Pharmacology of Atropine, Scopolamine, and Glycopyrrolate:

Atropine is a naturally occurring tertiary amine that is capable of inhibiting the activation of muscarinic receptors. These receptors are found primarily on autonomic effector cells that are innervated by postganglionic parasympathetic nerves but are also present in ganglia and on some cells. At usual doses of the drug, the principal effect of atropine is competitive antagonism of cholinergic stimuli at muscarinic receptors, with little or no effect at nicotinic receptors. Atropine is derived from flowering plants in the family Solanaceae (e.g., deadly nightshade [Atropa belladonna, named for Atropos, the Fate of Greek mythology who cuts the thread of life], mandrake [Mandragora officinarum], or jimsonweed [Datura stramonium]). Venetian women dropped the juice of deadly nightshade into their eyes to produce mydriasis, which was thought to enhance beauty (hence, the name belladonna, which, translated from Italian, is beautiful woman). Although atropine is used today to treat pesticide poisoning, Solanaceae plants have been used since 200 AD as biologic weapons to poison liquids for drinking (e.g., water, wine). Pharmacokinetics Absorption Atropine is well absorbed from the gastrointestinal tract (i.e., from the upper small intestine). It is also well absorbed following intramuscular administration or from the tracheobroncheal tree following inhalation. Distribution Atropine undergoes rapid distribution throughout the body and 50% is plasma protein bound. Atropine crosses the blood-brain barrier and the placenta. Elimination plasma half-life of atropine is 2 to 3 h; it is metabolized in the liver, with 30% to 50% of the drug excreted unchanged in the urine.

Pharmacologic Properties

Gastrointestinal System

Atropine reduces the volume of saliva and gastric secretions. The motility of the entire gastrointestinal tract, from esophagus to colon, is decreased, prolonging transit time. Atropine causes lower esophageal sphincter relaxation through an antimuscarinic mechanism. Cardiovascular System The effect of atropine on the heart is dose dependent. An intravenously administered dose of 0.4 to 0.6 mg causes a transient decrease in heart rate of approximately 8 beats/min. This decrease was once believed to be caused by central vagal stimulation.

However, the mechanism is not fully elucidated. Larger doses of atropine cause progressively increasing tachycardia by blocking vagal effects on M2 receptors on the sinoatrial node; by the same mechanism, atropine can reverse sinus bradycardia secondary to extracardiac causes, but it has little or no effect on sinus bradycardia caused by intrinsic disease of the sinoatrial node. High doses (> 3 mg) may cause cutaneous vasodilation.

Respiratory System Atropine reduces the volume of secretions from the nose, mouth, pharynx, and bronchi. Along with many other anticholinergic drugs (e.g., ipratropium), it relaxes the smooth muscles of the bronchi and bronchioles, with resultant decreases in airway resistance.
Central Nervous System Atropine is one of the few anticholinergic agents to cross the blood-brain barrier, stimulating the medulla and higher cerebral centers. Higher doses are associated with restlessness, irritability, disorientation, and delirium. Even higher doses produce hallucinations and coma. This constellation of symptoms and signs, called central anticholinergic syndrome, can be treated with physostigmine.

Genitourinary System Atropine decreases the tone and amplitude of ureter and bladder contractions, which is one of the reasons why belladonna and opium suppositories are administered to patients who have bladder spasms in response to a urinary catheter. The relaxation effect is more pronounced in neurogenic bladders. Bladder capacity is increased, and incontinence is relieved as uninhibited contractions are reduced. The renal pelves, calyces, and ureters are dilated.

Ophthalmic Response Atropine blocks responses of the sphincter muscle of the iris and the accommodative muscle of the ciliary body of the lens to cholinergic stimulation, resulting in mydriasis

Each transdermal Scopolamine patch contains 1.5 mg scopolamine base and is formulated to deliver in vivo approximately 1 mg scopolamine over 3 days. The patch is applied to the skin of the postauricular area for 3 days. It is important to wash the hands after handling the patch because blurry vision may occur as a result of a temporary increase in the size of the pupil. Because of the anticholinergic effects of scopolamine, the elderly and patients with hepatic

and/or renal impairment have an increased likelihood of central nervous system effects. Urinary retention may occur, especially in the elderly and patients with urinary bladder neck obstruction. Adverse effects of the scopolamine patch include bradyarrhythmia, hypotension, tachycardia, rash, xerostomia, confusion, dizziness, memory impairment, meningism, restlessness, somnolence, anisocoria, blurred vision, conjunctivitis, dry eye syndrome, glaucoma, eye itching, mydriasis, hallucinations, psychotic disorder, dysuria, and signs and symptoms of withdrawal. Scopolamine is no longer available in intravenous or intramuscular form.

Glycopyrrolate - is a synthetic antimuscarinic with a quaternary ammonium that has anticholinergic properties similar to those of atropine (see Table 63.1); however, unlike atropine, glycopyrrolate is completely ionized at physiologic pH. Pharmacokinetics Absorption With intravenous injection, the typical onset of action of glycopyrrolate occurs within 1 min; with intramuscular administration, it is approximately 15 to 30 min, with peak effects occurring within approximately 30 to 45 min. Compared with atropine and scopolamine, glycopyrrolate is a more potent antisialogogue (effects persisting for up to 7 h) and has a longer duration of action (vagal blocking effects persist for 2 to 3 h). Distribution The in vivo metabolism of glycopyrrolate in humans has not been studied. Elimination After intravenous administration, the mean half-life of glycopyrrolate is 45 to 60 min, and after intramuscular administration, it is 30 to 75 min. Pharmacologic Properties Gastrointestinal System Glycopyrrolate completely inhibits gastrointestinal motility but does not change gastric pH or the volume of gastric secretions. Cardiovascular System Glycopyrrolate has minimal effects on heart rate. Central Nervous System The structure of glycopyrrolate prevents it from crossing lipid barriers; therefore, unlike atropine and scopolamine, glycopyrrolate does not cross the blood-brain barrier, and the resultant effects on the central nervous system are limited.