

Chapter 16

Web Text Box 2

Cigarettes, mushrooms and insecticides

Nicotine is one of the most addictive substances known. The reason for this is still unclear. The muscle weakness that new smokers experience is due to nicotine binding to and blocking nicotinic acetylcholine receptors on the muscle cells (book page 274), but we are still not sure how nicotine acts in the brain to cause a pleasurable experience.

The fly agaric mushroom *Amanita muscaria* is seldom taken recreationally. Its popular use is more prosaic, in killing flies, hence its English and Latin names. However, Robert Graves has argued that it was used by the classical Greeks and by the Vikings to produce a state of berserk strength with hallucinations. Any such use would be highly dangerous: muscarine acts by stimulating the muscarinic acetylcholine receptor (see Text Box 16.1, Ionotropic and metabotropic receptors for the same transmitter) and the difference between a dose of muscarine large enough to cause pharmacological effects and a lethal one is very small.

Amanita muscaria has an even more dangerous relative, *Amanita phalloides*, the death cap mushroom. The toxin it produces, phalloidin, does not affect acetylcholine signaling. Instead, it interferes with the actin cytoskeleton.

Farmers and others who suffer insecticide toxicity show similar symptoms to those of muscarine poisoning. This is because these insecticides work by blocking the enzyme acetylcholinesterase which breaks down acetylcholine. With the enzyme blocked, acetylcholine hangs around in the extracellular medium, stimulating the receptor for longer than it should. Nerve gases developed to kill people (like Sarin, released in the Tokyo subway by members of the Aum cult in 1995) work in the same way. Paradoxically, sufferers are treated with another toxin, atropine, from the deadly nightshade plant. Atropine turns off the muscarinic acetylcholine receptor.