

Study Questions

Choose the **ONE** best answer.

4.1 Botulinum toxin blocks the release of acetylcholine from cholinergic nerve terminals. Which of the following is a possible effect of botulinum toxin?

- A. Skeletal muscle paralysis.
- B. Improvement of myasthenia gravis symptoms.
- C. Increased salivation.
- D. Reduced heart rate.

Correct answer = A. Acetylcholine released by cholinergic neurons acts on nicotinic receptors in the skeletal muscle cells to cause contraction. Therefore, blockade of ACh release causes skeletal muscle paralysis. Myasthenia gravis is an autoimmune disease where antibodies are produced against nicotinic receptors and inactivate nicotinic receptors. A reduction in ACh release therefore worsens (not improves) the symptoms of this condition. Reduction in ACh release by botulinum toxin causes reduction in secretions including saliva (not increase in salivation) causing dry mouth and an increase (not reduction) in heart rate due to reduced vagal activity.

4.2 A dentist would like to reduce salivation in a patient in preparation for an oral surgical procedure. Which of the following strategies will be useful in reducing salivation?

- A. Activate nicotinic receptors in the salivary glands.
- B. Block nicotinic receptors in the salivary glands.
- C. Activate muscarinic receptors in the salivary glands.
- D. Block muscarinic receptors in the salivary glands.

Correct answer = D. Salivary glands contain muscarinic receptors, not nicotinic receptors. Activation of muscarinic receptors in the salivary glands causes secretion of saliva. Blocking muscarinic receptors, using drugs such as atropine, reduces salivary secretions and makes the mouth dry.

4.3 Which of the following is a systemic effect of a muscarinic agonist?

- A. Reduced heart rate (bradycardia).
- B. Increased blood pressure.
- C. Mydriasis (dilation of the pupil).
- D. Reduced urinary frequency.
- E. Constipation.

Correct answer = A. A muscarinic agonist binds to and activates muscarinic receptors in the heart, endothelial cells (blood vessels), the gut, and iris sphincter (eye) and urinary bladder wall muscles, in addition to several other tissues. Activation of muscarinic receptors by an agonist causes a reduction in heart rate, constriction of circular muscles in the iris sphincter leading to constriction of the pupil (miosis), increased GI motility (hence, diarrhea, not constipation), and contraction of bladder muscles leading to an increase (not decrease) in urination frequency. In the endothelial cells of blood vessels, muscarinic activation produces release of nitric oxide that causes vasorelaxation and a reduction (not increase) in blood pressure.

4.4 If an ophthalmologist wants to dilate the pupils for an eye examination, which of the following drugs/classes of drugs could be theoretically useful?

- A. Muscarinic receptor activator (agonist).
- B. Muscarinic receptor inhibitor (antagonist).
- C. Acetylcholine.
- D. Pilocarpine.
- E. Neostigmine.

Correct answer = B. Muscarinic agonists (for example, ACh, pilocarpine) contract the circular smooth muscles in the iris sphincter and constrict the pupil (miosis). Anticholinesterases (for example, neostigmine, physostigmine) also cause miosis by increasing the level of ACh. Muscarinic antagonists, on the other hand, relax the circular smooth muscles in the iris sphincter and cause dilation of the pupil (mydriasis).

4.5 In Alzheimer's disease, there is a deficiency of cholinergic neuronal function in the brain. Theoretically, which of the following strategies will be useful in treating the symptoms of Alzheimer's disease?

- A. Inhibiting cholinergic receptors in the brain.
- B. Inhibiting the release of acetylcholine in the brain.
- C. Inhibiting the acetylcholinesterase enzyme in the brain.
- D. Activating the acetylcholinesterase enzyme in the brain.

Correct answer = C. Since there is already a deficiency in brain cholinergic function in Alzheimer's disease, inhibiting cholinergic receptors or inhibiting the release of ACh will worsen the condition. Activating the acetylcholinesterase enzyme will increase the degradation of ACh, which will again worsen the condition. However, inhibiting the acetylcholinesterase enzyme will help to increase the levels of ACh in the brain and thereby help to relieve the symptoms of Alzheimer's disease.

4.6 An elderly female who lives in a farm house was brought to the emergency room in serious condition after ingesting a liquid from an unlabeled bottle found near her bed, apparently in a suicide attempt. She presented with diarrhea, frequent urination, convulsions, breathing difficulties, constricted pupils (miosis), and excessive salivation. Which of the following is correct regarding this patient?

- A. She most likely consumed an organophosphate pesticide.
- B. The symptoms are consistent with sympathetic activation.
- C. Her symptoms can be treated using an anticholinesterase agent.
- D. Her symptoms can be treated using a cholinergic agonist.

Correct answer = A. The symptoms are consistent with that of cholinergic crisis. **Since the elderly female lives on a farm and since the symptoms are consistent with that of cholinergic crisis (usually caused by cholinesterase inhibitors)**, it may be assumed that she has consumed an organophosphate pesticide (irreversible cholinesterase inhibitor). Assuming that the symptoms are caused by organophosphate poisoning, administering an anticholinesterase agent or a cholinergic agonist will worsen the condition. The symptoms are not consistent with that of sympathetic activation, as sympathetic activation will cause symptoms opposite to that of cholinergic crisis seen in this patient.

4.7 Sarin is a volatile nerve agent that inhibits cholinesterase enzymes. Which of the following symptoms would you expect to see in a patient exposed to sarin?

- A. Urinary retention.
- B. Tachycardia.
- C. Constriction of pupils (miosis).
- D. Dilation of the pupils (mydriasis).
- E. Dry mouth.

Correct answer = C. Sarin is an organophosphate nerve gas that inhibits cholinesterase enzymes and increases ACh levels. Therefore, symptoms of cholinergic crisis (increased urination, bradycardia, excessive secretions, constriction of pupils, etc.) should be expected in patients exposed to sarin. Urinary retention, tachycardia, mydriasis, and dry mouth are usually seen with muscarinic antagonists.

4.8 Head and neck irradiation in cancer patients can decrease salivary secretion and cause dry mouth. All of the following drugs or classes of drugs are theoretically useful in improving secretion of saliva in these patients *except*:

- A. Muscarinic antagonists.
- B. Muscarinic agonists.
- C. Anticholinesterase agents.
- D. Pilocarpine.
- E. Neostigmine.

Correct answer = A. Activation of muscarinic receptors in the salivary glands causes secretion of saliva. This can be achieved in theory by using a muscarinic agonist such as pilocarpine or an anticholinesterase agent such as neostigmine (increases levels of ACh). Muscarinic antagonists (anticholinergic drugs) will reduce salivary secretion and worsen dry mouth.

4.9 Which of the following drugs or classes of drugs will be useful in treating the symptoms of myasthenia gravis?

- A. Nicotinic antagonists.
- B. Muscarinic agonists.
- C. Muscarinic antagonists.
- D. Anticholinesterase agents.

Correct answer = D. The function of nicotinic receptors in skeletal muscles is diminished in myasthenia gravis due to the development of antibodies to nicotinic receptors in the patient's body (autoimmune disease). Any drug that can increase the levels of ACh in the neuromuscular junction can improve symptoms in myasthenia gravis. Thus, cholinesterase inhibitors help to improve the symptoms of myasthenia gravis. Muscarinic drugs have no role in myasthenia gravis, and nicotinic antagonists will worsen the symptoms.

4.10 *Atropa belladonna* is a plant that contains atropine (a muscarinic antagonist). Which of the following drugs or classes of drugs will be useful in treating poisoning with belladonna?

- A. Malathion.
- B. Physostigmine.
- C. Muscarinic antagonists.
- D. Nicotinic antagonists.

Correct answer = B. Atropine is a competitive muscarinic receptor antagonist that causes anticholinergic effects. Muscarinic agonists or any other drugs that can increase the levels of ACh will be able to counteract the effects of atropine. Thus, anticholinesterases such as malathion and physostigmine can counteract the effects of atropine in theory. However, malathion being an irreversible inhibitor of acetylcholinesterase is not used for systemic treatment in patients. Muscarinic antagonists will worsen the toxicity of atropine. Nicotinic antagonists could worsen the toxicity by acting on parasympathetic ganglionic receptors and thus reducing the release of ACh.