Fact or Fiction?

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Poison or Medicine, Toxin or Drug?

"Poisons surround us. It's not just too much of a bad thing like arsenic that can cause trouble, it's too much of nearly anything. Too much vitamin A, hypervitaminosis A, can cause liver damage. Too much vitamin D can damage the kidneys. Too much water can result in hyponatremia, a dilution of the blood's salt content, which disrupts brain heart, and muscle function," reports Cathy Newman.[1]

However, more and more research studies are revealing that a little bit of some poisons can be quite helpful to human health. Examples include botulinum, carbon monoxide, hydrogen sulfide and epibatidine, the toxic that native Indians use to make poison darts.

Botulinum

Botulinum is one of the most poisonous substances known (see Table 1 for some comparisons). A gram of botulinum toxin, if dispersed and ingested, could kill 20 million people.[1] Yet, do you know anyone who has had Botox treatment to remove wrinkles? This is botulinum toxin in extremely dilute form. Other applications include relief of migraines, a cure for crossed eyes, and a treatment for the spastic conditions of multiple sclerosis and cerebral palsy. Researchers in Britain report that the combination of botulinum and a protein from the Mediterranean coral tree could provide a treatment for the chronic pain that afflicts millions of people, including cancer patients.[2]

Leon Fleisher, one of the world's premier concert pianists, became afflicted with focal dystonia, a misfiring of the brain that causes muscles to contract into abnormal, and sometimes painful positions. This career threatening disorder often strikes those who depend on small motor skills: musicians, writers, surgeons. After treatments with botulinum toxin, Fleisher is performing and touring again, and recently released his first two-handed recording in 40 years.[1]

Table 1
Hold a nickel in your hand. Here's how many lethal doses equal that nickel's weight[1]

Thallium	5
1080 Rat Poison	7
Cyanide	25
Strychnine	50
Nicotine	111
Botulinum	100,000,000
Anthrax	500,000,000

Carbon monoxide

Carbon monoxide is an example of a "pollutant" that is important for human existence. This deadly gas that kills thousands each year offers potential help for a number of medical issues.[3]

Although carbon monoxide inhalation can be lethal, our bodies make the molecule naturally in small amounts when an enzyme called heme-oxygenase-1 (HO-1) breaks down a portion of the blood protein hemoglobin.[4] Ventilator-induced lung injury (VILI) is a major cause of morbidity and mortality in intensive care units. The stress-inducible gene product, HO-1 and carbon monoxide, a major by product of the oxygenase catalysis of heme, have been shown to confer potent anti-inflammatory effects in models of tissue and cellular injury. Tomas Dolinay notes, "The data from this work leads to a tempting speculation that inhaled CO might be useful in minimizing VILI."[5]

Small amounts of carbon monoxide might alleviate symptoms of multiple sclerosis, a study in mice suggests. The finding may offer a treatment for MS, which strikes when a person's immune system damages the fatty sheaths that protect nerve fibers in the brain and spinal cord.[4]

Other studies of laboratory animals suggest that carbon monoxide in small doses can prevent injury to blood vessels caused by surgery. In this study, rats that inhaled carbon monoxide-laced air for one hour before angioplasty had much less subsequent artery blockage than did rats not receiving the gas. Rats that underwent a vessel transplant also fared significantly better if given carbon monoxide before and after the surgery.[6]

Hydrogen sulfide

Hydrogen sulfide, the compound that gives rotten eggs their odor, can be lethal at high concentrations. Yet researchers in Seattle reported that exposure to hydrogen sulfide gas can lower the heart rate, metabolism and body temperature in lab mice.[7] Mice in the study revived and appeared healthy when exposure to the gas ended. This is one step in helping researchers understand about hibernation and torpor in animals.[8]

Why is this of interest? This type of suspended animation could offer protection for humans after a heart attack or stroke, and it could help people survive while waiting for an organ transplant. Clinical trials with humans have found no significant harmful effects

and more trials are in progress.[9]

Epibatidine

Epibatidine is the toxic chemical which a tropical frog arms itself against its predators. Not only is epibatidine very toxic, and the reason it is used by native Indians to make poison, but it also turns out to be a superb painkiller. It is two hundred times stronger than morphine.[10]

The chemical formula for epibatidine is $C_{11}H_{13}N_2Cl$. Notice that it contains chlorine, which makes it an organochlorine compound. Bad stuff, let's get rid of it, say many environmentalists. Jonathan Adler notes, "The campaign to phase out the use of chlorine, a staple of modern industrial chemistry, perhaps best illustrates environmental groups' absolutist approach to risk assessment and their success at building political support. The anti-chlorine crusade was a fringe campaign initiated by Greenpeace, but it has attracted adherents from throughout the environmental community." It's endorsed to varying degrees by the National Wildlife Federation, Environmental Defense Fund, Natural Resources Defense Council, Sierra Club, U.S. Public Interest Research Group, National Audubon Society, Citizens for a Better Environment in Chicago and World Wildlife Fund.[11]

Since epibatidine comes from frogs, what do you do to get rid of this chlorine product? As John Emsley points out, "Epibatidine is an organochlorine compound, which confounds somewhat the environmentalists' belief that organochlorines are entirely manufactured chemicals that cause disease and damage the environment. Epibatidine is highly dangerous, but it is perfectly natural. It would seem a little unfair on the frogs to eradicate them because they are making a dangerous organochlorine molecule."[10]

The epibatidine story is only just starting. As Emsley notes, "It might well end a better painkiller, or a pill that smokers can take if they want to stop smoking. It might even result in a pill that will enhance learning or improve our enjoyment of intellectual pursuits."

Others

Nitrogen oxides are major components of air pollution from auto exhaust and industrial combustion. Yet nitric oxide was named "Molecule of the Year" by *Science* magazine in 1992 because small controlled doses are extraordinarily beneficial to the body.[12] More on the benefits of nitrogen oxides can be found in the April 2002 issue of this column.

On the other hand, low doses of some items that are very important for our daily existence can be quite dangerous. Oxygen is one example. If you breathe pure oxygen at normal room pressure, you will suffer chest pain, coughing and a sore throat within six hours. Hospitals have found that premature babies placed in incubators that were filled with oxygen-enriched air went blind because of oxygen damage to their retinas.

Summary

Edward Calabrese of the University of Massachusetts-Amherst is a strong proponent of hormesis, a scientific name that means low doses help and high doses hurt. He's concerned that if researchers don't begin regularly probing the effects of agents at very low doses, scientists will continue to miss important health impacts - both good and bad of pollutants, drugs and other agents. Janet Raloff points out, "Regulatory agencies don't require scientists to evaluate a poison at exposures below that at which no harm is apparent. This dose is referred to as the NOAEL, for 'no observable adverse-effects level."[14]

Two obvious benefits can accrue from testing effects at low doses: (1) medical help might be found from items otherwise known to be toxic and (2) if traces of certain pollutants are not as dangerous as previous estimates had suggested, perhaps some overly stringent regulations could be changed. Dream on. P&SF

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