

Nicotine: Addictive and spreads cancer?

Nicotine appears to be one of those things some people could die for — in more ways than one. One new study suggests it may promote the spread of cancer cells, while another indicates higher doses of nicotine replacements may be necessary to help smokers stop using tobacco.

At first, nicotine managed to keep clear of the fiery debate over whether tar and other tobacco constituents caused health problems. Then it was indicted in heart disease, and later found to cause a true physical addiction in many users (SN: 1/18/86, p.44). No longer the hidden ingredient, nicotine now is being studied in a broad range of research projects, including two reported last week in San Diego at the American Cancer Society's annual science writers' seminar.

At the University of South Alabama in Mobile, Gesina L. Longenecker and her co-workers are assessing the interaction of tumor cells, nicotine and blood platelets. Other studies had shown that platelets (cell fragments essential in blood clotting) can be activated by tumor cells. These activated platelets attach to the cells, protect them from the immune system and apparently help them work their way through the blood vessel walls during metastasis, or spread, of the cancer.

The Alabama group found that cultured cells from a human muscle cancer also produce significant amounts of prostacyclin, a substance released routinely from blood vessel walls that *inhibits* platelet activation and prevents unwanted clotting in the circulation. Thus these tumor cells, paradoxically, appear to release a negative signal that in effect slows the spread of cancer while at the same time promoting it.

But nicotine upsets this balancing act, says Longenecker, by inhibiting the production of prostacyclin by cancer cells, much as it inhibits prostacyclin produced by blood vessels. In addition, preliminary data suggest that nicotine increases the number of circulating tumor cells that stick to the sides of blood vessels. Longenecker explains that this would make nicotine not an initiator or promotor of cancer by itself, but perhaps a cofactor that aids metastasis.

Although the effect has been studied in only one type of cancer, Longenecker says it could be important to varying degrees in numerous types of cancer. Does this mean that smoking could enhance the spread of many, if not all, types of cancer? And should cancer patients be told to stop tobacco use, given the pleasure they may receive from smoking or chewing tobacco?

The answers are complicated by the

fact that only 20 percent of smokers are able to quit the habit "cold turkey."

At last week's seminar, Jack E. Henningfield, from the National Institute of Drug Abuse (NIDA), said nicotine addiction "is a special sort of compulsive behavior," similar to heroin and cocaine addiction in its behavioral and physical effects. Because a tolerance to nicotine builds over time, Henningfield says many tobacco users may require nicotine replacements like nicotine gum for a longer time and in larger doses than currently recommended by physicians. (Only half of the nicotine from the prescription chewing gum actually reaches the bloodstream.)

"The most desirable situation is no nicotine," he says, "but it could be given much longer safely." That would make it more likely to help the more than 60 percent of smokers who fail to stop, even after seven attempts, he says.

Despite the dangers of nicotine use, Henningfield feels that it is often a "trade-off" necessary to eliminate exposure to carcinogens in tobacco. Despite research on nicotine substitutes at NIDA's Addiction Research Center in Baltimore, nothing has been found to take its place for the addict, says Henningfield. NIDA studies are being done on smokeless cigarettes, suppositories and skin patches containing nicotine.

— D.D. Edwards

Less colitis among smokers

After all the bad news about its link to cancer and other diseases, does smoking tobacco actually have a positive health effect? Maybe so, according to a study by physicians in Seattle and Denver published in the March 19 *NEW ENGLAND JOURNAL OF MEDICINE*.

Investigating previous reports that smokers have a decreased risk of developing ulcerative colitis compared with nonsmokers, the researchers did a case-control study using former and current smokers served by a Seattle-based health maintenance organization. They found that people who had given up smoking were twice as likely as nonsmokers to develop the rare but serious disease, which is an inflammation of intestinal walls. Those currently smoking, however, had a 40 percent lower risk of developing the colitis than did those who never smoked.

Although the number of cigarettes used by current smokers did not seem to affect colitis incidence, the risk of disease rose among reformed smokers in proportion to the total number of cigarettes smoked before quitting. The authors say there are "currently no plausible biologic explanations" for the apparent protective effect, and suggest that weight gain and a host of other factors be investigated. □

AIDS vaccine: Time for human tests?

Four years after the AIDS virus was first identified, researchers are beginning to embark on human trials of vaccines against the deadly disease. As of March 30, according to a Food and Drug Administration spokesman, three research groups in the United States had applied to the FDA for permission to test their candidate vaccines in the first phase of human trials, which is designed to test vaccine safety in a few people. And two weeks ago, a French scientist reported that he had injected himself and other volunteers in Zaire with one experimental AIDS vaccine (SN: 3/28/87, p.198).

"I think it is virtually certain that there will be initial [U.S.] clinical studies [during] this calendar year," the FDA's Gerald V. Quinnan told reporters last week at an international AIDS vaccine workshop held at the National Institutes of Health in Bethesda, Md.

But while testing in human subjects is viewed by some as a milestone in AIDS vaccine research, scientists caution that a safe and effective vaccine — assuming one is indeed found — is years, if not decades, away. Moreover, not all researchers agree that human studies are yet warranted.

One of the most hotly debated questions at the workshop was whether researchers should have to show that their vaccine protects chimpanzees against AIDS infection before any — but especially large-scale efficacy — human studies are undertaken. Chimps are the only nonhuman animals that can be infected with the virus, although they have yet to develop full-blown AIDS symptoms. So far, chimps inoculated with some vaccines have produced antibodies and shown other immune responses to the AIDS virus. But no studies are known to have shown that a vaccine has actually protected chimps against an infection.

Quinnan and others argue that human trials of vaccines should not be barred on this basis alone, because the chimp immune system may not be a good model for that of humans. Moreover, they note, these chimps have been given a large intravenous dose of the AIDS virus, whereas humans are infected with AIDS through sexual and other kinds of contact. But other scientists say they'd be uneasy about going ahead with full-scale human tests before protection is shown in chimps. Most workshop participants agreed that the chimpanzee's role in vaccine development will be an evolving question. Still, asked one scientist, "Once we start down the road of giving vaccines to humans, how far can we go without knowing that they are efficacious? The public pressure to push on will be considerable."

— S. Weisburd