Medical Committee
The University of Jordan

PHARMACOLOGY

Lecture No.: 24

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SHEET

SLIDES

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Adrenoreceptor Blockers

β-Blockers

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- 2.4 Pharmacodynamics of β-adrenoreceptor antagonists.
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In the previous lectures we discussed the α-adrenoreceptor antagonists and part of β-adrenoreceptor antagonists {1→2.4} and we finished the pharmacological effects of propranolol (general β -Blockers that block all three subtypes of receptors).

Written by Mohammed Nawaiseh

❖ Discussing each drug individually:

1) Metoprolol, Atenolol:

I-They are β1-selective .

Q) **What are the actions that will not happen while using Metoprolol and Atenolol in respect that they are β1-selective (assuming using normal concentrations; because selectivity is lost at high concentrations of the drug) ?**

A) Generally, all the actions that are mediated through β2-receptors blockade will **not** be shown significantly by Metoprolol and Atenolol, like:

1- Bronchoconstriction, it won't occur significantly.

2-There won't be an increase in blood pressure; because there is no blocking for β_2-receptors, so there will be a vasodilatation in the blood vessels.

3-Problem of hypoglycemia in insulin users is not that significant, but because selectivity might be lost at high concentrations of the drug, hypoglycemia might occur.(The doctors should be careful while adjusting the dose for the patients).

II) Are **safer** in patients who experience bronchoconstriction with propranolol.

III) May be preferable for myocardial infarction in patients having diabetes (especially insulin users), peripheral vascular disease, chronic obstructive pulmonary disease {COPD}.

Note: Peripheral vascular disease is due to atherosclerosis in the blood vessels of skeletal muscles (obstruction; less blood supply),so if these β-Blockers were given to these patients their condition will not progress; because these drugs don't affect β2-receptors in general, so they are not going to produce constriction in the blood vessels of skeletal muscles.

2) Nadolol: This drug is similar to propranolol, but its duration of action is longer. It has a very long duration of action.

3) Timolol: This drug is used topically (as eye drops) for treatment of **glaucoma** to reduce intraocular pressure.

4) Pindolol, Acebutolol and Oxprenolol:

These drugs have partial β-Agonist activity (which partially activate β-receptors) so they are less likely to cause bradycardia and plasma lipids' abnormalities.

Q) **Why these drugs don't cause abnormalities in plasma lipids?**

A) The reason is not known; because we don't know why β-Blockers (in general) cause abnormalities in plasma lipids.

Q) **Why these drugs are less likely to cause bradycardia?**

A) Because they cause partial stimulation for β1-Receptors , so they decrease the probability of bradycardia in comparison for example with propranolol in which the pulse can reach 50 or even 48.

5) Labetalol:

This drug is a mixed (α and β) Blocker; because it's available as chiral isomers, and the same molecule has two isomers. (Racemic mixture)

- Some of these isomers are inactive (S,S) isomer and (R,S) isomer.
- The (S, R) - isomer is a potent α1-selective blocker.
- The (R, R) - isomer is a potent β-blocker (not selective; it blocks β1 and β2 receptors) .

Q) **When α1-receptors are blocked what will happen to blood vessels?**

A) α-blockers cause vasodilatation and this causes reflex sympathetic stimulation (because by definition all α1-Blockers cause reflex sympathetic stimulation) but part of this reflex will be blocked (reduced) by effect on β1 receptors.

In other words, although it's an α blocker it is not associated with significant tachycardia because β1 receptors are blocked and β_1 receptors are the ones responsible for SA node stimulation, so SA node won't be stimulated. As a result, there will be reduced blood pressure with less reflex tachycardia than only α-blockers.

6) Carvedilol: very important relatively new drug

- It is a **nonselective β-receptor antagonist** with some capacity to block α1-adrenergic receptors.
- It's prescribed a lot by cardiologists; important in chronic heart failure patients.
- It's like Labetalol {a mixed (α and β) blocker} which is a nonselective β-blocker and selective α1-blocker.

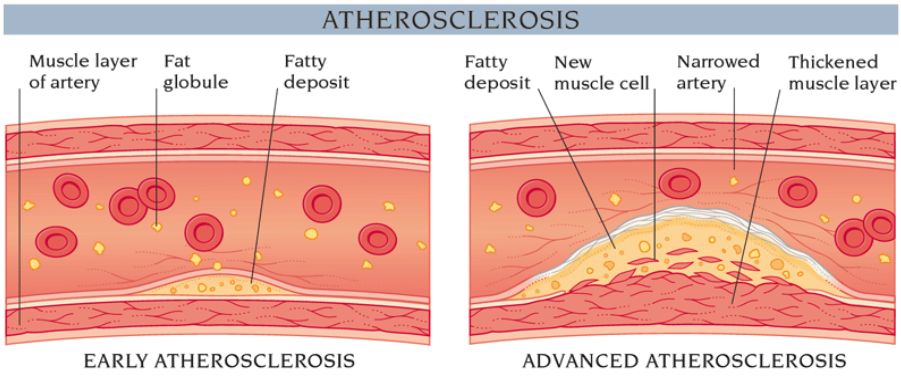
#This drug has two other important functions (actions):

1) It attenuates (decreases) oxygen free radical-initiated lipid peroxidation .
The first step in atherosclerosis {تصلب الشرايين} is the oxidation of LDL cholesterol and this oxidation initiates the process of atherosclerosis(which is the main problem in cardio vascular diseases, and leads to cerebrovascular accident (CVA) (stroke in the brain),kidney damage and eye damage. So this is an extremely important function.

Q) **What does carvedilol do with respect to atherosclerosis?**

A) This drug inhibits the oxidation of lipids and delays (stops, retards) atherosclerosis.

2) It inhibits vascular smooth muscle **mitogenesis** (mitosis, cell division):
Because mitogenesis increases the thickness of smooth muscles in blood vessels, the musculosa will be thicker and thick musculosa by itself will narrow the blood vessels.
*Both vasoconstriction and increase in smooth muscle cells' mass of blood vessels cause narrowing of blood vessels; because it will press the lumen of the blood vessel. Also the response to vasoconstrictors will be more and the obstruction will increase(this also will be inhibited by carvedilol).This is very important in the remodeling of the heart.



#Analogy (تشبيه) to the increase in response to vasoconstrictors when there is an increase in mitogenesis of smooth muscle cells in blood vessels(thicker musculosa): If there is two persons; the first one with high muscle mass and the second with normal muscle mass; stimulation to muscles in equal magnitude will cause more effect (stronger contractility) in the first person. And the same thing goes with thicker musculosa; it will respond more to vasoconstrictors because there is more muscle mass.

Q) **What does remodeling of the heart mean?**

A) When there is a disease in the heart (ex: cardiac ischemia) to the extent of inducing heart failure there will be remodeling of the heart (اعادة تصميم او تشكيل). It refers to the changes in size, shape, structure and physiology of the heart after injury to the myocardium. This remodeling happens by many changes including smooth muscle proliferation(thicker musculosa) in the blood vessels within the cardiac muscle (coronary arteries that branch to small arterioles).During remodeling, in case of cardiac ischemia for example ,healing will occur by scar formation (fibrosis; fibrous tissue not cardiac muscle).
This process(remodeling of the heart) can be stopped from progressing or partially reversed by using **carvedilol**, so this drug is very important in cases of heart disease when there is thickening in the muscle mass of blood vessels.
-Hypertension also cause thickening of the smooth muscles of blood vessels; because these smooth muscles will resist the increased pressure and increased cardiac output, and that means that there will be increased contraction in these smooth muscles ;therefore they will undergo hypertrophy and hyperplasia (adaptation) and as a result these smooth muscles will be thicker.

Q) Are β-blockers (in general) used in the treatment of heart failure patients?

A) No, β-blockers are contraindicated in patients with acute or chronic heart failure because they worsen it. However, **carvedilol** is given in chronic heart failure patients (not in acute heart failure).

Note: In case of heart failure patients, the heart is unable to contract normally and pump enough blood to the body .So, if β-blockers are given to these patients ,they will reduce the contractility of the heart more and can cause death.

If a patient with a heart failure (acute) came to the doctor, firstly the doctor should treat the heart failure, and when the patient has recovered, the doctor can give him\her small doses of carvedilol to reverse the remodeling of the heart and to stop the propagation of atherosclerosis by inhibiting oxidation.

Note: **Metoprolol** and **Bisoprolol** can be used in the treatment of chronic heart failure. However, **carvedilol** is the main drug used by cardiologists for such cases.

7) Esmolol:

-This drug has a short half life (10 minutes).

- This drug is usually given intravenously.
- This drug is used in the treatment of supraventricular arrhythmias, and the main goal of this treatment is to prevent the progression to ventricular arrhythmias.
- Supraventricular arrhythmias can be transmitted through the AV node and become ventricular arrhythmias.

Q) **How do β-Blockers prevent ventricular arrhythmias?**

A) β-blockers decrease the velocity of conduction through the AV node and prolong the refractory period and that makes β-blockers effective in controlling ventricular rate in supraventricular arrhythmias and prevents the possible occurrence of ventricular arrhythmias.

Q) Why is prevention of ventricular arrhythmias very important?

A) Because of the importance of ventricles in respect with cardiac out flow (more important than the atria). The atria collect blood and 75% of this blood flow spontaneously by gravity to the ventricles and 25% needs atrial contraction. However, ventricles need to contract efficiently to pump blood to the whole body. So it's very important to not have any problems in ventricular contraction.

-Thyrotoxicosis (hyperthyroidism) : In thyrotoxicosis there is up regulation in β-receptors due to thyroid hormones .This can cause tachycardia and cardiac supraventricular arrhythmias (because β-receptors work on SA node and increase chronotropic effect).So, non-selective β-blockers(ex: propranolol) can be used to antagonize the effect of thyrotoxicosis ,to treat the supraventricular arrhythmias and tachycardia that happen in thyrotoxicosis.(selective β-blockers are not used because all β- receptors will undergo up-regulation).

Therapeutic uses of β-adrenoreceptor antagonists:

1)**Hypertension**

2) **Supraventricular** and **ventricular cardiac arrhythmias**

A. They slow ventricular response rate in patients with atrial fibrillation (abnormal heart rhythm.) or flutter due to reduction in AV node conduction velocity and an increased refractory period.

B. They reduce ventricular ectopic beats precipitated by catecholamines.

#Note: ventricular arrhythmias of ectopic beats are found especially in persons who smoke and drink a lot of tea and coffee. They experience a lot of weird beats in the heart, these beats are called **extrasystoles beats**.

-ventricular arrhythmia is very dangerous and can cause death, but extrasystoles beats aren't that serious unless it evolves into ventricular arrhythmias.

Note: An **ectopic pacemaker** is an excitable group of cells that cause a premature heart beat outside the normally functioning SA node of the human heart. It can cause tachycardia, bradycardia or ventricular arrhythmias. In a normal heart beat rhythm, the SA node usually suppresses the ectopic pacemaker activity due to the higher impulse rate of the SA node. However, if the SA node is not working, ectopic pacemaker activity may take over the natural heart rhythm.

C. Sotalol is an antiarryhthmic drug that has other additional mechanisms beside β-blockade.

3) **Ischemic heart disease**

Ischemic heart diseases happen when the oxygen supply to the myocardium is not enough to meet the metabolic needs of the myocardium ,whether the blood flow increases (as in anemia)or decreases (due to hypoxia).

Q) How β-Blockers can be useful in ischemic heart disease?

A) β-Blockers don't supply more oxygen instead they reduce cardiac work and reduce the requirement (demand)for oxygen; because of the negative(chronotropic and inotropic)effect .

4) **Heart failure**: β-blockers are contraindicated in heart failure except these three β-antagonists that have been proved to be useful in chronic heart failure (Metoprolol, Bisoprolol & Carvedilol) if used correctly. These drugs may worsen acute heart failure so they must be used after the acute attack **only**. But they are used during or after the treatment of chronic heart failure.

5) **Glaucoma**: **Timolol**.

6) **Hyperthyroidism**:

Up-regulation of β-receptors due to thyroid hormones will cause excessive sympathetic activity associated with this condition. With increased amount of receptors and according to the law of mass action, the released catecholamines will bind more to the receptors (randomly). This can cause tachycardia and cardiac supraventricular arrhythmias (because β-receptors work in SA node and increase chronotropic effect).In this case a non-selective β-blockers (ex: propranolol) is used to reverse the sympathetic over activity associated with hyperthyroidism (not a treatment for hyperthyroidism).

7) Prevention of **migraine headache** (not treatment):

Some β-blockers can be used to reduce the intensity and frequency of migraine headache, because migraine is a vascular headache. However, β-blockers can't be used for treatment (only prevention); because it might worsen it. The mechanism is not known.

Migraine: صداع نصفي
cluster headache:صداع في مكان معين في الدماغ
Both of them are a vascular disease, but they have different mechanisms.

8) Treatment of **anxiety** and **tremors** associated with sympathetic over activity.
Especially in drugs that cross blood brain barrier (lipid –soluble) like propranolol that causes sedation and also nightmares.
Note: Propranolol (single dose) can be used to reduce performance anxiety (not psychiatric anxiety) before going to an interview or exams or any stressful events. If taken in high doses, it might lead to sleeping (sedation is the first stage of sleep).

9) Reduction of **portal vein pressure** in patients with hepatic cirrhosis.

Cirrhosis is a slowly progressing disease in which healthy **liver** tissue is replaced with scar tissue, eventually preventing the **liver** from functioning properly. The scar tissue blocks the flow of blood through the **liver** and slows the processing of nutrients, hormones, drugs, and naturally produced toxins. This blockage of blood flow will increase the pressure within the portal vein. **Propranolol and Nadolol (non-selective) is used in this case.**

Hypertension has three types:

1) Portal hypertension: Is caused by hepatic cirrhosis (is the worst hypertension).

2) Pulmonary hypertension: worse than systemic hypertension . 50% of patients with pulmonary hypertension can live only up to 5 years. (It was mentioned when we talked about sympathetic drugs that it cause loss of appetite and reduce body weight and adversely cause pulmonary hypertension and valve disease).

3) Systemic hypertension: (High blood pressure in systemic arteries- we covered it through this course) Patients with this type of hypertension, if they are treated , can live for (30-40)years.

Important note: In liver cirrhosis, the liver function is greatly affected and as a result there will be no metabolism in the liver and first pass effect is reduced. The drug will bypass the portal circulation and a normal dose of propranolol (40mg) can lead to toxicity (20 times increase in the effect).

Adverse effects of β-adrenoreceptor antagonists:

1) **Drug allergy**:

Any drug can cause allergy and GI tract irritation in particular patients; because drugs are foreign molecules that will bind to certain proteins(become haptens) and produce antibodies which will cause allergy.

2) **Sedation**, **sleep disturbances**, **depression (rarely)**, **psychotic reactions**, **nightmares** – (CNS):

- Drugs that reduce sympathetic activity (these drugs must be lipid soluble; to cross blood brain barrier) can cause depression. Hence, drugs that are used for treatment of depression usually increase sympathetic activity.

- This adverse effect is not caused by all β-blockers, such as Atenolol; it doesn't cause sedation nor nightmares nor depression, because it is water soluble and doesn't cross blood brain barrier.

-Reserpine (rarely used today) causes depletion of sympathetic NT and causes depression.

3) Worsening of **bronchial asthma**; because they cause bronchoconstriction through blocking of β2-Receptors.

4) Worsening of **peripheral vascular disease** and **vasospastic** conditions through blocking of β2-receptors.

Q) Peripheral vascular disease happens in which cases?

1) Elderly patients.
2) Middle aged patients (around forties 40-49) with high concentration of cholesterol, which causes premature atherosclerosis.
3) Diabetic patients with premature atherosclerosis.

* Atherosclerosis starts in young age and progresses with time. Diabetes and high concentration of cholesterol accelerates the progression of atherosclerosis.

* Patients with peripheral vascular disease have atherosclerosis that affects all blood vessels in the body especially the blood vessels that supply lower limb-skeletal muscles and decreases the blood supply(ischemia). When these patients walk for just short distances they will experience pain in their calf muscles; because the oxygen demand is increased .This pain will be relieved when they stop walking and that's because the oxygen demand is decreased.

This is called **intermittent claudication** (clinical diagnosis given for muscle pain, classically in the calf muscle, which occurs during exercise, such as walking, and is relieved by a short period of rest due to poor circulation) . B-blockers can't be given to these patients because they reduce cardiac output by reducing heart rate and contractility and the blood supply further decreases.

In general, ischemia causes pain, even myocardial ischemia, because it releases substances that stimulate pain receptors.

*The second case is **vasospasm-Raynaud's phenomenon** (inherited): Which is a sudden contraction of normal blood vessels especially in cold weather and this will cause noticeable necrosis in the skin of fingers and toes (black dots). It is different than atherosclerosis and other mechanical obstruction. Those individuals will get worse with β-blockers due to vasoconstriction by blocking β_2 receptors .

5) **Heart failure**: Reduction of cardiac output and cardiac decompensation .

6) **Bradycardia** : reduced heart rate .

7) **Atrioventricular block** and **cardiac arrest**:

Delay of conduction and prolonged refractory period .This will physiologically separate atria from ventricles and they will work without coordination.

Normally, when the ventricles contract the atria relax and vice versa. Therefore, when the AV node is cut (blocked) the ventricles and atria will work

without coordination. Eventually, atrioventricular block and excessive bradycardia will cause cardiac arrest (very dangerous).

8) **Masking the symptoms of, and delaying recovery from, hypoglycemia in diabetic patients taking insulin (β2).**

9) **Withdrawal syndrome**:

Using β-blockers chronically will cause up-regulation (increase number) of receptors during treatment. Up-regulation in the presence of β-blockers is going to block these excess receptors ,so there is no problem. But when the drug is stopped the receptors are excessively presented, catecholamines (epinephrine and norepinephrine) in the circulation will find more receptors and the action will be increased. This will cause the **rebound effects** (exaggeration of the condition they were used to treat).

Examples:

I- If β-blockers were used to treat hypertension and the patient for example had blood pressure 140/90 before using the treatment and the blood pressure was normalized after the use of β-blockers. If the treatment is stopped suddenly the blood pressure will increase more and become higher (180/110) (rebound effect).

II-Angina pectoris:{ذبحة صدرية} ischemia with pain but without heart damage.

If the patient stopped the drug suddenly, myocardial infarction could happen.

III-Patients with cardiac arrhythmias were given propranolol and then the drug was stopped suddenly ,this will cause excessive arrhythmias (can cause heart failure and death).

Q) **What the doctors do to prevent withdrawal syndrome (rebound effect)?**

A) Tapering of the dose (gradual reduction, to reverse up-regulation but not to the extent of down-regulation) rather than sudden withdrawal.

For example, if your patient takes a 40mg-dose 4 times daily, he should take 30mg-dose 4 times daily for a week as a first step. Then you lower the dose each week until you stop the drug

Note: Before prescribing the drug to the patient the doctor should warn him\her about the dangerous effects of stopping the drug suddenly to prevent withdrawal syndrome (rebound effect). **Never Ever Stop The Drug Suddenly.**

Done by: Mohammed Bassam Nawaiseh .

Review Test

1. Botulinum toxin causes paralysis by
(A) Inhibiting choline acetyltransferase
(B) Blocking transport of choline into neurons
(C) Blocking release of acetylcholine from storage vesicles
(D) Inhibiting acetylcholinesterase
(E) Blocking the synapse at ganglia

2. Which of the following neurotransmitters interacts with guanethidine?
(A) Acetylcholine
(B) Epinephrine
(C) Dopamine
(D) Norepinephrine
(E) Serotonin

3. What is the mechanism of action of cocaine?
(A) Propagation of action of norepinephrine by inhibiting its active transport from the synapse
(B) Oxidative deamination of norepinephrine in nerve terminals and the effector cells
(C) Inhibition of metabolism of norepinephrine in nerve terminals
(D) Potentiation of tyrosine hydroxylase, the rate-limiting enzyme in the synthesis of norepinephrine
(E) Promotion of release of norepinephrine from adrenergic nerve endings

4. What class of medications does bethanechol belong to?
(A) Nicotinic blockers
(B) α-Agonists
(C) β1-Blockers
(D) β2-Blockers
(E) Muscarinic agonists

5. A 38-year-old farmer is brought to the ER by his wife with symptoms of sudden difficulty breathing, sweatiness, and anxiety. He was spraying insecticide when this happened. It has been 25 minutes since the symptoms started. The patient is emergently intubated and given atropine and another medication that acts to reactivate acetylcholinesterase. What medication is it?
(A) Physostigmine
(B) Propranolol
(C) Pralidoxime
(D) Phenylephrine
(E) Pancuronium

6. A 78-year-old man with Parkinson disease experiences worsening of his symptoms. He is already taking levodopa. Since the disease is characterized by degeneration of dopaminergic neurons, leading to the lack of inhibition of cholinergic neurons, the addition of which medication is likely to help alleviate the patient's symptoms?
(A) Benztropine
(B) Reserpine
(C) Doxazocin
(D) Timolol
(E) Tubocurarine

7. A 66-year-old woman with a long history of heavy smoking presents to her doctor with complaints of shortness of breath and chronic coughing that has been present for about 2 years and has been worsening in

frequency. The doctor decides to prescribe a bronchodilator agent that has minimal cardiac side effects, since the patient also has an extensive cardiac history. Which medication did the doctor likely prescribe?
(A) Albuterol
(B) Prazosin
(C) Atenolol
(D) Ipratropium
(E) Pseudoephedrine

8. Which of the following medications is used to prevent premature labor?
(A) Tamsulosin
(B) Cevimeline
(C) Atracurium
(D) Tolterodine
(E) Terbutaline

9. A floor nurse pages you about a patient who is having chest pain. You order an electrocardiogram
and rush to see the patient.
He describes the pain as tight pressure and is demonstrably sweating and gasping for air. The ECG comes back with acute ST-segment elevations in inferior leads, and you diagnose a myocardial infarction. You start giving the patient oxygen and give him sublingual nitroglycerin and morphine for pain. You also give him another medication, which you have read may prolong his survival in this dire situation. What class of medication is it?
(A) β-Blocker
(B) α-Agonist
(C) Muscarinic agonist
(D) Neuromuscular blocker
(E) Dopamine agonist

10. A 35-year-old woman presents to your office for a regular check-up. Her only complaint is recurrent migraine headaches, which have increased in frequency over the years. On examination, her blood pressure is elevated at 150/70 . You decide to start her on antihypertensive therapy that is also used for prophylaxis of migraines. Which medication is it?
(A) Clonidine
(B) Prazosin
(C) Hydrochlorothiazide
(D) Propranolol
(E) Verapamil

11 . In contrast to propranolol, metoprolol
(A) Is used for the management of hypertension
(B) Has greater selectivity for β2-adrenoceptors
(C) May be beneficial for the acute treatment of migraine headache
(D) Is less likely to precipitate bronchoconstriction
in patients with asthma

12. Which of the following drugs is used to diagnose myasthenia gravis?
(A) Atropine
(B) Neostigmine
(C) Bethanechol
(D) Edrophonium
(E) Pralidoxime

13. Pilocarpine reduces intraocular pressure
in patients with glaucoma because it
(A) Activates nicotinic cholinoceptors
(B) is a muscarinic cholinoceptor agonist.
(C) Selectively inhibits peripheral activity of sympathetic ganglia
(D) Inhibits acetylcholinesterase

14. Drug X causes an increase in blood pressure and a decrease in heart rate when administered to a patient intravenously. If an antagonist at ganglionic nicotinic receptors is administered first, drug X causes an increase in blood pressure and an increase in heart rate. Drug X most likely is
(A) Propranolol
(B) Norepinephrine
(C) Isoproterenol
(D) Terbutaline
(E) Curare

15. Poisoning with an insecticide containing an acetylcholinesterase inhibitor is best managed by administration of which one of the following agents?
(A) Physostigmine
(B) Bethanechol
(C) Propranolol
(D) Pilocarpine
(E) Atropine

16. Receptor actions of acetylcholine are mimicked by nicotine at which one of the following sites?
(A) Adrenal medullary chromaffin cells
(B) Urinary bladder smooth muscle cells
(C) Iris circular (constrictor) muscle
(D) Heart sinoatrial pacemaker cells

17. Muscarinic cholinoceptor agonists may cause vasodilation through the release of endothelial
(A) Histamine
(B) Norepinephrine
(C) Acetylcholine
(D) Nitric oxide

18. Emergency treatment of acute heart failure is best managed with which of the following drugs?
(A) Metaproterenol
(B) Phenylephrine
(C) Dobutamine
(D) Norepinephrine
(E) Isoproterenol

19. Which one of the following agents, when applied topically to the eye, would cause both mydriasis and cycloplegia?
(A) Phenylephrine
(B) Carbachol
(C) Prazosin
(D) Atropine

20. Neostigmine would be expected to reverse which one of the following conditions?
(A) Paralysis of skeletal muscle induced by a competitive, nondepolarizing muscle relaxant
(B) Paralysis of skeletal muscle induced by a depolarizing muscle relaxant
(C) Cardiac slowing induced by stimulation of the vagus nerve
(D) Miosis induced by bright light

21. Topical application of timolol to the eye would be expected to induce which of the following?
(A) Miosis
(B) Mydriasis
(C) Decreased formation of aqueous humor
(D) Increased outflow of aqueous Humor

22. Phenylephrine is used to treat patients with nasal mucosa stuffiness because it causes vasoconstriction by
(A) Blocking nicotinic cholinoceptors
(B) Blocking β-adrenoceptors
(C) Stimulating α-adrenoceptors
(D) Stimulating muscarinic Cholinoceptors

Q)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22
A)	C	D	A	E	C	A	D	E	A	D	D	D	B	B	E	A	D	C	D	A	C	C

Explanation for some questions

6. The answer is A. Benztropine, an antimuscarinic agent, is used as an adjunct for the treatment of Parkinson disease. Reserpine is a norepinephrine uptake inhibitor occasionally used for the treatment of hypertension. Timolol is a β-blocker used for glaucoma. Tubocurarine is a neuromuscular blocker used in anesthesia.

7. The answer is D. Ipratropium bromide is used extensively for chronic obstructive pulmonary disease (COPD), which is the most likely diagnosis in this case. It acts by antagonizing muscarinic receptors in bronchial smooth muscle, thereby causing bronchodilation.

9. The answer is A. β-Blockers such as atenolol are now part of management of acute myocardial infarction, along with oxygen, nitroglycerin, and morphine. They reduce sympathetic activity and heart contractility, thereby reducing the oxygen demand.

10. The answer is D. The β-blocker propranolol is a good choice for an antihypertensive medication; however, it is also successfully used for other indications, such as prophylaxis of migraine headaches.

14. The answer is B. In the absence of a nicotinic receptor antagonist, norepinephrine may result in a reflex baroreceptor-mediated increase in vagal activity. The presence of such an agent unmasks the direct stimulant effect of norepinephrine on heart rate.

16. The answer is A. Nicotinic cholinoceptors are found in adrenal medullary chromaffin cells. At the other sites, acetylcholine activates muscarinic cholinoceptors.

17. The answer is D. nitric oxide is similar to EDRF

18. The answer is C. Dobutamine, a relatively selective β1-adrenoceptor agonist, increases cardiac output and lowers peripheral resistance.

19. The answer is D. Atropine produces both mydriasis and cycloplegia (the inability to accommodate for near vision). Phenylephrine causes mydriasis without cycloplegia. Carbachol causes pupillary constriction. Prazosin is an α-adrenoceptor antagonist.

20. The answer is A. Acetylcholine accumulation due to neostigmine inhibition of cholinesterase will reverse the action of the competitive neuromuscular blocking agents.