ФАРМАКОЛОГИЯ
В ВОПРОСАХ И ОТВЕТАХ

Учебно-методическое пособие
для студентов 3 курса факультета по подготовке
специалистов для зарубежных стран

PHARMACOLOGY
IN QUESTIONS AND ANSWERS

Textbook
for the 3rd year students of faculty on preparation
of experts for foreign countries

Гомель
ГомГМУ
2011
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Содержит тестовый контроль (MCQ's) по основным разделам фармакологии в соответствии с требованиями типовой программы для студентов высших медицинских вузов.

Ответы на заданные вопросы приведены после соответствующих разделов и могут быть использованы для углубления знаний студентов по фармакологии.

На основе приведенных тестов создана компьютерная версия, которая используется для предэкзаменационного тестирования.

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**LIST OF ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE</td>
<td>angiotensin converting enzyme</td>
</tr>
<tr>
<td>AT</td>
<td>antithrombin</td>
</tr>
<tr>
<td>AV</td>
<td>atrioventricular</td>
</tr>
<tr>
<td>AMP</td>
<td>adenosine monophosphate</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>COX</td>
<td>cyclooxygenase</td>
</tr>
<tr>
<td>cAMP</td>
<td>3,5-cyclic adenosine monophosphate</td>
</tr>
<tr>
<td>cGMP</td>
<td>3,5-cyclic guanosine monophosphate</td>
</tr>
<tr>
<td>DOCA</td>
<td>desoxycorticosterone acetate</td>
</tr>
<tr>
<td>DOPA</td>
<td>dihydroxyphenyl alanine</td>
</tr>
<tr>
<td>DEC</td>
<td>diethyl carbamazine citrate</td>
</tr>
<tr>
<td>DNA</td>
<td>deoxyribose nucleic acid</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>etc.</td>
<td>et cetera (and so on)</td>
</tr>
<tr>
<td>e.g.</td>
<td>exempli gratia (for example)</td>
</tr>
<tr>
<td>GABA</td>
<td>gamma aminobutyrie acid</td>
</tr>
<tr>
<td>g.i.t.</td>
<td>gastrointestinal tract</td>
</tr>
<tr>
<td>HMG CoA</td>
<td>hydroxymethyl glutaryl coenzyme A reductase</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>i.e.</td>
<td>id est (that is)</td>
</tr>
<tr>
<td>IL</td>
<td>interleucine</td>
</tr>
<tr>
<td>INH</td>
<td>isonicotinic acid hydrazide</td>
</tr>
<tr>
<td>LTs</td>
<td>leukotriene(s)</td>
</tr>
<tr>
<td>MAO</td>
<td>monoamine oxidase</td>
</tr>
<tr>
<td>mRNA</td>
<td>messenger ribonucleic acid</td>
</tr>
<tr>
<td>NO</td>
<td>nitric oxide</td>
</tr>
<tr>
<td>O. volvulus</td>
<td>onchocerca volvulus</td>
</tr>
<tr>
<td>P. falciparum</td>
<td>plasmodium falciparum</td>
</tr>
<tr>
<td>P. vivax</td>
<td>plasmodium vivax</td>
</tr>
<tr>
<td>PGI₂</td>
<td>prostacycline</td>
</tr>
<tr>
<td>PG</td>
<td>prostaglandin</td>
</tr>
<tr>
<td>PGs</td>
<td>prostaglandin(s)</td>
</tr>
<tr>
<td>PAF</td>
<td>platelet activating factor</td>
</tr>
<tr>
<td>PAS</td>
<td>paraamino salicylic acid</td>
</tr>
<tr>
<td>RNA</td>
<td>ribonucleic acid</td>
</tr>
<tr>
<td>S. haematobium</td>
<td>schistosoma haematobium</td>
</tr>
<tr>
<td>T₁/₂</td>
<td>half-life period</td>
</tr>
<tr>
<td>TxA₂</td>
<td>thromboxane A₂</td>
</tr>
<tr>
<td>t-RNA</td>
<td>transfer ribonucleic acid</td>
</tr>
<tr>
<td>W. bancrofti</td>
<td>wuchereria bancrofti</td>
</tr>
</tbody>
</table>
INTRODUCTION

At present testing have been wide-spread used for control of knowledge. It enable to give objective estimation of knowledge during minimal time.

Representative textbook of test controls «Pharmacology in questions and answers» consists of more than 100 tests with different level of complexity.

Test controls are divided according to basic pharmacological groups:
— neurotropic drugs;
— drugs acting on different organs and systems;
— drugs acting on metabolic and pathologic processes;
— antimicrobial drugs.

There are 4 answers on each questions, one of its is correct. Correct answers are given at the end of every section. It helps to use test both for teaching and self-control and control of student’s knowledge in pre-examination testing.

Methodical work with the textbook will promote learning of basic knowledge of pharmacology and may be good basis for following learning pharmacotherapy and successful take the examination for confirmation of certificate of degree in homeland country.
I. NEUROTROPIC DRUGS

1. Which of the following is NOT a catecholamine:
   Variants of the answer:
   a) Epinephrine;
   b) Norepinephrine;
   c) Dopamine;
   d) Phenylephrine.

2. Action of Atropine are all EXCEPT:
   Variants of the answer:
   a) Bronchoconstriction;
   b) Tachycardia;
   c) Mydriasis;
   d) CNS stimulation.

3. Which of the following is FALSE about Pentazocine:
   Variants of the answer:
   a) Decreased vomiting and constipation as compared to Morphine;
   b) Risk of addiction is less than that with Morphine;
   c) Risk of addiction is more than that with Morphine;
   d) It is agonist-antagonist.

4. Which of the following drugs acts on \( \mu \) receptors of the CNS:
   Variants of the answer:
   a) Morphine;
   b) Buprenorphine;
   c) Pethidine;
   d) Pentazocine.

5. Which of the following is NOT inotropic drug:
   Variants of the answer:
   a) Dopamine;
   b) Isoprenaline;
   c) Amrinone;
   d) Amiodarone.

6. Pralidoxime acts by:
   Variants of the answer:
   a) Reactivating cholinesterase enzyme;
   b) Promoting synthesis of cholinesterase;
   c) Promoting synthesis of acetylcholine;
   d) direct action on cholinergic receptors.

7. Clonidine is a:
   Variants of the answer:
   a) \( \alpha_1 \)-selective agonist;
b) $\alpha_2$-selective agonist;
c) $\alpha_1$-selective antagonist;
d) $\alpha_2$-selective antagonist.

8. Propranolol is indicated in all of the following conditions EXCEPT:
Variants of the answer:
  a) thyrotoxicosis;
  b) variant angina;
  c) migraine;
  d) hypertension.

9. Anti-adrenergic drug which crosses the blood brain barrier minimally is:
Variants of the answer:
  a) Propranolol;
  b) Atenolol;
  c) Oxprenolol;
  d) Alprenolol.

10. All of the following are features of sympathetic stimulation of the heart, EXCEPT:
Variants of the answer:
  a) increase contractility;
  b) increase heart rate;
  c) increase refractory period;
  d) increase conduction.

11. Shortest acting neuromuscular blocking agent is:
Variants of the answer:
  a) pancuronium;
  b) atracurium;
  c) mivacurium;
  d) vecuronium.

12. Which of the following antiepileptic drugs acts by the release of the inhibiting transmitter GABA:
Variants of the answer:
  a) valproic acid;
  b) Diazepam;
  c) Ethambutol;
  d) Phenytoin.

13. Flumazenil is a:
Variants of the answer:
  a) Benzodiazepine antagonist;
  b) Benzodiazepine agonist;
  c) adrenergic blocking agent;
  d) opioid antagonist.
14. The most common side effect associated with chronic use of Phenothiazines is:
Variants of the answer:
a) akinesia;
b) parkinsonism;
c) tardive dyskinesia;
d) muscular dystonia.

15. All of the following may be seen with neuroleptic malignant syndrome EXCEPT:
Variants of the answer:
a) hypothermia;
b) altered consciousness;
c) muscle rigidity;
d) involuntary movements.

16. Low doses of aspirin used in myocardial infarction act by:
Variants of the answer:
a) inhibiting thromboxane synthetase;
b) inhibit cyclooxygenase;
c) releasing endothelium-derived relaxing factor;
d) high protein binding activity.

17. All are classified as reversible anticholinesterases EXCEPT:
Variants of the answer:
a) Ambenonium;
b) Physostigmine;
c) Pyridostigmine;
d) Echothiophate.

18. Agent used as a diagnostic test for myasthenia gravis is:
Variants of the answer:
a) Phentolamine;
b) Edrophonium;
c) Echothiophate;
d) Glucagon.

19. In treatment of cardiac failure, Dobutamine acts by all of the following mechanisms EXCEPT:
Variants of the answer:
a) α-receptors agonism;
b) ß-adrenergic receptors agonism;
c) Dopamine receptor agonism;
d) increasing force of contraction.

20. Neostigmine is a:
Variants of the answer:
a) primary ammonium compound;
b) secondary ammonium compound;
c) tertiary ammonium compound;
d) quaternary ammonium compound.

21. **Drug of choice in acute central anticholinergic syndrome is:**
   *Variants of the answer:*
   a) Neostigmine;
   b) Physostigmine;
   c) Tacrine;
   d) 4-aminopyridine.

22. **Selective $\alpha_{1A}$-blocker is:**
   *Variants of the answer:*
   a) Prazosin;
   b) Terazosin;
   c) Tamsulosin;
   d) Indapamide.

23. **$\beta_1$-selective agonist is:**
   *Variants of the answer:*
   a) Terbutaline;
   b) Albuterol;
   c) Dobutamine;
   d) Isoprenaline.

24. **All of the following are selective $\beta_1$-blockers EXCEPT:**
   *Variants of the answer:*
   a) Atenolol;
   b) Metoprolol;
   c) Labetalol;
   d) Betaxolol.

25. **Selegiline is a selective inhibitor of:**
   *Variants of the answer:*
   a) MAO-A;
   b) MAO-B;
   c) Dopamine;
   d) Norepinephrine-uptake.

26. **$\beta$-blocker with peripheral vasodilator action is:**
   *Variants of the answer:*
   a) Carvedilol;
   b) Propranolol;
   c) Atenolol;
   d) Acebutolol.
27. **Diagnosis of myasthenia gravis is by using:**
*Variants of the answer:*
   a) Edrophonium;
   b) Neostigmine;
   c) Succinylcholine;
   d) Atropine.

28. **Drug of choice for epilepsy in pregnancy is:**
*Variants of the answer:*
   a) Carbamazepine;
   b) Sodium valproate;
   c) Phenobarbitone;
   d) Phenytoin.

29. **A patient of parkinsonism is managed with L-dopa. If vitamine B-complex is administered concurrently:**
*Variants of the answer:*
   a) the action of L-dopa in brain will be potentiated;
   b) decarboxylation of L-dopa in brain will be decreased;
   c) side effects will be ameliorated;
   d) decreased efficacy will result.

30. **All of the following statements are true EXCEPT:**
*Variants of the answer:*
   a) intravenous Noradrenaline increases systolic and diastolic blood pressure and causes tachycardia;
   b) intravenous Adrenaline increases systolic, decreases diastolic blood pressure and causes tachycardia;
   c) intravenous Isoprenaline causes no change in systolic, decreases diastolic blood pressure and causes tachycardia;
   d) Dopamine decreases peripheral resistance and improves renal perfusion.

31. **FALSE statement about Selegiline is:**
*Variants of the answer:*
   a) it is a MAO-A inhibitor;
   b) does not cause «cheese» reaction;
   c) may be used in «on-off phenomenon»;
   d) it is used in parkinsonism.

32. **During introduction agent for non-inhalated narcosis in patient there was increase of blood pressure, tachycardia, involuntary movements, and hallucinations. What drug may cause this symptoms:**
*Variants of the answer:*
   a) Propofol;
   b) Ketamine;
   c) Thiopental sodium;
   d) Hexobarbital.
1. The answer is D (Phenylephrine):
The three closely related endogenous catecholamines are:
- Noradrenaline;
- Adrenaline;
- Dopamine.
Tyrosine hydroxylase is the rate-limiting enzyme in catecholamine synthesis.

2. The answer is A (bronchoconstriction):
All visceral smooth muscles that receive parasympathetic motor innervation are relaxed by Atropine.
Atropine causes:
- relaxed smooth muscles of bronchus — causes bronchodilatation;
- relaxed smooth muscles of the stomach and intestine — causes constipation;
- relaxed smooth muscles of urethra and bladder — causes urinary retention;
- relaxed smooth muscles of iris — causes mydriasis;
- inhibits parasympathetic outflow to the heart — causes tachycardia.

3. The answer is C (risk of addiction is more than that with Morphine):
Pentazocine is an opioid with mixed receptor action and is classified as an agonist-antagonist. It is agonist at \( \kappa \) (kappa) receptor and antagonist / partial agonist at \( \mu \) (mu) receptor.
Pentazocine is mainly used as an oral / parenteral analgesic for post-operative and moderately severe pain.
Its profile of action is similar to Morphine and is differences:
- Analgesia is lower in efficacy than Morphine and is different in character being mostly spinal (\( \kappa_1 \)).
- Cardiac work is increased: it causes tachycardia and rise in blood pressure due to sympathetic stimulation and is better avoided in coronary ischemia and myocardial infarction.
- Sedation and respiratory depression is less than Morphine.
- Vomiting is less frequent.
- Biliary spasm and constipation are less severe.
- Subjective effects are pleasurable and abuse liability is present although it is lower than that with Morphine.

4. The answer is A (Morphine):
- Morphine and other opioids exert their actions by interacting with specific receptors present on neurons in the CNS in peripheral tissues.
- Three types of opioid receptors have been identified i.e. \( \mu \), \( \kappa \) and \( \delta \).
- The \( \mu \)-receptors is characterized by its high affinity for Morphine.
Characteristic of some opioids is represented in the table 1.

Table 1 — Receptor Subtype activity of some representative opioids

<table>
<thead>
<tr>
<th>Drug</th>
<th>µ (Mu)</th>
<th>δ (Delta)</th>
<th>κ (Kappa)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Opioid peptides</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enkephalins</td>
<td>agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td>β-Endorphin</td>
<td>agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td>Dynorphin</td>
<td>weak agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td><strong>Agonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Codeine</td>
<td>weak agonist</td>
<td>weak agonist</td>
<td></td>
</tr>
<tr>
<td>Etorphine</td>
<td>agonist</td>
<td>agonist</td>
<td>agonist</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meperidine</td>
<td>agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methadone</td>
<td>agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>agonist</td>
<td>weak agonist</td>
<td>weak agonist</td>
</tr>
<tr>
<td>Butorphanol</td>
<td>antagonist or partial agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td><strong>Partial agonist-antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>partial agonist</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dezocine</td>
<td>partial agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td>Nalbuphine</td>
<td>antagonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td>Pentazocine</td>
<td>antagonist or partial agonist</td>
<td></td>
<td>agonist</td>
</tr>
<tr>
<td><strong>Antagonists</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naloxone</td>
<td>antagonist</td>
<td>antagonist</td>
<td>antagonist</td>
</tr>
</tbody>
</table>

5. The answer is D (amiodarone):

Amiodarone is not an inotropic agent, but a «long acting anti-arrhythmic» belonging to class III antiarrhythmic drugs. It causes myocardial depression and fall in blood pressure on intravenous injection.

Amrinone is a selective phosphodiesterase III inhibitor. It is termed as an inodilator, the major effects being positive inotropic action and vasodilation.

Dopamine and Isoprenaline both cause inotropic action and may be used in cardiogenic shock.

6. The answer is A (Reactivating Cholinestrase enzyme):

Pralidoxime (2-PAM) regenerates cholinesterase enzyme in organophosphate poisoning (but needs to be given before ageing of the enzyme occurs). It is contraindicated in Carbamate poisoning.

7. The answer is B (α2-selective agonist):

α₁-agonists are Phenylephrine, Methoxamine;
α₁-blocker is Prazosin;
α₂-agonist is Clonidine;
α₂-blockers are Yohimbine, Rauwolscine.
8. The answer is B (variant angina):

β-blockers decrease the frequency and severity of attacks and increases exercise tolerance in classical angina. They act by reducing cardiac work and $O_2$ consumption.

Variant (prinzmetal's angina) occurs at rest and is due to coronary artery spasm. Non-selective β-blocker (e.g., Propranolol) can actually worsen variant angina due to unopposed α-mediated coronary vasospasm, and are therefore contraindicated in variant angina.

Other adverse effects of propranolol are:
- accentuates myocardial insufficiency and can worsen cardiac heart failure;
- dradycardia;
- worsen chronic obstructive pulmonary disease;
- impaired carbohydrate tolerance;
- altered plasma lipid profile;
- rebound hypertension and worsening of angina (on withdrawal);
- worsening of peripheral vascular disease;
- contraindicated in partial or complete heart block. Arrest may occur.

9. The answer is B (Atenolol):

Drugs which are lipid in-soluble, do not cross blood brain barrier. Three β-blockers are lipid insoluble:
- Atenolol;
- Nadolol;
- Sotalol.

All of these three share certain common characteristics which are frequently asked:
- do not cross blood brain barrier and therefore produce no the CNS effects;
- have good renal excretion;
- have no membrane stabilizing activity;
- are incompletely absorbed orally;
- are long acting;
- are effective in narrow dose range.

(Note: lipid soluble agents are primarily metabolized in liver and so have shorter $T_{1/2}$)

10. The answer is C (Increased refractory period):

Features of sympathetic stimulation of heart are (due to β actions):
- Increase of heart rate — arrhythmia may occur;
- Increase of force of cardiac contraction;
- Systole is shortened more than diastole;
- Cardiac output and $O_2$ consumption of the heart are markedly increased;
- Conduction velocity in the conductive tissues of heart is increased;
- Refractory period of all types of cardiac cells is reduced.
This makes sense, because with a fight or flight response, heart rate increases, as a consequence of:
— increase of conduction velocity;
— decrease of refractory period (so that cardiac tissue becomes excitable in a shorter span of time).

11. The Answer is C (Mivacurium):
- shortest acting neuromuscular blocking drugs — Succinylcholine (3–6 min);
- shortest acting depolarizing blocking drugs — Succinylcholine (3–6 min);
- shortest acting non-depolarizing blocking drugs — Mivacurium (12–20 min).
The choices in this question are only of non-depolarizing type neuromuscular blocking drugs. So the answer becomes Mivacurium.

12. The answer is A (valproic acid):
Valproate appears to act by multiple mechanisms:
- Augmentation of release of inhibitory transmitter GABA, by inhibiting its degradation, and may also by increasing its synthesis (i. e. like Diazepam).
- Phenytoin like frequency dependent prolongation of Na⁺ channel inactivation.
- Attenuation of Ca²⁺ mediated «T» current (Ethosuximide-like).

Diazepam — is an agonist at an allosteric benzodiazepine site which is an integral part of the GABA_A receptor — CI⁻ channel complex. The benzodiazepine receptor increases the frequency of Cl⁻ channel opening, and enhances GABA induced hyper-polarization (i. e. have only GABA facilitatory, but no GABA mimetic action).

Phenytoin — Phenytoin has a stabilizing influence on neuronal membrane. This is achieved by prolonging the inactivated state of the voltage sensitive neuronal Na⁺ channel. Facilitation of GABA responses occurs, but at higher concentration.

Ethambutol — is a tuberculostatic drug with unclear mechanism, and interferes with mycolic acid incorporation in cell wall, and inhibits RNA synthesis. It has nothing got to do with GABA.

13. The answer is A (Benzodiazepine antagonist):
Flumazenil is itself a «benzodiazepine analogue» but with minimal intrinsic activity (~0).
It therefore acts as a competitive antagonist at the Benzodiazepine receptors and reverses their effects.

14. The answer is C (tardive dyskinesia):
All the options mentioned in the question are. Extrapyramidal disorders seen with administration of Phenothiazines. However tardive dyskinesia is the one, which occurs with chronic use, all others manifesting as more acute responses. Extrapyramidal syndromes seen with administration of Phenothiazines:
- Muscular dystonia:
— occurs within few hours of a single dose, or at the most within the first week of therapy;
— manifested as bizarre muscle spasms, mostly involving linguo-facial muscles – grimacing, tetricollis and locked jaw.
  • Parkinsonism: appears between 1–4 weeks of therapy
  • Akethesia: this appears between 1–8 weeks of therapy.
  • Manifests as a feeling of restlessness, agitation, discomfort manifested as a compelling desire to move about (but without anxiety).
  • Tardive dyskinesia: occurs late in therapy sometimes even after withdrawal of neuroleptic (most common chronic or late complication). It manifests as purposeless involuntary facial movements, such as constant chewing, puffing of cheeks, lip licking, and also choreoathetoid movements of limbs.
  • Rabbit syndrome: occurs after years of therapy, but is a rare complication. It manifests as perioral tremors.

15. The answer is A (hypothermia):
Neuroleptic malignant syndrome is a life threatening disorder that occurs in patients who are extremely sensitive to the extrapyramidal effects of antipsychotics. This syndrome is believed to result from an excessively rapid blockage of post synaptic dopaminergic receptors. A severe form of extrapyramidal syndrome follows.
Features:
  • initial symptom is marked muscular rigidity;
  • fever, may ensue often reaching dangerous levels (hyperthermia);
  • autonomic instability and altered blood pressure and pulse rate (is a mid-brain manifestation);
  • stress leukocytosis;
  • elevated creatine kinase isoenzymes (due to muscle damage).
Treatment:
  — Vigorous treatment with antiparkinsonian agents is worthwhile early in the course.
  — Muscle relaxant, particularly diazepam are often helpful.
  — Other relaxants such as dantrolene (direct) may be helpful.

16. The answer is B (inhibit cyclooxygenase):
Aspirin inhibits thromboxane synthesis but not thromboxane synthetase. Thromboxane A₂ is a product of arachidonic acid (via cyclooxygenase pathway) that causes:
  • change in platelet shape;
  • release of platelet granules;
  • aggregation of platelets.
Aspirin inhibits thromboxane A₂ by irreversible acetylation of the enzyme cyclooxygenase (inhibition of cyclooxygenase).
Although inhibition of cyclooxygenase also inhibits PGI\(_2\) i.e. prostaglandins which inhibit aggregation, the effect on platelet thromboxane A\(_2\) predominants — and therefore its effect is inhibition of platelet aggregation and hence benefit in myocardium infarction.

Aspirin inhibits cyclooxygenase irreversibly. Platelets do not have nuclei and cannot synthesize new proteins. Therefore new cyclooxygenase cannot be synthesized by platelets during its entire lifetime (10 days). Small doses are therefore able to exert antithrombotic effects for several days. Other salicylates and non-steroidal anti-inflammatory drugs also inhibit cyclooxygenase but have a shorter inhibitory action because they cannot acetylate cyclooxygenase i.e. their action is reversible.

17. The answer is D (Echothiophate):
Echothiophate is an irreversible organophosphate (anticholinesterase). Examples of anticholinesterases are represented in the table 2.

<table>
<thead>
<tr>
<th>Reversible</th>
<th>Irreversible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbamate</td>
<td>Organophosphates</td>
</tr>
<tr>
<td>Acridine:</td>
<td>Carbamates:</td>
</tr>
<tr>
<td>• Physostigmine</td>
<td>• Echothiophate</td>
</tr>
<tr>
<td>• Tacrine</td>
<td>• Cabaryl</td>
</tr>
<tr>
<td>• Neostigmine</td>
<td>• Dyflos (Disfluorophosphate)</td>
</tr>
<tr>
<td>• Pyridostigmine</td>
<td>• Propoxur</td>
</tr>
<tr>
<td>• Edrophonium</td>
<td>• Parathion, malathion</td>
</tr>
<tr>
<td>• Ambenonium</td>
<td>• Diazinon</td>
</tr>
</tbody>
</table>

18. The answer is B (Edrophonium):
Edrophonium because of its short duration of action (10–30 mm) is chosen as the diagnostic agent for myasthenia gravis.

Edrophonium injected slowly intravenously improves muscle strength only in myasthenia gravis and not in other muscular dystrophies.

19. The answer is C (dopaminergic receptors):
Remember:
- Dobutamine is a derivative of Dopamine but not a D\(_1\) or D\(_2\) receptor agonist.
- it acts on both \(\alpha\)- and \(\beta\)-receptors (more selective action on \(\beta_1\), receptors).
Only prominent action is increase in force of cardiac contraction and output (without significant change in heart rate, peripheral resistance, and blood pressure).

20. The answer is D (quaternary ammonium compound):
Neostigmine is a reversible anticholinesterase. It is derived from a synthetic source. It is a *quaternary ammonium compound* with poor oral absorption.

It does not effectively penetrate the cornea and does not cross blood brain barrier.
21. The answer is B (Physostigmine):

Physostigmine (a natural alkaloid) is a tertiary amino derivative and is rapidly absorbed from gastro-intestinal tract and parenteral sites. It effectively penetrates the cornea and crosses blood brain barrier. Physostigmine therefore antagonizes both central as well as peripheral actions.

Neostigmine is derived from a synthetic source. It is a quaternary ammonium compound with poor oral absorption. It does not effectively penetrate the cornea and does not cross blood brain barrier. Thus for a central anticholinergic syndrome neostigmine would be ineffective.

Tacrine is a recently developed Acridine compound which interacts with cholinesterase in a fashion similar to the reversible cholinesterase inhibitors. It crosses blood brain barrier and has a longer duration of action. It is used in Alzheimer's disease or «chronic central anticholinergic syndrome» and not as an acute treatment as asked in this question.

22. The answer is C (Tamsulosin):

Subtypes of $\alpha_1$- and $\alpha_2$-receptors have now been delineated.
$\alpha_{1A}$ subtype predominates in prostate and bladder base.
$\alpha_{1B}$ subtype predominates in vascular smooth muscles (also $\alpha_{1D}$)

Tamsulosin is a selective $\alpha_{1A}$-blocker: it increases the urine flow rate and reduces residual urine volume in patients with benign hypertrophy of prostate without significantly altering blood pressure or heart rate.

The only significant side effect: retrograde ejaculation

Prazosin and Terazosin are selective $\alpha_1$-blockers but not selective $\alpha_{1A}$

23. The answer is C (Dobutamine):

Dobutamine is a relatively selective $\beta$-agonist. Though it acts on both $\alpha$- and $\beta$-receptors, the only prominent action of clinically employed doses is its $\beta$ action, i.e. an increase in force of cardiac contraction and output (without a significant change in heart rate, blood pressure and peripheral resistance).

Dobutamine is a derivative of dopamine but not a $D_1$ or $D_2$ agonist.
Albuterol (Salbutamol) and Terbutaline are all selective $\beta_2$-agonists.

24. The answer is C (Labetalol):

Selective $\beta_1$, blockers are:
- Atenolol;
- Acebutolol;
- Bisoprolol;
- Betaxolol;
- Celiprolol;
- Esmolol and Metoprolol.

Labetalol is a non selective ($\beta_1$ and $\beta_2$) $\beta$-blocker with additional $\alpha$-blocking property as well. Other congeners of this group are Carvedilol and Dilevalol.
25. The answer is B (MAO-B):
Selegiline (Deprenyl) is a selective MAO-B inhibitor. It predominates in the brain and blood platelets.
- Non selective MAO inhibitors include: Phenelzine, Isocarboxazid, Tranilcypromine.
- Selective MAO-A are: Clorgiline, Moclobemide.
- Selective MAO-B are: Selegiline (Deprenyl).

26. The Answer is A (Carvedilol):
Carvedilol is both an α- and β-receptor blocker and belongs to the same family as Labetalol and Dilevalol.
Carvedilol:
- is β₁+β₂+α₁-adrenoceptor blocker;
- produces vasodilation due to α₁ blockage as well as direct action;
- has antioxidant properties as well.
Vasodilation may be produced by β₂-agonists or α₁-blockers
Propranolol, Atenolol and Acebutolol are all β-blockers and therefore will not produce vasodilatation.

27. The answer is A (Edrophonium):
Diagnosis tests for myasthenia gravis include two types of tests:
- Ameliorative test: uses Edrophonium. Edrophonium (anticholinesterase) injected slowly intravenously improves muscle strength only in myasthenia gravis and not in other muscular dystrophies.
- Provocative test: myasthenics are sensitive to d-tubocurarine. Intravenous d-tubocurarine causes marked weakness in myasthenia, but is ineffective in non-myasthenics.

28. The answer is C (Phenobarbitone):
Phenobarbitone is considered the drug of choice in pregnancy.

29. The answer is D (Decreased efficacy will result):

\[
\text{L-Dopa} \xrightarrow{\text{Decarboxylase}} \text{Dopamine}
\]

Pyridoxine (Vit B₆) is a cofactor for DOPA decarboxylase.
Pharmacologic doses of Pyridoxine enhance the peripheral (extracerebral) decarboxylation of Levodopa, and as such, less is available to cross the brain. This may therefore prevent its therapeutic effect, unless a peripheral decarboxylase inhibitor is also taken.

Carbidopa and Benserazide are peripheral decarboxylase inhibitors and enhance the action of Levodopa. More of it is available to cross the blood brain barrier to reach the site of action.
30. The answer is A (intravenous Noradrenalin increases systolic and diastolic blood pressure and causes tachycardia)

Comparative characteristic of different adrenomimetics is represented in the table 3.

Table 3 — Influence of different adrenomimetics on cardio-vascular system

<table>
<thead>
<tr>
<th>Adrenomimetic</th>
<th>Action</th>
<th>Effect on Blood Pressure</th>
<th>Effect on Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoprenaline:</td>
<td>(β₁+β₂)</td>
<td>Systolic blood pressure shows little change or may even fall.</td>
<td>Heart rate is increased by a direct action</td>
</tr>
<tr>
<td></td>
<td>No α action</td>
<td>Diastolic blood pressure falls.</td>
<td></td>
</tr>
<tr>
<td>Noradrenaline:</td>
<td>(α₁+α₂+β₁)</td>
<td>Increases both systolic and diastolic blood pressure.</td>
<td>Heart rate is slowed (reflexly due to rise of blood pressure)</td>
</tr>
<tr>
<td></td>
<td>No β₂ action</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenaline:</td>
<td>(α₁+α₂+β₁+β₂)</td>
<td>Systolic blood pressure is increased due to increase in force of myocardial contraction and increase in cardiac output.</td>
<td>Heart rate is increased by direct action</td>
</tr>
<tr>
<td>Dopamine:</td>
<td>(D₁+D₂+α₁+α₂+β₁)</td>
<td>D₁ receptors in renal and mesenteric blood vessels are very sensitive. Intravenous infusion of low doses of Dopamine dilates mesenteric vessels and improves renal perfusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No β₂ action</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

31. The answer is A (It is a MAO-A inhibitor):

- **Selegiline (Deprenyl)** is a selective MAO-B inhibitor. MAO-B inhibitors are predominantly found in the brain and blood platelets.
  - Unlike nonselective MAO inhibitors, Selegiline in normal to low doses does not interfere with peripheral metabolism of dietary amines. Consequently catecholamine accumulation, hypertensive reaction («cheese» reaction) does not develop.
  - Selegiline retards intracerebral degradation of Dopamine, facilitating dopaminergic transmission and this is responsible for therapeutic benefit in parkinsonism.
  - Fluctuations in clinical response to Levodopa are often seen as treatment continues. When these fluctuations are unrelated to timing of dose, they are referred to as «on and off phenomenon». The «off period» is that of akinesia and it alternates with «on periods» is a period of improved mobility.
  - Patients may be benefited by:
    - Taking their medication at more frequent intervals in smaller doses during the day.
    - Addition of dopamine agonist: selegiline may reduce mild on-off phenomenon.

32. Answer is B (Ketamine):

Ketamine induce so called «dissociative anesthesia» — profound analgesia, immobility, amnesia with light sleep and felling of dissociation from ones own body and surrounding. Respiration is not depressed, reflexes are not abolished and muscle tone increases. Heart rate, cardiac output and blood pressure are elevated due to sympathetic stimulation. It may cause emergence delirium, hallucinations and involuntary movements in up to 50 % patients.
II. DRUGS ACTING ON DIFFERENT ORGANS AND SYSTEMS

1. Side-effects of Captopril are all EXCEPT:
   Variants of the answer:
   a) cough;
   b) hyperkalemia;
   c) renal dysfunction;
   d) hemolytic anemia.

2. Which of the following is NOT true about Enalapril:
   Variants of the answer:
   a) it is a pro-drug;
   b) it is a di-peptide;
   c) it is more effective than Captopril;
   d) it has less adverse effects.

3. Which of the following has the shortest plasma half-life:
   Variants of the answer:
   a) Propranolol;
   b) Esmolol;
   c) Timolol;
   d) Atenolol.

4. Which of the following does NOT cause bradycardia:
   Variants of the answer:
   a) Propranolol;
   b) Hydralazine;
   c) Clonidine;
   d) Reserpine.

5. All the following are true of Cholestyramine EXCEPT:
   Variants of the answer:
   a) are basic ion exchange resins;
   b) cause compensatory increase in HMG CoA reductase activity;
   c) may cause constipation, steatorrhea;
   d) patient acceptability is good.

6. Intracranial pressure may be increased by all of the following drugs EXCEPT:
   Variants of the answer:
   a) hypervitaminosis A;
   b) Corticosteroids;
   c) Quinolones;
   d) Aminoglycosides.
7. **Furosemide and Thiazides have similar properties in the following:**

*Variants of the answer:*

a) duration of action;
b) site of action;
c) effect on urate excretion;
d) well absorbed orally.

8. **All of the following statements about antianginal action of nitrates are true EXCEPT:**

*Variants of the answer:*

a) decrease of myocardial O₂ consumption;
b) decreases both pre and after load;
c) increase of total coronary flow;
d) cause favorable redistribution of coronary flow.

9. **Drug of choice in paroxysmal supraventricular tachycardia is:**

*Variants of the answer:*

a) Verapamil;
b) Propranolol;
c) Cardioversion;
d) Digoxin.

10. **Predominant arteriolar dilators include all of the following EXCEPT:**

*Variants of the answer:*

a) Sodium Nitroprusside;
b) Diazoxide;
c) Hydralazine;
d) Minoxidil.

11. **Which of the following antihypertensive drugs is devoid of any central action:**

*Variants of the answer:*

a) Clonidine;
b) α-methyldopa;
c) Propranolol;
d) Indapamide.

12. **True statement about Omeprazole is:**

*Variants of the answer:*

a) it may cause leomyosarcoma;
b) it is a nitrosource;
c) it may induce carcinoid tumors in rats;
d) it is more frequently used by the intravenous route than orally.
13. **Gynecomastia may be associated with administration of:**
   *Variants of the answer:*
   a) ranitidine;
   b) cimetidine;
   c) terfenadine;
   d) omeprazole.

14. **Which of the following antiarrhythmic drugs causes prolonged repolarization of ventricles and effective refractory period:**
   *Variants of the answer:*
   a) Amiodarone;
   b) Propranolol;
   c) Verapamil;
   d) Quinidine.

15. **All of the following are side effects of Amiodarone EXCEPT:**
   *Variants of the answer:*
   a) pulmonary fibrosis;
   b) corneal microdeposits;
   c) thyroid dysfunction;
   d) osteoporosis.

16. **Most commonly postural hypotension is seen with:**
   *Variants of the answer:*
   a) Prazosin;
   b) Nifedipine;
   c) Atenolol;
   d) ACE inhibitors.

17. **Which of the following drugs acts as a HMG-CoA reductase inhibitor:**
   *Variants of the answer:*
   a) Gemfibrozil;
   b) Clofibrate;
   c) Lovastatin;
   d) Probucol.

18. **Low molecular weight heparin therapy is associated with all EXCEPT:**
   *Variants of the answer:*
   a) less chances of bleeding;
   b) single dose per day;
   c) easy filterability by glomerular capillaries;
   d) high biological interaction to plasma proteins.
19. **Low doses of Aspirin used in myocardial infarction act by:**
Variants of the answer:
a) inhibiting thromboxane synthetase;
b) inhibit cyclooxygenase;
c) releasing endothelium-derived relaxing factor;
d) high protein binding activity.

20. **All of the following statements are true about nitrates EXCEPT:**
Variants of the answer:
a) it releases NO;
b) it causes vasodilatation;
c) it decreases atrio-ventricular conduction;
d) it has high first pass metabolism.

21. **Dipyridamole acts by:**
Variants of the answer:
a) Adenosine uptake inhibition;
b) inhibiting thromboxane A²;
c) stimulating PGI₂ synthesis;
d) inhibiting PGI₂ synthesis.

22. **Systemic lupus erythematosus like syndrome is most commonly associated with administration of:**
Variants of the answer:
a) Rifampicin;
b) Procainamide;
c) Digoxin;
d) Phenytoin.

23. **Coronary «steal phenomenon» is caused by:**
Variants of the answer:
a) Dipyridamole;
b) Diltiazem;
c) Propranolol;
d) Verapamil.

24. **The nitrate which does NOT undergo 1st pass metabolism is:**
Variants of the answer:
a) Isosorbide mononitrate;
b) Nitroglycerine;
c) Pentaerythritol tetranitrate;
d) Isosorbide dinitrate.
25. **Enalapril is contraindicated in all of the following EXCEPT:**

*Variants of the answer:*
- a) diabetic nephropathy with albuminuria;
- b) single kidney;
- c) bilateral renal artery stenosis;
- d) hyperkalemia.

26. **A 6 years old child presents with malignant hypertension. The drug of choice is:**

*Variants of the answer:*
- a) Sodium Nitroprusside;
- b) Sublingual Nifedipine;
- c) Furosemide;
- d) Enalapril.

27. **Which of the following is NOT given in a patient with pheochromocytoma:**

*Variants of the answer:*
- a) Atenolol;
- b) Prazosin;
- c) Nitroprusside;
- d) Metyrosine.

28. **Drug causing hirsutism and gynecomastia:**

*Variants of the answer:*
- a) Spironolactone;
- b) Rifampicin;
- c) Penicillin;
- d) Bumetanide.

29. **Spironolactone is contraindicated with of the following:**

*Variants of the answer:*
- a) Enalapril;
- b) Atenolol;
- c) Verapamil;
- d) none of the above.

30. **Which one of the following drug causes increased concentration of Na\(^+\) and CI in urine with normal bicarbonate:**

*Variants of the answer:*
- a) Etacrynic acid;
- b) Furosemide;
- c) Acetazolamide;
- d) Bumetanide.
31. A patient is taking 40 mg Famotidine, Sucralfate and Antacid tablets. This treatment is irrational because of:
Variants of the answer:
   a) Sucralfate decreases the absorption of Famotidine;
   b) Sucralfate increases the toxicity of Famotidine;
   c) Sucralfate decreases absorption of antacids;
   d) Sucralfate polymerises only when gastric pH is less than 4.

32. β-blocker that can be used in renal failure is all EXCEPT:
Variants of the answer:
   a) Propranolol;
   b) Pindolol;
   c) Sotalol;
   d) Oxprenolol.

33. Digoxin is NOT indicated in:
Variants of the answer:
   a) atrial flutter;
   b) atrial fibrillation;
   c) high output failure;
   d) paroxysmal supraventricular tachycardia.

34. All of the following statements are true about Theophylline EXCEPT:
Variants of the answer:
   a) increase in dose is required in cardiopulmonary disease;
   b) it increases cAMP;
   c) increase in dose is required in smokers;
   d) it inhibits phosphodiesterase.
ANSWERS

1. The answer is D (hemolytic anemia):
Hemolytic anemia is not a side effect of Captopril.
• Captopril is an ACE inhibitor which inhibits the converting enzyme responsible for conversion of Angiotensin I to Angiotensin II.
• Adverse effects of Captopril have been frequently asked and need to be remembered.

Side Effects of Captopril:
— hypotension;
— hyperkalemia;
— acute renal failure;
— proteinuria;
— cough;
— dysgeusia;
— rashes;
— urticaria;
— photodermatitis;
— angioedema;
— headache;
— nausea;
— dizziness;
— bowel upset.

Dysgeusia is a reversible loss or alteration of taste sensation due to Captopril.
Cough is not dose related and appears to be caused by inhibition of bradykinin / substance P breakdown in lungs.

Acute renal failure is precipitated by ACE inhibitors in patients with bilateral renal artery stenosis. It is contraindicated in these patients.

Fetal damage: fetal growth retardation, hypoplasia of organs and fetal death may occur if ACE inhibitors are given during late half of pregnancy. ACE inhibitor are contraindicated in pregnancy.

2. The answer is B (it is dipeptide):
• Enalapril is a prodrug converted in the body to Enalaprilat.
• It is a tripeptide analogue, not a dipeptide.

Enalapril has the same pharmacological therapeutic and adverse affect profile as Captopril bit offers certain advantages which are often asked in prostaglandin entrance examinations:
— absorption is not affected by food;
— more potent;
— onset of action is slower: less likely to cause first dose hypotension;
— duration of action is longer: single daily administration;
— rashes and dysgeusia is less frequent.
3. The answer is B (Esmolol):
Esmolol is an ultra-shot acting β₁-blocker devoid of partial agonistic or membrane stabilizing action. Its plasma T₁/₂ is as short as < 10 min. (table 4).

Table 4 — The half-life period of some β-blockers

<table>
<thead>
<tr>
<th>Agent</th>
<th>T₁/₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timolol</td>
<td>3–5 hours</td>
</tr>
<tr>
<td>Propranolol</td>
<td>4–5 hours</td>
</tr>
<tr>
<td>Atenolol</td>
<td>6–9 hours</td>
</tr>
<tr>
<td>Esmolol</td>
<td>&lt; 10 min.</td>
</tr>
</tbody>
</table>

4. The answer is B (Hydralazine):
Hydralazine causes reflex tachycardia by the following mechanism:

- Hydralazine is a directly acting «arteriolar» dilator (vasodilator)
- Reduces total peripheral resistance (TPR)
- Reflex tachycardia

- Clonidine (central sympatholytic) causes decrease in sympathetic out flow and fall in blood pressure and bradycardia.

- Reserpine (inhibits active amine transport and monoamines are gradually depleted) causes decreased sympathetic out flow (depletion of Noradrenalin at nerve endings) and fall in blood pressure and bradycardia.

- Propanolol (non-selective β-blocker) blocks sympathetic activity and decreases blood pressure and bradycardia.

5. The answer is D (patient acceptability is good):
Though safe, Cholestyramine is unpalatable; inconvenient; causes nausea, flatulence, heart burn, constipation, steatorrhea and deficiency of fat soluble vitamins. Patients acceptability is poor.

Cholestyramine is a hypolipidemic drug which acts as a bile acid sequestrant:

Binds bile acid in intestine and is itself neither digested nor absorbed

Interruption of entero-hepatic circulation

Enhanced extraction of bile acid and Cholesterol (Cholesterol is absorbed with the help of bile salts)

Compensatory increase of hepatic HMG CoA reductase occurs and results in enhanced Cholesterol synthesis, thereby blunting the long term effectiveness.

They are basic ion exchange resins supplied in chloride form.

These resins are useful only when low density lipoprotein cholesterol levels are raised, but not in other types.
6. The answer is D (Aminoglycosides):
Drugs raising intracranial pressure are:
- Amiodarone;
- Steroids (both Glucocorticoids and Mineralocorticoids);
- hypervitaminosis A;
- oral contraceptives;
- Tetracyclines;
- Quinolones.
Aminoglycosides do not penetrate the cerebrospinal fluid and have not been mentioned as a cause of raised intracranial pressure.

7. The answer is D (well absorbed orally):
- both Furosemide and Thiazides are well absorbed orally (Thiazide more than Furosemide).
- Furosemide has a quick onset with a short duration of action. Thiazide action starts in 1 hour, but the duration is variable.
- Furosemide acts on thick ascending limb of Henle’s loop (site II), while Thiazides act on early distal tubule (site III).
- Furosemide has a lower incidence of hyperuricemia than Thiazides.

8. The answer is C (increase total coronary flow):
Pharmacologic actions of Nitrates are:
- Preload reduction by dilating veins more than arteries.
- After load reduction. They just dilate veins more than the arteries. Therefore they decrease blood pressure and decrease myocardial O₂ consumption.
- Re-distribution of coronary flow, but do not appreciably increase coronary flow.
- They have more effect on larger, angiographically visible arteries, than arterioles.

Note:
- Nitrates increase free radical NO in smooth muscle cells – increase cGMP.
- All nitrates undergo extensive 1st pass metabolism in liver (except Isosorbide mononitrate).
- Arterioles are regulated by autonomic and local metabolic mechanisms.
- Propranolol also does not increase total coronary flow.

9. The answer is A (Verapamil):
Drug of choice in paroxysmal supraventricular tachycardia:
1st Adenosine — by rapid intravenous injection;
2nd Verapamil.

10. The answer is A (Sodium Nitroprusside):
Sodium Nitroprusside: relaxes both resistance and capacitance vessels i.e. relaxes arteries and veins.
**Diazoxide:** relaxes resistance vessels, without an effect on capacitance vessels.

**Note:**
- It is a K\(^+\) channel opener. It causes marked Na\(^+\) and water retention.

**Hydralazine:** a directly acting arteriolar dilator, with little action on venous capacitance vessels.

**Minoxidil:** pattern of action resembling Hydralazine. Side effects are excess hair growth on face, back and arms.

11. **The answer is D (Indapamide):**
- **Methyldopa and Clonidine** diminish central sympathetic outflow, by stimulating the central α\(_2\)-receptors that diminishes vasomotor outflow.
- **Propranolol and Reserpine** may exert some sympatholytic effects at the CNS level.
- **Indapamide** is weak diuretic, and it reduces blood pressure at much lower dosage. It probably exerts additional vasodilator action through direct action on vascular smooth muscle cell. It has no central action.

12. **The answer is C (may induce carcinoid tumor in rats):**
- Omeprazole inhibit proton pump (H\(^+\)-K\(^+\) ATPase inhibitor), irreversible. During prolonged use it decreases gastric acid output that causes increase of gastrin levels in blood. As a result it found to induce proliferation of parietal cells and gastric carcinoid tumors in rats.

13. **The answer is B (Cimetidine):**
- Cimetidine (but not other H\(_2\)-blockers). It:
  - has anti-androgenic action (by displacing Dihydrotachysterol from receptor);
  - increases plasma prolactin levels;
  - inhibits degradation of estradiol by liver.
  - Therefore it cause gynecomastia, loss of libido, impotence and temporary decrease in sperm count.

**Also note:**
- Cimetidine inhibits cytochrome p450 i.e. inhibits metabolism of many drugs.
- Antacids reduce absorption of all H\(_2\)-blockers.

14. **The answer is A (Amiodarone):**
- Antiarrhythmic agents that prolong repolarization and effective refractory period belong to Class III.
  - These include: Amiodarone and Bretylium (this also has class II properties).

15. **The answer is D (osteoporosis):**
- Side effects:
  - thyroid dysfunction: mainly hypothyroidism but hyperthyroidism (rarely) may occur;
• peripheral neuropathy;
• myocardial depression;
• lung fibrosis (pulmonary fibrosis);
• corneal microdeposits;
• photosensitization.

16. The answer is A (Prazosin):
Prazosin causes postural hypotension – first dose effect.

Prazosin is a highly selective $\alpha_1$-blocker. It blocks sympathetic mediated vasoconstriction and produces fall in blood pressure which is attended only by mild tachycardia. Postural hypotension is specially marked in the beginning, so much so, that dizziness and fainting may occur. This is often referred to as the «first dose effect».

ACE inhibitors induce hypotension but postural hypotension is not a problem.

Nifedipine also induces hypotension. Postural hypotension may occur but is not as prominent as with Prazosin.

Atenololum is a selective $\beta$-antagonist and does not dilate vessels. Therefore no postural hypotension.

Remember: postural hypotension $\rightarrow$ Prazosin
Rebound hypertension $\rightarrow$ Clonidine.

17. The answer is C (Lovastatin):

HMG CoA reductase inhibitors include:
• Lovastatin;
• Simvastatin;
• other Statins.

— HMG CoA reductase is the rate limiting enzyme for cholesterol synthesis. These drugs therefore act by inhibiting cholesterol synthesis.

— These inhibitors are the first choice drugs for: primary hyperlipidemia with increased low density lipoproteins and total cholesterol levels, with or without elevated triglyceride levels (type IIa, IIb, V).

— Its side effects are frequently asked and need to be remembered:

1) Liver damage: evaluate liver function and hepatic transaminases periodically.

2) Myopathy and rhabdomyolysis monitor plasma creatine phosphokinase periodically. This complication is seen specially in patients who suffer from renal insufficiency or taking drugs such as:
• Gemfibrosil;
• Itraconazole;
• Cyclosporine;
• Niacin;
• Erythromycin.

3) Bleeding tendency: evaluate prothrombin time regularly. These inhibitors increase coumarin levels.
4) Contraindicated in pregnant and lactating mothers.

18. The answer is D (high biological interaction to plasma proteins):
• Bleeding chances are less: low molecular weight heparins have a different anticoagulant profile.
  — They selectively inhibit factor Xa with little effect on AT and coagulation in general.
  — They act only by inducing conformational change in AT III.
  — They appear to have lesser antiplatelet action.
As a result they have a small effect on a prothrombin time and whole blood clotting time.
  Since a prothrombin time/clothing times are not prolonged (much) laboratory monitoring is not needed, and the incidence of hemorrhagic complication is less.
• Single dose per day: these have a longer and more consistent monoexponential $T_{1/2}$.
  Once daily subcutaneous administration is sufficient and advised.
• They are easily filtered from glomerular capillaries because of there smaller molecular weight.

19. The answer is B (inhibit cyclooxygenase):
Aspirin inhibits thromboxane synthesis but not «thromboxane synthetase».
  Tx A$_2$ is a product of arachidonic acid (via cyclooxygenase pathway) that causes:
  — change in platelet shape;
  — release of platelet granules;
  — aggregation of platelets.
  Aspirin inhibits Tx A$_2$ by irreversible acetylation of the enzyme cyclooxygenase (inhibition of COX).
  Although inhibition of COX also inhibits PGI$_2$ i.e. prostaglandins which inhibit aggregation, the effect on platelet TxA$_2$ predominants – and therefore the net effect is inhibition of platelet aggregation and hence benefit in myocardium infarction.
  Aspirin inhibits COX irreversibly. Platelets do not have nuclei and cannot synthesize new proteins. Therefore new COX cannot be synthesized by platelets during its entire lifetime (10 days). Small doses are therefore able to exert antithrombotic effects for several days. Other salicylates and non-steroidal anti-inflammatory drugs also inhibit COX but have a shorter inhibitory action, because they cannot acetylate COX i.e. their action is reversible.
20. The answer is C (it decreases atrio-ventricular conduction):
Nitrates are rapidly denitrated in the smooth muscle cells to release: NO and:
• NO is an endothelium derived «relaxing factor» and causes vasodilatation consequent to relaxation. This action is mediated via cGMP.
• The most prominent action is exerted on vascular smooth muscles.
• Action is more on veins (predominantly venous dilatation) than on arteries. Thus they reduce preload more than after load.
• Also they cause favorable redistribution of blood flow to ischemic areas, although they do not appreciably increase the total coronary flow.

21. The answer is A (Adenosine uptake inhibition):
Dipyridamole is a unique example of pharmacological success but therapeutic failure.
Pharmacological success:
• Dipyridamole prevents uptake and degradation of Adenosine, which is a local mediator for autoregulation of coronary dilatation and an increases total coronary flow.
• This brings about powerful coronary dilatation and an increase total flow.
• It dilates resistance vessels and abolishes autoregulation.
Therapeutic failure:
• Cardiac work is not decreased (because venous return is not reduced).
• Blood pressure is minimally altered. Does not give symptomatic benefit.
• Does not avert ECG changes of angina.
This therapeutic failure has been explained by «coronary steal phenomenon» i.e. by dilating resistance vessels in the non-ischemic zone as well, it diverts the already reduced blood flow away from the ischemic zones and therefore does not benefit angina.

22. The answer is B (Procainamide):
Several drugs can cause a syndrome resembling systemic lupus erythematosus. This syndrome is rare with all except Procainamide and Hydralazine, which are the most frequent offenders.
Note that while Phenytoin also may cause such a syndrome, this is a rare entity with Phenytoin and therefore the best answer here is Procainamide.

23. The answer is A (Dipyridamole):
Dipyridamole is a powerful coronary dilator. It dilates resistance vessels and abolishes autoregulation by dilating ischemic vessels in the non-ischemic zones as well, it directs the already reduced blood flow, away from the ischemic zone.
This is called «coronary steal phenomenon» and is responsible for therapeutic failure of Dipyridamole.
24. The answer is A (Isosorbide mononitrate):
All nitrates except isosorbide mononitrate undergo extensive but variable first pass metabolism in liver.
Thus Isosorbide mononitrate is the only nitrate with minimal 1st pass metabolism.

25. The answer is A (diabetic nephropathy with albuminuria):
• ACE inhibitors are the drugs of choice for diabetic nephropathy with albuminuria. Prolonged ACE inhibitor therapy has found to prevent or delay end stage renal disease in both Insulin dependent as well as Insulin non-dependent diabetics.

Albuminuria (an index to nephropathy) remains stable in those treated with ACE inhibitors. All patients with diabetic nephropathy, whether hypotensive or normotensive deserve ACE inhibitor therapy.
• ACE inhibitors are contraindicated in patients with a single kidney or bilateral renal artery stenosis. Acute renal failure is precipitated by ACE inhibitors in patients with bilateral renal artery stenosis, due to dilation of efferent arteriole, and hence a fall in glomerular filtration pressure.
• Hyperkalemia may be precipitated by ACE inhibitors, because of inhibition renin-angiotensin system. Thus presence of hyperkalemia is a contraindication.
• Pregnancy is also a contraindication.

26. The answer is A (Sodium Nitroprusside):
The drugs most commonly used to treat hypertensive emergencies are:
• Nitroprusside;
• Diazoxide.
Nitroprusside is generally the agent of choice, as it acts almost instantaneously and dose response can be easily titrated.

27. The answer is A (Atenolol):
The treatment of choice for pheochromocytoma is surgical, laparoscopic removal of tumor or tumors being the procedure of choice.

Medical management before operation involves the following:
• α-blockade is the basis of management in the preoperative period. Phenoxybenzamine is the agent of choice here. α1-selective antagonists such as Prazosin may also be used.
• Nitroprusside may be used initially for the management of hypertensive crisis.
• Calcium channel blockers (Nifedipine and Nicardipine) may be used as alternatives.
• ACE inhibitors may also be used for the same.
• β-blockers should not be employed prior to establishing effective receptor blockage, since unopposed β-receptor blockage could theoretically cause blood
pressure elevation from increased vasoconstriction. Atenolol however is a selective β1-agonist, and acts on the heart and not a peripheral blood vessels. Tachyarrhythmias are treated with intravenous Atenolol, Esmolol or Lidocaine.

- Metyrosine is a competitive inhibitor of tyrosine hydroxylase and interferes with synthesis of dopamine.

For in-operable tumors or metastatic tumors, Metyrosine may be added to reduce catecholamine synthesis.

Thus while all can be used in the management of pheochromocytoma, β-blocker is the one agent, out of the above, that has a dangerous potential, all others being distinctly beneficial.

28. The answer is A (Spironolactone):

Side effects of Spironolactone include hirsutism, gynecomastia, impotence and menstrual irregularities.

Spironolactone is a steroid, chemically related to the mineralocorticoid Aldosterone. Its mechanism of action as well as side effects can both be explained by this nature.

Mechanism of action:

Being related to Aldosterone, it binds Aldosterone receptors and thus inhibits Na+ reabsorption and K+ excretion, thereby acting as a saluretic (Na+ excretion) and K+ sparing diuretic. This also explains its site of action which is same as that of Aldosterone i.e. late distal tubule and collecting duct.

Side effects include: hirsutism, gynecomastia, impotence and menstrual irregularities. Most serious side effect however is hyperkalemia.

Uses: Spironolactone is especially useful as a diuretic in cirrhotic and nephrotic edema.

It breaks the resistance to thiazide diuretic that develops due to secondary hyperaldosteronism and reestablishes the response. Thus it is particularly employed in refractory edema.

29. The answer is A (Enalapril):

As we have just talked before, hyperkalemia is the most serious side effect with Spironolactone therapy. Hyperkalemia is also an important risk in patients on ACE inhibitors and if the two are given concomitantly significant rise of K+ to dangerous levels can occur.

30. The answer is A (Ethacrynic Acid):

Ethacrynic acid is a loop diuretic and acts by inhibiting Na+–K+–2Cl− transport in ascending Henle's loop. Thus it inhibits reabsorption of Na+ and Cl− ions and promotes excretion of these electrolytes in urine. Unlike other loop diuretics however, it does not inhibit carbonic anhydrase, and therefore it lines not cause any increase in HCO3− excretion in urine. This explains the situation in the question i.e. increased sodium and chloride in urine with normal bicarbonate.
Characteristic of some diuretics:
- Most marked kaliuresis ($K^+$ excretion) is caused by Acetazolamide.
- Most marked natriuresis ($Na^+$ excretion) is caused by Furosemide.
- Most marked chloride excretion is caused by Etacrynic acid.
- Diuretic which inhibits chloride excretion is Acetazolamide (Pretest).

That is why it causes metabolic acidosis.
- Diuretics which do not promote bicarbonate excretion: Etacrynic acid, Thiazide like diuretics e.g. Indapamide, Metazoline, Chlorthalidone.
- Diuretics which maximally promotes uric acid excretion: Acetazolamide (by alkalinizing urine).

31. The answer is D (Sucralfate polymerizes only when gastric pH is less than 4):
Sucralfate is ulcer protective agent. It preferentially and strongly adheres to the ulcer base, especially duodenal, and acts as a physical barrier preventing acid, pepsin and bile from coming in contact with the ulcer base. However, this protective action is attributed to Sucralfate because of certain properties which are achieved only in acidic medium:
- Acidic medium gives it a viscous consistency.
- It polymerizes at pH < 4 by cross linkages of molecule assuming sticky gel like consistency.

It is this viscous and gel like properties that are responsible for its action.
When antacids are given concurrently they raise the pH of gastric secretion and this interferes with the very basic mechanism of action of sucralfate (requires pH < 4) and thus makes them ineffective.

32. The answer is C (Sotalol):
- Sotalol: unlike other β-blockers, Sotalol is excreted mostly unchanged in urine, and this takes place by glomerular filtration. Since it is primarily excreted via urine, therefore it should not be used in renal failure.
- Pindolol: about 40 % of oral dose of Pindolol is excreted in urine as unchanged drug. Pindolol is also secreted by the renal tubules, and as such its renal clearance exceeds the glomerular filtration route.

The elimination of the drug in patients with liver/renal disease has been reported to be reduced, but it is probably necessary to alter the Pindolol dosage only in patients with severe renal or hepatic impairment. It may be given in mild-moderate renal failure.
- Propranolol and Oxprenolol: mainly eliminated by hepatic route. These can therefore be used in renal failure.

33. The answer is C (high output failure):
Cardiac glycosides primarily mitigate systolic function. Digitalis causes a dose dependent increase in force of contraction of heart i.e. positive inotropic action.
Best results are therefore obtained when:

- Myocardium is not primarily damaged e.g. hypertrophy, valvular defects.
- Failure is low output type.

Poor response and more toxicity is likely when:

- Myocardium has been damaged: e.g. by ischemia, inflammation (myocardial) or thiamine deficiency.
- High output failure (e.g. anemia)

Digitalis is used in atrial flutter, atrial fibrillation and paroxysmal supraventricular tachycardia.

Atrial fibrillation: Digitalis is drug of choice for controlling ventricular rate in atrial fibrillation whether associated with cardiac heart failure or not, though it is incapable of curing atrial fibrillation.

Atrial flutter: Digitalis enhances the degree of AV block and thus:
- reduces ventricular rate;
- prevents sudden shift of AV block to lower degree;
- may convert atrial flutter to atrial fibrillation, which is a welcome response as control of ventricular rate is easier in atrial fibrillation than in atrial flutter.

Paroxysmal supraventricular tachycardia: Digitalis may be used however it is now reserved for preventing recurrence. Adenosine (drug of choice) and Verapamil are more effective, less toxic and acts faster than digitalis.

34. Answer is A (increase in dose is required in cardiopulmonary disease):

Mechanism of action of Theophylline (or other Methylxanthine): inhibit phosphodiesterase enzyme which degrades cyclic nucleotides such as AMP. The concentration of these cyclic nucleotides (AMP) is therefore increased.

Factors which need dose reduction are:
- age more than 60 yrs;
- pneumonia;
- cardiac heart failure;
- liver Failure;
- drugs which inhibit Theophylline metabolism.

Thus cardiopulmonary disease demands reduction and not an increase in dosage.
III. DRUGS ACTING ON METABOLIC AND PATHOLOGIC PROCESSES

1. Which of the following steroids can be administered by inhalation:
   
   *Variants of the answer:*
   
   a) Beclometasone;
   b) Betamethasone;
   c) Prednisolone;
   d) Hydrocortisone.

2. Which drug causes osteoporosis on long-term use:
   
   *Variants of the answer:*
   
   a) Estrogen;
   b) Progesterone;
   c) Gonadotropin releasing hormone analogues;
   d) Warfarin.

3. Estrogen acts on:
   
   *Variants of the answer:*
   
   a) cellular membrane receptors;
   b) cytoplasmic receptors;
   c) nuclear receptors;
   d) mitochondria.

4. Prolonged use of steroids may cause:
   
   *Variants of the answer:*
   
   a) decrease in bone matrix protein;
   b) hypoglycemia;
   c) hypotension;
   d) early healing of wound.

5. 1st drug to be used in anaphylactic shock is:
   
   *Variants of the answer:*
   
   a) subcutaneous Adrenaline;
   b) intravenous corticosteroid;
   c) Theophylline;
   d) Antihistaminic.

6. Which of the following has least glucocorticoid activity:
   
   *Variants of the answer:*
   
   a) Fludrocortisone;
   b) Dexamethasone;
   c) Triamcinolone;
   d) Betamethasone.
7. Which of the following drugs acts on «motilin» receptors:
Variants of the answer:
   a) Erythromycin;
   b) Tetracycline;
   c) Norfloxacin;
   d) Chloramphenicol.

8. All of the statements are true about fluoroquinolones EXCEPT:
Variants of the answer:
   a) suspected of having teratogenic potential;
   b) arthropathy of limb in children may occur;
   c) increase Theophylline toxicity;
   d) increase neuromuscular blocking action.

9. Difference between action of DEC and Ivermectin in a case of scrotal filariasis is:
Variants of the answer:
   a) DEC acts more effectively on microfilariae than Ivermectin;
   b) DEC acts only on microfilariae and Ivermectin acts only on adults;
   c) DEC acts on both microfilariae and adults while Ivermectin acts on adults only;
   d) DEC acts on adults and Ivermectin on microfilariae.

10. Cyclosporine acts by inhibiting the proliferation of:
Variants of the answer:
   a) IL1;
   b) IL2;
   c) IL6;
   d) Macrophages.

11. Side-effects of the Cisplatinum include all of the following EXCEPT:
Variants of the answer:
   a) nausea and vomiting;
   b) nephrotoxicity;
   c) blindness;
   d) ototoxicity.

12. Pancreatitis is a known side effect with administration of:
Variants of the answer:
   a) L-Asparaginase;
   b) Insulin;
   c) Cyclophosphamide;
   d) Vincristine.
13. All of the following are correct about steroids EXCEPT:

Variants of the answer:

a) inhibit the release of arachidonic acid from vessel wall through action of phospholipase A2;
   b) bind plasma membrane receptors and following internalization influence nuclear changes;
   c) inhibit vascular membrane permeability;
   d) increase glucose synthesis, glycogen deposition in liver.

14. All of the following statements are true EXCEPT:

Variants of the answer:

a) Prostaglandins and leukotrienes are derived from arachidonic acid;
   b) COX-I is an inducible enzyme;
   c) COX-II is induced by cytokines at sites of inflammation;
   d) Leukotrienes cause smooth muscle constriction.
1. **The answer is A (Beclometasone):**
   Inhaled steroids include:
   - Beclometasone dipropionate;
   - Budesonide;
   - Flunisolide;
   - Triamcinolone acetonide;
   - Fluticasone propionate.

   Properties of inhaled steroids:
   - Inhalational steroids have no role during acute attack of bronchial asthma or status asthmaticus.
   - They help by reducing need for reuse β-agonist inhalation and preventing episodes of acute asthma.

2. **The answer is C (Gonadotropin releasing hormone agonist analogues):**
   Adverse effects of Gonadotropin releasing hormone agonists include:
   - hot flashes;
   - loss of libido;
   - osteoporosis;
   - emotional liability;
   - vaginal dryness.

   There are many drugs causing osteoporosis. Some of them are:
   - Glucocorticoids;
   - Cyclosporine;
   - Cytotoxic drugs;
   - Anticonvulsants;
   - excessive alcohol;
   - Gonadotropin releasing hormone agonists;
   - Heparin;
   - Lithium;
   - excessive thyroxin;
   - Aluminum.

3. **The answer is B (cytoplasmic receptors):**
   Different hormones activate specific receptors. Examples are represented in table 5.
Table 5 — Receptor activation by the hormones

<table>
<thead>
<tr>
<th>Cell membrane receptors</th>
<th>Cytoplasmic receptors (Steroid hormones)</th>
<th>Nuclear receptors (Thyroid hormones)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>cAMP pathway</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenaline, Glucagon, Thyroid stimulating hormone, Follicle stimulating hormone, Luteinizing hormone, Parathyroid hormone, Calcitonin, Adrenocorticotropic hormone</td>
<td>Clucocorticoids</td>
<td>Thyroid hormones:</td>
</tr>
<tr>
<td></td>
<td>Mineralocorticoids</td>
<td>− Thyroxin;</td>
</tr>
<tr>
<td></td>
<td>Estrogens</td>
<td>− Tri-iodothyronine</td>
</tr>
<tr>
<td></td>
<td>Progestins</td>
<td></td>
</tr>
<tr>
<td><strong>Inositol trisphosphate₃ / Diacylglycerol generation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vasopressin / Oxytocin</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Tyrosine kinase activation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin / growth hormone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

4. The answer is A (decrease in bone matrix protein):
- Steroids are catabolic.
- Their function appears to maintain blood glucose levels (for brain) during starvation (causes hyperglycemia)
- Therefore they will not cause hypoglycemia.
- They suppress inflammatory response (all stages) and wound healing / scar formation.
- Steroids maintain tone of arterioles and myocardial contractility.
- They have a permissive role in development of hypertension.
- Its effects on bones are:
  — inhibit intestinal absorption and enhance renal excretion of Ca²⁺;
  — loss of osteoid (decreased formation and increased resorption).

5. The answer is A (subcutaneous Adrenaline):
The 1st thing one should do when dealing with a case of shock is to give the patient Epinephrine subcutaneously.

But:
- *Anaphylactic shock:* Epinephrine is drug of choice only and only in anaphylactic shock.
- *Septic shock:* volume expansion + blood spectrum antibiotics.
- *Cardiogenic shock:* inotropic agents, preferably Dobutamine.
- *Hypovolemic shock:* volume expansion with crystalloids.

The adrenergic drugs should not be considered a primary form of therapy in shock. In many instances the effect may be detrimental. Pressors are given only when hypotension persists after volume deficits are corrected.
Antihistamines do not have an immediate effect, but they may shorten the dilation of the reaction. Steroids have no significant effect for 6–12 hours. However they may prevent relapse or recurrence of severe reactions.

6. The answer is C (Triamcinolone):
Comparative characteristic of some glucocorticoids and mineralcorticoids is represented in the following table 6.

Table 6 — Characteristic of some corticosteroids

<table>
<thead>
<tr>
<th>Glucocorticoids</th>
<th>Glucocorticoid activity</th>
<th>Mineralocorticoid activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dexamethasone</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>2. Betamethasone</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>3. Paramethasone</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>4. Triamcinolone</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>5. Prednisolone</td>
<td>4</td>
<td>0.8</td>
</tr>
<tr>
<td>6. Hydrocortisone</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>7. Cortisone</td>
<td>0.8</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Mineralocorticoids

<table>
<thead>
<tr>
<th>Mineralocorticoids</th>
<th>Mineralocorticoid activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Aldosterone</td>
<td>0.3</td>
</tr>
<tr>
<td>2. Fludrocortisone</td>
<td>10</td>
</tr>
<tr>
<td>3. DOCA</td>
<td>0</td>
</tr>
</tbody>
</table>

Thus the only mineralocorticoid with significant Glucocorticoid activity is Fludrocortisone (10) and its activity is more than all Glucocorticoids below Paramethasone.

Remember:
- Agents with zero mineralocorticoid activity:
  - Triamcinolone;
  - Paramethasone;
  - Dexamethasone;
  - Betamethasone.
- Agents with zero Glucocorticoid activity:
  - DOCA.

7. The answer is A (Erythromycin):
Erythromycin stimulates «motilin» receptors in the g.i.t.
Thereby it:
- induces gastric contractions;
- hastens gastric emptying;
- promotes intestinal motility.
However contribution of this to the gastrointestinal side effects is not known.
8. The answer is D (increased neuromuscular blocking action):
- Fluoroquinolones are contraindicated in children less than 18 years of age, because of evidence in animals of cartilage damage in developing joints.
- They are contraindicated in pregnancy because of concern for the developing fetus (teratogenicity).
- Fluoroquinolones are enzyme inhibitors and thus inhibit the metabolism of many drugs.
- Plasma concentration of Theophylline is increased because of inhibition of its metabolism and this result in Theophylline toxicity.
- Fluoroquinolones have no neuromuscular blocking properties.

**Antibiotics with neuromuscular blocking properties are:**
- Aminoglycosides;
- Tetracycline;
- Polypeptide antibiotics;
- Clindamycin;
- Lincomycin.

9. The answer is D (DEC acts on adults, and Ivermectin on microfilariae):

**DEC:**
- causes rapid disappearance of microfilariae of W. bancrofti, W. malayi and Loa loa from the human peripheral blood. The Microfilariae of W. bancrofti in a hydrocoele however are not affected;
- DEC acts by sensitizing the microfilariae, so that they become susceptible to phagocytosis;
- DEC kills the adult worms of W. malayi and Loa loa, and possibly those of W. bancrofti;
- DEC has no action against adult worms of O. volvulus.

**Ivermectin:**
- Ivermectin on the other hand is the drug of choice for Onchocerciasis.
- It acts via a GABA agonistic action causing paralysis of the parasite.
- It has no lethal action against the adult worms.

In a case of Scotalfilariasis (with a hydrocoele) DEC will be effective against the adult worms, and Ivermectin against the microfilariae.

10. The answer is B (IL$_2$) :
Cyclosporine is an immunosuppressant agent.
It markedly and selectively inhibits:
- T-lymphocyte proliferation;
- IL$_2$ cytokine production;
- CD$_4$ molecule is involved;
- Response of inducer T-cell to IL$_1$ with out any effect on suppressor T cells.
11. The answer is C (blindness):

*Cisplatin* is a platinum containing, anti-neoplastic drug, classified in a «miscellaneous» group.

*It has very important and frequently asked side effects:*
- high emetic potential;
- high renal toxicity: the most important dose dependent toxicity is renal impairment;
- tinnitus and deafness: ototoxicity;
- neuropathy;
- hyperuricemia.

12. The answer is A (L-Asparaginase).

*L-Asparaginase*: the most typical side effects are liver damage, pancreatitis and CNS symptoms (due to defective protein synthesis). Being a foreign protein, it produces allergic reactions in a significant percentage of patients – even anaphylaxis can occur.

*Insulin*: the most typical side effects are hypoglycemia, allergic reaction (due to contaminating proteins), edema (due to Na\(^+\) retention) and local reaction such as swelling, erythema, stinging and lipodystrophy.

*Cyclophosphamide* has prominent immunosuppressant effect. Other prominent side effects are alopecia and cystitis due to metabolite acrolein.

*Vincristine*: prominent adverse effects are peripheral neuropathy and alopecia.

13. The answer is B (bind plasma membrane receptors and following internalization influence, nuclear changes):

Mechanism of action of steroid hormone is bind either:
- to receptors located either in the nucleus (e.g. estrogen);
- receptors in cytoplasm (e.g. Glucocorticoids).

*They do not bind to cell membrane receptors.*

Those steroid receptors that are located in cytoplasm also migrate promptly to the nucleus as soon as they bind their ligands. Binding of receptor hormone complex to DNA within the nucleus increases the transcription of mRNA's which are translated in the ribosomes and increased quantities of proteins are produced that bring about the alteration in cell function.

*Action on carbohydrate metabolism:*

The function of Glucocorticoids is oriented around maintaining the blood glucose levels during starvation. They promote:
- glycogen deposition in liver by activation of glycogen synthetase;
- gluconeogenesis;
- inhibit glucose utilization by peripheral tissue.
Anti-inflammatory action:

• Coticosteroids induce lipocortins in macrophages, endothelial and fibroblasts. Lipocortins inhibit phospholipase A\textsubscript{2} and thus decrease production of PGs LTs and PAF.

• The anti-inflammatory action is non specific and covers all components and stages of inflammation. This includes reduction of:
  – increased capillary permeability;
  – local exudation;
  – cellular infiltration;
  – phagocyte activity.

Glucocorticoids interfere at several steps in the inflammatory response, but the most important overall mechanism appears to be limitation of recruitment of inflammatory cells at the local sites.

14. The answer is B (COX-I is an inducible enzymes):

Prostaglandins, prostocyclins and Tx A\textsubscript{2} are produced from arachidonic acid by the enzyme COX.

COX exists in two isoforms:

- **COX-I**: constitutive isoform: serves physiological housekeeping function.
- **COX-II**: inductive isoform: normally present in minute quantities. It is induced by cytokines and other signal molecules at site of inflammation.

**Leukotrienes** are produced from arachidonic acid via the lipoxygenase pathway.

Leukotrienes also called «slow reactive substance of anaphylaxis» contract most smooth muscles. They are potent bronchoconstrictors and are most important mediators of human allergic asthma:

• LT-B\textsubscript{4} is highly chemotactic.
• LT-C\textsubscript{4} and D\textsubscript{4}: increase capillary permeability.

Vasodilatation i.e. relaxant action on blood vessels has not been seen.
IV. ANTIMICROBIAL DRUGS

1. All the following drugs cause pulmonary fibrosis EXCEPT:
   Variants of the answer:
   a) Busulfan;
   b) Methotrexate;
   c) Doxorubicin;
   d) Bleomycin.

2. All the following antibiotics act on the cell wall EXCEPT:
   Variants of the answer:
   a) Ampicillin;
   b) Bacitracin;
   c) Cycloserine;
   d) Griseofulvin.

3. Advantages of the 3rd generation cephalosporins over the 1st and the 2nd generation cephalosporins is that they are:
   Variants of the answer:
   a) β-lactamase sensitive;
   b) not orally administered;
   c) effective against Gram-positive bacteria;
   d) effective against Gram-negative bacteria.

4. The anti-malarial drugs effective in pre-erythrocytic phase in liver are:
   Variants of the answer:
   a) Proguanil;
   b) Chloroquine;
   c) Pyrimethamine;
   d) Quinine.

5. Which of the following statements is FALSE about Acyclovir:
   Variants of the answer:
   a) it inhibits DNA synthesis and viral replication;
   b) it is effective against influenza;
   c) it has low toxicity for host cells;
   d) renal impairment necessitates dose reduction.

6. All the following antimicrobial agents are used topically EXCEPT:
   Variants of the answer:
   a) Clotrimazole;
   b) Griseofulvin;
   c) Nystatin;
   d) Miconazole.
7. Interstitial nephritis is most commonly seen with:
   Variants of the answer:
   a) Methicillin;
   b) Ampicillin;
   c) Amoxicillin;
   d) Cloxacillin.

8. Maximum amount of photosensitivity is seen with:
   Variants of the answer:
   a) Ciprofloxacin;
   b) Ofloxacin;
   c) Pefloxacin;
   d) Norfloxacin.

9. Administration of one of the following drug is known to result in neuropsychiatric symptoms:
   Variants of the answer:
   a) Rifampicin;
   b) Cycloserine;
   c) Ethionamide;
   d) Cephalosporin.

10. Oral contraceptive failure may be seen with:
    Variants of the answer:
    a) Rifampicin;
    b) Cimetidine;
    c) Propranolol;
    d) Ethambutol.

11. Following drugs may be used for pseudomonas infection EXCEPT:
    Variants of the answer:
    a) Pefloxacine;
    b) Azithromycin;
    c) Imipenem;
    d) Ceftazidime.

12. Clindamycin acts by inhibiting:
    Variants of the answer:
    a) protein synthesis;
    b) DNA gyrase;
    c) cell wall synthesis;
    d) lysosomal enzyme.
13. Albendazole may be used for treatment of all of the following conditions EXCEPT:
  Variants of the answer:
  a) enterobius;
  b) ascariasis;
  c) ankylostor;
  d) shistosomiases.

14. Gynecomastia may be caused by all EXCEPT:
  Variants of the answer:
  a) Cimetidine;
  b) Ranitidine;
  c) Ketoconazole;
  d) Spironolactone.

15. All of the following are examples of bactericidal EXCEPT:
  Variants of the answer:
  a) INH;
  b) Rifampicin;
  c) Ethambutol;
  d) Pirazinamide.

16. All of the following are drugs for anti-tubercular treatment EXCEPT:
  Variants of the answer:
  a) Kanamycin;
  b) Cycloserine;
  c) 5-flucytosine;
  d) Ofloxacin.

17. Mechanism of action of erythromycin is interference with:
  Variants of the answer:
  a) transcription;
  b) translation;
  c) translocation;
  d) signal transduction.

18. A patient has hepatic encephalopathy. The drugs used for gut sterilization in this patient is:
  Variants of the answer:
  a) Neomycin;
  b) Netilmicin;
  c) Bleomycin;
  d) none of the above.
19. A patient taking both Ketoconazole and Terfenadine is prone for:
Variants of the answer:
a) cardiac arrhythmia;
b) toxicity of Ketoconazole;
c) congestive cardiac failure;
d) all of the above.

20. The treatment of contacts of meningococcal meningitis is by:
Variants of the answer:
a) Rifampicin;
b) Erythromycin;
c) Penicillin;
d) Cephalosporin.

21. Drug of choice for malaria during pregnancy is:
Variants of the answer:
a) Chloroquine;
b) Quinine;
c) Primaquine;
d) Mepaquine.

22. Which of the following is NOT an anti-pseudomonal agent?
Variants of the answer:
a) Vancomycin;
b) Ticarcillin;
c) Ceftazidime;
d) Tobramycin.

23. Which anti HIV drug does NOT cause peripheral neuropathy:
Variants of the answer:
a) Lamivudine;
b) Stavudine;
c) Didanosine;
d) Zalcitabine.

24. Mechanism of action of Tetracycline is:
Variants of the answer:
a) binds to A site and inhibit attachment of t-RNA;
b) inhibits peptidyl transferase;
c) causes misreading of mRNA;
d) causes termination of peptide chain elongation.
ANSWERS

1. The answer is C (Doxorubicin):
   Drugs causing pulmonary infiltrates often present with interstitial pulmo-
   nary disease or pulmonary fibrosis. These include:
   • Acyclovir;
   • Amiodarone;
   • Bleomycin;
   • Busulfan;
   • Carmustine;
   • Chlorambucil;
   • Cyclophosphamide;
   • Gold;
   • Melphalan;
   • Methysergide;
   • Mitomycin C;
   • Nitrofurantoin;
   • Procarbazine;
   • Sulfonamides.

2. The answer is D (Griseofulvin):
   Drugs inhibiting cell wall synthesis:
   • Penicillins (e.g. Ampicillin, Amoxicillin, Penicillin G, V, etc.);
   • Cephalosporins;
   • Cycloserine;
   • Vancomycin;
   • Bacitracin.

3. The answer is D (effective against Gram-negative bacteria):
   The 3rd generation of cephalosporins:
   • parenteral:
     — Cefotaxime;
     — Ceftriaxone;
     — Ceftrizoxime;
     — Ceftazidime;
     — Cefoperazone;
     — Cefepime.
   • Oral:
     — Cefixime
   Characteristic features:
   — Highly augmented activity against Gram-negative enterobacteriaceae.
   — Highly resistant to β-lactamase from Gram-negative bacteria.
   — Less active on Gram-positive cocci.
   — All except one are intravenous preparations.
4. The answer is A (Proguanil):
The pre-erythrocytic phase in the liver is targeted for causal prophylaxis. Two anti-malarial drugs are effective for causal prophylaxis (table 7):
- Proguanil (Chlorguanide) is used primarily for Plasmodium falciparum.
- Primaquine:
  - is used for all species of malariae;
  - is not used in mass programmes because of toxic potential.

Table 7 — Activity of different agent against pre-erythrocytic phase

<table>
<thead>
<tr>
<th>Agent</th>
<th>Activity against pre-erythrocytic phase</th>
<th>Plasmodium falciparum</th>
<th>Plasmodium vivax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proguanil</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Primaquine</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Quinine</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Mepacrine</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Pyrimethamine</td>
<td>−</td>
<td>−</td>
<td>−</td>
</tr>
</tbody>
</table>

5. The answer is B (it is effective against influenza):
Acyclovir inhibits DNA synthesis and viral replication:
- inhibits herpes virus DNA polymerase competitively;
- gets incorporated in viral DNA and stops lengthening of DNA strand. The terminated DNA inhibits DNA polymerase irreversibly.
Acyclovir is preferentially taken up by cells which are infected with the herpes virus. Because of selective generation of the active inhibitor in the virus infected cells and it greater inhibitory effect on viral DNA synthesis, Acyclovir has low toxicity for host cells.
Acyclovir primarily excreted unchanged in urine, both by glomerular filtration and tubular secretion. Renal impairment necessitates dose reduction.
Acyclovir is effective against Herpes group of viruses and not against influenza. Spectrum includes:
- herpes simplex: encephalitis, keratitis, genital and mucocutaneous;
- herpes zoster;
- chicken pox.

6. The answer is B (Griseofulvin):
Griseofulvin is used systemically for dermatophytosis. It is ineffective topically.

Nystatin is used only locally (available as ointment).
Clotrimazole is effective in topical treatment of tinea infections.
Miconazole is effective with cutaneous application for tinea, pityriasis, otomycosis, cutaneous and vulvo-vaginal candidiasis.
7. The answer is A (Methicillin):

All Penicillins (mostly so Methicillins) can cause interstitial nephritis.
The most common side effect of all Penicillins is hypersensitivity.
The drug-specific most common side effects are (apart from hypersensitivity):
- Methicillin — interstitial nephritis;
- Oxacillin — hepatitis;
- Nafcillin — neutropenia;
- Ampicillin — diarrhea.

8. The answer is C (Pefloxacin):

Photosensitivity has been reported with Lomefloxacin and Pefloxacin. Photosensitivity can be severe, specially with Lomefloxacin.
Keep Lomefloxacin as the 1st choice and Pefloxacin as the 2nd.
Lomefloxacin has not been given in the option, so Pefloxacin becomes the answer of choice here.

9. The answer is B (Cycloserine):

Cycloserine is used as an anti-tubercular agent, inhibiting cell wall synthesis. Cycloserine has very high CNS toxicity. It may cause:
- psychosis;
- convulsions (may be prevented by pyridoxine);
- tremors;
- headache;
- sleepiness.

10. The Answer is A (Rifampicin):

Contraceptive failure can occur if the following drugs are used concurrently with oral contraceptives.
- Enzyme inducer (i.e. increases metabolism of both estrogen and progestins):
  — Rifampicin;
  — Phenytoin;
  — Phenobarbitone;
  — Primidone;
  — Carbamazepine.

Note:
Cimetidine inhibits drug metabolizing enzymes.
- Suppression of intestinal microflora:
  — Tetracyclines;
  — Ampicillin.
Mechanism: no deconjugation of estrogens secreted in bile.
Therefore interrupts enterohepatic circulation.
11. The answer is B (Azitromycin):
Azitromycin is a macrocycle antibiotic. It does not act on pseudomonas.
Important: during Pseudomonas aerogenosa infection:
- therapy of the 1st choice: antipseudomonal Penicillin + Aminoglycoside;
- therapy of the second choice:
  - antipseudomonal Penicillin + Quinolone;
  - antipseudomonal Cephalosporin;
  - imipenem or Meropenem;
  - aztreonam ± aminoglycoside

Drugs for pseudomonas include:
- Antipseudomonal Pencillins:
  - Carboxypenicillins: e.g. Carbenicillin and Ticarcillin;
  - Ureidopenicillins: e.g. Azlocillin, Mezlocilline, Piperacillin.
- Antipseudomonal cephalosporins:
  - Ceftazidime;
  - Cefoperazone (excreted with bile therefore not given with probenacide);
  - Other the 3rd generation of Cephalosporins (but these are not dependable).
- Imipenem: it is the most broad spectrum β-lactam antibiotic (active against pseudomonas).
  Limiting feature of Imipenem is its rapid hydrolysis by the enzyme dehydropeptidase-I located on brush border of renal tubular cells. Solution to this problem is combination with Cilastatin which is a reversible inhibitor of dehydropeptidase-I.
- Aztreonam: it is a β-lactam antibiotic with only one lactam ring i.e. monobactam.
  - inhibits pseudomonas;
  - is resistant to β-lactamase.
- Quinolones: e.g. Ciprofloxacin
- Aminoglycosides: Gentamycin, Tobramycin and Amikacin are used for gram negative infections. Streptomycin is used for Gram-positive infections.
  Outstanding feature of Amikacin is its resistance to bacterial aminoglycoside inactivating enzymes.
- Polypeptides like Polymyxin B and Colistin may be used. Colistin is more potent in pseudomonas.

Remember:
- Vancomycin does not act on pseudomonas.
- Bacitracin does not act on pseudomonas.

12. The answer is A (protein synthesis):

Clindamycin. Mechanism of action is similar to that of erythromycin i.e. inhibits protein synthesis by binding with 50S ribosome unit and inhibiting process of translocation.
Very important:
• inhibiting protein synthesis:
  – Tetracycline (30S);
  – Chloramphenicol (50S);
  – Erythromycin (50S);
  – Clindamycin (50S).
• Antibiotics inhibiting cell wall synthesis:
  – Penicillins;
  – Cephalosporins;
  – Vancomycin;
  – Bacitracin;
  – Cycloserine.
• Antibiotic inhibiting DNA Gyrase: Fluoroquinolones e.g. Ciprofloxacin
• Antibiotic causing misreading of mRNA code: Aminoglycosides (bactericidal effect).

13. The answer is D (Schistosomiasis):

*Albendazole* is not used for *schistosomiasis*. It is used for all other infections mentioned (table 8).

<table>
<thead>
<tr>
<th>Disease</th>
<th>Drug of choice</th>
<th>Alternatives</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Enterobius</td>
<td>Mebendazole</td>
<td>Albendazole / Pyrantel pamoate</td>
</tr>
<tr>
<td>2. Ascaris</td>
<td>Albendazole</td>
<td>Mebendazole / Pyrantel pamoate</td>
</tr>
<tr>
<td>3. Schistosoma</td>
<td>Praziquantel</td>
<td>Metrifonate (for Schistosoma haematobium)</td>
</tr>
<tr>
<td>4. Strongyloides</td>
<td>Ivermectin</td>
<td>Oxamniquine (for schistosoma mansoni)</td>
</tr>
<tr>
<td>5. Dracunculus</td>
<td>Metronidazole + Worm removal</td>
<td>Albendazole / Thiabendazole Thiabendazole + Worm removal</td>
</tr>
</tbody>
</table>

14. The answer is B (Ranitidine):

*Cimetidine* has antiandrogenic action and may cause gynecomastia but not ranitidine.

Agents causing gynecomastia:
• Estrogen and testosterone;
• calcium channel blockers and digitalis;
• isonicotinic acid hydrazide, and Ethionamide;
• Griseofulvin and Ketoconazole;
• Spironolactone;
• Reserpine and methyldopa;
• Phenytoin;
• Clomiphene;
• Cimetidine.
15. The answer is C (Ethambutol):
Ethambutol is tuberculostatic and not tuberculocidal.
Others are all bactericidal.
Remember: Ethambutol is contraindicated in children below 6 years of age.
This is so, because young children may be unable to report an early visual impairment, which is the most important dose and duration dependent toxicity.
Ethambutol is one of the few antitubercular treatment drugs that are not hepatotoxic.

16. The answer is C (5-Flucytosine):
5-Flucytosine is an antifungal agent and has no antitubercular activity.
Some antitubercular drugs are represented in the table 9.

Table 9 — Antitubercular drugs

<table>
<thead>
<tr>
<th>Second line drugs include:</th>
<th>And newer agents:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Thiacetazone</td>
<td>1. Ciprofloxacin</td>
</tr>
<tr>
<td>2. PAS</td>
<td>2. Ofloxacin</td>
</tr>
<tr>
<td>3. Ethionamide</td>
<td>3. Clarithromycin</td>
</tr>
<tr>
<td>5. Kanamycin</td>
<td>5. Rifabutin</td>
</tr>
<tr>
<td>6. Amikacin</td>
<td></td>
</tr>
<tr>
<td>7. Capreomycin</td>
<td></td>
</tr>
</tbody>
</table>

17. The answer is C (translocation):
Erythromycin combines with 50S ribosome subunit and interferes with translocation.

18. The answer is A (Neomycin):
Normally ammonia is produced by colonic bacteria. This is absorbed and converted to urea by liver. In severe hepatic failure detoxification of ammonia, does not occur, and blood levels of ammonia rise and produce encephalopathy.
Neomycin is specially suited for this purpose because:
• it is highly effective against coliforms.
• development of resistance is not a problem.
• absorption from the g.i.t. is minimal.

19. The Answer is A (cardiac arrhythmia):
Terfenadine blocks cardiac K⁺ channels in overdose and may produce polymorphic ventricular tachycardia or <<torsades de pointes>>.
Toxicity is markedly increased in:
• Liver disease.
• Concurrent administration of inhibitors of cytochrome p450 e.g.
  – Erythromycin, Clarithromycin (Azitromycin and Fluconazole have been found safe);
Ketoconazole, Itraconazole. Thus a patient administered both Ketoconazole and Terfenadine is prone for Terfenadine toxicity (i.e. cardiac arrhythmia) and not Ketoconazole toxicity.

20. The answer is A (Rifampicin):
Contacts: chemoprophylaxis has been suggested for close contacts. Rifampicin is the drug of choice unless the organism is known to be sensitive to Sulfadiazine. Chemoprophylaxis of some disease is represented in the table 10.

Table 10 — Drug of choice for chemoprophylaxis of some disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Tetanus</th>
<th>Penicillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>Amantadine</td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>Chloroquine</td>
<td></td>
</tr>
<tr>
<td>Cholera</td>
<td>Tetracycline</td>
<td></td>
</tr>
<tr>
<td>Plague</td>
<td>Tetracycline</td>
<td></td>
</tr>
<tr>
<td>Bacterial conjunctivitis</td>
<td>Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Pertussis</td>
<td>Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Meningococcal meningitis</td>
<td>Rifampicin</td>
<td></td>
</tr>
</tbody>
</table>

21. The answer is A (Chloroquine):
Prophylaxis of malaria in pregnancy:
• best course is weekly Chloroquine with or without proguanil.
• in areas with Chloroquine-resistant malaria, Mefloquine can be used, except in first trimester.
• drugs contraindicated in pregnancy are Doxycycline and Primaquine.

22. The answer is A (Vancomycin):
Vancomycin is a glycopeptide antibiotic. It is bactericidal to gram positive cocci, Neisseria, Clostridia and Diphtheroids. It does not act on gram negative bacilli such as pseudomonas.

It is the drug of choice for:
• antibiotic associated pseudo-membranous colitis;
• Methicillin resistant Staphylococcus aureus.
Its side effects have been asked frequently:
• ototoxic;
• nephrotoxic;
• red-man syndrome: rapid intravenous injection of Vancomycin is associated with intense flushing. This is called «red-man syndrome».

Other drugs mentioned in the question are all active against pseudomonas.
23. The answer is A (Lamivudine):

*Lamivudine*: potential side effects are headache, insomnia, fatigue and gastrointestinal discomfort, though these are typically mild. Peripheral neuropathy has not been mentioned as a side effect.

*Stavudine*: the major dose limiting toxicity is dose related peripheral sensory neuropathy.

*Didanosine*: the major clinical toxicity associated with Didanosine therapy is dose dependent pancreatitis. Other adverse effects include painful peripheral neuropathy, diarrhea, hyperuricemia, cardiomyopathy, retinal changes and optic neuritis.

*Zalcitabin*: it is associated with a dose dependent peripheral neuropathy, that can be treatment limiting in 10–20 % of patients, but appears to be slowly reversible if treatment is stopped promptly.

The other major reported toxicities include:
- oral and esophageal ulceration;
- pancreatitis (less common than with Didanosine);
- headache, nausea, rash, arthralgias, cardiomyopathy etc.

Thus the answer is Lamivudin.

24. The answer is A (bind to A site and inhibit attachment of t-RNA):

*Tetracycline* inhibits protein synthesis by binding to 30S ribosomes in susceptible organism. Subsequent to such binding, attachment of aminoacyl t-RNA to the «A» site on the mRNA ribosome complex is inhibited. As a result peptide chain fails to grow. Tetracycline is bacteriostatic.

Antibiotics which act on 50S ribosome:
- Clindamycin;
- Chloramphenicol;
- Erythromycin.

Antibiotics which act on 30S ribosome:
- Tetracycline;
- Aminoglycosides.

*Aminoglycosides*: interfere with polysome formation and cause misreading of mRNA code.

*Erythromycin and Clindamycin*: interfere with translocation of the elongated peptide chain from «A» to «P» site. *Synthesis therefore may be prematurity terminated.*
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