Question 1: What is meant by quantal release of neurotransmitter?

Answer: The elementary unit of a neurotransmitter release is the content of one synaptic vesicle. Each vesicle contains several thousand transmitter molecules. The total amount of transmitter released at a synapse is a multiple of this number, depending on how many vesicles release their contents into the synaptic cleft. The amplitude of postsynaptic EPSP is a multiple of the response to the contents of one vesicle. It reflects the number of transmitter molecules in one synaptic vesicle and the number of postsynaptic receptors available at the synapse.

Question 2: You apply ACh and activate nicotinic receptors on a muscle cell. Which way will current flow through the receptor channels when V_m = –60 mV? When V_m = 0 mV? When V_m = 60 mV? Why?

Answer: Nicotonic ACh receptors are permeable to both sodium and potassium. When V_m = –60 mV, net current flow through ACh-gated ion channels is inward, toward the equilibrium potential of sodium, causing depolarization. At V_m = 60 mV, the direction of net current flow through the ACh-gated ion channels is outward, toward the equilibrium potential of potassium, causing the membrane potential to become less positive. The critical value of membrane potential at which the direction of current flow reverses is called the reversal potential. In this case, the reversal potential is 0 mV because this is the value between the equilibrium potentials of sodium and potassium. At 0 mV, no current flows.

Question 3: In this chapter, we discussed a GABA-gated ion channel that is permeable to Cl^-. GABA also activates a G-protein-coupled receptor called the $GABA_B$ receptor, which causes potassium-selective channels to open. What effect would $GABA_B$ receptor activation have on the membrane potential?

Answer: Activated GABA-gated Cl^- ion channels bring the membrane toward the equilibrium potential for Cl^-, which is –65 mV. If the membrane potential was less negative than –65 mV when the transmitter was released, activation would cause hyperpolarization. The activation of $GABA_B$ receptors causes potassium-selective channels to open. As a result, $GABA_B$ activation brings membrane potential toward the equilibrium potential of potassium, which is –80 mV. If the membrane potential was less negative than –80 mV when the transmitter was released, activation would also cause hyperpolarization. This channel might also impact the neuron by shunting inhibition, allowing a depolarizing current from an excitatory synapse to leak out. This, in turn, decreases the likelihood of action potential. The action of a G-protein-coupled receptor is, however, slower than that of the GABA-gated Cl^- ion channel or a typical excitatory synapse. Therefore, its effects would be slower to occur and would last longer.

Question 4: You think you have discovered a new neurotransmitter, and you are studying its effect on a neuron. The reversal potential for the response caused by the new chemical is –60 mV. Is this substance excitatory or inhibitory? Why?

Answer: If the new chemical has a reversal potential of –60 mV, the substance is likely to be inhibitory. The reversal potential reflects the types of ions the membrane is permeable to after the application of the neurotransmitter. A reversal potential of –60 mV suggests that the neurotransmitter activates ion channels that make the membrane more negative. If a neurotransmitter causes the membrane to move toward a value that is more negative than the action potential threshold, the neuron becomes less likely to fire an action potential, which means it is inhibited.

Question 5: A drug called strychnine, isolated from the seeds of a tree native in India and commonly used as rat poison, blocks the effects of glycine. Is strychnine an agonist or an antagonist of the glycine receptor?

Answer: Strychnine is an antagonist of glycine at its receptor. Mild strychnine poisoning enhances the startle and other reflexes and resembles hyperekplexia. High doses can eliminate glycine-mediated inhibition in circuits of the spinal cord and the brain stem. This leads to uncontrollable seizures and unchecked muscular contractions, spasms, and paralysis of respiratory muscles. It might ultimately result in painful, agonizing death from asphyxiation.

Question 6: How does nerve gas cause respiratory paralysis?

Answer: Nerve gases interfere with synaptic transmission at the neuromuscular junction by inhibiting AChE. Uninterrupted exposure to high concentrations of ACh for several seconds leads to a process called *desensitization*. In this process, transmitter-gated channels close despite the continued presence of ACh. Normally, the rapid destruction of ACh by AChE prevents desensitization. However, if AChE is inhibited by nerve gas, ACh receptors will be desensitized and neuromuscular transmission will fail, causing respiratory paralysis.

Question 7: Why is an excitatory synapse on the soma more effective in evoking action potentials in the postsynaptic neuron than an excitatory synapse on the tip of a dendrite?

Answer: A current entering the sites of synaptic contact must spread to the spike-initiation zone and this zone must be depolarized beyond its threshold to generate an action potential. In addition, depolarization decreases as a function of distance along a dendrite. As a result, the effectiveness of an excitatory synapse for triggering an action potential depends on how far

the synapse is from the spike-initiation zone. Because the soma is closer to the spike-initiation zone, an excitatory synapse on the soma is more effective for evoking action potentials than an excitatory synapse on the tip of a dendrite.

Question 8: What are the steps that lead to increased excitability in a neuron when NE is released presynaptically?

Answer: The steps that increase the excitability of a neuron when NE is released presynaptically are:

1. The NE receptor bound to a β receptor activates G-protein in the membrane.

2. G-protein activates the adenylyl cyclase enzyme.

3. Adenylyl cyclase converts ATP into the second messenger cAMP.

4. cAMP activates a protein, kinase.

5. Kinase causes a potassium channel to close by attaching a phosphate group to it.

This produces little change in membrane potential but increases the membrane resistance and increases the length constant of dendrites. This enhances the response that a weak or a distant excitatory synapse produces. This effect can last longer than that of the presence of the transmitter.