Seventh Edition

Medical Pharmacology

As per the latest
CBME Guidelines
Competency Based Undergraduate Curriculum for the Indian Medical Graduate

Padmaja Udaykumar

Dedicated to Education
CBS Publishers & Distributors Pvt Ltd

Contents

Unit III: **Autacoids and Related Drugs**

Unit IV: **Anaesthetics**

Unit V: Central Nervous System

Unit VI: Drugs Acting on the Kidney

Unit VII: **Blood**

Unit VIII: **Cardiovascular System**

Unit IX: **Respiratory System**

Unit X: **Gastrointestinal Tract**

Unit XI: **Drugs used in Haematological Disorders**

Unit XII: **Drugs used in Endocrine Disorders**

Unit XIII: **Chemotherapy**

Unit XIV: **Immunopharmacology**

Unit XV: **Toxicology**

Unit XVI: **Miscellaneous Topics**

CHAPTER 1

Principles of Pharmacology, Evidence-based Medicine and Routes of Drug Administration

Competency achievement: The student should be able to:

PH 1.1 Define and describe the principles of pharmacology and pharmacotherapeutics.[1]

PH 1.2 Describe the basis of evidence-based medicine and therapeutic drug monitoring.[2]

Pharmacology is the science that deals with the study of drugs and their interaction with the living systems. The word pharmacology is derived from the Greek word—***Pharmacon*** meaning an active principle and ***logos*** meaning a discourse.

HISTORICAL ASPECTS

The useful and toxic effects of many plant and animal products were known to man since ancient times. In fact, there has been a quest for drugs and remedies since the existence of mankind itself.

In early days, there was a close relationship between religion and the treatment of diseases. The knowledge of the use of drugs often rested with the priest or holyman. Drugs were thought to be magical in their actions. Several cultures like the Chinese, Greek, Indian, Roman, Persian, European and many others contributed a great deal to the development of medicine in early times. The drug prescriptions included preparations from herbs, plants, animals and minerals. However, written information on remedies used in early times is lacking.

The Indian and the Chinese writings are amongst the oldest written material in medicine. India's earliest pharmacological writings are from the 'Vedas'. Rigveda (3000 BC) has description of some medicines. An ancient Indian physician Charaka, and then, Sushruta and Vagbhata, described many herbal preparations included in **'Ayurveda'** (meaning the science of life). Indians practiced vaccination as early as 550 BC.

'Pen Tsao' the Chinese materia medica was written as early as 1700 BC and it contained classification of medicinal plants and some preparations of plants, metals and animals.

The Egyptian medical papyri (1600 BC) described several preparations. The largest of them, Ebers Papyrus lists some 800 preparations.

The Greeks studied the toxic effects of various plant extracts. Their contribution to the growth of modern medicine is significant. **Hippocrates** (460–377 BC), a Greek physician, studied the cause of disease and wrote on the ethics of medicine and recommended judicious use of drugs. Galen (130–201 BC), also a Greek physician, practiced in Rome and put forth a doctrine that diseases are due to an imbalance of fluids—blood, phlegm, black bile and yellow bile. He believed that drugs had some properties like warmth, coldness, dryness or humidity and also thought that it is beneficial to use a combination of drugs to obtain these effects.

In the Middle Ages, many herbal gardens were cultivated by the monasteries. **Paracelsus** the **'Grandfather of Pharmacology'** born in Switzerland was the son of a physician. He

Pharmacoeconomics deals with the cost, i.e. economic aspects of drugs used therapeutically.

Pharmacogenetics (and pharmacogenomics) is the science that deals with the study of genetic basis for variation in drug responses (*see* page 54).

Pharmacoepidemiology is the study of both the useful and adverse effects of drugs on large number of people.

Pharmacovigilance is related to the detection, assessment, understanding and prevention of adverse effects of drugs (*see* page 65).

Toxicology deals with the adverse effects of drugs and also the study of poisons, i.e. detection, prevention and treatment of poisoning *(Toxicon = poison in Greek)*.

Chemotherapy is the use of drugs and chemicals for the treatment of infections. The term now also includes the use of chemical compounds to treat malignancies.

Essential medicines are those that satisfy the healthcare needs of majority of the population and should be available at all times in adequate amounts and in the appropriate dosage forms (*see* page 74) as defined by the WHO.

Orphan drugs are drugs to be used for prevention and treatment of rare diseases.

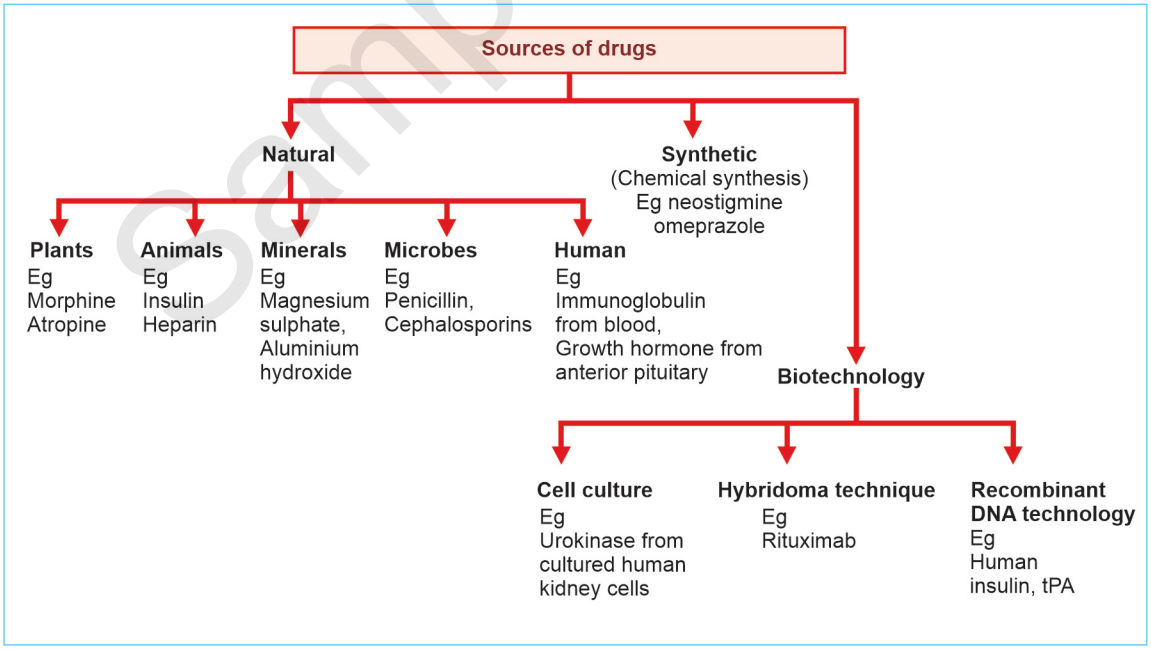
Pharmacopoeia is the official publication containing information on drugs (*see* page 72).

Pharmacy is the science of identification, compounding and dispensing of drugs. It also includes collection, isolation, purification, synthesis and standardization of medicinal substances.

Chronopharmacology is the science that involves the correlation of drug effects to the circadian rhythm to obtain optimum therapeutic effect and minimize the adverse effects, e.g. bronchospasm usually occurs at night. Blood pressure rises at dawn and dusk and is the lowest at midnight (*see* page 73). **Chronotherapy** is the administration of drugs to match the circadian rhythm. ***Chronobiotics*** are drugs that can be used to modify or reset the circadian rhythm. They find application mostly in conditions like sleep disorders and jet lag.

SOURCES OF DRUGS

The sources of drugs could be natural, or synthetic and biotechnology.



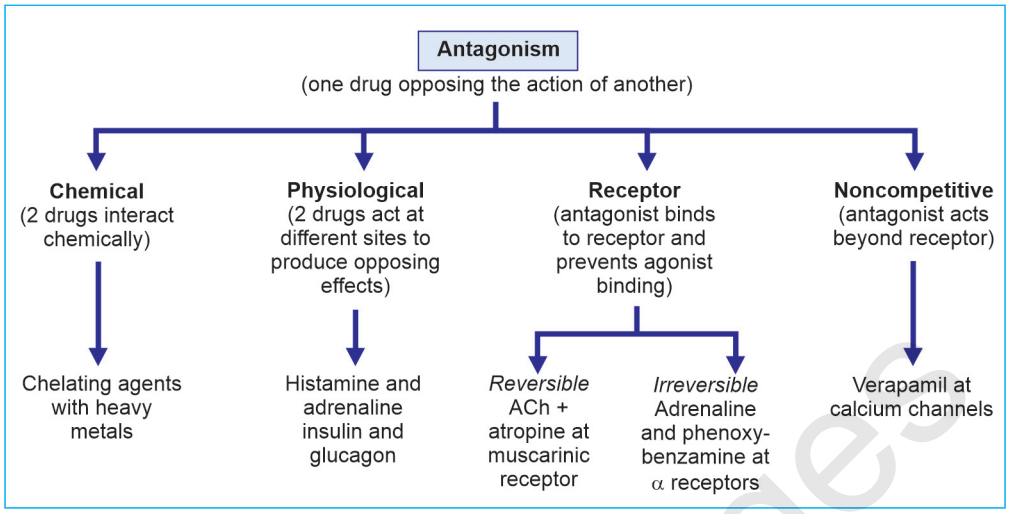


Fig. 3.9: Types of antagonism with examples

3. Antagonism at the Receptor Level

The antagonist binds to the receptor and inhibits the binding of the agonist to the receptor. Such antagonism may be reversible or irreversible.

Reversible or competitive antagonism: The agonist and antagonist compete for the same receptor. When a fixed concentration of an agonist is employed and the dose of the antagonist is progressively increased, the response to the agonist is progressively diminished. However, by increasing the concentration of the agonist, the antagonism can be overcome. It is thus reversible antagonism. The same maximal response can still be obtained by increasing the dose of the agonist. It is also called **surmountable** or **equilibrium type** of antagonism. This is the most common type of antagonism. Acetylcholine and atropine compete at muscarinic receptors. The antagonism can be overcome by increasing the concentration of acetylcholine at the receptor. Tubocurarine and acetylcholine compete for the nicotinic receptors at the neuromuscular junction. The dose response curve of the agonist shifts to the right (Fig. 3.10) in the presence of competitive antagonists.

Clinical significance: When an antagonist is used therapeutically, it should be borne in mind that the extent of inhibition brought about by a reversible antagonist depends on the concentration of the agonist. Therefore, the dose of the antagonist should be adjusted to get the optimum response, e.g. propranolol is used to block β adrenergic receptors. An increased amount of the endogenous agonists noradrenaline and adrenaline are released in stress and the dose of the antagonist (propranolol) needed would also be more in such situations.

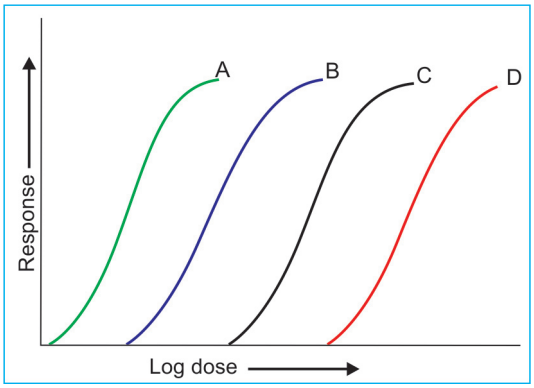


Fig. 3.10: Dose response curves of an agonist: A in the absence of competitive antagonist; B, C and D in the presence of increasing doses of a reversible competitive antagonist

Irreversible antagonism: The antagonist binds by covalent bonds to the receptor and it binds so firmly that it dissociates very slowly or not at all. Thus it blocks the action of the agonist and the blockade cannot be overcome by increasing the dose of the agonist and hence it is irreversible antagonism. In this type of antagonism, the duration of action is usually long since the effect remains till the new receptors are synthesized, e.g. adrenaline and phenoxybenzamine at alpha adrenergic receptors. This antagonism is also called **non-equilibrium** type of antagonism.

There is progressive flattening of the dose response curve (Fig. 3.11).

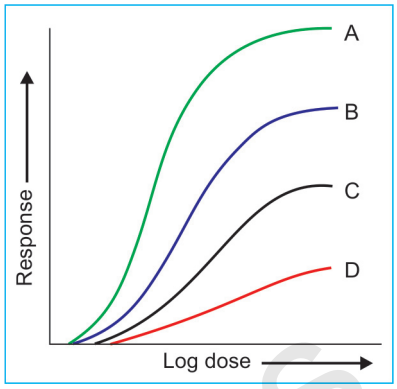


Fig. 3.11: Dose response curves of an agonist A, in the absence of antagonist, B, C, and D in the presence of increasing doses of an irreversible antagonist

4. Noncompetitive Antagonism

The antagonist blocks at the level of the receptor–effector linkage, i.e. at a different site beyond the receptor and not on the receptor. There is flattening as well as some rightward shift of the dose response curve (Fig. 3.12). For example, verapamil blocks the cardiac calcium channels and inhibits the entry of Ca^{++} during depolarisation. It thereby antagonises the effect of cardiac stimulants like isoprenaline and adrenaline. Since non-competitive antagonism is often confused with irreversible antagonism, they are compared in the table (below).

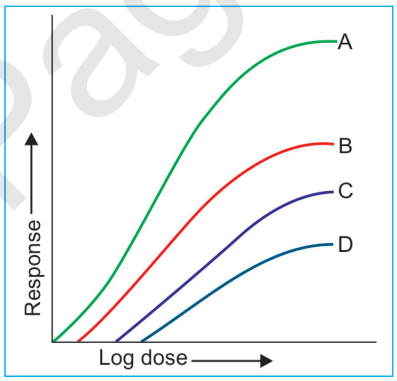


Fig. 3.12: Non-competitive antagonism—there is flattening as well as some rightward shift of DRC

FACTORS THAT MODIFY THE EFFECTS OF DRUGS

The same dose of a drug can produce different degrees of response in different patients and even in the same patient under different situations. Various factors modify the response to a drug. They are:

1. Body weight: The recommended dose is calculated for medium built persons. For the obese and underweight persons, the dose has to be calculated individually. Though body surface area is a better parameter for more accurate calculation of the dose, it is inconvenient and hence not generally used.

COMPARE AND CONTRAST

Parameter	*Irreversible antagonism*	*Non-competitive antagonism*
Receptor binding	Yes	Not involved
Mode of action	Binding irreversible or very long lasting	Binding at a different site than receptor
Example	Phenoxybenzamine at α receptors	Verapamil at Ca^{++} channels
DRC	Progressive flattening	Flattening and rightward shift

Table 5.2: Important drug schedules

Schedule	*Features*	*Examples*
Schedule H drugs—to be sold under "prescription only"	• Warning to be given on the label: Schedule H drug. Warning: To be sold on the prescription of registered medical practitioner only • Symbol R_x should be printed prominently on the left hand top corner of the label • If the drug is covered under Narcotic Drugs and Psychotropic Substances Act, symbol NR_x should be printed instead of R_x • The rules for sale are same as for schedule X drugs	Acyclovir Alprazolam Amitriptyline Atenolol Azathioprine Bacampicillin Barbiturates Antibiotics
Schedule X: Psychotropic drugs	• The label should contain the warning: "Schedule X drug" • Symbol X R_x in red letters on left hand top corner • Warning: To be sold on presciption of a registered medical practitioner only • Schedule X drugs should be stored under lock and key • Drugs should not be dispensed more than once unless such an instruction is given in the prescription • No substitute or alternative drug should be given • The prescription should be in duplicate and a copy should be retained for at least 2 years • On the cash bill, the purchaser's signature should be taken.	Amphetamine Barbiturates Methaqualone Glutethimide
NDCT-2019	Describes requirements and guidelines for new drug and clinical trials	
Other important drug schedules:		
Schedule C	Includes biological and special (intravenous) products Druggists require separate license for sale of these drugs	Insulin, adrenaline
Schedule E	Includes poisons and drugs under Ayurvedic, Siddha and Unani systems of medicine. It applies to the storage and sale of such drugs.	
Schedule F, F1	Include vaccines and sera	
Schedule G	For these drugs, label should have the warning—'Caution: It is dangerous to take this preparation except under medical supervision'. Containers should be labelled in red bottles against white background	Ethosuximide; anticancer drugs like bleomycin; hormones antidiabetics like insulin, glibenclamide
Schedule S	Prescribes standards for cosmetics	

7. Blank space should be avoided between direction and the signature of the doctor. If blank space is present, it should be striked off to avoid misuse of the space to obtain drugs illegally.

PARTS OF THE PRESCRIPTION

1. Date of writing the prescription.
2. Address of the prescriber—preferrably prescriptions are written on the letter pad with doctor's name and address printed at the top.
3. Name, age, sex and address of the patient.
4. Superscription—the symbol R_x meaning 'take thou' is also considered as an invocation to the Greek Gods of healing—Jupitor and Horus.
5. Drug name and strength. This is the body of the prescription—also called inscription. Abbreviations should never be used.

CHAPTER 6

Adrenergic Agonists and Antagonists

OVERVIEW

The nervous system is divided into central and peripheral nervous systems (Fig. 6.1). The peripheral nervous system consists of autonomic and somatic nervous systems. The autonomic nervous system (ANS) is **not under voluntary control** and, therefore, was so named by Langley (*Autos* = self, *nomos* = governing—in Greek). The ANS innervates the **heart**, the **smooth muscles**, the **glands** and the **viscera** and controls the functions of these organs (Fig. 6.2).

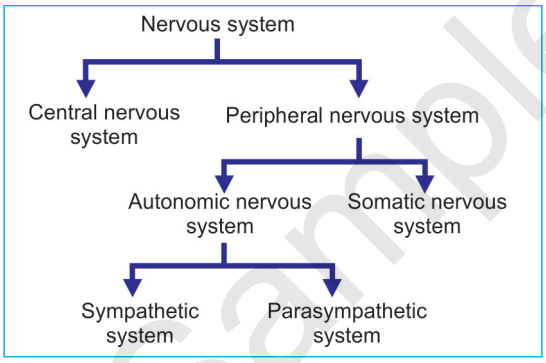


Fig. 6.1: Nervous system

The centres for autonomic reflexes are present in the hypothalamus, medulla and spinal cord. Hypothalamus coordinates the autonomic activity.

The ANS consists of two major divisions—the **sympathetic** and the **parasympathetic** (Fig. 6.4). Most of the viscera have both sympathetic and parasympathetic innervation. ***The two divisions have opposing effects and normally their effects are in a state of equilibrium.*** The prime function of the sympathetic

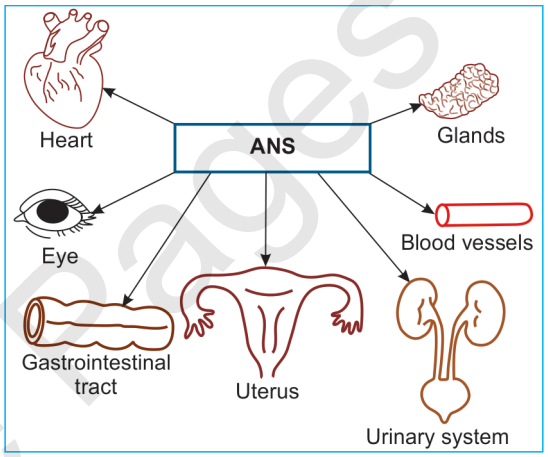


Fig. 6.2: Structures under the control of autonomic nervous system

system is to help a person to adjust to stress and prepare the body for **fight or flight reactions**, while the parasympathetic mainly participates in **tissue building reactions.** Man can survive and remain alive without sympathetic system (if maintained stress-free) but not without parasympathetic.

AUTONOMIC INNERVATION

Like the somatic nervous system, autonomic innervation also has an afferent, a center and an efferent.

Autonomic afferents: The autonomic afferents (Fig. 6.3) are carried in visceral nerves through nonmyelinated fibres. For example, the parasympathetic afferents are carried by the 9th and 10th cranial nerves. The autonomic efferent innervation consists of a myelinated preganglionic fibre which synapses with the postganglionic fibre. The postganglionic fibre

Table 7.5: Salient features of atropine derivatives

	Derivative	*Preparations and dose*	*Indications*	*Comments*
1.	Homatropine	HOMIDE 1, 2% eye drops; 1–2 drops	For fundoscopy and in iritis to produce mydriasis, it also produces cycloplegia	Duration of mydriasis 1–3 days
2.	Cyclopentolate	CYCLOMID 0.5, 1% eye drops; 1–2 drops	To produce cycloplegia	Mydriasis up to 24 hrs
3.	Tropicamide	TROPICAMET, TROMIDE 0.5, 15% eye drops 1–2 drops	Mydriasis for fundoscopy	Mydriasis 3–6 hrs—shortest acting
4.	Propantheline	PROBANTHINE 15 mg tab; 15–30 mg TDS	Peptic ulcer	Gastric emptying is delayed
5.	Oxyphenonium	ANTRENYL 5, 10 mg tab; 5–10 mg	Peptic ulcer, GI hypermotility	Delays gastric emptying; NM blockade in higher dose
6.	Clidinium	NORMAXIN 2.5 mg with dicyclomine 10 mg + chlordiazepoxide 5 mg; 2.5–5 mg oral	Peptic ulcer, colic, IBS	May be combined with BZD for dyspepsia
7.	Glycopyrrolate	PYROLATE 0.2 mg/ml, 1 ml amp, 10 ml vial; 0.1 –0.3 mg IM; 1–2 mg oral	Preanaesthetic medication	Does not cross BBB – No CNS effects
8.	Dicyclomine	CYCLOPAM 20 mg with paracetamol 500 mg; 20 mg/ml inj. 10–20 mg TDS	Motion sickness, morning sickness, antispasmodic in dysmenorrhoea, IBS	Also has antiemetic properties
9.	Valethamate	EPIDOSIN 10 mg tab, 8 mg inj.; 10 mg oral, 8 mg IM	Spasmolytic, dilatation of cervix	—
10.	Oxybutynin	OXYSPASS, OXYBUTIN 2.5, 5 mg tab; 5 mg BD-TDS	Urinary disorders—to increase bladder holding capacity	Can also be instilled directly into bladder or applied transdermally
11.	Tolterodine	TORQ 1, 2 mg tab; 2 mg BD	Urinary disorders—to reduce urinary urgency and frequency	Dose to be reduced in patients receiving microsomal enzyme inhibitors
12.	Flavoxate	URISPAS 200 mg tab; 200 mg TDS	Urinary disorders—to reduce urinary urgency and frequency as in cystitis, urethritis and prostatitis	Also has local anesthetic and analgesic properties
13.	Darifenacin	DARITEN 7.5 mg OD	Over active bladder	—
14.	Benzhexol	ARTANE, PACITANE 2 mg tab; 2–12 mg/day	Drug-induced EPS	FDC with antipsychotics available
15.	Ipratropium	IPRAVENT 20 μg and 40 μg/puff; 20–40 μg 3–4 times a day inhalation	COPD, bronchial asthma	More useful in COPD than asthma
16.	Tiotropium	TIOVA 18 μg ROTACAPS; 18 μg OD	COPD, bronchial asthma	Longer acting than ipratropium

IBS: Irritable bowel syndrome FDC: Fixed dose combination
EPS: Extrapyramidal symptoms NM: Neuromuscular

CHAPTER 8

Skeletal Muscle Relaxants

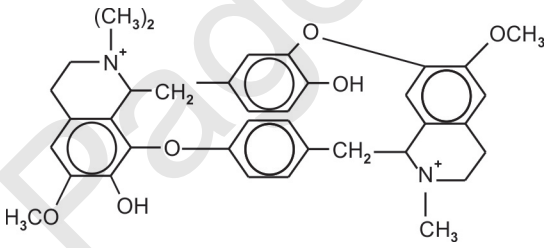
Competency achievement: The student should be able to:

PH 1.15 Describe mechanism/s of action, types, doses, side effects, indications and contraindications of skeletal muscle relaxants .[1]

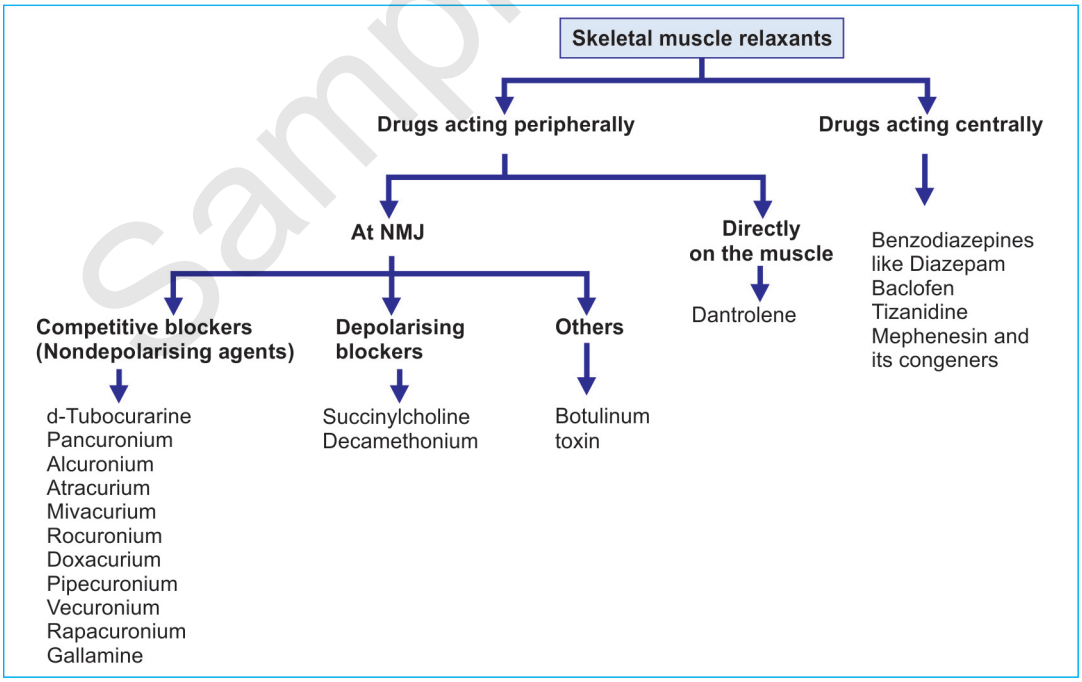
Skeletal muscle relaxants (SMRs) are drugs that reduce the muscle tone either by acting peripherally at the neuromuscular junction (neuromuscular blockers) or centrally in the cerebrospinal axis or directly on the contractile mechanism. They reduce the spasticity in a variety of neurological conditions and are also useful in surgeries.

Skeletal muscle relaxants may be classified as given in Flowchart 8.1.

Structure of d-Tubocurarine



Flowchart 8.1: Classification of skeletal muscle relaxants



1. PERIPHERALLY ACTING SKELETAL MUSCLE RELAXANTS

Neuromuscular Blockers (NMB)

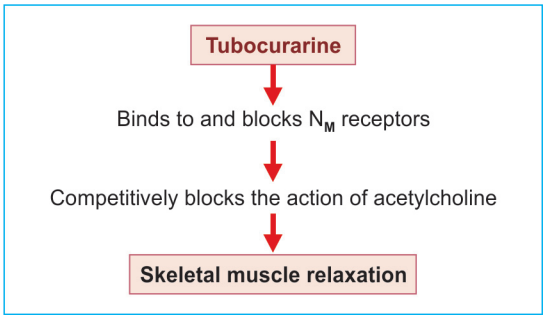
A. Competitive Blockers

d-Tubocurarine: Curare was used by the South American Indians as arrow poison for hunting wild animals because curare paralysed the animals. On extensive research, the active principle from curare, **tubocurarine** was identified.

d-Tubocurarine (d-Tc) is the dextrorotatory quaternery ammonium alkaloid obtained from the plant *Chondrodendron tomentosum* and plants of the *Strychnos* species (l-tubocurarine is less potent). Several synthetic agents have been developed. All these are quaternary ammonium compounds because of which they are not well absorbed, do not cross the BBB and are quickly excreted.

Mechanism of Action

Non-depolarising blockers bind to N_M nicotinic receptors (*see* Fig. 7.3, page 111) on the motor end plate and block the actions of acetylcholine by competitive blockade (Fig. 8.1). These compounds slowly dissociate from the receptors and transmission is gradually restored. Thus, the action of d-Tc is reversible. Increasing the concentration of the agonist acetylcholine at the NMJ also overcomes the blockade. This can be done by the administration of anticholinesterases like neostigmine.



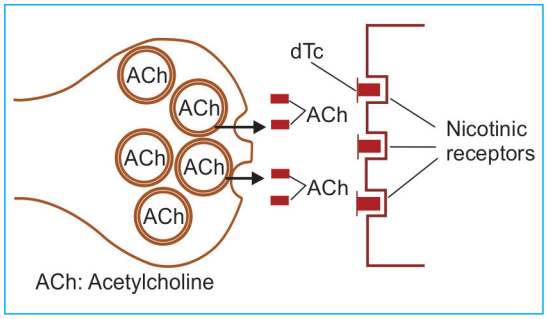


Fig. 8.1: d-Tc molecules bind to nicotinic receptors and prevent the binding of ACh on these receptors

Pharmacological Actions

Skeletal muscle: On parenteral administration, tubocurarine initially causes muscular weakness followed by flaccid paralysis. Small muscles of the eyes and fingers are the first to be affected, followed by those of the limbs, neck and trunk. Later the intercostal muscles and finally the diaphragm are paralysed and respiration stops. Consciousness is not affected throughout. Recovery occurs in the reverse order, i.e. the diaphragm is the first to recover. The effect lasts for 30–60 minutes (Table 8.1).

Autonomic ganglia: In high doses tubocurarine can block autonomic ganglia and adrenal medulla resulting in hypotension.

Histamine release: Tubocurarine can cause histamine release from the mast cells leading to bronchospasm, increased tracheobronchial and gastric secretions. Histamine release also contributes to hypotension. Some of the other NMBs also release histamine. They release histamine by a direct effect on the mast cells.

Pharmacokinetics

Tubocurarine and other NMBs are quaternary ammonium compounds, hence not absorbed orally. They are given either IM or IV.

Adverse Reactions

1. Respiratory paralysis and prolonged apnea—patient should be given artificial ventilation. Neostigmine or edrophonium

Table 10.3: Properties of some commonly used NSAIDs

NSAID	*Properties*	*Adverse effects*	*Uses*
Aspirin	Analgesic, anti-inflammatory, rheumatic fever, rheumatoid, psoriatic and osteoarthritis, closure of PDA; to delay labor or antiplatelet activity in post-stroke and post-MI	Gastritis, nausea, allergic reactions, precipitation of bronchial asthma, nephrotoxicity, hepatotoxicity, Reye's syndrome, delayed onset of labour, salicylism	Antiplatelet activity even in low dose, **good anti-inflammatory,** analgesic, Uricosuric agent. Irreversible inhibitor of COX-1 and COX-2
Paracetamol	Fever, as analgesic in headache, backache, dysmenorrhoea, myalgia and other painful conditions	Less gastric irritant, large doses—hepatotoxicity (toxic metabolite N-acetyl-benzoquinone-imine)	Good analgesic, antipyretic but weak anti-inflammatory (weak PG inhibition in the periphery). Antidote: n-acetylcysteine
Diclofenac	Chronic inflammatory conditions, rheumatoid arthritis, osteoarthritis, acute musculoskeletal pain and post-operative pain	Same as aspirin	Good concentration in **synovial fluid,** adverse effects milder; **aceclofenac** is longer acting and more gastric friendly
Ibuprofen, naproxen	Analgesic anti-inflammatory, and antipyretic, all actions milder than aspirin	Same as aspirin, but milder	Good analgesic, anti-inflammatory, antipyretic
Piroxicam	Arthritis, musculoskeletal pain	Same as aspirin, but milder gastric irritant.	Good analgesic, antipyretic anti-inflammatory. **Longer acting—OD dose**
Phenylbutazone	Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis	Same as aspirin, but more salt and water retention, more toxic than aspirin.	Salt and water retention, poor analgesic, antipyretic **Not preferred**
Indomethacin	Rheumatoid, psoriatic arthritis; good anti-inflammatory and antipyretic but toxicity is high	Toxicity high-peptic ulceration, oedema, agranulocytosis, hypothyroidism, insomnia, vertigo, optic neuritis, blurred vision, convulsions	Because of toxicity, it is **withdrawn** in many countries
Mephenamic acid	Dysmenorrhoea, myalgias	Gastric irritation, diarrhoea	Efficacy low, more toxic, contraindicated in children, used for short periods
Celecoxib	Good anti-inflammatory, analgesic, antipyretic	Higher risk of CV thrombotic events; Nausea, gastritis—milder, rashes, drowsiness, dizziness, nephrotoxicity, hepatotoxicity	Does not inhibit platelet aggregation, highly selective COX-2 inhibitor

of the risk of hepatotoxicity, nimesulide is **now banned** in most countries including India.

SELECTIVE COX-2 INHIBITORS

Coxibs

Though NSAIDs are extremely useful drugs, they are poorly tolerated particularly when they are used for long periods. Gastric irritation is the common side effect which limits its use. Selective inhibition of COX-2 was found to be advantageous because COX-2 is involved in inflammation and COX-1 which is protective on gastroduodenal mucosa is spared (Fig. 10.2). Some of the older NSAIDs have relative selectivity for selective COX-2 (meloxicam) but

COMPARE AND CONTRAST

Aspirin and Celecoxib (nonselective and selective COX-2 inhibitors)

Features	*Aspirin*	*Celecoxib*
Chemistry	Salicylic acid derivative	Sulfonamide derivative
COX inhibition	Non-selective (COX-1, COX-2)	Selective COX-2 inhibitor
Ulcerogenic effect on gastric mucosa	+++ (Significant)	+ (Mild)
t½	Short (2–3 hours)	Long (6–12 hours)
Effect on platelet function	Inhibits platelet aggregation	Does not
Risk of Reye's syndrome in children	Present	Nil
Risk of thrombosis, atherogenesis	Nil	Present
Cardiovascular toxicity	No significant effect	Risk of MI
Cerebrovascular toxicity	No significant effect	Risk of stroke
Use in post-MI patients	Recommended	Contraindicated
Prominent action	Analgesic, antipyretic, anti-inflammatory	Analgesic, antipyretic, anti-inflammatory
PG synthesis	Inhibited	Inhibited

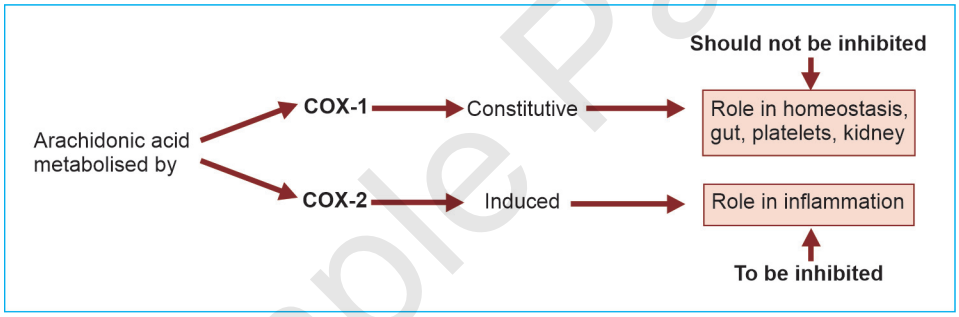


Fig. 10.2: Role of COX-1 amd COX-2

highly selective COX-2 inhibitors with several times greater selectivity for COX-2 have been synthesized—like the coxibs—**celecoxib, parecoxib and etoricoxib.** These drugs have analgesic, anti-inflammatory and antipyretic effects like non-selective NSAIDs but with much less gastric ulcerogenic effects. They also do not inhibit platelet aggregation because COX-1 is involved in platelet function. However, many of the coxibs have been withdrawn due to the adverse effects.

Adverse Effects

Clinical studies have shown that use of selective COX-2 inhibitors increase the risk of cardiovascular and cerebrovascular thrombotic events—**may increase the risk of myocardial infarction and stroke. Hence most of them (like rofecoxib) were withdrawn** from the market and the others are under supervision. They are indicated only in patients who cannot tolerate NSAIDs and are at a high risk of developing peptic ulcer.

Celecoxib

Celecoxib, a diaryl substituted compound is highly selective COX-2 (10–20 times) inhibitor. It has good anti-inflammatory, analgesic and antipyretic properties but does not affect platelet aggregation. In such indications too, they should be used in the minimum effective dose for a short period only.

CHAPTER 21

CNS Stimulants and Drugs of Abuse

Competency achievement: The student should be able to:

PH 1.22 Describe drugs of abuse (dependence, addiction, stimulants, depressants, psychedelics, drugs used for criminal offences).[1]

PH 1.23 Describe the process and mechanism of drug deaddiction.[2]

Drugs that have a predominantly stimulant effect on the CNS may be broadly divided into:

1. **Respiratory stimulants**
   Doxapram, nikethamide
2. **Psychomotor stimulants**
   Amphetamine, cocaine, methylxanthines
3. **Convulsants**
   Leptazol, strychnine.

RESPIRATORY STIMULANTS

Respiratory stimulants are also called ***analeptics***. These drugs stimulate respiration and are sometimes used to treat respiratory failure. Though they may bring about temporary improvement in respiration, the mortality is not reduced. They have a low safety margin and may produce convulsions. The availability of ventilators has reduced the need for analeptics.

Doxapram appears to act mainly on the brainstem and spinal cord and increase the activity of medullary respiratory and vasomotor centres. Doxapram in low doses can selectively stimulate respiration. Given intravenously as an infusion.

1–2 mg/kg/hr or 40–80 mg IM.

Adverse effects are nausea, cough, restlessness, muscle twitching, hypertension, tachycardia, arrhythmias and convulsions.

Uses

1. Doxapram is occasionally used IV as an analeptic in acute respiratory failure.
2. Apnoea in premature infants not responding to theophylline.

Nikethamide is not used because of the risk of convulsions.

PSYCHOMOTOR STIMULANTS

Amphetamine and **dextroamphetamine** are sympathomimetic drugs (*see* page 91).

Cocaine is a CNS stimulant, produces euphoria and is a drug of abuse (*see* page 182).

Methylxanthines

Caffeine, theophylline and theobromine are the naturally occurring xanthine alkaloids. The beverages—coffee contains caffeine; tea contains theophylline and caffeine; cocoa has caffeine and theobromine.

Actions

CNS: Caffeine and theophylline are CNS stimulants. They bring about an increase in mental alertness, a reduction of fatigue, produce a sense of well-being and improve motor activity and performance with a clearer flow of thought. Caffeine stimulates the respiratory centre. Higher doses produce irritability, nervousness, restlessness,

insomnia, excitement and headache. High doses can result in convulsions.

CVS: Methylxanthines increase the force of contraction of the myocardium and increase the heart rate and, therefore, increase the cardiac output. But, they also produce peripheral vasodilatation which tends to decrease the BP. The changes in BP are, therefore, not consistent. Caffeine causes vasoconstriction of cerebral blood vessels.

Kidneys: The xanthines have a diuretic effect and thereby increase the urine output.

Smooth muscle: Xanthines cause relaxation of smooth muscles especially the bronchial smooth muscle (*see* page 399).

Skeletal muscle: Xanthines enhance the power of muscle contraction and thereby increase the capacity to do muscular work by both a central stimulant effect and the peripheral actions.

GI tract: Xanthines increase the secretion of acid and pepsin in the stomach and are gastric irritants.

Pharmacokinetics

Methylxanthines are well absorbed orally, widely distributed and are extensively metabolised in the liver; t½ 7–12 hr. In higher doses t½ may be prolonged due to saturation of metabolizing enzymes. Premature infants have a longer t½ of 24–36 hr.

Adverse Effects

Adverse effects include nervousness, insomnia, tremors, tachycardia, hypotension, arrhythmias, headache, gastritis, nausea, vomiting, epigastric pain and diuresis. High doses produce convulsions. Tolerance develops after sometime. Habituation to caffeine is common.

Uses

i *Headache:* Because of the effect of caffeine on cerebral blood vessels, it is combined with ergotamine for the relief of migraine headache. Caffeine is also combined with aspirin/paracetamol for the treatment of headache.

ii. *Bronchial asthma:* Theophylline is used in the treatment of bronchial asthma.

iii. *Apnoea in premature infants:* Episodes of prolonged apnoea (>15–20 sec) may be seen in premature infants which if too frequent may result in neurologic and other tissue damage due to hypoxia. When no primary cause can be detected, methylxanthines may be used orally or IV. Theophylline or caffeine may be used for 1–3 weeks to reduce the duration of episodes of apnoea which may be seen in premature babies.

CONVULSANTS

Strychnine is an alkaloid obtained from the seeds of *Nux vomica*. On administration, it produces tonic convulsions—opisthotonus followed by coma and death. It acts as a competitive antagonist of the inhibitory neurotransmitter glycine—mainly stimulates the spinal cord and in higher doses the entire nervous system. **Strychnine is of no therapeutic value.** Poisoning can be treated by IV diazepam or clonazepam. Ventilatory support may be needed. 1:1000 potassium permanganate solution or tannic acid 2% solution can be used to adsorb the alkaloid and prevent its absorption. All sensory stimuli produce exaggerated reflexes and should, therefore, be avoided.

Leptazol or pentylene tetrazol is a CNS stimulant. By a direct effect on the central neurons, it produces convulsions. It is mostly used as an experimental drug to induce convulsions. Poisoning with leptazol is treated with diazepam.

NOOTROPICS

Nootropics are drugs that improve memory and cognition. They are also called cognition enhancers.

Ranolazine is orally effective with a bioavailability of 30–50%. It prolongs QT interval and, therefore, should be avoided with other drugs that prolong QT interval. It can also cause weakness, postural hypotension, dizziness, headache and constipation.

Dose: 500 mg sustained release tablets BD. RANEXA 100, 500 mg tab.

Oxyphedrine acts by improving myocardial metabolism in hypoxia. However, its efficacy is yet to be proved.

PHARMACOTHERAPY OF ANGINA

Exertional Angina

Coronary angioplasty with insertion of a stent is the preferred treatment in presence of significant narrowing of the coronary arteries. Coronary artery surgery is done when there is severe narrowing. Pharmacotherapy may be an alternative in some patients.

Acute attack: Sublingual nitroglycerin is the drug of choice. If the pain does not subside in 5 minutes, repeat the dose. After the relief of pain, the tablet should be discarded.

Acute prophylaxis: Sublingual nitroglycerin given 15 minutes before an exertion (e.g. walking uphill) can prevent the attack. The prophylactic effect lasts for 30 minutes.

Chronic prophylaxis: Long-acting nitrates or β-blockers (preferred) or calcium channel blockers can be used. All are given orally. If one drug is not effective, a combination of drugs may be used.

Combination of Drugs in Angina

1. *Nitrates + β-blockers:* Very effective in exertional angina. Reflex tachycardia due to nitrates is countered by β-blockers. Ventricular dilatation due to β-blockers is opposed by nitrates.
2. *Nifedipine + β-blockers:* The antianginal effects are additive. Reflex tachycardia due to nifedipine is countered by β-blockers.
3. *Nitrates + CCBs:* Nitrates decrease preload, CCBs reduce afterload and the combination reduces cardiac workload.
4. *CCBs + β-blockers + nitrates:* If the angina is not controlled by 2 drug combinations, 3 drugs can be used. Nitrates reduce preload, CCBs reduce afterload while β-blockers decrease heart rate. This combination is useful in severe angina.

Vasospastic Angina

Nitroglycerin and nifedipine given sublingually and amlodipine are effective in preventing and treating vasospastic episodes.

Unstable Angina

Unstable angina includes:

- Patients with exertional angina developing angina **at rest.**
- Severe, prolonged anginal attacks without ECG evidence of MI.
- Angina developing after myocardial infarction.

Such patients with unstable angina are at a high risk of developing MI or sudden death and need hospitalisation and rigorous treatment for its prevention. The primary goal of treatment is to increase myocardial blood flow.

Drugs used in Unstable Angina

1. *Aspirin:* Platelet aggregation can occlude narrowed coronary arteries and can also release potent vasoconstrictors. Aspirin (75–300 mg daily) prevents platelet aggregation and thereby could prevent myocardial infarction.
2. *Heparin:* In high-risk patients, IV/SC heparin reduces pain.
3. *Nitrates:* Intravenous nitroglycerin reduces the cardiac workload and relieves pain.
4. *Other drugs:* β-adrenergic blockers like atenolol (50–100 mg daily) and; if they are contraindicated, calcium channel blockers like diltiazem and verapamil may be given. Glycoprotein receptor antagonists (abciximab, epitifibatide and tirofiban) inhibit the final steps of platelet aggregation and are being tried in unstable angina.

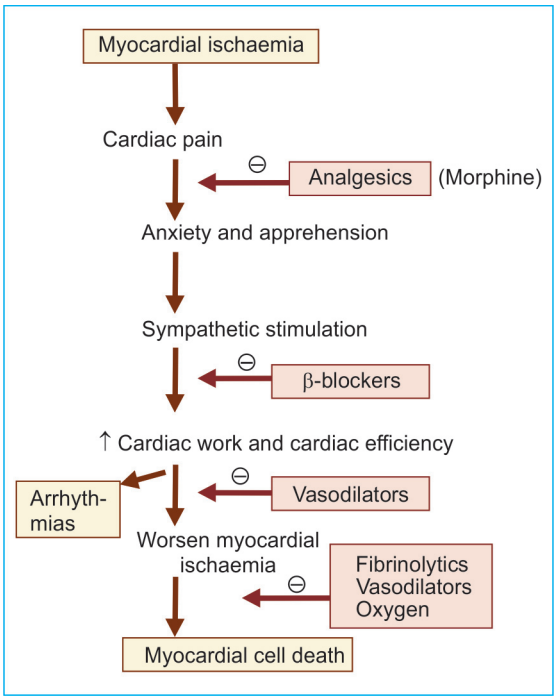


Fig. 28.4: Pathophysiology and sites of drug action in myocardial infarction

DRUGS USED IN MYOCARDIAL INFARCTION

Coronary heart disease is the most important cause of premature death, particularly in the developed countries.

Rupture of an atheromatous plaque in the coronary artery (Fig. 28.4) results in an occlusive thrombus leading to acute myocardial infarction. Symptoms include severe substernal pain radiating to the left shoulder, medial aspect of the left arm with nausea, vomiting, sweating, palpitation and shortness of breath. Patients appear pale and apprehensive. The process of infarction gradually develops (unless it is severe) over 6–8 hours after which there is cell death in the infarcted area. Timely intervention can reduce the extent of damage. Coronary angioplasty with a stent inserted to recanalise the coronary artery is the preferred option. The immediate objective of treatment is to limit the myocardial ischaemia and the consequent cell death. Drugs used are given below:

Immediate Treatment

1. *Analgesics and antianxiety drugs:* Pain due to myocardial ischaemia evokes anxiety and apprehension which result in sympathetic overactivity. This itself could prove deleterious to the heart. Hence a good analgesic, like morphine 10 mg or pethidine 50 mg, is given intravenously through an IV cannula. They relieve pain and thereby reduce anxiety. Hence the demerits of sympathetic overactivity are reduced. Diazepam may also be given to reduce anxiety and produce sedation.
2. *Thrombolytics:* Can limit the extent of damage and reduce mortality, if started at the onset of symptoms. They should be started at the earliest possible (within 6–12 hr). Streptokinase 1.5 million units infusion is given over 1 hour. Urokinase or alteplase may be given as alternatives as 15 mg bolus and 0.5 mg/kg over the next 90 minutes.

   Anistreplase is a form of streptokinase which is convenient to use because it is long acting and, therefore, can be used as a single IV injection. Alteplase is expensive and hence is mostly reserved for patients in whom streptokinase cannot be used (*see* page 309).

   Thrombolytics should be **started at the earliest possible** (within 6–12 hours) because they can limit the extent of damage and reduce mortality.
3. *Antiplatelet drugs:* 300 mg of soluble aspirin should be given orally immediately at the onset of symptoms. It reduces mortality and improves the effect of thrombolysis. Aspirin should be continued for long term (75–150 mg/day) even after the patient recovers from MI. Patients allergic to aspirin may be given oral clopidogrel.
4. *Anticoagulants:* Heparin may be given to prevent the extension of thrombus and also to prevent deep vein thrombosis.
5. *Oxygen:* High flow oxygen should be given by inhalation.

CHAPTER 30

Hypolipidaemic Drugs

Competency achievement: The student should be able to:

PH 1.31 Describe the mechanisms of action, types, doses, side effects, indications and contraindications of the drugs used in the management of dyslipidemias.[1]

Hyperlipoproteinaemias (HPL) are conditions in which the concentration of cholesterol or triglyceride (TG) carrying lipoproteins in the plasma is elevated above normal (Table 30.1). Increase in lipoproteins can hasten the development of atherosclerosis and is a risk factor for myocardial infarction.

Lipids and proteins form complexes called lipoproteins and circulate in the blood vessels. There are four types of lipoproteins:

- Low density lipoproteins (LDL)
- High density lipoproteins (HDL)
- Very low density lipoproteins (VLDL)
- Chylomicrons.

LDL is the primary carrier of cholesterol while VLDL is of triglycerides. There are different pathways for the transport of endogenous and exogenous lipids (Fig. 30.1). In the exogenous pathway, cholesterol and triglycerides absorbed from the gut are transported as chylomicrons. They are hydrolysed to chylomicron remnants by the action of lipoprotein lipase (LPL) and free fatty acids are released which are taken up by muscle and adipose tissue. The chylomicron remnants are transported to the liver.

In the endogenous pathway, cholesterol and triglycerides from the liver are carried as VLDL to the muscle and adipose tissue. Here the triglycerides in VLDL are hydrolysed and free fatty acids released. Thus intermediate density lipoprotein (IDL) and then LDL are formed by the action of lipoprotein lipase. Cells have LDL receptors and LDL is taken up into the cell. When the LDL plasma levels rise, LDL is taken up by the scavenger macrophages. In this process, they are oxidised and such LDL is atherogenic.

Excess cholesterol from the cells is transported to the liver for excretion by reverse cholesterol transport. High density lipoproteins (HDL) take part in this process. They also antagonise atherogenesis by other mechanisms including antiplatelet—aggregatory effect, anticoagulant and other effects. High density lipoproteins decrease the risk of coronary heart disease, are called protective lipoproteins and higher plasma levels of HDL are thus desirable.

Types of Hyperlipoproteinaemias

Based on the lipoprotein fraction that is elevated, lipoprotein disorders may be

Table 30.1: Plasma lipid levels (mg/dl)

	Total CH	*LDL – CH*	*HDL – CH*	*TGs*
Desirable	<200	<100	>40 (men), >50 (women)	<150
Borderline	200–239	130–159	–	150–199
High	>240	>160	>60	>200

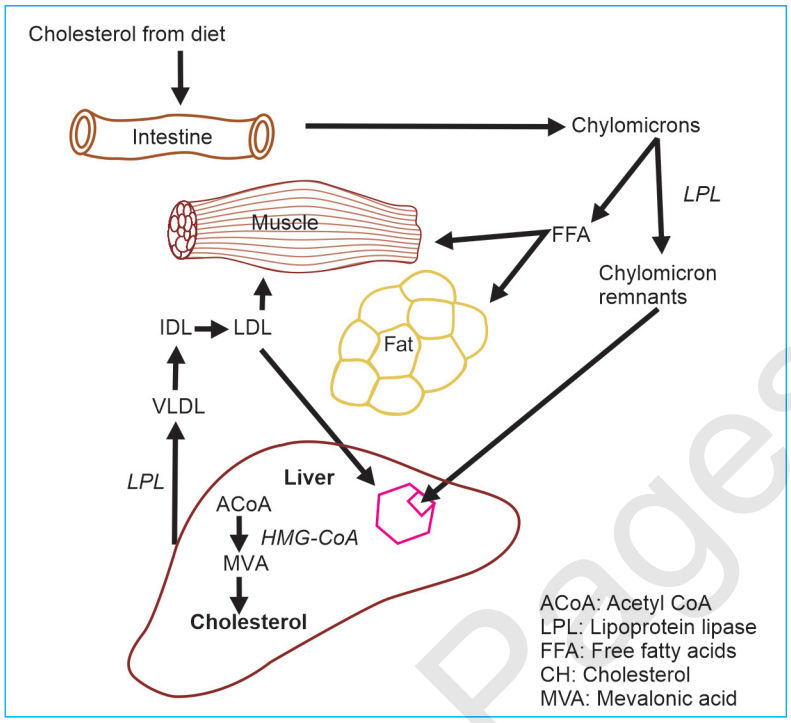


Fig. 30.1: Endogenous and exogenous pathways of lipid transport

broadly grouped into primary and secondary hyperlipidaemias (Table 30.2). Secondary hyperlipidaemias may be secondary to an underlying disorder.

HYPOLIPIDAEMICS

Elevated plasma levels of LDL cholesterol and low levels of HDL cholesterol enhance the risk of CHD along with the other risk factors, viz. smoking, family history of coronary artery disease, male sex, metabolic syndrome, diabetes mellitus and hypertension. Hence hypercholesterolaemia needs to be controlled.

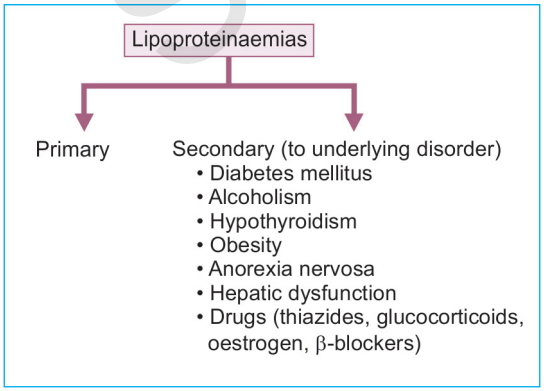


Table 30.2: Types of primary hyperlipoproteinaemias

Type	*Disorder*	*Plasma lipids raised*
I.	Familial LPL deficiency	C, TG
IIa.	Familial hypercholesterolaemia	C
IIb.	Polygenic hypercholesterolaemia	C
III.	Familial dysbetalipoproteinaemia	C, TG
IV.	Hypertriglyceridaemia	TG
V.	Familial combined hyperlipidaemia	C, TG

C: Cholesterol, TG: Triglycerides, LPL: Lipoprotein lipase

Hypolipidaemics are drugs that lower plasma lipid levels in the body.

HMG-CoA Reductase Inhibitors (Statins)

Hydroxymethylglutaryl-CoA (HMG-CoA) is the rate-controlling enzyme in the biosynthesis of cholesterol.

CHAPTER 44

General Considerations

Competency achievement: The student should be able to:

PH 1.42 Describe general principles of chemotherapy.[1]

PH 1.43 Describe and discuss the rational use of antimicrobials including antibiotic stewardship program.[2]

Chemotherapy can be defined as the use of a chemical substance in infectious diseases to destroy microorganisms without damaging the host tissues.

Antibiotics are substances produced by microorganisms which suppress the growth of or destroy other microorganisms at low concentrations.

Pasteur and Joubert were the first to identify that microorganisms could destroy other microorganisms. **Paul Ehrlich** 'The **Father of Modern Chemotherapy'** coined the term 'chemotherapy'. He showed that certain dyes can destroy microbes and demonstrated that methylene blue can be used in malaria. He synthesized many arsenical compounds for the treatment of syphilis and sleeping sickness. Paul Ehrlich was awarded Nobel Prize for his work on chemotherapy. The evolution of chemotherapy can be studied in three periods.

i. Pre-Ehrlich era—before 1891
ii. The period of Paul Ehrlich
iii. Post-Ehrlich era—after 1935

Domagk in 1935 demonstrated that prontosil, a sulfonamide dye, is effective in some infections. Domagk was awarded Nobel Prize for his work. **Sir Alexander Fleming** discovered penicillin in 1928. He was studying different variants of staphylococci and found that a fungus was contaminating one of the culture plates. This fungus, *Penicillium notatum*, produced a substance which inhibited the growth of a variety of microorganisms. The substance was named Penicillin. It needed extensive research and purification for clinical use. In 1941, penicillin was first used therapeutically on a policeman. The discovery of penicillin is described as the beginning of the 'golden era' of antibiotics. In the last 60 years, several powerful antibiotics and their semisynthetic derivatives have been produced.

Many infectious diseases, which were earlier incurable, can now be treated with just a few doses of antimicrobial drugs. Thus the development of antimicrobial drugs is one of the important advances of modern medicine. In fact, antimicrobials are one of the most commonly prescribed drugs but are often the most over used or misused drugs.

Mechanisms of Action of Antimicrobials

The structure and composition of the bacterial cell differs from the mammalian cells in many aspects. This has made it possible to some extent to design antibacterials to act on such structures, enzymes, etc. to make them more selective to bacteria and less toxic to the human beings. Thus, antibiotics target different sites on the bacterial cell like:

1. *Cell wall:* Beta lactams and glycopeptides (vancomycin) inhibit the synthesis of bacterial cell wall. As a result, bacteria with

Classification

Based on the site of action

Antimicrobials may be classified (Fig. 44.1) as drugs that:

1. ***Inhibit cell wall synthesis***
   Penicillins, cephalosporins, carbapenems, monobactam, vancomycin, teicoplanin, bacitracin, cycloserine.
2. ***Damage cell membranes***
   (causing leakage of cell contents)
   Polymyxins, amphotericin B, nystatin.
3. ***Bind to ribosomes and inhibit protein synthesis***
   50S—erythromycin, chloramphenicol clindamycin, streptogramins, linezolid
   30S—tetracyclines, aminoglycosides
4. ***Inhibit DNA gyrase***
   Fluoroquinolones
5. ***Inhibit DNA function***
   (↓DNA dependent RNA polymerase)
   Rifampicin
6. ***Interfere with metabolic steps***
   (Antimetabolite action)
   Sulfonamides, sulfones, trimethoprim, pyrimethamine

weak cell walls are formed which swell and burst due to difference in tonicity.

2. *Cell membrane:* Polymyxins alter the permeability of the cell membrane leading to leakage of cell contents followed by cell death. Amphotericin B causes leakage of fungal cell contents to damage the cell membrane leading to cell death.
3. *Protein synthesis:* Several antimicrobials act by interfering with the protein synthesis. The bacterial ribosome has a 50S and a 30S subunit and mammalian ribosome has 60S and 40S subunits which are involved in protein synthesis. Antimicrobials like amino glycosides, tetracyclines, chloramphenicol and macrolides bind to and interfere with the activity of 30S or 50S ribosomal subunits in the bacteria and thereby inhibit protein synthesis.

   Antibacterials may interfere with nucleic acid synthesis either by inhibitng DNA or RNA polymerase (e.g. rifampicin) or by inhibiting the enzyme DNA gyrase (quinolones).
4. *Metabolic pathway:* Drugs like sulfonamides interfere with the metabolic pathway of the bacteria, block the enzymes involved in

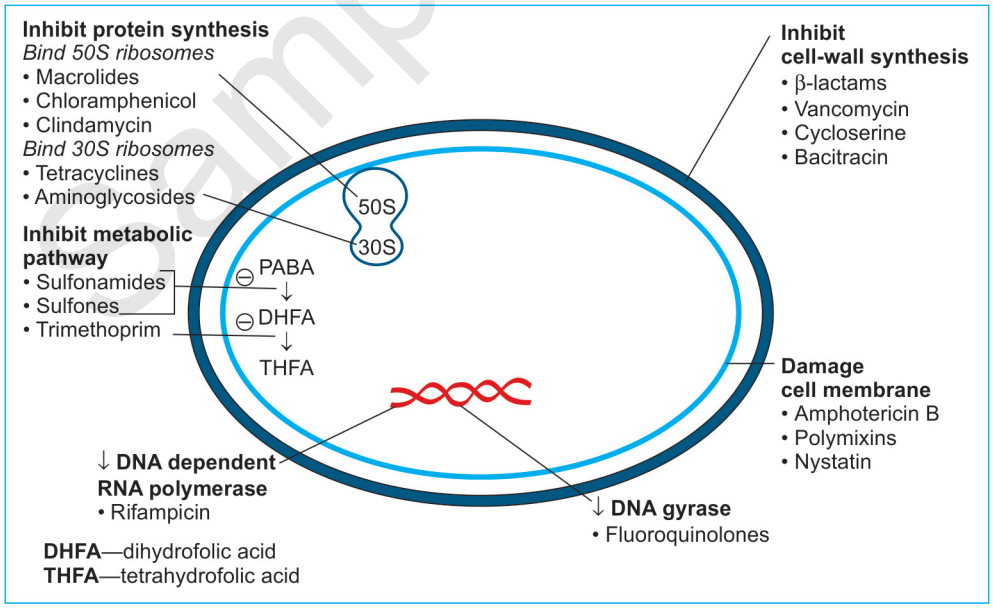


Fig. 44.1: Classification of antimicrobials based on their mechanisms of action

Table 60.2: Some specific antidotes for drugs and chemicals

Agent causing toxicity	*Antidote*	*Dose*
1. Paracetamol	N-acetyl cysteine	Oral 140 mg/kg followed by 70 mg/kg every 4 hr, or IV 150 mg/kg infusion over 15 min repeated as required.
2. Morphine and other opioids	Naloxone	1–2 mg IV repeated every 10–15 minutes.
3. Heparin	Protamine Sulphate	1 mg IV for every 100 units of heparin.
4. Cyanide	Sodium nitrate + Sodium thiosulfate	10 ml of 3% solution IV 50 ml of 25% solution IV
5. Organophosphates	Atropine, Oximes	2 mg IV repeated every 10 minutes Pralidoxime 1 gram IV every 3–4 hr 3 doses
6. Theophylline, caffeine	Esmolol	25–50 µg/kg/min- IV
7. Atropine	Physostigmine	1–2 mg IV slowly (or SC) may be repeated if symptoms reappear
8. Curare and other non-depolarizing skeletal muscle relaxants	Neostigmine	2 mg IV repeated as required.
9. Copper	d-penicillamine	100 mg/kg/day orally in 4 divided doses for 3–7 days.
10. Iron	Desferrioxamine	15 mg/kg/hr IV (100 mg desferrioxamine binds 8.5 mg of iron)
11. Arsenic	Dimercaprol	Ist day 400–800 mg deep IM in divided doses; 2nd and 3rd day 200–400 mg; 4th day onwards 100–200 mg
12. Lead	Calcium disodium edetate	1 g in 250 ml saline infusion twice a day.
13. Streptokinase and other fibrinolytics	Epsilon amino caproic acid	5 g oral or IV followed by 1 g hrly till bleeding stops (Max 30 gm in 24 hr)
14. Insulin	Glucose	50 ml of 50% solution.
15. Digitalis	Digoxin specific antibody fragments	10 vials (DIGI FAB) emperic therapy or specific $\text{No. of vials} = \frac{\text{Total digoxin consumed}}{0.5}$
16. Methanol, ethylene glycol	Ethanol or Fomepizole	10% ethanol is given orally –0.7 mg/kg loading Dose: 0.15 ml/kg infusion. loading dose 15 mg/kg repeated every 12 hours.
17. Carbon monoxide	Oxygen	100% by high-flow non-rebreathing mask.
18. Nitrites	Methylene blue	0.1% solution slow IV in the dose of 1–2 mg/kg body weight.
19. Warfarin	Vitamin K_1 oxide, fresh blood	10 mg IM followed by 5 mg 4 hrly As required.
20. Benzodiazepines	Flumazenil	0.2 mg IV repeated as required (Max. 3 mg)
21. Iodine	Sodium thiosulphate	1–5%, solution orally

tracheal tube may be inserted. Patient should be put in lateral position.

ii. If breathing is depressed, artificial ventilation should be given. Oxygen may be needed.

iii. *Circulation:* Circulatory status should be assessed by pulse rate, blood pressure and urine output. Suitable IV fluids should be given. Generally 1 litre of normal saline with 1 litre of dextrose

CHAPTER 62

Dietary Supplements, Nutraceuticals, Vitamins, Herbal Medicines and Enzymes in Therapy

Competency achievement: The student should be able to:
PH 1.61 Describe and discuss dietary supplements and nutraceuticals.[1]

DIETARY SUPPLEMENTS AND NUTRACEUTICALS

Dietary supplements are given along with the diet as a pill, capsule, tablet or liquid. Dietary supplements are not meant to replace food but are to be used in addition to food for health maintenance. The supplements include vitamins, minerals, herbals, botanicals, amino acids, enzymes and also some substances that have not been proved as being essential but could be having a beneficial biological effect.

Examples:

- Vitamin D supplements in people who do not get sufficient exposure to ultraviolet light.
- Calcium supplements to reduce risk of osteoporotic fractures.
- Protein supplements in people recovering from chronic illness or injury.
- Amino acids individually or in combination. Taurine is a popular supplement claimed to improve sports performance.
- Glucosamine—used as a nutrient for cartilage in osteoarthritis of knee.
- Body building supplements like high protein drinks, branched chain amino acids, glutamine, arginine, essential fatty acids, and creatinine are used by those involved in body building, weight lifters and athletes to increase lean body mass.

NUTRACEUTICALS

A nutraceutical (also called bioceutical or superfood) is a pharmaceutical compound that could produce beneficial effects to the user. It is a food or fortified food product that supplements the diet and also assists in treating or preventing disease. The term "nutraceutical" was coined in 1989 by Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine.

Nutraceuticals based on their source:

- Plant—tomato, garlic
- Animal—shark liver oil, cod liver oil.
- Mineral—calcium, magnesium, phosphorus.
- Microorganism—bifido-bacterium, lacto-bacilli.

Compare and Contrast

Nutraceutical	*Pharmaceutical*
Nutraceutical is used to prevent diseases	Pharmaceutical is used for prevention and treatment of diseases
Referred to as health product	Referred to as drug.
No license is needed to sell	Requires a license from the regulatory body
No prescription is required for purchasing	Can be purchased only by prescription (except OTC drugs)

Uses: They may be used to improve health, delay the process of aging, prevent chronic disease, increase life expectancy or support the structure or function of the body.

Some Nutraceuticals

- Coenzyme Q10 or ubiquinone used as purified nutritional supplement is an antioxidant. It has been tried in hypertension, heart failure and IHD. An interesting application is in prevention of statin-induced myopathy. Coenzyme Q10 levels may be reduced on administration of statins which may have a role in myopathy
- *Flax seeds:* Prevent mammary, colon and rectal cancers. Reduces blood pressure in hypertensive patients, reduces risk of diabetes and coronary artery disease.
- *Spirulina* has an immunostimulant property, used in arthritis and for delaying aging process.
- *Bitter gourd* has a hypoglycemic effect. The extract of bitter gourd increases the rate of glycogen synthesis by 4–5 fold in liver.
- *Garlic* used in the treatment of hyperlipidemia
- *Turmeric (curcuminoids)* has antimicrobial and anti-inflammatory activity. Recent findings indicate that it also is an integrase enzyme inhibitor.
- *Tomato lycopenes* prevents prostate cancer.
- *Fenugreek* has a laxative, expectorant and demulcent property.

Thus diet rich in nutraceuticals, along with regular exercise, stress reduction and maintenance of healthy body weight, will maximize health and reduce disease risk.

VITAMINS

Vitamins are organic compounds essential for normal metabolism in the body. They are supplied by the diet. A balanced diet supplies adequate amounts of vitamins to fulfill the daily requirement. The requirement is increased during periods of rapid growth, pregnancy and lactation. Vitamin deficiencies result in characteristic signs and symptoms.

Vitamins are grouped into fat-soluble and water-soluble vitamins (Table 62.1).

Fat-soluble Vitamins

Vitamin A

Vitamin A is present in the diet as retinol, dehydroretinol or as carotenoids. Carotenoids are pigments present in green yellow vegetables and fruits and are converted in the body to retinol.

Physiological functions: Vitamin A has an important role in dark adaptation. It is essential for the synthesis of rhodopsin, the photosensitive pigment of rods. Vitamin A is also essential for maintenance of the integrity of epithelial cells, for growth and cell-mediated immunity.

Signs and symptoms of deficiency: Xerophthalmia (dryness of eyes), Bitot's spots in the conjunctiva, night blindness, diarrhoea, dry and rough skin are seen in early stages. In the later stages, keratomalacia, perforation of the cornea, necrosis and blindness can occur.

Daily requirement 3000–5000 IU/day.

Uses: In the prophylaxis and treatment of vitamin A deficiency.

1. *Prophylaxis:* 3000–5000 IU/day in presence of increased requirement.
2. *Treatment:* 50,000–1,00,000 IU intramuscularly or orally for 1–3 days followed by oral supplementation.
3. *Acne:* Retinoic acid or synthetic analogs of vitamin A like tretinoin or isotretinoin are used.

Hypervitaminosis A: Since vitamin A is a fat-soluble vitamin, it accumulates in the body on prolonged administration. The symptoms are dry skin (hyperkeratosis), anorexia, fever, alopecia, anaemia, oedema, headache, skin ulcers and tenderness over the bones.

Seventh Edition

Medical Pharmacology

is the thoroughly revised, enlarged and updated edition of the popular textbook. The book retains its simplicity, lucidity and clarity of writing—the hallmark features well appreciated by the medical students as well as the teachers.

The textbook covers all the topics as per the latest CBME Guidelines | Competency Based Undergraduate Curriculum for the Indian Medical Graduate prescribed by Medical Council of India (now structured as National Medical Commission).

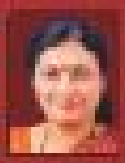
Besides being the 'must read' for undergraduate medical students, the text also caters to the needs of the candidates preparing for postgraduate entrance and other competitive examinations. Students and teachers of dental sciences, pharmacy, nursing and other paramedical courses will find it particularly useful just like the other editions.

Highlights of the Seventh Edition

- New features, flowcharts and diagrams, added to explain the recent concepts
- Text completely revised, recast and enlarged to accommodate the latest curriculum prescribed by MCI
- New topics prescribed under the CBME guidelines have been added at relevant positions in the text
- Flowcharts explain every important mechanism of action
- Boxes made more functional and useful to the reader
- Text revision and enlargements based on reviews and comments by superspecialists and subject experts
- Student-friendly format followed
- Text and tables focus on clinical relevance
- Many mnemonics throughout the book help memorizing
- COMPARE AND CONTRAST series makes the textbook complete in giving an analytic edge.

Padmaja Udaykumar MD

is Professor and Head, Department of Pharmacology, and Former Vice Dean, Father Muller Medical College, Mangalore, Karnataka. She has a keen interest in medical education with an experience in teaching of more than 30 years and has been on the boards of studies of many universities. She has published several titles and this is the 22nd book in the series of textbooks meant for medical, dental, nursing, physiotherapy and pharmacy students. Her other publications brought out by CBSPD are *Pharmacology Companion* and *Pharmacology for Pharmacy Students*. She also has several research papers to her credit. She has rich experience in clinical pharmacology; conducted and coordinated several clinical trials; and has been advising clinicians on the appropriate and rational use of drugs.



CBS Publishers & Distributors Pvt Ltd

4819/XCI, Prahlad Street, 24 Ansari Road, Daryaganj, New Delhi 110 002, India

E-mail: delhi@cbspd.com, cbspubs@airtelmail.in; Website: www.cbspd.com

New Delhi | Bengaluru | Chennai | Kochi | Kolkata | Mumbai

Hyderabad | Jharkhand | Nagpur | Patna | Pune | Uttarakhand