Chemistry

Clue to cigarettes' role in emphysema

Though the link between cigarette smoking and emphysema seems firmly established, researchers are still puzzling over the precise chemical role of tobacco smoke in the destruction of lung tissue. Chemists at Louisiana State University in Baton Rouge have teased out a new clue: a biologically aggressive role for a chemical produced by interactions between relatively nontoxic chemicals in smoke and in the lung.

The body is peppered with proteases, valuable enzymes that foster the breakdown of proteins. Within the lung, however, these enzymes must be held in check to avoid the risk that they will begin a wholesale chopping up of structural tissue – a process that can lead to emphysema. Nature has seeded the lung with antiproteases to inhibit these enzymes. Suppression of the antiproteases is the most widely accepted explanation for how smoking leads to emphysema. The remaining question has been how smoke shuts down antiproteases.

Juan J. Moreno and William A. Pryor now describe evidence indicating that peroxynitrite ($O=NOO^-$) is one of the agents responsible. Many biochemists had suspected that the antiproteases' nemesis was a potent, biologically damaging free radical, such as hydroxyl ($HO^\bullet$) – and that peroxynitrite production constituted one step along the path to creation of the radical. But in the May/June CHEMICAL RESEARCH IN TOXICOLOGY, Moreno and Pryor show that peroxynitrite can by itself inactivate the most abundant lung antiprotease, alpha-1 PI.

Peroxynitrite forms during reactions between two free radicals: nitric oxide (NO) in smoke and the superoxide (O_2^-) produced in the lung. "Though neither of the parent compounds are powerful oxidants," Pryor notes, "together they form a potent oxidant." Indeed, their offspring appears to inactivate the lung-protecting alpha-1 PI by donating an oxygen atom to methionine, one of its amino-acid building blocks.

Radical concerns over drinking water

Animal studies have suggested that chlorine ingestion alters the body's handling of cholesterol and fats. For example, an Environmental Protection Agency study showed that drinking highly chlorinated water "subtly but noticeably shifted" a mouse's transport of cholesterol from high-density lipoproteins (the "good" lipoproteins) in the blood to the "bad" low-density lipoproteins, which foster atherosclerosis (SN: 6/3/89, p.342). J. Peter Bercz, who headed that study, now reports that hypochlorite – a very reactive by-product of standard water chlorination – can also destroy polyunsaturated fatty acids (PUFAs), including those essential to health.

"It's certainly possible," he says, that the new finding might play a role in the altered lipoprotein metabolism seen in animals drinking chlorinated water.

Hypochlorite (OCl^-), a powerful bleaching agent and disinfectant, develops in water treated with pure (free) chlorine. Bercz put each of seven biologically essential PUFAs into hypochlorite-laced water. The ensuing chemical reactions effectively cleaved these PUFAs into fragments of varying lengths. The complex series of processes responsible for the PUFAs' destruction involved both the stripping of electrons (oxidation) and the incorporation, at least temporarily, of chlorine, he reports in the May/June CHEMICAL RESEARCH IN TOXICOLOGY. Indeed, he notes, oxidant-spawned free radicals "really destroy these sensitive PUFAs," producing changes similar to those responsible for rancid flavors in aging fatty foods. In animals, such oxidized PUFAs have also been associated with liver and immune-system toxicity and with pre-atherosclerotic changes.

Unsaturated fatty acids contain one or more carbon double bonds, or "valence bonds," capable of accepting an electron. The new data show that the hypochlorite-initiated fragmentation of PUFAs begins at these double bonds. However – and paradoxically, Bercz admits – the more such double bonds a PUFA possesses, the less susceptible it proves to oxidation.

A 1979 change in the Safe Drinking Water Act has encouraged many municipalities to switch their disinfectant from free chlorine to monochloramine. This increasingly popular oxidant kills bacteria without generating high levels of potentially toxic chlorinated organics. The new study now also shows that these "monochloramines are totally inert," says Bercz.

Chronic ingestion of hypochlorite or foods treated with chlorine bleach – from white flour to butchered meats – "should be viewed not only as a potential cause for decreased bioavailability of essential PUFAs [from foods], but also as a factor in generating reactive . . . toxicants," including those capable of altering DNA, Bercz concludes.

Radical protection for athletes

Competitive athletes continually push to better their records, but such strenuous pursuits exact a price. The high consumption of oxygen bathes the body in biologically damaging, oxygen-derived free radicals. However, at least five new studies indicate that certain dietary supplements can help limit or repair muscle damage from these oxidants. All were presented last month at the American College of Sports Medicine's annual meeting in Dallas.

For instance, Christopher Baldi and his colleagues at Ithaca (N.Y.) College assayed malondialdehyde (MDA), a characteristic marker of muscle oxidation, in 25 college-age women before and after a vigorous, 30-minute treadmill run. The exercise raised urinary MDA levels by 32 percent in women who did not receive supplements, the researchers found. Surprisingly, postexercise MDA levels fell by 28 percent among the remaining women, all of whom had taken 400 international units of vitamin E daily for three months. This suggests that antioxidants "may actually reverse oxidative stress during exercise," concludes Robert R. Jenkins, who led the study.

Ian Gillam of the Phillip Institute of Technology in Melbourne, Australia, and his colleagues recorded signs of a similar suppression of muscle oxidation in elite, high-endurance athletes after just four weeks of antioxidant supplements. The researchers recruited a total of 12 cross-country skiers, endurance runners and triathletes at the Australian Institute of Sport, an Olympic training center. Half took 1,000 international units of vitamin E and 1,000 milligrams of vitamin C daily; the rest received sugar pills. After four weeks, each group switched to the other's supplements.

After vitamin supplementation, "there was a 25 percent reduction in tissue oxidation," as evidenced by levels of two enzymes assayed in the blood, Gillam says. This suggests not only that the membranes in muscle – and probably the heart – are less damaged by oxidant stress during normal training if supplements are taken, but also that red blood cells sustain less damage, he says. Gillam's team also found signs that vitamins E and C altered concentrations of two hormones in the blood. A reduction in the normal ratio of testosterone to cortisol serves as a marker of "overtraining syndrome," a condition that can provoke a range of symptoms and diminish athletic performance. After supplementation, testosterone-cortisone ratios in these athletes actually increased.

"We don't have hard scientific evidence yet that we can improve [athletic] performance with antioxidant supplementation, but there's lots of evidence . . . that supplementation protects against damage [during training and competition]," concludes antioxidant specialist Lester Packer of the University of California, Berkeley, who organized a meeting session on this topic.