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## Smoking indictment: most serious yet

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Ever since the Surgeon General of the Public Health Service first reported on the health dangers of cigarette smoking in 1964, the Surgeon General of each succeeding Administration has done the same. Now the latest Surgeon General's report on the subject, that of C. Everett Koop, has just been released, and as he points out, it "is in some respects the most serious indictment of cigarette smoking which the Public Health Service has yet made."

This report, unlike previous ones, concentrates exclusively on scientific data linking cigarette smoking to cancer. One of the reasons, Koop explains, is that total death rates from cancer, alone among the major causes of death, have shown no major decline during a period when deaths from heart disease, infectious diseases and accidents have fallen. This lack of major decline is due almost completely to cigarette smoking.

Here are the report's main conclusions:

- Almost one-third of all current cancer deaths are due to cigarette smoking. Cigarette smoking is a major cause of not just lung cancer but of cancers of the larynx, oral cavity and esophagus. It is also

a contributor to the development of bladder, pancreas and kidney cancers, and may also be responsible for stomach and cervical cancers.

- Three epidemiologic studies have been published that explore the possibility that passive exposure to cigarette smoke causes lung cancer. Two of the studies have found a statistically significant link between nonsmoking wives' risk of lung cancer and the extent of their husbands' smoking. In the third study, the risk of lung cancer among nonsmoking wives of smoking husbands was also increased, but the risk was not statistically significant. "Although the currently available evidence is not sufficient to conclude that passive or involuntary smoking causes lung cancer in nonsmokers," the report asserts, "the evidence does raise concern about a possible serious health problem."

- While cigarettes appear to be the major culprit as far as cancer is concerned, pipes and cigars are also "causal factors" for cancers of the lung, larynx, mouth and esophagus. Tobacco and alcohol used together increase the risks of larynx, mouth and esophagus cancers. Long-term snuff use seems to be implicated in mouth cancer.

A similar indictment of cigarette smoking has also just been issued by the American Cancer Society. (See page 138, this issue.) □

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## Mixed bag of tumor cells

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The overwhelming reason for the failure of anti-cancer drug therapies is the diversity of cells within the tumor, says George Poste of the Smith Kline and French Laboratories in Philadelphia. Speaking at the New York Academy of Sciences Conference on Cell Proliferation, Cancer and Cancer Therapy, he described "depressing complexities" of tumor cell populations. But recent advances in understanding how the cell diversity is generated have important implications for therapy.

The two areas of tumor cell heterogeneity most important therapeutically are drug resistance characteristics and the ability of cells to leave the primary tumor and cause a tumor in a new site. Many laboratories have reported that within a single animal tumor some cells are more likely to metastasize than others. Only recently has a human tumor been shown to be similarly diverse. Poste reports that individual cells of a human melanoma, each cloned and implanted into an immune-deficient mouse less than three weeks old, result in a wide variation of metastatic ability. Some clones caused no lung tumors in the mice, while others caused more than 100.

"A tumor is an incredible mosaic of cells," Poste says. "Not only is it metastatically heterogeneous, but superimposed on that challenging problem [are] ... dif-

ferential sensitivities to therapy." When cells from a single tumor are exposed to an anti-cancer drug, some cells prove sensitive while others are resistant.

The heterogeneity of cells within a tumor arises even in a population grown from a single cell. This variance may reflect selective pressure applied either by the host defense system or by medical therapy. Poste finds a stability within a tumor comprised of cells with a variety of drug resistance characteristics. "There must be some kind of interaction within a polyclonal tumor," he says. "Some 'equilibrium state' is reached."

Poste artificially creates a model of such a tumor by mixing cells of six clones marked with different drug resistances. He sees no significant shift in their characteristics. However, after he applies the drugs that destroy four of the six subpopulations, new cell variants rapidly emerge. Rapid emergence of variants has also been demonstrated in tumors growing in mice.

The therapeutic implications of this finding are that treatments that remove most of the cancerous cells may give rise to cells with different characteristics than those in the original tumor. "It may be necessary to hit with rapid staging of successive therapy to blunt the drive to new variants," Poste suggests. "You need to ablate all these subpopulations."

—J. A. Miller

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## Prion: scrapie agent in disguise

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From what's appeared in various newspapers over the past week about a viral-like agent called a prion, one would think that it had just arrived on earth from outer-space. For instance, Lewis Thomas of the Memorial Sloan-Kettering Cancer Center in New York is quoted in a wire service article on the subject as saying: "If it is not made up of nucleic acid and can nonetheless replicate itself, it will surely be one of the strangest of all creatures on this planet."

What's all the hoopla about? It started last December when Stanley B. Prusiner and colleagues at the University of California at San Francisco Medical School published in the *PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES* and *SCIENCE* five lines of evidence arguing that the scrapie agent, a so-called slow virus agent that causes a fatal neurological disease in sheep, is comprised solely of protein, as opposed to conventional viruses made of nucleic acid cores surrounded by protein coats and to viroids made of nucleic acid without protein coats (SN: 12/5/81, p. 259). This possibility was intriguing, because if it really turned out to be the case, it would be, in the words of Michael McKinley, one of Prusiner's colleagues, "heresy as far as molecular biology goes." In other words, it would demonstrate that at least one life form, or at least semi-life form, could exist without containing genetic material.

Since then several things have tossed the scrapie agent into the limelight. Prusiner and his team have come up with still a sixth line of evidence that the agent is composed solely of protein—when it is treated with urea, there is a marked decrease in infectivity. Prusiner has also dubbed the agent, on the basis of their findings, a "prion," meaning that it is both proteinaceous and infectious. Then last week, when a California newspaper ran an article about that scrappy scrapie agent-turned-prion, other newspapers and wire services around the country jumped on the bandwagon. The result: An agent known for several centuries was hailed as a "previously unknown life form."

Still another misleading aspect of the current flurry of publicity over the prion is that it implies that this agent, or at least fellow slow viruses, cause a spate of conventional diseases, from diabetes, Parkinson's disease and rheumatoid arthritis to multiple sclerosis, lupus and senile dementia. But as McKinley told *SCIENCE NEWS*, "there has not been any report of a human being affected or afflicted with scrapie." In fact, there is no definitive evidence to date that any of the slow viruses can cause human diseases with the exception of kuru and Creutzfeldt-Jakob disease (SN: 4/14/73, p. 245). —J. A. Treichel