed megaloblastic anemia, alone in Addisonian pernicious anemia, other vitamin B deficient state and malignancy.

**Precautions**

Women receiving antiepileptic therapy need counseling before starting.

**Adverse effects**

Rarely G.I.T upsets and hypersensitivity reactions

**Drug interactions**

Antiepileptic drugs.
**Vitamin A**

Vitamin A has a number of important function in the body. It plays an essential role in the function of the retina. It is necessary for growth and differentiation of epithelial tissue and is required for growth of bone, reproduction and embryonic development. Together with certain carotenoids, it appears to enhance the function of the immune system, to reduce the consequence of some infectious disease, and to protect against the development of certain malignancies.

**Dose**

In treatment of xerophthalmia, 200,000 units of vitamin A should be given on diagnosis. The dose is repeated next day and an additional dose given 2 weeks later. Child less than 1 year, given half the dose.

**Indications**

Prophylaxis and treatment of vitamin A deficiency states especially in susceptible periods (infancy, pregnancy and lactation) or in patients with steatorrhea, severe biliary obstruction or liver cirrhosis. In some skin disorders e.g. acne, psoriasis and Dariers disease.

**Contraindications**

Hepatic disease, hypercholesterolemia, hypertriglyceridemia, sunburn, retinoid hypersensitivity.

**Precautions**

Large doses during the first trimester of pregnancy.

**Adverse effects**

Large doses may lead to hypervitaminosis A characterized by dry pruritic skin, disturbed hair growth, anorexia, oedema, lip fissures and pathological hepatic changes. In infants signs of increased intracranial tension are early signs of toxicity.

**Drug interactions**

Benzoyl peroxide, cimetidine, diltiazem, erythromycin, verapamil, salicylic acid, rifampin, ketoconazole, phenobarbital.

**Patient instructions**

Do not take more than the recommended doses.

**Vitamin E**

Vitamin E displays no notable pharmacological effects or toxicity. In acting as an antioxidant, Vitamin E presumably prevents oxidation of essential cellular constituents. Signs of vitamin E deficiency include structural and functional vitamin E abnormalities of many organs and organ systems. Attending these morphological alterations are biochemical defects that appear to involve fatty acids metabolism and numerous other enzyme systems. Notable is the fact that many deficiency signs and symptoms in animals superficially resemble disease states in humans.
Dose
100 IU capsules and fort 400 IU capsules. Daily requirement 10-30 mg.

Pharmacological action
Anti-oxidant and anti-sterility.

Indications
Vitamin supplements, muscular dystrophy, peripheral vascular disease cardiopathies and megaloblastic anemia.

Vitamin B₁₂ Cyanocobalamin
Metabolic functions of vitamin B₁₂

The coenzymes are essential for cell growth and replication. They are essential for maintenance of normal myelin sheath and maturation of other cell types. They are required for methionine synthesis and isomerization of methylmalonyl COA to succinyl COA.

Dose
In treatment of deficiency states 250-1000 micrograms on alternate days for 1-2 weeks then 250 micrograms/week till blood counts return to normal. Maintenance dose is 1000 micrograms/month in presence of neurological deficits 1000 micrograms are given on alternate days till signs of improvement occur. In prophylaxis of vitamin B₁₂ deficiency 250-1000 micrograms/month.

Indications
Prophylaxis and treatment of vitamin B₁₂ deficiency states, which may occur in strict vegetarians, malabsorption syndromes, following gastrectomy and in pernicious anaemia.

Precautions
should be administered after confirmation of diagnosis.

Adverse effects
Hypersensitivity reactions.

Drug interactions
Aminoglycosides, aminosalicylic acid, anticonvulsants, biguanides, chloramphenicol, cholestyramine, cimetidine, colchicine, potassium salts, methyldopa and oral contraceptives.

Cholecalciferol and Ergocalciferol
The term vitamin D covers a range of compounds including ergocalciferol (vitamin D₂) and cholecalciferol (vitamin D₃) which are equipotent and either can be used to prevent and treat rickets.

Simple deficiency of vitamin D occurs in those who have an inadequate dietary intake or who fail to produce enough cholecalciferol in their skin in response to ultraviolet light.
Dose
In prevention of vitamin D deficiency 10 micrograms (400 units)/day. In treatment up to 1mg (40,000 units)/day. In treatment of hypocalcaemia up to (200,000)/day.

Indications
Prophylaxis and treatment of vitamin D deficiency states and in hypocalcaemia of hypoparathyroidism.

Contraindications
Hypercalceamia, metastatic calcification.

Precautions
Breast-feeding with large doses. With the administration of large doses check plasma calcium concentrations.

Adverse effects
Overdose may lead to anorexia, lassitude, nausea, vomiting, diarrhoea, thirst, weight loss and increased calcium and phosphate in plasma and urine.

Drug interactions
Barbiturates and anticonvulsants, digitalis glycoside, thiazide diuretics, verapamil, mineral oil.

Patient instructions
Avoid simultaneous use of mineral oil while taking vitamin D. Avoid use of nonprescribing drugs including magnesium-containing antacids and multivitamin containing vitamin D.

Vitamin B complex
Indications
Deficiency states, which may be severe with chronic alcoholism.

All items see vitamin B_6, B_12.

Vitamin K activity is associated with at least two distinct natural substances designated as vitamin K_1 and vitamin K_2:

Vitamin K (phytomenadione)
Vitamin K_1 is found in plants and it is the only natural vitamin K available for therapeutic use.

Dose
10 mg tablets and 10 mg amp (1-50 mg repeated after 8 hours IM or IV)

Pharmacological action
Stimulates hepatic synthesis of coagulant factors, prothrombin. Most rapid action (within 4 hours) and not toxic.

Indications
In bleeding disorders due to deficiency of uptake or malabsorption from intestine in obstructive jaundice (injection) and coumarin anticoagulant toxicity.
Vitamin C (Ascorbic Acid)

**Dose**
Prophylaxis of vitamin C deficiency states 25-75 mg/day. Treatment of scurvy up to 1g/day in divided doses.

**Indications**
Treatment of scurvy, to control idiopathic methemoglobinaemia and in urine acidification. (The use of vitamin C in respiratory infections and wound healing is not yet scientifically proved).

**Precautions**
Use with caution in kidney stones or a history of kidney stones, vitamin C appears in milk, consult your doctor before you begin breast-feeding.

**Adverse effects**
Large doses for long time lead to kidney stones (oxalate), rebound scurvy in persons taking large doses and suddenly stop and in the off-spring of mother taking large doses.

**Drug interactions**
The following drugs interact with vitamin C: Contraceptives, sulphonamides, warfarin.

---

16.2 Minerals

16.2.1 Calcium Salt

**Calcium Gluconate**

**Dose**
In osteoporosis oral 800 mg/day. In hypocalcaemia tetany or hyperkalemia, initial IV injection of 10mL (2.25 mmol) following by continuous IV infusion of 40mL (9 mmol)/day.

**Indications**
Prevention and treatment of deficiency childhood, pregnancy, lactation and old age, osteoporosis, hypocalcaemic tetany, hyperkalaemia and in cardiac resuscitation.

**Contraindications**
Conditions associated with hypercalcaemia, hypercalciuria (some firms of malignant disease)

**Precautions**
In parenteral injection, monitor calcium plasma concentration. Avoid IM injection in children.

**Adverse effects**
Bradycardia, arrhythmia and irritation after IV administration.

**Drug interactions**
Tetracycline, cardiac glycosides and thiazide diuretics.
Calcium Carbonate

It is used in treatment of renal osteodystrophy (renal rickets) in chronic renal failure due to reduced ability to convert 25 (OH) D3 to calcitriol. Aluminium deposition in bone may also play a role. Oral calcium carbonate is a phosphate binder and calcium supplement.

16.2.2 Ferrous salt

Iron (ferrous salts)

Dose

Therapy 120-180 mg/day in divided doses. Prophylaxis 60 mg/day. Child therapy in divided doses up to 1-year 36 mg/day; 1-5 year’s 72 mg/day; 6-12 years 120 mg/day.

Indications

Iron deficiency anaemia.

Contraindications

Haemosiderosis, hemochromatosis, patient receiving repeated blood transfusion, parenteral iron therapy.

Precautions

Should not be administered for longer than 6 months, pregnancy, peptic ulcer, regional enteritis, and ulcerative colitis.

Adverse effects

G.I.T upset in the form of altered bowel habits, nausea and epigastric pain.

Drug interactions

Magnesium trisilicate, tetracyclines, ciprofloxacin, levodopa, penicillamine, zinc.

Zinc salt

Dose

Effervescent tablets 1 tablet in water 1-3 times/day after meals.

Indications

Zinc deficiency, which may occur with inadequate diet intake, malabsorption states or increased body loss in trauma and burns and with IV feeding.

Contraindications

Fluoroquinolones (ciprofloxacin), tetracyclines (oxytetracyclin).

Precautions

Allergy to zinc supplements, not recommended during pregnancy.

Adverse effects

Abdominal pain and dyspepsia.

Drug interactions

Iron, tetracyclines, ciprofloxacin and penicillamine.

Patient instructions

If stomach upset or nausea occurs, take with food or liquid. Avoid taking with foods high in bran, calcium, phosphorus or phytate.
16.3 Blood Restorative

Electrolytes for Infusion

These are indicated in cases of hemorrhage, shock, distributed electrolytes in blood or for supplying fluids or food for patients who are unable to maintain oral intake.

Potassium Chloride 15%
(parentral)

**Dose**

10-40 m Eq/hour IV

**Indications**

In electrolyte imbalance.

**Contraindications**

Several renal impairment with concomitant oliguria, hyperkalaemia, renal failure, anuria, trauma, use of potassium sparing diuretics.

**Precautions**

The concentration of the IV Infusion not exceeds 3.2 g/ml, pregnancy category c, lactation, and decreased renal functions.

**Adverse effects**

Minor: diarrhoea, nausea, stomach pains, vomiting. Major: anxiety, bloody or black, tarry stools, confusion, difficulty in breathing, unusual weakness, abdominal pain.

**Drug interactions**

Amiloride, spironolactone, triameterene leads to hyperkalemia. Digoxin leads to heart problems.

**Potassium Chloride (oral)**

**Dose**

In prophylaxis, 2-4 g/day (smaller doses are given in renal impairment). For treatment, 10-15 g/day for days or weeks.

**Indications**

In prophylaxis and treatment of potassium depletion.

**Contraindications**

Renal failure and in cases where plasma potassium concentration is above 5 mmol/L.

**Precautions**

Intestinal stricture and history of peptic ulcer.

**Adverse effects**

Nausea, vomiting, oesophageal and small bowel ulceration.

**Drug interactions**

ACE inhibitors, cyclosporin, and potassium sparing diuretics.

**Patient instructions**

Take after meals with food and full glass of water. Swallow tablets whole,
without chewing, sucking or crushing. Warn patient not to use salt substitutes and to avoid salt free food. Avoid ingestion of large amounts of potassium through excessive intake of foods such as avocados, bananas, broccoli.

**Sodium Bicarbonate 4.2 % and 8.4 %**

**Dose**

In severe acidosis, sodium bicarbonate 1.26 % should be infused with isotonic saline. A total volume up to 6 L (4L sodium chloride and 2 L sodium bicarbonate) may be necessary in adults. In severe acidosis without depletion 50 ml of 8.5% are IV administered.

**Indications**

Treatment of metabolic acidosis and in the emergency management of hyperkalemia.

**Contraindications**

Loss of chloride from vomiting. Hypertension, hypocalcemia, convulsions or CHF.

**Precautions**

Monitor plasma pH.

**Adverse effects**


**Drug interactions**

Amphetamine, dextroamphetamine, ephedrine, pseudoephedrine, dobutamine, dopamine, and ketoconazole, lithium.

**Patient instructions**

Do not take with milk.

**Ringer lactate solution**

**Indications**

Diabetic ketoacidosis.

**Contraindications**

Metabolic acidosis and impaired hepatic function. Avoid OTC medications containing sodium bicarbonate. Not to use maximum dose of antacids for more than 2 weeks

**Precautions**

Allergy to pyridoxine. Pyridoxine appears in breast milk, consult your doctor before begin breast-feeding.

**Adverse effects**

Large doses (2 mg/day) for a long time lead to severe peripheral neuropathy.

**Drug interactions**

Levodopa, isoniazid, penicillamine and oral contraceptives.

Patient interactions: Enteric-coated tablets do not cut, crush or chew, and swallow whole with a glass of water.
Common source of vitamin B6. (Liver, eggs, meat, whole-grain, bread and cereals, soybeans, vegetables).

**Sodium Chloride 0.18% plus Dextrose 5%**

**Indications**
Replacement of fluid and electrolytes in case of combined sodium chloride and water depletion as in persistent vomiting.

**Precautions**
Restrict intake in renal impairment, heart failure and in hypertension, peripheral and pulmonary oedema, and toxaemia of pregnancy. Jugular venous pressure should be assessed.

**Adverse effects**
Administration of large doses may give rise to sodium accumulation and oedema.

**Sodium Chloride 0.9 % and 0.45 %**

**Dose**
In severe depletion (4-8 L) give 2-3 l of 0.9 % over 2-3 hours thereafter at slower rates.

**Indications**
Sodium depletion as in gastroenteritis, diabetic ketoacidosis, ileus and ascites.

**Precautions**
Assess central venous pressure and avoid excessive administration. Restrict intake in impaired renal function. Cardiac failure, pulmonary oedema, toxaemia of pregnancy.

**Adverse effects**
Administration of large doses may give rise to sodium accumulation and oedema.

**16.4 Plasma Proteins and Plasma Expanders**

The plasma volume is contracted as a result of simple loss of fluid and electrolytes as in chlorea, diabetic ketoacidosis or Addison's crisis which may be corrected by simple replacement of fluids and electrolytes.

Ideal plasma expander should: Have a high MW to be retained in the circulation for sufficient time. Have an osmotic pressure comparable to that of plasma. Not have an antigenic, allergic, pyretic or toxic effects. Not interfere with typing or cross matching of blood. Being pharmacologically inert, except for its physical properties. Being stable on storage, easily sterilized and transported. Have a suitable viscosity.

**Human Albumin (4-5%)**

**Dose**
Plasma albumin level 2.5 positive or negative 0.5 g/100 ml.
**Indications**

Acute or sub-acute loss of plasma volume in burns, trauma and complications of surgery and in plasma exchange

**Human Albumin (20-25%)**

**Dose**

Total plasma protein level 5.2 g/100 ml, this is best achieved with albumin 25% solution.

**Indications**

Severe hypoalbuminemia associated with decreased plasma volume and generalized oedema and as adjunct in the management of hyperbilirubinemia by exchange transfusion in the newborn.

**Contraindications**

Heart failure and severe anemia.

**Precautions**

History of CVS disorders, risk of further hemorrhages or shock due to rise in blood pressure. Correct dehydration when administrating the concentrated solution.

**Adverse effects**

Hypotension after rapid infusion. Allergic or pyogenic reactions fever and chills.

**Patient instructions**

Monitor for dehydration, patient may require additional fluids. Do not administer if solution is cloudy. Administer slowly. Do not dilute.

**Dextrans 70 (6% Dextran in saline or 5% dextrose)**

**Dose**

IV infusion after moderate to severe haemorrhage, 500-1000 ml rapidly initially followed by 500 ml later if necessary. In severe burns, up to 3000 ml in the first few days with electrolytes.

**Indications**

In short-term blood volume expansion and in the prophylaxis of post surgical thrombo-embolic disease.

**Contraindications**

Severe congestive heart failure, renal failure, bleeding disorders such as thrombocytopenia.

**Precautions**

Congestive heart failure, renal impairment. Blood samples for cross matching should ideally be withdrawn before dextran infusion.

**Adverse effects**

Rarely anaphylactic reaction, urticarial and other hypersensitivity.

**Drug interactions**

Dextran may interfere with blood group cross matching or biochemical measurements and these should be carried out before the infusion.
SECTION XVII

SKELETAL MUSCLE RELAXANTS

In this section:

17.1 Central Muscle Relaxants 207
17.2 Peripheral Muscle Relaxants 207
17.3 Antirheumatics 209
17.4 Antigout 213
17. Skeletal Muscle Rela-
xants
They include two major groups: Neuro-muscular blockers: Cause paralysis and are used during surgical procedures. Their site of action is at the NMJ. Spasmolytics: They are used to decrease spasticity in neurological conditions as low back syndrome and rheumatism with muscle spasm.

17.1 Central Muscle Rela-
xants
They act on the spinal cord and subcortical brain areas inhibiting multisynaptic reflexes involved in producing and maintaining muscle spasm. They don’t directly relax tense muscles.

Orphenadrine
Dose
100 mg tablets orally 2-3 times daily.

Indications
Skeletal muscle spasticity, painful muscle spasms in neuromuscular, musculoskeletal disorders e.g. myalgia, rheumatic diseases.

Contraindications
Myasthenia gravis, motor weakness, myopathy with decreased muscle tone.

17.2 Peripheral Muscle Relaxants
They are injected intravenously as anesthetic adjuvents to produce muscle relaxation during general anaesthesia.

Pancuronium Bromide
Dose
Adult and children IV 0.06-0.1 mg/kg, neonate IV 0.02 mg/kg.

Indications
Induction of non-depolarizing muscle relaxation of medium duration.

Contraindications
Severe respiratory insufficiency.

Precautions
Hepatic impairment, respiratory insufficiency, history of asthma or hypersensitivity, to neuromuscular blockers. Reduce dose in obesity and in renal impairment. Patients should have their respiration assisted or controlled until drug is antagonized.

Adverse effects
Dose-related tachycardia, slight hypotension.

Drug interactions
Aminoglycosides, clindamycin, lincomycin, polymyxins, verapamil, quinidine, propranolol, cholinergics, parenteral magnesium and lithium.
**Patient instructions**

Reassure patient that breathing will return to normal after pancuronium is discontinued. Maintain calm environment.

**Atracurium Besylate**

**Dose**

25-50 mg amp. Initial dose 0.5 mg/kg, onset 2-3 min and duration 20-45 min.

**Indications**

They are anesthetic adjuvents in thoracic and upper abdominal operations. Aids endoscopy (laryngo-, broncho- and esophagoscopy), for endotracheal intubations, ECT therapy, orthopedic manipulations (fractures or dislocations), stabilization of chest wall in chest crush injury, control muscle spasms in acute convulsive states (tetanus, drugs...), to rest motor end-plate in myasthenia gravis crisis.

**Drug interactions**

Ether, chlorpromazine and aminoglycosides (potentiation).

Antagonists: Neostigmine methyl sulphate 1-2.5 mg with atropine 1mg to avoid excessive vagal stimulation.

Elimination: Renal (less than5%) and ester hydrolysis in plasma (Hoffmann elimination is pH and temperature-dependent process) with laudanosine product which has CNS stimulant in high concentration, under goes renal and hepatic elimination.

---

**Gallamine Triethiodide**

**Dose**

40 mg IV (1 mg/kg for adults and 4mg/year age for children) as non-depolarizing muscle relaxant. It has 1/5 curare activity, rapid immediate onset (2-3 min), and duration 15-30 min with selective parasympatholytic action on heart sinus bradycardia and arrhythmias.

**Contraindications**

In patients sensitive to iodides and renal disorders (mainly renal excretion).

**Neostigmine**

**Dose**

For several of non-depolarizing neuro-muscular blockers: I. V injection, 1-5 mg after or with atropine sulphate 0.6-1.2 mg. Others, oral, 15-30 mg with a total dose of 75-300 mg/day (usually maximum tolerated dose is 180 mg/day).

**Indications**

Reversal of non-depolarizing neuro-muscle blockers and in myasthenia gravis. As antidote for certain muscle relaxant drugs used during surgery. To prevent and treat distension and urinary retention following surgery.

**Contraindications**

Intestinal or urinary obstruction, recent intestinal or bladder surgery.
Precautions
Asthma, bradycardia, recent myocardial infarction, epilepsy, Parkinsonism, hypotension, vagotoniapeptic ulceration and in pregnancy.

Adverse effects
Nausea, vomiting increased saliva-tion, diarrhoea and abdominal cramps, muscle spasm. Overdose: Cholinergic crisis, rash associated with bromide salt, hypotension.

Drug interactions
Quinidine, clindamycin, lincomycin, polymyxins, propranolol, chloroquine, muscle relaxants (depolarizing and non-depolarizing) and lithium.

Patient Instructions
Inform physician if adverse effects occur. Long term use may induce toler-ance, which requires dosage ad-justment.

17.3 Antirheumatics
17.3.1 Non steroidal anti-inflammatory Drugs (NSAIDs)
Non-opioid analgesics are particularly suitable for pain in musculoskeletal condition, wherease the opioid analgesics are more suitable for moderate to severe visceral pain. Low concentra-tion of aspirin and indomethacin inhibit the enzymatic production of prostaglandins, prostaglandins are released whenever cell are damaged and appear in inflammatory exudates, non steroidal anti-inflammatory drug inhibit the biosynthesis and release of prostaglandin.

However the NSAIDs do not generally inhibit the formation of eicosanoids such as leukotrienes which also contribute to inflammation, nor do they affect the synthesis of numerous other inflammatory mediators. Non opioid analgesic with anti-inflammatory activity include salicylates such as acetyl salicylic acid and other NSAIDs such as ibuprofen. Non opioid analgesic with little or no anti-inflammatory activity include paracetamol.

Acetyl Salicylic Acid
Aspirin (acetyl salicylic acid) is still the most widely prescribed analgesic-antipyretic and anti-inflammatory agent, and it is the standard for comparison and evaluation of the others.

Dose
300-900 mg every 4-6 hours, when necessary, maximum 4 mg daily.

Indications
Used for mild to moderate pain, fever, inflammation and the prevention of myocardial infarction and stroke.

Contra indications: GIT ulcer, gout, bleeding tendencies and allergy. Chil-dren under 12 years and with breast-feeding, pregnancy, asthma and nasal polyps.
Precautions
Asthma, allergic diseases, impaired liver and kidney functions. Prolonged medication with salicylates requires medical supervision.

Adverse effects
GIT disturbances, increased bleeding time, Reye syndrome, and precipitation of allergic attacks. Chronic over dosage leads to salicilism.

Drug interactions
Antacids, anticoagulants, anti-epileptic, cytotoxic, diuretics, uricosuric, metoclopramide, domperidone and alcohol.

Patient instructions
Take with food or after meals. Do not crush or chew. Take with a full glass of water.

Diclofenac
Dose
75-150 mg/day in 2-3 divided doses after meals. Children (over 1 year): 1-3 mg/kg/day in divided doses.

Indications
For the relief of pain and inflammation.

Contraindications
GIT ulceration, porphyria.

Precautions
Long-term treatment with diclofenac should be accompanied with blood counts.

Adverse effects
GIT ulceration, hypersensitivity reactions.

Drug interactions
Digoxin, lithium, methotrexate, cyclosporin and triamterene and salicylates.

Patient instructions
Do not take part in any activity that requires alertness. Tell your dentist that you are taking that drug as it prolonges bleeding time.

Ibuprofen
Dose
1.2-1.8 g/day in divided dose preferably after meals (max. 2.4 g/day).

Indications
Management of mild to moderate pain and antipyretic.

Contraindications
Patients with active peptic ulceration.

Precautions
May provoke bronchospasm in patients with asthma. Should be given cautiously to elderly, patients with
history of peptic ulcer, cardiovascular, liver or kidney disorders.

**Adverse effects**

GIT ulceration, hypersensitivity reactions.

**Drug interactions**

Antihypertensives, cardiac glycosides, cytotoxics, diuretics and lithium.

**Patient instructions**

Similar to diclofenac.

**Ketoprofen**

**Dose**

50 to 100 mg twice daily with food.

**Indications**

Management of mild to moderate pain and antipyretic.

**Contraindications**

Should not be given to patients with known hypersensitivity to aspirin and pregnancy.

**Precautions**

May provoke bronchospasm in patients with asthma, should be given cautiously to elderly and patients with history of peptic ulcer, cardiovascular, liver or kidney disorders.

**Adverse effects**

GIT ulceration, hypersensitivity reactions.

**Drug interactions**

Probenecid, lithium and methotrexate.

**Patient instructions**

Stomach problems if you drink alcohol while being treated with this medication.

**17.3.2 Analgesic Antipyretics**

**Paracetamol**

**Dose**

0.5-1 g every 4-6 hours with a maximum of 4 g/day. Children under 3 months 10 mg/kg, 3 months-1 year: 60-120 mg/kg, 1-5 years: 120-250 mg/kg and 6-12 years: 250-500 mg/kg. These doses may be repeated every 4-6 hours if necessary with maximum of 4 doses.

**Indications**

Management of mild to moderate pain and pyrexia, acute migraineous attacks, tension headache.

**Contraindications**

Should not be given to patients with hepatic and renal damage and alcoholism.

**Precautions**

Hepatic impairment, renal impairment, alcohol dependence, pregnancy and breast-feeding.
Adverse effects
Rashes, blood disorders and acute pancreatitis after prolonged use. Acute poisoning may lead to liver damage.

Drug interactions
Anion exchange resin, metoclopramide and domperidone.

Patient instructions
Do not exceed the maximum recommended daily dosage of 4 g. Do not use with other anti-inflammatory agents.

17.3.3 Anti-Migraine
Treatment of acute attacks may be non-specific using simple analgesic, or specific using ergotamine, if nausea and vomiting are features of the attack, an anti-emetic drug may be given.

Ergotamine should be considered only when attacks are unresponsive to non-opioid analgesics.

To be fully effective, ergotamine must be taken in adequate amount as early as possible during each attack.

Ergotamine Tartrate
Dose
1-2 mg repeated half an hour later if necessary (max. 6 mg/day and 12 mg/week) co-administration of caffeine (100 mg) enhances the effect of ergotamine.

Indications
Treatment of migraine and cluster headache.

Contra indications: Severe hypertension, sepsis, peripheral vascular disease, pregnancy, ischaemic heart disease, porphyria.

Precautions
Should be administered with care in severe hyperthyroidism and anemia and should not be used for prophylaxis. Discontinue in cases of numbness or tingling of extremities.

Adverse effects
Nausea and vomiting, weakness and muscle pain, symptoms of peripheral vasoconstriction and CVS disturbances, drug dependence.

Drug interactions
Caffeine, beta-blockers and macrolide antibiotics.

Patient instructions
Avoid any food to which you are allergic, and make your headache worse. Avoid exposure to cold. Elderly patients are more sensitive.

Sumatriptan
Dose
100 mg tablets and 0.5 mg ampoule SC injection. Oral: 25-100 mg. Injection 6-12 mg (response rate at 2 hour, 75%).
Indications

Migraine headache. It is effective when the prodromal symptoms starts and second dose after 2-4 hours then every 6-8 hours until symptoms subside.

Adverse effects

Nausea, vomiting, malaise, dizziness, pain and redness at site of injection (40 %), chest pressure (5%).

Contraindications

Coronary artery disease, hypertension, peripheral or cerebral vascular disease.

Drug interactions

Ergot alkaloids, lithium, antidepressants (MAOIs and SSRIs) serotonin syndrome.

17.4 Antigout

Acute attacks of gout are usually treated with high doses of an NSAIDs such as Indometacin, Ibuprofen has a weaker anti-inflammatory property than other NSAIDs so unsuitable for treatment of gout.

Colchicine is an alternative for those patients in whom NSAIDs are contra-indicated, its use is limited by toxicity with high doses.

For long term control of gout in patients who have frequent attacks, the xanthine oxidase inhibitor allopurinol may be used to reduce production of uric acid.

The intiation of allopurinol treatment may precipitate an acute attack therefore colchicines or a suitable NSAIDs should be used as a prophylactic and continued for at least one month after the hyperuricaemia has been corrected.

Allopurinol

Dose

100-300 mg tablets 2-3 times/day depending on the level of uric acid in the blood then maintaince 100 mg/d when the serum level is between 3-8 mg. It is combined with clochicine to avoid acute exacerbation as anti-inflammatory).

Pharmacological action

It blocks uric acid synthesis by increase oxypurines clearance greater than uric acid.

Indications

In chronic gouty arthritis and marked elevation of uric acid in blood (hyperuricemia) e.g.1-cytotoxic drugs (massive breakdown of purine in nucleoproteins as an end product) e.g. Leukemia. 2- Decreased uric acid excretion e.g. chronic renal failure (end-stage). 3- Endogenous metabolic error e.g. glycine, uric acid or disturbed glutamine metabolism.
Adverse effects
Skin rash and precipitation of acute gouty attack.

Colchicine

Dose
1 mg initially, followed by 0.5 mg every 2-3 hours until relief of pain or vomiting or diarrhoea occurs. Do not repeat within 3 days.

Indications
Treatment of acute gout, short-term prophylaxis during initial therapy alluprinol and uricosuric drugs. It is also useful in amyloidosis, familial Mediterranean and Behcet's disease.

Contraindications
Severe GIT, cardiac, hematologic, liver or renal disease. Pregnancy and breast-feeding.

Precautions
Frequent blood counts are recommended on chronic use.

Adverse effects
Nausea, vomiting, and abdominal pain. Excessive doses may lead to diarrhoea and GIT bleeding. On prolonged use blood disorders may develop.

Drug interactions
Cyclosporin, cynacobolamin, diuretics and NSAIDS and alcohol.

Patient instructions
It is important to understand how to take it and when it should be stopped. If you miss a dose; do not double the next dose.
SECTION XVIII

OPHTHALMIC PREPARATIONS

In this section:

18.1 Antivirals 216
18.2 Local Anaesthetics 216
18.3 Antibiotics 216
18.4 Steroids 216
18.5 Sulphonamides 217
18.6 Antihistaminics and/or Decongestants 217
18.7 Preparations for Glaucoma 217
18.8 Miotics 219
18.9 Mydriatics 220
18. Ophthalmic Preparations

Preparation for eye should be sterile when formulated.

Use of single-application containers is preferable, multiple-application preparations include antimicrobial preservatives.

18.1 Antivirals

Acyclovir

See under antiviral drugs.

18.2 Local Anaesthetics

Topical local anaesthetics are employed for simple ophthalmological procedures and for short operative procedures involving the cornea and conjunctiva.

Benoxinate (oxybuprocaine)

Pharmacological action

It is soluble primary local anaesthetic.

Indication: For ophthalmic use. Produce little or no mydriasis. (0.4 % solution) Skin ointment e.g. dermatosis, itching (1%). Urethral instrumentation (0.2%).

18.3 Antibiotics

Blepharitis, conjunctivitis, keratitis and endophthalmitis are common acute infections of the eye and can be treated topically. However, in some cases, for example, in gonococcal conjunctivitis, both topical and systemic anti-infective treatment may be necessary.

Blepharitis and conjunctivitis are often caused by staphylococcus, while keratitis and endophthalmitis may be bacterial, viral, or fungal.

Bacterial blepharitis is treated with an anti-bacterial eye ointment or drops, although most cases of acute bacterial conjunctivitis may resolve spontaneously, anti-infective treatment shorten the infectious process.

Chloramphenicol (0.5 and 1%)

See chloramphenicol.

Oxytetracycline HCL (1%)

See Tetracycline.

Eye Drops: Apply 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 are used during day) or 4-6 times/day (alone).

18.4 Steroids

Before administration of an ophthalmic corticosteroid, the possibility of bacterial, viral or fungal infection should be excluded.

Treatment should be the lowest effective dose for the shortest possible
time; if long-term therapy (more than 6 weeks) is unavoidable, withdrawal of an ophthalmic corticosteroid should be gradual to avoid relapse.

**Dexamethasone**
See Dexamethasone.

### 18.5 Sulphonamides

**Sulphacetamide sodium 10%**
See Sulphacetamide.

### 18.6 Antihistaminics and/or Decongestants

**Phenylephrine**
**Pharmacological action**
It is a mono-hydroxy-phenyl alkylamine and has a direct sympathomimetic action mainly on alpha-receptors and little beta effect on the heart.

**Dose**
Local: 0.5 – 1 % solution (nasal drops and spray). Injection IM 5 -10 mg. Included in nasal and throat decongestant mixtures.

**Indications**
Vaso-constrictor, nasal decongestant and mydriatic (irritant). In hypotensive states.

### 18.7 Preparations for Glaucoma

Glaucoma is normally associated with raised intra-ocular pressure and eventual damage to the optic nerve, which may result in blindness. The rise in pressure is almost always due to reduced outflow of aqueous humour, the inflow remaining constant.

The most common condition is chronic open-angle Glaucoma (chronic simple Glaucoma) in which the intra-ocular pressure increases gradually and the condition is usually asymptomatic unit well advanced. In contrast, angle-closure Glaucoma (closed-angle Glaucoma) usually occurs as an acute emergency resulting from a rapid rise in intra-ocular pressure; if treatment is delayed, chronic angle-closure Glaucoma may develop.

Ocular hypertension is a condition in which intra-ocular pressure is raised without signs of optic nerve damage.

Drugs used in the treatment of Glaucoma lower the intra-ocular pressure by a variety of mechanisms including reduction in secretion of aqueous humour by the ciliary body, or increasing the outflow of the aqueous humour by opening of the trabecular network.

Anti-glaucoma drugs used include topical application of a beta-blocker (beta-adrenoceptor antagonist), a miotic, or a sympathomimetic such as epinephrine; systemic administration...
of a carbonic anhydrase inhibitor may be used as an adjunct.

**Timolol (0.25% - 0.5%)**

**Dose**
One drop twice daily.

**Indications**
Management of open angle glaucoma and some cases of secondary glaucoma.

**Contraindications**
Since systemic absorption may occur, these eye drops are contraindicated in asthma, obstructive lung disease, bradycardia, heart block or heart failure.

**Precautions**
Older people (risk of keratitis) if used in angle-closure glaucoma, use with miotic and not single.

**Adverse effects**
Allergic conjunctivitis, transitory dry eye, transient stinging and granulomatous anterior uveitis (with Metipranolol), burning, pain, itching keratitis, diplopia and allergic blepharitis.

**Drug interactions**
If systemic absorption occurs, these drugs can interact with other drugs (alcohol, anesthetics, amiodarone, lidocaine, rifampicin, fluoxamine, anti-diabetics), anxiolytics, hypnotics, cardiac glycosides, cholinergics, antipsychotics, ergotamine, sympathomimetics, theophylline, thyroxine, cimetidine, diuretics, and carbadoxolone.

**Patient instructions**
Do not allow the tip of the dispensing container to contact the eye, to avoid bacterial contamination. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 10 minutes. Contact lenses should be removed; lenses may be reinserted 15 minutes following administrations. Protect from light.

**Metipranolol**

**Dose**
1 drop should be taken at bedtime.

**Indications**
For the treatment of intraocular pressure in chronic open angle glaucoma.

**Contraindications**
Bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second-degree and third degree atrioventricular block, cardiac failure, cardiogenic shock.

**Precautions**
Pregnancy category C, patient with cerebrovascular insufficiency, bronchial disease, and sulphite sensitivity, thyroid disorder, diabetes mellitus and may mask hypoglycemic symptoms in patients with insulin-dependant diabetes.
**Adverse effects**

Ocular effect includes burning, stinging at instillation, photophobia, and excessive lacrimation.

**Betaxolol**

Causes temporary blurred vision; serious systemic reactions include bronchospasm, bradycardia, CHF, heart block, cerebrovascular ischemia and depression.

**Drug interactions**

Oral B-adrenergic blocking agents, calcium channel blockers, digoxin, and quinidine.

**Patient instructions**

Wash hands before drug administration, not allow dropper to come into contact with any surface including eyelashes. Report these symptoms to physician, eye infection, inflammation, rash, itching or decreased vision or sudden eye pain. Monitor glucose level carefully.

**18.8 Miotics**

A miotic such as pilocarpine, through its parasympathomimetic action, contracts the iris sphincter muscle and the ciliary muscle and opens the trabecular net work, it is used in chronic open-angle glaucoma either alone or, if required, as an adjunct with a beta-blocker epinephrine or a systemic carbonic anhydrase inhibitor. However, it is not advisable to use pilocarpine after surgery because of a risk of posterior synechiae forming, systemic absorption of topically applied pilocarpine can occur producing muscarinic-like adverse effect.

**Pilocarpine**

**Dose**

Apply drops 3-6 times/day.

**Indications**

To reduce intra-ocular pressure in open angle glaucoma, as a part in the emergency treatment of closed angle glaucoma prior to surgery, to antagonize the effect of mydriatics and cycloplegics on the eye and in some surgical procedure in the eye.

**Contraindications**

Acute iritis, acute uvitis and some cases of secondary glaucoma.

**Precautions**

Used with severe cautions in patients with history of retinal detachment, young patients with high myopia. Miosis may cause difficulty with dark adaptation, high or low cranial abrasion, asthma, hyperthyroidism, peptic ulcer, Parkinson’s disease, U.T obstruction.

**Adverse effects**

Ciliary’s spasm, ocular pain and irritation, blurred vision, myopia and browache.
Drug interactions
β-blockers, topical NSAIDs.

Patient instructions
If over dosage occurs, flush eyes with water. Caution while driving at night or performing tasks in poor illumination. Keep bottle tightly closed when out of use. Wash hands with soap and water.

18.9 Mydriatics
Antimuscarinics, by blocking the cholinergic effects of acetyl choline, paralyse the pupillary constrictor muscles causing dilation of the pupil (mydriasis) and paralyse the ciliary muscles resulting in paralysis of accommodation (cycloplegia).

Mydriasis may precipitate acute angle-closure glaucoma particularly in elderly or long-sighted patients.

In patients with dark iridic pigmentation, higher concentrations of mydriatic drugs are usually required and care should be taken to avoid overdosing.

Atropine
Dose
Uveitis, 1-2 drop 4 times/day. Child, 1 drops 3 times/day. Refraction in children, 1 drops 2 times/day for 3 days of examination and then one hour before examination.

Indications
To produce cycloplegia for refraction in young children, in children with convergent strabismus. In iridocyclitis to prevent posterior synechiae.

Contraindications
Glaucoma. Not use in infants below 3 months with an association between cycloplegia and amblyopia.

Precautions
Atropine ointment is preferred in children below 5 years. Avoid driving is allowed 1-2 hours after mydriasis.

Adverse effects
Contact dermatitis, toxic systemic reactions may occur in extremes of age, nasal congestion, altered taste, may precipitate acute narrow-angle glaucoma in old patients.

Drug interactions
Haloperidol, phenothiazines.

Patient instructions
dim room lighting to comfortable level or provide sun glasses if necessary. Provide lubricating eye drops in xerophthalmia. Notify physician in ocular pain.
SECTION IX

EAR, NOSE AND OROPHARYNX
DRUGS

In this section:

19.1 Antibiotics 222
19.2 Decongestants 222
19.3 Systemic Decongestants 224
19. Ear, Nose and Oropharynx Drugs

19.1 Antibiotics

Chloramphenicol (Ear Drops)

**Dose**

Apply bid or tid.

**Indications**

Used in eye infections and bacterial infections of the outer ear.

**Contraindications**

Perforated tympanic membrane, trivial infections, prophylactic use, fungal disease of ocular structure, and mycobacterial infection of eye.

**Adverse effects**

Blood disorders including reversible and irreversible aplastic anaemia (with reports of resulting leukaemia), peripheral neuritis, optic neuritis, erythema multiforme, nausea, vomiting, diarrhoea, stomatitis, glossitis, nocturnal haemoglobinuria reported, gery syndrome (abdominal distention, pallid cyanosis, circulatory collapse) may follow excessive doees in neonates with immature hepatic metabolism.

**Drug interactions**

Inhibits CYP2C9 and increase serum concentrations of phenytoin, warfarin and sulphonylurea, phenobarbital and rifampin can decrease serum levels of chloramphenicol.

19.2 Decongestants

19.2.1 Local sympathomimetics

**Oxymetazoline**

**Pharmacological action**

Sympathomimetic for topical use.

**Indications**

Nasal decongestant. In common colds, flu and allergic rhinitis.

**Dose**

Nasal drops 0.025% (Infantile) and 0.05% (Adult). Nasal sprays 0.05% and gel.

**Precautions**

In patient with hypertension.

**Xylometazoline**

**Pharmacological action**

Sympathomimetic for topical use.

**Indications**

Nasal decongestant

**Dose**

Nasal drops 0.5% (Infantile) and 1% (Adult). Nasal spray 1%.
Precautions
In patient with hypertension.

Tetrahydrozoline
0.05%, 0.5% eye and nasal drops.

19.2.2 Systemic antihistamines
Clemastine
Dose
1 mg tablets, 0.5 mg/5mL syrup and 1 mg. amp. 1-2 doses/day and when needed.

Pharmacological action
Systemic antihistaminic.

Indications
Similar to diphenhydramine.

Adverse effects
Less sedation and psychomotor impairment.

Dimethindene, Phenylephrine and Neomycin
Nasal spray.

Pharmacological action
Decongestant, anti-allergic and anti-septic nasal spray.

Diphenhydramine
Dose
Syrup tid.

Indications
Nasal pharyngeal allergy, hay fever, pruritus, urticaria, medication allergies and common cold.

Adverse effects
Sedation, hypnosis and psychomotor impairment.

Fexofenadine
Dose
120 mg tablets/day.

Precautions
Machinary workers and driving that need alertness.

Pharmacological action, Indications, Adverse effects: see Acrivastine.
Ketotifen
Dose
1 mg. Tablets, 1 mg/5mL syrup, 1 mg/1mL. Drops 1-2 times/day.

Loratadine
Dose
Loratadine tablets and syrup should be taken once daily.

Indications
Long-acting antihistamine, symptomatic relief of seasonal allergic rhinitis.

Contraindications
Allergic reactions to cyproheptadine, azatadine, astemazole, brompheniramine, carbenoxamine, clemastine, hydroxyzine.

Precautions
If you have ever had asthma, blood vessel disease, glaucoma, high blood pressure, kidney, liver disease, peptic ulcers, inform your doctor. Nursing mothers not to use

Adverse effects
Anxiety, depression, feeling faint, shortness of breath, change in menstruation, breast pain, constipation, dry mouth, rash, urine discoloration, yellowing of eyes or skin.

Drug interactions
MAOIs, TCA, CNS depressant.

Patient instructions
Wear protective clothing and use an effective sunscreen. If there is constipation, increase the amount of fibre in your diet, exercise and drink more water. If you feel dizzy site and be careful on stairs. Should always be administrated on an empty stomach.

19.3 Systemic Decongestants

Carbinoxamine plus Phenylephrine
Systemic nasal decongestant and anti-allergic

Dose
Capsule 3 times/day.

Chlorpheniramine plus Phenylephrine
Systemic nasal decongestant and anti-allergic

Dose
Syrup 3-4 times/day.

Indications
Common cold.

Budesonide
Dose
50 microgram/dose as nasal aerosol and 200 microgram/dose aerosol.
Pharmacological action
Plain nasal corticosteroid.

Indications
Nasal allergy (50 microgram). Anti-asthmatic corticoid by 200-microgram inhalation.

Adverse effects
Inhalation leads to horseness of voice and fungal infection in throat.

Pseudoephedrine
Systemic nasal, throat decongestant and bronchodilator.

Dose
Tablets 3-4 times/day.

Indications
Common cold and allergic bronchitis.

Pseudoephedrine plus triprolidine
Systemic nasal decongestant, anti-allergic and bronchodilators.

Dose
Tablets and syrup.

Indications
Common cold, allergic rhinitis and bronchitis, high fever and anti-tussive.

Acrivastine
Pharmacological action
Systemic anti-histaminic (long duration).

Dose
8 mg capsule sid or bid.

Indications
Similar to diphenhydramine.

Adverse effects
Less psychomotor impairment and less sedation.

Naphazoline Hcl plus Chlorpheniramine maleate
Dose
2-3 drops 3-4 times daily.

Indications
Nasal congestion due to common cold and sinusitis, to promote nasal or sinus drainage, to relieve air block, pressure pain in air travel.

Contraindications
Breast feeding (oral agents only), coronary artery disease, glaucoma.

Precautions
Angina, diabetes mellitus, dizziness, hyperthyroidism, insomnia, prostatic hypertrophy, nursing women, patients of 60 years and older.
Adverse effects
Nervousness, dizziness, sleeplessness with excessive eye sensitivity to light, use of topical decongestants more likely in infants and in nasal discharge, hypertension, rebound congestion, convulsions, depression, anorexia, tremor, headache, weakness.

Drug interactions
Furazolidone, guanethidine, MAOIs, Methyldopa, tricyclic antidepressants, rawolfia alkaloids.

Patient instructions
Not to be used by more than one person to prevent spread of infection.

Cetirizine
Systemic anti-histaminic (long duration

Dose
10 mg tablets 1-2/day.
SECTION XX

DERMATOLOGICAL DRUGS

In this section:

20.1 Antibiotics 228
20.2 Sulphonamides 229
20.3 Local Anti-Fungals 230
20.4 Antiviral 230
20.5 Antiparasites 231
20.6 Corticosteroids 232
20.7 Keratolytic 233
20.8 Protective and Soothing Agents 233
20.9 Local Antipruritic and Ectoparasiticides 234
20.10 Acne Preparations 234
20.11 Antiseptics and Disinfectants 235
20 Dermatological Drugs

The primary role of the skin is to act as a barrier and this role is well served by its structure, a multi layered epithelium of squamous cells.

The outer most layer, the stratum corneum has relative impermeability to chemical, physical agent.

20.1 Antibiotics

Most skin and soft tissue infections are caused by streptococcus pyogenes or staphylococcus aureus, in general, systemic antibiotics such as penicillins, erythromycin or cephalosporin are favored for all but the most localized infections, since deeper infections are beyond the reach of topical preparation.

The microbiology of skin infections is changing, however, and there is increasing incidence of infections caused by strains of Staph. aureus that are resistant to many antibiotics.

Systemic antibiotics are also used to treat non infectious dermatological diseases such as acne vulgaris.

Tetracycline

Dose
Apply 1-3 times/day.

Indications
Acne vulgaris, impetigo and susceptible skin infections.

Contraindications
Hypersensitivity to any tetracycline.

Precautions
Overgrowth of non-susceptible organisms may occur. Stains clothing.

Adverse effects
Rarely local hypersensitivity reactions.

Drug interactions
May interfere with bactericidal actions of penicillins.

Patient instructions
Topical medication may stain clothes. Avoid exposure to sunlight and using sunscreen or wear protective clothing to avoid photosensitivity. Notify the patient that topical use may result in burning sensation.

Fucidic acid

Pharmacological action
Bactericidal antibiotic by interrupting protein synthesis and by inhibiting translocation on the ribosome (erythromycin – like).

Spectrum: against lactamase-producing Staphylococcus aureus, Gram-positive bacteria and Neisseria.

Preparations: Topical ointment and cream 2%.
Indications
Pyodermia, infected wound.

Clindamycin
Dose
1% gel to be applied on dry skin and cover all the infected area 2-3 times daily.

Indications
Used for the treatment of acne vulgaris.

Contraindications
Allergic reactions to clindamycin.

Precautions
Tell your physician if you are pregnant or breast-feeding.

Adverse effects
Dry skin, oily skin, itching.

Drug interactions
If you are using another topical medication it is best to apply them at different times to reduce skin irritation.

Patient instructions
You should avoid getting this medication in your eyes, nose, or mouth.

Doxycycline
Dose
Adult and child over 8 years 200 mg capsules on first day then 100 mg daily.

Indications
Pelvic inflammatory disease and other infections of skin by susceptible organisms.

Contraindications
Pregnancy, children, porphyria, systemic lupus erythematosus.

Precautions
Hepatic impairment, breast-feeding, photosensitivity reported.

Adverse effects
GIT disturbance, erythema, photosensitivity, headache, visual disturbance, hepatotoxicity and pancreatitis.

Patient instructions
Capsules should be swallowed whole with plenty of fluid while sitting or standing.

20.2 Sulphonamides
Silver Sulphadiazine
Pharmacological action
Broad spectrum against gram-positive bacteria (streptococcus, staphylococcus and Clostridium welchii) and gram negative bacteria (neisseria and
enterobacteria). Non-irritant with high penetration.

**Indications**

Topical cream 1% in Burns and wounds.

**20.3 Local Anti-Fungals**

Fungal infections of hair, skin and nail are a major source of morbidity throughout the world.

The primary effect of most antifungal drugs is to prevent colonization of new tissue by the organism, any agent should be used for a minimum of 4 weeks to eradicate the infection.

**Econazole**

**Pharmacological action**

Fungicidal against dermatophytes and candida.

**Indications**

Topical for cutaneous fungal infection as 1% cream, topical powder and topical spray.

**Clotrimazole**

**Dose**

Apply 2-3 times/day for 14 days after lesions have healed.

**Indications**

Ringworm infections (other than nail and scalp ring worms) and in candidal skin infections.

**Contraindications**

Allergy to clotrimazole.

**Precautions**


**Adverse effects**

Occasional skin irritation or sensitivity, erythema, stinging, blistering, peeling, oedema, and pruritus.

**Patient instructions**

Avoid contact with eyes, do not use on scalp or nails. Avoid use of occlusive wrappings or dressing. Continue use until a full course of therapy is completed.

**20.4 Antiviral**

Anti-viral agents such as acyclovir are used to treat serious viral infections that involve the skin particularly those caused by the herpes simplex, varicella-zoster virus.

**Acyclovir**

**Dose**

Apply on the skin to cover all the infected area for 3 hour 6 times/day for 7 days.

**Indications**

Treatment of initial episodes of herpes genitalis and some muco-cutaneous
RSV infections in immunocompromised patients.

**Contraindications**
Allergy to the drug.

**Precautions**
Pregnancy (category c), lactation (excreted in breast milk). Care must be taken to avoid getting drug in eyes. Sexual intercourse must be avoided when lesions are present.

Adverse effect: Topical applications to herpes lesions can be painful, burning or stinging and pruritis.

**Drug interactions**
Zidovudine increases propensity for lethargy, do not add acyclovir to biologic or colloidal fluids.

**Patient instructions**
Avoid sexual intercourse. Teach patient to apply ointment with finger cot or glove. Start treatment as soon as symptoms occur.

20.5 Antiparasites

**Benzyl benzoate**

**Dose**
In scabies apply 25% over the whole body (excluding head and neck), repeat without bathing on next day and wash off 24 hours later.

**Indications**
Scabies and pediculosis.

**Contraindications**
Inflamed or broken skin.

**Precautions**
Children, avoid contact with eyes.

**Adverse effects**
Local irritation particularly in children.

**Permethrin**

**Dose**
Apply to clean damp hair and leave for 10 minutes, rinse and dry.

**Indications**
Pediculosis (lice but less effective against eggs).

**Contraindications**
Inflamed or broken skin.

**Precautions**
Avoid contact with eyes, in children below 2 years use only under medical supervision.

**Adverse effects**
Pruritis, erythema, stinging of scalp.
Patient instructions
Avoid contact with open cuts, eyes, nose, mouth or other mucous membranes. If contact occurs the eye and the drug flush the eye thoroughly with tap water for several minutes Discontinue use if severe irritation develops. Change clothing and bed linens the morning following application.

20.6 Corticosteroids
Glucocorticoids exert anti-inflammatory, immuno suppressive and catabolic effect on skin.

Betamethasone cream
Dose
Apply thinly 2-3 times/day reducing strength and frequency as condition responds.

Indications
Severe inflammatory skin disorders e.g. eczema unresponsive to less potent corticosteroids.

Contraindications
Untreated bacterial, fungal or viral skin infection. It is not used on face, groin or axilla or for ophthalmic treatment.

Precautions
Application of more than 100 g/week of 0.1% preparation is likely to cause adrenal suppression.

Adverse effects
Spread and worsening of untreated local infection, thinning of the skin, increased hair growth, perioral dermatitis and acne.

Drug interactions
Does not interact with any other medications as long as it is used according to directions.

Patient instructions
Should be stored at room temperature (never frozen). If irritation develops, immediately discontinue its use and notify your doctor. It is not for use in the eyes or mucous membranes. If this medication is used on a child’s diaper area, do not put tight-fitting diapers or plastic parts on the child.

Hydrocortisone cream
Dose
Apply thin 2-3 times/day reducing strength and frequency as condition responds.

Indications
Mild inflammatory skin disorders.

Contraindications
Untreated bacterial, fungal or viral skin lesions, ulcerative skin lesions.

Precautions
The same as Betamethasone.
Adverse effects
Spread and worsening of untreated infections, thinning of skin, irreversible striae atrophica, increased hair growth, perioral dermatitis, acne at site of application, mild depigmentation and vellus hair.

20.7 Keratolytic
These are mild caustics used for softening and removing the horny layer of the skin. They are used particularly in the chronic scaling conditions especially psoriasis. Salicylic acid 2% is the first choice.

Tretinoin is an alternative; other keratolytics include propylene glycol, tars, sulphur, canthridine and resorcinol.

Coal Tar products
Dose
Apply 1-3 times/day starting with the lowest strength.

Indications
Chronic eczema and psoriasis, it has both anti-pruritic and keratolytic properties.

Contraindications
Not applied on broken or inflamed skin.

Precautions
Coal tar stains skin, hair and fabric.
Precautions
Contact sensitivity to lanolin and wool alcohol present in ointments may occur.

Adverse effects
Local sensitivity reactions.

Drug interactions
Zinc forms complexes with tetracyclines.

Patient instructions
If irritation develops while using this medication, immediately discontinue its use and notify your doctor. Use this medication only for your current condition. Do not use it for another problem or give it to other to use.

Dexpanthenol
Function: It is related to a vitamin (Pantothenic acid) included with multivitamin combinations in syrup form. It is one member of the vitamin B complex that enters in the formation of co-enzyme A in some important metabolic pathaways e.g. acety-CoA and aceto-acetyl COA in fat metabolic pathways and Krebs cycle.

20.9 Local Antipruritic and Ectoparasiticides
Crotamiton
Dose
Topical for head lice apply 1% cream rinse to hair one time after washing hair, leave for no longer than 10 minutes and rinse with water.

Indications
Active against lice (including unwatched eggs) and mites (e.g. scabies).

Contraindications
Documented allergy to any pyrethroid or vehicle component.

Precautions
Pregnancy, breast-feeding, avoid contact with eyes.

Adverse effects
transient burning, stinging, tingling occurs in about 10% of patients. Itching, oedema and erythema are often symptoms of scabies skin irritation.

Drug interactions
No interactions.

Patient instructions
Wash hair and towel. Apply cream rinse to saturate hair, scalp, especially behind ears and on the nape of neck.

20.10 Acne Preparations
Skin cleansing and degreasing by week antiseptics and detergents. Mild keratolytics (exfoliating) to unblock pilosebaceous ducts, e.g. benzoyl peroxide, sulphur and salicylic acid. Anti-microbial therapy (tetracyclines, erythromycin, clindamycin, cotri-
moxazole) are used over months to suppress bacterial lipolysis which generates inflammatory fatty acids. Topical adrenal steroids to reduce the inflammation.

Vitamin A derivatives to reduce sebaceous production and keratinization. Topical tretinoin (retinoic acid) or oral isotretinoin are used only in the severe cystic acne as they are highly toxic and teratogenic. Hormonal therapy to decrease androgen production or effect by using oestrogen or the anti-androgen cyproterone.

**Benzoyl peroxide**

**Dose**

Apply once daily for the first few days increase frequency of application from 2 to 3 times daily

**Indications**

Mild to moderate acne vulgaris and oily skin.

**Contraindications**

If severe diarrhoea, stomach pain and cramps or bloody stools occur. Allergy to benzoic acid, cinnamon or any ingredients of the medications.

**Precautions**

Do not treat diarrhoea associated with benzamycin use without consulting your doctor.

**Adverse effects**

Excessive dryness, peeling, facial swelling, oiliness, redness, oedema stinging, burning on application, excessive hair growth, and loss of skin pigment.

**Drug interactions**

Dietary supplements with benzoyl peroxide.

**Patient instructions**

Keep away from eyes, mouth, lips, inside the nose, highly inflamed or damaged skin. If dryness, itching, swelling, redness. Use moisturizers, cool compresses, or topical steroids. Water-based cosmetics may be used after benzoyl peroxide use. Cleansers (washes and bar soap) use once or twice daily on affected skin.

**20.11 Antiseptics and Disinfectants**

**Povidone iodine**

**Pharmacological action**

Topical antiseptic and disinfectant.

Uses: For cleansing skin and wounds. In burns, infected skin abrasions and ulcers by dressing.

Preparation: Paint 10%, solution 7.5% and 4% for shampoo and soap liquid.
In this section:

BCG Vaccine 238
OPV, Oral Polio Vaccine (Sabin) 239
IPV, Inactivated Polio Vaccine (Salk) 239
Hepatitis B Vaccine 239
Hepatitis A Vaccine 240
DTP Vaccine 240
Tetanus Vaccine 241
Diphtheria Antitoxin 241
Measles 241
MMR Vaccine 242
Typhoid Vaccine 242
Cholera Vaccine 242
Viral Influenza Vaccine 242
Meningococcal Vaccine 243
Yellow Fever Vaccine 243
Varicella Vaccine 243
Pneumococcal Vaccine 244
Rabies Vaccine 244
Polyvalent Anti Scorpion Venom 244
Polyvalent Anti Snake Venom 245
Anti Tetanic Serum (Tetanus Antitoxin) 245
Human Anti Haemophilic Factor VIII 245
Anti D Antibody (Rh Immunoglobulin) 246
21. Vaccines and Sera

A preparation, consisting of killed, pre-treated, or living microorganisms or molecules derived from them, which are used in vaccination.

Principle of Vaccination

Protection from diseases by inducing secondary immune response leading to the antibody production.

Attributes of a good vaccine: Ability to obtain the appropriate immune response for the particular pathogen leading to long term protection. Safe: should not cause disease. Stable: Retain immunogenicity, despite adverse storage conditions prior to administration. Inexpensive.

Types of vaccines

Live vaccines

Live attenuated Vaccines: Organisms whose virulence has been artificially reduced. Live recombinant vaccines: It is possible; using genetic engineering to introduce a gene coding for an immunogenic protein from one organism into the genome of another (such as varicella virus) the organism expressing a foreign gene is called a recombinant organism. Following injection into the subject, the recombinant organism will replicate and express sufficient amounts of the foreign protein to induce a specific immune response to the protein.

Immune response: Both cell mediated immunity and antibody responses are good. Life long immunity.

Safety: Danger of reversion to virulence. May cause disease in immunocompromised.

Stability: Organisms in the vaccine must remain viable in order to infect and replicate in the host. Vaccine preparations are therefore very sensitive to adverse storage conditions. Maintenance of the cold chain is very important.

Expense: cheap to prepare.

Killed Vaccines

Killed inactivated vaccines: When safe live vaccines are not available. The organism is propagated in bulk, in vitro and inactivated with either beta-propiolactone or formaldehyde. Not infectious and are therefore relatively safe.

Recombinant proteins: Immunogenic proteins of virulent organisms, synthesized artificially by introducing the gene coding for the protein into an expression vector, such as E. coli or yeasts. The protein of interest can be extracted from lysates of the expression vector, then concentrated and purified for use as a vaccine (e.g. Hepatitis B vaccine).

Immune response: Poor; Response, it is short lived, enhanced by incorporation of adjuvant.
Safety: Inactivated, therefore cannot replicate in the host and cause disease.

Stability: Efficacy does not rely on the viability of the organisms. Withstand more adverse storage conditions. Expensive.

**BCG Vaccine**

**Pharmacological action**

This vaccine is used to prevent tuberculosis.

**Dose**

0.1 ml intradermal, in the left Deltoid area.

**Indications**

Compulsory in Egypt for the newly born in the first 3 months of life and a booster dose at school entry.

At risk personnel: contacts of patients with T.B (e.g. medical personnel, mine workers (silicosis) with precaution to be preceded by tuberculin test (must be negative).

Success of immunization: At the injection site, a small scar appears in a week, progresses to a papule then to an ulcer that heals in 6-12 weeks.

**Tuberculin test (Mantoux test):**

**Dose**

5 tuberculin units (purified protein derivatives), 0.1 ml in the flexor surface of the forearm. Result: After 48–72 hours to show result: If reaction (induration area) more than 10 mm (positive result): previous vaccination or infection must be investigated. If induration less than 5 mm (negative result), it indicates absence of immunity against T.B and must be vaccinated by BCG or anergy. If induration 5-9 mm (doubtful result) must be repeated by 25 tuberculin units.

**BCG-T**

Nature: Each 1 ml contains: 30 mg/ml liquid BCG + Diluted solution 25% as a stabilizing mechanism.

**Indications**

Treatment of urinary bladder carcinoma "in situ" Treatment of urethral cell carcinoma "in situ"

Dose and route of administration: Both the dose and duration depend upon: The general condition of the patient. The reaction to the previous dose of the vaccine. It is given one dose/week for 6 successive weeks or as prescribed by the physician. It is instilled intravesical.

**Contraindications**

Pregnancy and lactation, positive Tuberculin test with clinically active T.B, immunodeficiency syndromes, and patients treated with immunosuppressive drugs.

**Precautions**

Should be instilled under complete aseptic conditions. Traumatic catheterization can produce BCGaemia
(systemic BCG infection) and administration should be delayed until healing occurs.

**OPV, Oral Polio Vaccine (Sabin)**

It is a live attenuated vaccine. It is currently preferred in children for two reasons: It interrupts fecal–oral transmission by inducing secretory IgA in the GIT. IgA is induced by the live virus because it replicates in the GIT, whereas the killed vaccine does not. It is given orally and so is more readily accepted than the killed vaccine which must be injected.

**Precautions**

It must be kept refrigerated to prevent heat inactivation of the live virus. Infection of the GIT by other enteroviruses can limit replication of the vaccine virus and reduce protection so the vaccine is given in winter. It can cause disease in immunodeficient persons and therefore should not be given to them.

The duration of immunity is thought to be longer with the live vaccine than with the killed one, but booster doses are recommended with both.

It should be given at 2, 4, 6 and 18 months of age with a booster at school age. Another dose is added in endemic areas at 9 months of age.

**IPV, Inactivated Polio Vaccine (Salk)**

It is a killed vaccine, used in two special instances: Initial vaccination of previously unimmunized adults, because the risk of disease from live vaccine is higher in adults than in children.

Vaccination of immunodeficient individuals: It is recommended to start this vaccination as soon as 2 months of age in a schedule of 3 injections at least one month apart.

Boosters: One year after the last injection then every 10 years. Dose: 0.5 ml IM or SC.

**Hepatitis B Vaccine**

**Nature:** Recombinant vaccine.

**Indications**

Compulsory at 2, 4 and 6 months infants. High-risk personnel (medical and paramedical), drug abusers and contacts to Hepatitis B patients 0, 1 and 6 months interval or 0, 1, 2 and a booster at one year.

Special schedules: 0, 1, 2, 6 months for Dialysis and Immunocompromised. 0, 7, and 21 days to babies born to hep. B positive mothers.

Route of administration: IM in the deltid region in children and anterolateral aspect of thigh in infants.
Dose
0.5 ml less than 10 yrs and 1.0 ml more than 10 yrs age, 2 ml in dialysis and immunocompromised patients.

**Hepatitis A Vaccine**

Nature: A vaccine for hepatitis A has been developed from formal inactivated, cell culture – derived virus.

Dose and route of administration: 18 years old: 0.5 ml. 19 years and above: 1 ml. It is given as two doses with a six month interval which appears to induce high levels of neutralizing antibodies.

**Indications**
The vaccine is recommended for adults who are not immune to hepatitis A.

**Hepatitis A and B vaccine**

It is a combined Hepatitis A and B vaccine.

Dose and route of administration: 1 ml IM in the deltoid region. It is given in a schedule of 0, 1 and 6 months.

Advantages: of a single injection and hence avoiding multiple injections with production of the same immunity level. It is not given below the age of 16 years old.

**DTP Vaccine**

**Pharmacological action**
Vaccine to prevent Diphtheria, Pertussis and Tetanus.

**Indications**
Compulsory in Egypt for infants. Doses are given at 2, 4, 6 and 18 months of age.

Contra indications: Children older than 4 years. Children less than 4 years with history of epilepsy or convulsions (due to the pertussis content of the vaccine). If first dose is associated with convulsions; give DT vaccine.

**Dose**
0.5 ml IM

**DT Vaccine**

**Pharmacological action**
Vaccine used to prevent Diphtheria and Tetanus.

**Indications**
At school age. Used when DPT is contraindicated: Above 4 years old children. Below 4 years old children with history of convulsions or epilepsy, or if first dose of DPT caused convulsions.

**Dose**
0.5 ml IM
**Hepatitis B plus DTP Vaccine**

It is a combined DTP and Hepatitis B vaccine formed of: Diphtheria toxoid, Tetanus toxoid, inactivated whole cell Bordetella Pertussis strain and Recombinant Hepatitis B virus surface antigen.

**Indications**

It is indicated for active immunization against Diphtheria, Tetanus, Pertussis and Hepatitis B in infants from 6 weeks onwards.

Dose and route of administration: A dose of 0.5 ml by IM injection is recommended and given in the anterolateral aspect of the thigh.

Schedule of immunization: At 2, 4 and 6 months of infancy.

**Adverse effects**

Pain, swelling and fever. If convulsions occur due to the Pertussis portion of the vaccine, continue with DT and Hepatitis B vaccines separately.

**Tetanus Vaccine**

**Pharmacological action**

Vaccine used to prevent tetanus.

**Indications**

Pregnant females in the 5th and 6th months of pregnancy followed by a booster dose in each of the next 3 pregnancies. At risk individuals who are liable to injuries.

**Dose**

0.5 ml SC or IM

**Diphtheria Antitoxin**

It should be given immediately on the basis of clinical impression because there is a delay in the laboratory diagnostic procedures. The toxin binds rapidly and invisibly to cells and once bound it cannot be neutralized by anti-toxin. The function of anti-toxin is therefore to neutralize unbound toxin in the blood. Because the antiserum is prepared in horses, the patient must be tested for hypersensitivity first, and medications for the treatment of anaphylaxis must be available.

**Measles**

Prevention of measles: With live attenuated vaccine the vaccine is effective and cause few Adverse effects.

**Pharmacological action**

Given to children at the age of 9 months in endemic areas and in developed areas it is given at the age of 15 months combined with mumps and rubella (MMR).

**Dose**

0.5 ml by SC injection.

**Contraindications**

Being a live vaccine, it should not be given to pregnant women or immuno-
compromised patients. It gives long lasting immunity.

**MMR Vaccine**

Nature: Live attenuated vaccine: It is a combined vaccine for prevention of measles, mumps and rubella viruses.

**Pharmacological action**

Given to children at the age of 15 months with a recommended booster dose at school age.

**Dose**

0.5 ml by SC injection.

Life long immunity.

**Typhoid Vaccine**

**Pharmacological action**

The vaccine used to prevent Typhoid Fever.

**Indications**

High risk personnel as food handlers. Travellers to endemic areas. Medical personnel dealing with patients.

**Dose**

2 Doses of SC injection with 1 to 4 weeks apart. First dose 0.5 ml second 1 ml. gives protection for 2 years. A booster is given every 2 years.

**Cholera Vaccine**

Composition: Cholera vaccine is prepared from killed Vibrio cholera from the two main serotypes, Inaba and Ogawa.

**Indications**

Cholera vaccine is recommended for prophylaxis against cholera.

**Contraindications**

Pregnancy, TB infection and acute febrile conditions.

**Dose**

Route of administration and schedule of vaccination: Children 1-5 years: 0.25 ml is given by IM or deep SC injection, followed by a second dose of 0.25 ml within 1-4 weeks. A booster of 0.5 ml is recommended 6 months after the primary vaccination. Individuals 5 years old and above: 1st dose: 0.5 ml 2nd dose: 0.5 ml 3rd dose: 1 ml With the same schedule and route of administration as children 1-5 years. Children below one year are not vaccinated.

**Viral Influenza Vaccine**

**Pharmacological action**

Killed influenza A and B strains of the virus. The vaccine usually contains the current antigenic newly strains. The virus in the vaccine is killed. It induces IgG which offers some protection, little secretory IgA appears on the respiratory mucosa. Yearly boosters are recommended and should be given shortly before the flu season e.g.: In October.
Indications
The vaccine should be given to people over the age of 65 years, to those with chronic diseases (particularly respiratory and cardiovascular conditions), immunocompromised patients and all those who want to reduce their risk of acquiring influenza.

Dose
The adult dose is 0.5 ml given once by IM or deep SC injection. For children below 3 years: two doses of 0.25 ml by IM or deep SC injection with a one month interval if not previously vaccinated but if previously vaccinated only one dose is given.

Meningococcal Vaccine
Composition: Contains the capsular polysaccharides of groups A, C, Y and W135 strains.

Indication: Preventing epidemics of meningitis and reducing the carrier state. The vaccine does not contain the B polysaccharide which is poorly immunogenic in humans.

Dose
0.5 ml by SC injection Immunity lasts for two years. It is not recommended to be given below two years of age because of poor immune response for the serogroup C and to a lesser extent for the serogroups W135 and Y.

Yellow Fever Vaccine
Nature: Live attenuated vaccine prepared by culture in chicken embryo.

Dose
0.5 ml by SC injection gives protection for 10 years.

Indications
Active immunization against yellow fever in tropical areas of Latin America and Africa. International travellers to endemic areas.

Adverse effects
Very rarely, Encephalitis.

Contraindications
Under 9 months of age.

Varicella Vaccine
Nature: Live attenuated.

Uses: For prophylaxis against Varicella and Herpes Zoster virus.

Dose
1 dose of 0.5 ml by SC injection after 1 year -13 years. Above 13 years old: 2 doses with one month interval.

Immunity: Life long immunity.

Contraindications
Acute febrile illness, HIV positive individuals, severly immunocompro-
mised (non HIV related), post solid organ transplantation or chronic immuno-suppressive therapy.

Varicella vaccination is indicated for susceptible persons in the following groups: Teachers of young children, day-care workers, residents and staff in institutional settings, college students. Family contacts. Immunocompromised patients. Non-pregnant women of childbearing age. Pregnancy should be avoided for one month following each dose of vaccine. International travellers.

**Pneumococcal Vaccine**


**Indications**

65 years of age or older. Between the ages of 2 and 65 years with one of the following conditions: Chronic cardiovascular disease (e.g.: congestive heart failure cardiomyopathy). Chronic pulmonary disease (e.g. COPD or emphysema). Chronic liver disease (e.g. Cirrhosis). Diabetes mellitus. Liver disease resulting from alcohol. Functional or anatomic asplenia (e.g. sickle cell anemia or splenectomy). Immunosuppressive conditions (e.g. congenital immunodeficiency, HIV infection, leukaemia, lymphoma, multiple myeloma, Hodgkin’s disease or generalized malignancy). Organ or bone marrow transplantation. Therapy with alkylating agents, anti-metabolites or systemic corticosteroids. Chronic renal failure or nephrotic syndrome.

Dose and route of administration: 0.5 ml by SC injection every two years.

Immunity: Two years.

**Rabies Vaccine**

Vaccine in current use is a human diploid cell culture derived vaccine (inactivated) which is safe. There are two situations where the vaccine is given: Post exposure prophylaxis, following the bite of a rabid animal: A course of 5 intramuscular injections, starting on the day of exposure. Hyper-immune rabies globulin may be also administered on the day of exposure in severe exposure. Pre exposure prophylaxis is used for protection of: Persons at risk: e.g. veterinary physicians and laboratory workers. The schedule is 2 doses. Further boosters every 2 years should be given if risk of exposure continues.

**Rabies Immune Globulin (RIG)**

Used in prevention of rabies in those who may have been exposed to the virus, half dose is infiltrated at the bite site and the other half given intramuscularly, the preparation contains a high titre of antibody made by hyper immunizing human volunteers with rabies vaccine, it is obtained from humans to avoid hypersensitivity reactions.

**Polyvalent Anti Scorpion Venom**

Prepared from purified plasma of healthy horses that have been immu-
nized against the most dangerous scorpions.

**Indications**
Treatment of poisoning from scorpion stings.

**Dose**
IM injection of 1–10 ml according to severity.

**Contraindications**
Hypersensitivity to horse serum.

**Polyvalent Anti Snake Venom**
Snake venom antiserum prepared from purified plasma of healthy horses that have been immunized against the most dangerous snakes.

**Dose**
20-40 ml by IM injection.

**Indications**
Venomous snake bites.

Contraindications: Sensitivity to horse serum.

**Anti Tetanic Serum (Tetanus Antitoxin)**
Prepared from purified healthy horse plasma after immunization by repeated injections with tetanus toxin.

**Dose**
1500 U IM

**Indications**
Tetanus prone wounds in unimmunized persons or if last dose of tetanus vaccine was more than 10 years.

**Contraindications**
Sensitivity to horse serum.

**Human Anti Haemophilic Factor VIII**
Dried purified plasma concentrate derived from healthy donors.

**Indications**
Haemophilia A (Factor VIII deficiency). Acquired factor VIII Deficiency

**Precautions**
Hypersensitivity to the product.

**Adverse effects**
Hypersensitivity (allergic) reactions.

interactions: None

**Dose**
Required units of factor VIII Body weight (Kg) x Desired Factor VIII Level rise (%) x 0.5
Desired level in minor bleeding and haematoma: 20 % Haemarthrosis: 40 % Minor operations: 80 % Major operations: 100 %

**Antigen D Antibody (Rh Immunoglobulin)**

Antibody against D (Rh antigen).

**Indications**

Prevention of Rh incompatibility that causes haemolytic disease of the newborn. It works by preventing sensitization of Rh negative woman that occurs when Rh positive foetal RBCs reach her blood circulation during pregnancy, labour or abortion. Prevention of sensitization of Rh negative individuals if Rh positive blood transfusion has been received. Treatment of ITP: Patients must be Rh positive and their spleen intact. It works by forming a complex with Rh positive RBCs that are destroyed in the spleen and sparing an equivalent amount of platelets.

Doses: Pregnancy and other obstetric conditions: 1500 IU by IM injection at 28 weeks gestation, 600 IU within 72 hours after delivery. 600 IU by IM injection in cases of abortion after 12 weeks. ITP: 125 IU/kg intravenously by slow injection.

**Contraindications**

Hypersensitivity to human immune globulin. Rh negative and/or splenectomised individuals in treatment of ITP.

**Adverse effects**

Hypersensitivity reactions.

**Precautions**

Treatment of ITP, if haemoglobin is less than 10 g/dl reduce dose. Hb less than 8 g/dl contraindicated.
SECTION XXII

ANAESTHETIC PREPARATIONS

In this section:

22.1 Local 248
22.2 General 249
22.3 Narcotic Analgesic 253
22 Anaesthetic Preparations

Anaesthetics may be fatal if used inappropriately and should be used by non-specialized personnel only as a last resort.

22.1 Local

Local anaesthetics act by causing a reversible block to conduction along nerve fibres. They are used very widely in dental practice, for brief and superficial interventions, for obstetric procedures, and for specialized techniques of local anaesthesia calling for highly developed skills. Where patient cooperation is required the patient must be psychologically prepared to accept the proposed procedure.

22.1.1 Parenteral

Bupivacaine (Carbocaine)

**Dose**

The suggested general maximum single dose is 150 mg followed if necessary by doses of 50 mg/2 hours, not more than 400 mg should be given daily.

For peripheral nerve block: 12.5-25 mg, for sympathetic nerve block: 50-125 mg, for lumbar epidural block 25-100 mg.

**Indications**

Bupivacaine is local anaesthetic related to xylocaine with more rapid onset and long duration. It is used for infiltration anaesthesia, peripheral and sympathetic nerve block, lumbar epidural block (surgery and labour) and dental or surgical procedures of the maxillary or mandibular regions.

Contra-indications: Intravenous regional anaesthesia, hypovolemia, cardiovascular system (C.V.S) disorders and hypersensitivity to the amide group.

**Precautions**

The dose should be reduced in the elderly, children, in debilitated patients and in cardiac or hepatic disease.

**Adverse effects**

CNS excitation manifested by restlessness, dizziness, tinnitus, blurred vision, nausea and vomiting. CVS disturbance as myocardial depression and hypotension.

**Drug interactions**

Anti-arrhythmic.

**Patient instructions**

Avoid contact of this medication with your eyes. Be sure to wash your hands thoroughly after use. Tell your doctor if you have ever had anaemia, or glucose 6 phosphate dehydrogenase enzyme deficiency.
Lidocaine (Xylocaine, Lignocaine)

Dose

By Injection maximum dose is 200 mg or 500 mg with solutions, which also contain adrenalin. Infiltration anaesthesia: 0.25-0.5%, with adrenaline 1 in 200000, using 2-50 ml of a 0.5% solution. Nerve blocks, epidural and caudal blocks with adrenaline 1 in 200000, 1% to a maximum of 50 ml, 2% to a maximum of 25 ml. Surface anaesthesia, usual strength hours 2-4%. In emergency ventricular tachyarrythmias, lidocaine is given as a bolus of 100 mg over few minutes followed by infusion of 2-4 mg/min.

Indications

Lidocaine is local anaesthetics with rapid onset and an intermediate duration of action. It is used for infiltration anaesthesia, nerve, epidural and caudal block and as a surface anaesthetic. It is used in emergency ventricular tachyarrythmias without heart block.

Contraindications

Hypersensitivty, porphyria, hypovolemia.

Precautions

Hepatic or renal insufficiency and impaired cardiac conduction. Children under age of 3 months are at increased risk.

Adverse effects

Hypotension, Bradycardia, Cardiac arrest and CNS stimulation.

Drug interactions

Other antiarrythmics, beta-blockers, diuretics and cimetidine.

22.1.2 Surface

Ethyl chloride (spray)

Indications

local anaesthetics in minor surgery (not recommended) and topically for relief of pain.

Precautions

Highly flammable. It should not be applied to broken skin or mucous membranes.

Adverse effects

Prolonged spraying onto skin can cause chemical frostbite. Hepatotoxic, nephrotoxic and hypotension.

22.2 General

It is a reversible state of analgesia, amnesia,loss of consciousness, inhibition of sensory and autonomic reflexes, and variable degrees of skeletal muscle relaxation. They are classified into:

Inhalation anaesthetics: They are either volatile liquids or gases. Volatile liquids: Halogenated agents: Halothane, enflurane, isoflurane. Ethers:


Others: etomidate, propanidid, viadril, althesin, and disoprofol.

**Molecular mechanism of action of general anaesthetics**

They depress neuronal activity by interfering with sodium influx or facilitating inhibitory synapses, e.g. GABA-chloride ion channel complex.

**22.2.1 Parenteral**

These drugs are able to induce rapid loss of consciousness when given parenterally.

**Ketamine Hcl**

**Dose**

An IV dose of 2 mg/kg over 60 sec. will induce surgical anaesthesia within 30 sec in lasting for 5-10 min. An IM dose of 10 mg/kg will induce anaesthesia within 3-4 min lasting 12-25 min.

**Indications**

It is indicated as the sole anaesthetics for diagnostic and short surgical procedures (especially in children), for induction of anaesthesia to be maintained by other anaesthetics or a supplementary anaesthetic.

**Contraindications**

Hypertension, increased intra-cranial or intra-ocular pressures.

**Adverse effects**

Emergence reaction on recovery (treated with diazepam), increased muscle tone, hypertension, tachycardia, respiratory depression, increased intra-ocular and cerebrospinal pressures.

**Drug interactions**

Halothane and phenobarbitone.

**Thiopentone (Thiopental) Sodium**

**Dose**

The dose for induction of anaesthesia varies widely, but a typical dose is 100-150 mg injected over 10-15 sec. Repeated according to response. For children the dose is 2-7 mg/kg. As a sole anesthetic, can be maintained by repeated doses as needed or by continuous IV infusion of a 0.2-0.4% solution. For the treatment of convulsive states the dose is 75-125 mg IV

**Indications**

Thiopentone sodium is used in the induction of general anaesthesia or the sole anaesthetics in minor surgical procedures of short duration. It is also
indicated in the management of convulsive states.

Contra-indications: Porphyria and respiratory diseases.

Precautions
Shock, dehydration, severe anemia, hyperkalemia, myasthenia gravis, myxedema, severe hepatic or renal diseases.

Adverse effects
Extravasation may lead to tissue necrosis; IV administration of concentrated solutions may lead to thrombophlebitis, respiratory depression, hypotension, post-operative vomiting, drowsiness and confusion.

Drug interactions
Sulphonamides, antihypertensives, antipsychotics, anxiolytics, hypnotics, beta-blockers and calcium channel blockers.

Fentanyl
Dose
1 ml/9 kg body weight IV over 5-10 minutes, peak action after 5 minutes with rapid recovery. Transdermal Fentanyl Patch: 100 microgram/hr for managed of chronic cancer pain. Onset after 6-12 hr and duration 8-12 hours.

Indications
It possesses a narcotic action and when combined with droperidol the preparation is known as Innovar (Fentanyl 0.05 mg + droperidol 2.5 mg/ml).

Adverse effects
Hypotension, bradycardia and respiratory depression.

Midazolam
Dose
5-15 mg amp.

Indications
Sedation, amnesia and anxiolysis. It induces IV anaesthesia for minor operations.

Propofol
Dose
200 mg ampoule.

Indications
IV induction of anaesthesia, maintenance of general anaesthesia. They produce a state of light anaesthesia not deep to permit surgery and mainly used in pre-anesthetic medication, simple administration, rapid induction, slower recovery, non-irritant or explosive., pre-anesthetic and post-operative sedation.

Adverse effects
Respiratory depression and cannot control depth of anaesthesia.
22.2.2 Inhalation
Pharmacological actions of inhalation anaesthetics

CNS: They decrease the metabolic rate of the brain and increase cerebral blood flow and may increase the intracranial pressure.

Respiratory system: All inhaled anaesthetics are respiratory depressants.

CVS: Halothane, enflurane, methoxyflurane and isoflurane reduce BP due to reduction in cardiac output. Ether, fluroxene do not reduce arterial BP.

ANS: There may be vagal or sympathetic activity.

GIT: Nausea and vomiting may occur during induction with an irritant agent like ether.

Liver: Transient depression of liver function may occur with all anaesthetics.

Kidney: All inhaled anesthetics decrease glomerular filtration rate and effective renal plasma flow.

Uterus: Halothane, enflurane and chloroform cause relaxation of uterine muscles.

Halothane
Dose
Anaesthesia may be induced with 2-4% v/v of halothane in oxygen or mixtures of nitrous oxide with oxygen.

Anaesthesia is maintained with concentrations of 0.5-2% v/v.

Indications
It is used for induction and maintenance of anaesthesia in major surgery in combination with oxygen or mixtures of nitrous oxide with oxygen.

Contra-indications: A history of unexplained jaundice or pyrexia in a patient following exposure to halothane during labour.

Precautions
Careful anaesthetic history should be taken. Repeated exposure to halothane in less than 3 months should be avoided.

Adverse effects
Cardiorespiratory depression, ventricular arrhythmias and malignant hyperpyrexia. Severe hepatotoxicity on repeated exposure.

Drug interactions
Antihypertensives, antipsychotics, anxiolytics, hypnotics, beta-blockers, calcium channel blockers, dopaminergic agonists and sympathomimetics.

Isoflurane
Dose
Induction should start with isoflurane concentration of 0.5% then increased to 1.5-3% producing anaesthesia within 10 min. Anaesthesia is main-
tained with a concentration of 1-2.5% with oxygen and nitrous oxide.

**Indications**

Used for induction and maintenance of general anaesthesia.

**Contraindications**

Patients prone to hyperpyrexia.

**Precautions**

Induction with isoflurane is as smooth as with halothane and used cautiously in patients with increased intracranial tension.

**Adverse effects**

Respiratory depression, cardiac arrhythmias and malignant hyperpyrexia and increased intracranial tension.

**Drug interactions**

Antihypertensives, antipsychotics, anxiolytics, hypnotics, beta-blockers and calcium channel blockers, dopaminergic agonists, sympathomimetics and muscle relaxants.

**Nitrous oxide**

**Dose**

Used with mixtures of oxygen (20%) for induction, and up to 50% for maintenance of anaesthesia or analgesia in obstetrics or dental operations.

**Indications**

Used for induction and maintenance of anaesthesia in conjunction with other anaesthesia and in sub anesthetic doses as analgesic.

Contra-indications: In patients with air-containing closed space.

**Precautions**

Add muscle relaxants. To avoid diffusion hypoxia, administer 100% O2 after discontinuation of nitrous oxide.

**Adverse effects**

Anaesthetic hypoxia. Prolonged use may lead to megaloblastic anemia, leucopenia and peripheral neuropathy.

**Drug interactions**

CNS depressants.

22.3 Narcotic Analgesic

(opioid analgesics)

Opium Alkaloids can be classified into two chemical classes: Phenanthrenes: The principal alkaloids of this group are morphine, codeine, and thebaine. Thebaine is a powerful convulsant and has no therapeutic uses. Benzylisoquinolines: Papaverine which is a smooth muscle relaxant with no central actions, and noscapine.
Butorphanol

Dose
As analgesics, 1-4 mg IM OR 0.5-2 MG IV Every 3-4 hours. With anaesthesia, 2 mg IM as pre-medication 60-90 minutes before surgery, for maintenance in balanced anaesthesia 0.5-1 mg IV

Indications
Analgesics in moderate to severe pain and as an adjunct to anaesthesia.

Contraindications
Like morphine. In addition, it should be avoided after myocardial infarction.

Precautions
May precipitate acute withdrawal symptoms if given to patients who have recently used opioid analgesics.

Adverse effects
Nausea, vomiting, and headache. Less respiratory depression, cardiovascular effects and dependence than morphine,

Drug interactions
Mexiletine, MAOI, anxiolytics, hypnotics, cisapride, domperidone, alcohol, metoclopramide, anesthetics and opioid analgesics.

Morphine

It is the most valuable analgesic for severe pain.

Dose
Acute pain, SC or IM injection of 10 mg every 4 hours if necessary. Child up to one month 150 microg/kg, 1-12 months 200 micro g/kg, 1-5 years 2.5-5 mg, 6-12 years 5-10 mg. Myocardial infarction, slow IV, 10 mg followed by 5-10 mg (reduce dose in elderly). Acute pulmonary oedema, 5-10 mg slow IV chronic pain, SC or IM 5-20 mg regularly every 4 hours.

Indications

Contraindications
Respiratory depression, during an attack of bronchial asthma, heart failure secondary to lung disease, acute alcoholism or head injuries. Fatal if co administered with MAOI.
**Precautions**

Used with extreme caution in newborns, patients with poor respiratory reserve, hypothyroidism, adrenocortical insufficiency, impaired renal or hepatic functions, prostatic hypertrophy, shock, inflammatory or obstructive bowel disease and myasthenia gravis.

**Adverse effects**

Nausea, vomiting, constipation, drowsiness, difficulty in micturition, biliary or ureteric spasm, dry mouth, Bradycardia, miosis and dependence. Larger doses produce respiratory depression and hypotension.

**Drug interactions**

Mexiletine, MAOIs, anxiolytics, hypnotics, cisapride, domperidone, metoclopramide, alcohol, anesthetics, buprenorphine, butorphanol, nalbuphine and pentazocine.

**Patient instructions**

Take with food or juice. Full effectiveness may not occur for 30-60 minutes after administration. Stool softener, fibre laxative, increased fluid intake and bulk in diet.

**Meperidin (Pethidine)**

Produce prompt but short-acting analgesia.

**Dose**

IM or SC 25-100 OR IV Infusion 25-50 mg. Child, 0.5-2 mg/kg IM Obstetric Analgesia, 50-100 mg IM OR SC repeated after 1-3 hours if necessary. Pre-medication 50-100 mg IM or SC 1 hour before operation. Adjunct to nitrous oxide - oxygen anaesthesia, 10-25 mg slow IV

**Indications**

Relieves most types of moderate to severe pain including labour pains. As pre-operative medication, as adjunct to anesthetics and with promethazine to produce basal narcosis.

**Contraindications**

Similar to morphine. And it is avoided in supraventricular tachycardia and history of convulsions.

**Precautions**

Similar to morphine.

**Adverse effects**

Similar to morphine, but less constipation.

**Drug interactions**

Mexiletine, MAOI, anxiolytics, hypnotics, cisapride, Domperidone, metoclopramide, alcohol, anaesthesia, buprenorphine and butorphanol, nalbuphine, pentazocine and cimetidine.

**Patient instructions**

Similar to morphine.
Tramadol

Pharmacological action

Narcotic analgesic.

Dose

50 mg. capsules and 100 mg ampoules.

Indications

Traumatic and postoperative pain.

Adverse effects

Addiction, respiratory depression (less than morphine).
Index

A

ACE-Inhibitors, 68
eratogen, 3
Acetyl Salicylic Acid, 208
  anti-platelet, 83
Acrivastine, 224
Acyclovir, 155
  eye, 215
  skin, 229
Adrenaline. See Epinephrine
Aflatoxin
  ADR-Hepatotoxicity, 32
Albumin, human
  20-25%, 204
  4-5%, 203
Aldosterone, 174
Allopurinol, 212
Alpha fetoprotein
  paediatrics, 9
Alpha Methyl dopa, 65
Aluminum hydroxide, 52
Aminoglycosides, 144
Aminophylline, 92
Aminopterin
  teratogen, 3
Amiodarone, 81
Amtriptyline, 117
Amlodipine, 72
Ammonium chloride
  drug interaction, 23
Amoxycillin, 142
Amphotericin B, 157
Anti D Antibody (Rh
  Immunoglobulin), 245
Anti Tetanic Serum (Tetanus
  Antitoxin), 244
Antidepressants, 117
Anti-Diabetics, 168
Antiepileptics, 120
Antihistaminics, 103

eye, 216
Antimuscarinics, 118
Antineoplastics
  breastfeeding, 5
  teratogen, 3
Antiparkinsonism, 118
Antipsychotics, 115
Antituberculous drugs, 152
Ascorbic Acid. See Vitamin C
Asparaginase, 185
Astemizole, 104
Atenolol, 73
Atorvastatin, 84
Atracurium Besylate, 207
Atropine
  antispasmodic, 59
  eye, 219

B

Barbiturates
  drug interaction, 23
  teratogen, 3
BCG Vaccine, 237
BCG-T, 237
Beclomethasone, 93
Benoxinate. See Oxybuprocaine
Benzoyl peroxide, 234
Benztropine, 119
Benzyl benzoate, 230
Benzyl Penicillin, 142
Beta-blockers
  angina, 75
  arrhythmia, 80
  hypertension, 72
Beta-carotene, 195
Beta-Lactams
  geriatric, 16
Betamethasone
  anti-allergy, 106
  skin, 231
Beta-stimulants
  anti-allergy, 105
  bronchodilator, 92
  heart failure, 78
Betaxolol, 218
Bezafibrates, 84
Biguanides, 169
Bisacodyl, 56
Bromhexine, 95
Bromocriptine
  breastfeeding, 5
Bronchodilators, 91
Budesonide, 223
Bupivacaine. See carbocaine
Butorphanol, 253

C
Calcitonin, 180
Calcium
  carbonate, 200
  gluconate, 199
Calcium channel blockers
  angina, 75
  arrhythmia, 81
  hypertension, 70
Carbamazepine, 121
  teratogen, 3
Carbidopa, 119
Carbimazole, 178
Carbinoxamine, 223
Carbocaine, 247
Carbocysteine, 95
Carboplatin, 185
Cardiac Glycosides, 77
Castellani paint, 165
Cefotaxime, 144
Ceftazidime, 144
Cephadroxil, 143
Cephalosporins, 143
Cephaloperazine, 144
Cetirizine, 105, 225
Cetrimide, 164
Chloral hydrate
  drug interaction, 23
Chlorambucil, 184
Chloramphenicol
  drug interaction, 23
  ear drops, 221
  eye, 215
  intestinal antiseptics, 58
Chlorhexidine gluconate, 164
Chloroquine, 160
Chloroxylenol, 165
Chlorpheniramine, 103
  ENT, 223, 224
Chlorpromazine, 115
Cholecalciferol, 197
Cholera Vaccine, 241
Choloramphenicol, 148
Cimetidine
  drug interaction, 23
Ciprofloxacin, 150
Cisplatin, 185
Clarithromycin, 146
Clemastine, 222
Clindamycin, 228
Clobutinol, 94
Clofazimine, 154
Clomiphen, 176
Clomipramine, 118
Clonazepam, 123
Clonidine, 66
Clotrimazole, 229
Cocaine
  teratogen, 3
Colchicine, 213
Contraceptives, 174
Co-trimoxazole, 149
  drug interaction, 23
Crotamiton, 233
Cushing's syndrome, 62
Cyanocobalamine. See Vitamin B₁₂
Cyclophosphamide, 183
Cyclosporin, 192
Cynara extract, 59
Cyproheptadine, 222
**D**

Dapsone, 154  
Daunomycin, 44  
Desmopressin Acetate, 171  
Dexamethasone, 172  
anti-allergy, 107  
eye, 216  
Dexpanthenol, 233  
Dextran, 204  
Dextromethorphan, 94  
Diazepam, 114  
Diclofenac, 209  
Diethylstilbesterol  
teratogen, 3  
Digitalis  
ADR, CVS, 44  
Digoxin, 77  
Diloxanide furoate, 160  
Dimethicone, 57  
Dimethindene, 105, 222  
Diphenhydramine, 222  
Diphtheria Antitoxin, 240  
Diuretics  
hypertension, 63  
Dobutamine, 78  
Domperidone, 48  
Dopamine, 78  
Doxorubicin, 189  
Doxycline, 148, 228  
DTP Vaccine, 239

**E**

Econazole, 158, 229  
Enoxaparin sodium, 87  
Epinephrine  
allergy, 105  
Epirubicin, 190  
Ergocalciferol, 197  
Ergotamine  
breastfeeding, 5  
tartrate, 211  
Erythema multiforme  
drug eruption, 42  
Erythromycin, 145  
Ethambutol, 153  
Ethamsylate, 87  
Ethanol  
teratogen, 3  
Ethyl chloride, 248  
Etoposide, 187

**F**

Fentanyl, 250  
Fexofenadine, 222  
Flubendazole, 162  
Fluconazole, 156  
Fludrocortisone  
anti-allergy, 106  
Flucortolone, 56  
Fluoroquinolones, 150  
Fluorouracil, 188  
Folic Acid, 195  
Fucidic acid, 227  
Furosemide, 64

**G**

Gallamine Triethiodide, 207  
Gelatin, 55  
Gemfibrozil, 84  
Gentamycin, 144  
paediatrics, 10  
Gentian violet, 165  
Glibenclamide, 170  
Glucocorticoids, 172  

drug interaction, 22  
Glycerine, 55  
Glyceryl trinitrate, 75  
Griseofulvin, 157  

drug interaction, 23  
Guaiaphenesin, 95
H
Harperol, 116
Halothane, 251
Helicobacter pylori, 49
Heparin, 85
Hepatitis A and B vaccine, 239
Hepatitis A Vaccine, 239
Hepatitis B Vaccine, 238
Hepatitis B, DTP Vaccine, 240
Human Anti Haemophilic Factor VIII, 244
Hydrochlorothiazide, 63
Hydrocortisone
  anti-allergy, 106
  haemorrhoids, 57
  skin, 231
Hydrogen Peroxide, 165
Hyoscine
  antispasmodic, 60

I
Ibuprofen, 209
Idarubicin, 190
Ifosfamide, 184
Imipramine, 117
Immunosuppressants, 192
  breastfeeding, 5
Insulin, 168
  bovine, 169
  human, 168
Interferon, 155
Iodine
  povidone, skin, 234
  teratogen, radioactive, 3
IPV, Inactivated Polio Vaccine (Salk), 238
Iron
  ferrous, 200
Isoflurane, 251
Isoniazid, 152
  drug eruption, 42
Isoprenaline, 79
Isosorbide dinitrate, 74
Itraconazole, 157

K
Kaolin, 54
Ketamine HCl, 249
Ketoprofen, 210
Ketotifen
  ENT, 223

L
Lactulose, 55
Levamisole, 162
Levodopa, 119
Levofloxacin, 151
Levotyroxine, 178
Lidocaine, 248
  arrhythmia, 80
Lignocaine, 57, See Lidocaine
Lisinopril, 69
Lithium
  ADR, CVS, 44
  breastfeeding, 5
  teratogen, 3
  Loop diuretics, 64
Loperamide, 54
Loratadine, 104
  ENT, 223
Losartan, 69

M
Macrolides, 145
Magenta Paint, 165
Magnesium sulphate, 59
Magnesium trisilicate, 52
Mannitol, 64
Measles, 240
Mebendazole, 162
Mebeverine, 60
<table>
<thead>
<tr>
<th>Meckel’s diverticulum</th>
<th>49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningococcal Vaccine</td>
<td>242</td>
</tr>
<tr>
<td>Meperidin. See Pethidine</td>
<td></td>
</tr>
<tr>
<td>Metformin</td>
<td>169</td>
</tr>
<tr>
<td>Methadone teratogen</td>
<td>3</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>188 teratogen</td>
</tr>
<tr>
<td>Metipranolol</td>
<td>217</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>47</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>159 breastfeeding, 6 drug interaction</td>
</tr>
<tr>
<td>Midazolam, 250</td>
<td></td>
</tr>
<tr>
<td>Midodrine</td>
<td>73</td>
</tr>
<tr>
<td>Miotics</td>
<td>218</td>
</tr>
<tr>
<td>Misoprostol breastfeeding</td>
<td>5</td>
</tr>
<tr>
<td>Mitomycin, 190</td>
<td></td>
</tr>
<tr>
<td>MMR Vaccine</td>
<td>241</td>
</tr>
<tr>
<td>Mono Amino Oxidase Inhibitors, MAOI drug interaction, 23</td>
<td></td>
</tr>
<tr>
<td>Morphine, 253</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naphazoline</td>
</tr>
<tr>
<td>Neomycin</td>
</tr>
<tr>
<td>Neostigmine</td>
</tr>
<tr>
<td>Niclosamide</td>
</tr>
<tr>
<td>Nicotine breastfeeding</td>
</tr>
<tr>
<td>Nitrates</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
</tr>
<tr>
<td>Nitrous oxide</td>
</tr>
<tr>
<td>Norethisterone</td>
</tr>
<tr>
<td>Norfloxacin</td>
</tr>
<tr>
<td>NSAIDs</td>
</tr>
<tr>
<td>Nystatin, 156</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octreotide</td>
</tr>
<tr>
<td>Oestradiol, ethinyl</td>
</tr>
<tr>
<td>Ofloxacin</td>
</tr>
<tr>
<td>Omeprazole</td>
</tr>
<tr>
<td>Ondansetron</td>
</tr>
<tr>
<td>OPV, Oral Polio Vaccine (Sabin)</td>
</tr>
<tr>
<td>Oral anticoagulants drug interaction</td>
</tr>
<tr>
<td>Oral hypoglycemics drug interaction</td>
</tr>
<tr>
<td>Oral rehydration solution</td>
</tr>
<tr>
<td>Orphenadrine</td>
</tr>
<tr>
<td>Osmotic diuretics</td>
</tr>
<tr>
<td>Ouabain</td>
</tr>
<tr>
<td>Oxybuprocaine</td>
</tr>
<tr>
<td>Oxymetazoline</td>
</tr>
<tr>
<td>Oxytetracycline eye. See tetracycline</td>
</tr>
<tr>
<td>Oxytocin, 171 uterus, 181</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paclitaxel, 191</td>
</tr>
<tr>
<td>Pancuronium Bromide</td>
</tr>
<tr>
<td>Paracetamol</td>
</tr>
<tr>
<td>Pectin</td>
</tr>
<tr>
<td>Penicillin Benzathine, G</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
antispasmodic, *paed*, 60
Phenylephrine, 216
decongestant, 222, 223
Phenytoin, 121
drug interaction, 22, 23
teratogen, 3
Phytomenadione. *See* Vitamin K
Pilocarpine, 218
Pipenzolate, 60
Pneumococcal Vaccine, 243
Polyvalent Anti Scorpion Venom, 243
Polyvalent Anti Snake Venom, 244
Potassium
  chloride, 201
  oral, 201
Praziquantel, 161
Prazosin, 68
Prednisolone, 173
  anti-allergy, 107
Probenecid
drug interaction, 23
Progesterone, 176
  medroxy acetate, 174
Promethazine, 104
Propofol, 250
Propranolol, 72
Proton pump inhibitors, 50
Pseudoephedrine, 224
Pyrazinamide, 153
Pyrazolones
drug interaction, 22
Pyrimethamine, 161

Q
Quinidine, 80
  ADR, CVS, 44
drug interaction, 23
Quinolones, 150
  breastfeeding, 6
  geriatric, 16

R
Rabies Immune Globulin (RIG), 243
Rabies Vaccine, 243
Radiopharmaceuticals
  breastfeeding, 6
Ranitidine, 51
Ribaverin, 155
Rifampicin, 152
drug interaction, 23
Ringer lactate, 202

S
Salbutamol, 92
Salicylates
drug interaction, 22
Senna Extract, 55
Silymarin, 58
Simethicone, 57
Sodium
  bicarbonate, 202
  bicarbonate, interaction, 23
  chloride, 203
  chloride, dextrose, 203
Sodium Cromoglycate, 93
Sodium Nitroprusside, 67
Sodium phosphate
  Enema, 58
Steatosis
  Hepatic injury, 34
Stevens-Johnson syndrome. *See* Erythema multiforme
Streptokinase, 82
Streptomycin, 154
  intestinal antiseptics, 58
Strophanthin-G. *See* Ouabain
Sulphacetamide, 216
Sulphadiazine, 166
  skin, 228
Sulphonamides, 149
drug interaction, 22
eye, 216
skin, 228
Sulphonylureas, 170
Sumatriptan, 211
Sympathomimetics
heart failure, 78

T

Tamoxifen, 191
Tar, 232
Taxanes, 191
Td Vaccine, 239
Terbutaline, 92
Tetanus Vaccine, 240
Tetracosatrin, 179, See Tetracosatrin
Tetracycline, 147
drug interactions, 22
paediatrics, 8
skin, 227
teratogen, 3
Tetrahydrozoline, 222
Theophylline, 91
Thiazides, 63
drug interaction, 22
Thiopental, 249
Thiopentone. See Thiopental
Thioridazine
ADR, CVS, 44
Thiouracil
propyl, 179
Thyroxin, 177
Timolol, 217
Tinidazole, 160
Tramadol, 255
Triamcinolone
anti-allergy, 106
Triprolidine, 224
Typhoid Vaccine, 241

V

Valproic acid, 122
drug interaction, 22, 23
teratogen, 3
Valsartan, 69
Vancomycin, 148
Varicella Vaccine, 242
Verapamil, 71
arrhythmia, 81
Vinblastine, 187
Vincristine, 186
Viral Influenza Vaccine, 241
Vitamin A, 196
teratogen, 3
Vitamin B
complex, 198
Vitamin B₁₂, 197
Vitamin C, 199
vitamin D. See Cholecalciferol
Vitamin E, 196
Vitamin K, 198
Haemostatics, 88
paediatrics, 8

W

Warfarin, 86

X

Xanthines, 91
Xylocaine. See Lidocaine
Xylometazoline, 221

Y

Yellow Fever Vaccine, 242

Z

Zinc, 200
Zinc oxide, 232
Zollinger-Ellison syndrome, 49, 50, 51