President’s Cancer Panel Stirs Up Environmental Health Community

By David C. Holzman

The President’s Cancer Panel released a report May 6 on reducing environmental pollutants and generated substantial controversy—not surprising, given its proposals for radical change in the way pollutants are regulated.

“In all my years in cancer research, I can’t recall ever seeing something like this coming from such a mainstream source,” David H. Gorski, M.D., Ph.D., wrote (favorably of the report) in his pseudonymous blog, “Respectful Insolence.” Gorski is a surgical oncologist at the Barbara Ann Karmanos Cancer Institute in Detroit. The report, he wrote, “blames weak laws, lax enforcement, and overlapping and conflicting regulatory authority, but more strongly, it blames the attitude that industrial chemicals are safe unless strong evidence that they are not safe emerges.”

Among the report’s substantive recommendations is a proposal to replace the current regulatory system, which requires the government to prove harm for a chemical that is already in use, to one in which the manufacturer must establish safety before that chemical is introduced into widespread use.

The report drew strong criticism from various quarters. For example, Michael J. Thun, M.D., vice president emeritus of the American Cancer Society, objected to “the unsupported claim” in the report that previous estimates had “grossly underestimated” the percentage of cancers attributable to environmental pollutants.

However, the ACS concurred with the need to improve testing of chemicals. Thun noted, though, that important scientific and other issues exist that must be resolved first. These include defining what the criteria for “safety” would be and “determining how some of the novel approaches for toxicity testing as described in a 2007 National Research Council report can be integrated into a regulatory framework.” The American Chemical Society estimated in 2007 that the number of chemicals in “significant” commercial use was 8,300.

The most vehement critics charge that the report ignores other major environmental causes of cancer—smoking, diet, infection, geophysical sources of radiation, and the like—to focus on pollutants and occupational exposures.

“They seem to almost totally ignore tobacco and smoking,” said F. Peter Guengerich, Ph.D., professor of biochemistry and director of the Center in Molecular Toxicology at Vanderbilt University School of Medicine. “Twenty-five percent of the cancer in this country is due to tobacco, and still 20% of Americans smoke.” Graham Colditz, M.D., Ph.D., referred to the “almost speculation . . . that we have to uncover more environmental exposures that must be causing cancer.” He said that the report lacks perspective on “the known causes, the modifiable causes, and the national priority for action to proceed based on what we already know.”

But some supporters, such as Richard Clapp, D.Sc., a professor of environmental health at Boston University School of Public Health, point out that the panel’s last report, published 2 years ago, was on lifestyle and cancer. So “you could argue . . . they gave [lifestyle] priority,” he said.

Tiny Fraction of Cancers?

Perhaps the most fundamental challenge to the report comes from several well-known studies suggesting that workplace exposures and environmental contaminants are responsible for only a tiny fraction of cancers. The panel and its supporters say that conclusion reflects a paucity of data.

Debates on this point often begin with the seminal paper by the British epidemiologists, the late Sir Richard Doll, M.D., of Oxford University, and Sir Richard Peto, FRS, director of the Clinical Trial Service Unit, Oxford University, that appeared in JNCI in June 1981. Doll and Peto estimated the burden of cancer from various etiological agents. They found, to many people’s surprise, that cancers from workplace exposures and environmental contaminants—4% and 2% of total cancers, respectively—were swamped by everything else, most notably smoking (30%) and diet (35%).

Various studies have since supported Doll and Peto. A 1995 study from the International Agency for Research on Cancer came to similar conclusions. Most recently, a meta-analysis of environmental...
exposures to pesticides through 2009 by Genevieve Van Maele-Fabry and colleagues, which appeared in Cancer Causes and Control in June, backs the contention that a very small fraction of cancers are associated with environmental pollutants.

But the President’s Cancer Panel and its supporters argue that there are still few data on this question. “There is less research today on environmental causes than there was 20 years ago,” said Jack Siemiatycki, Ph.D., an environmental health researcher at the University of Montreal, using the term environment in the broad sense rather than the narrow sense of environmental pollutants. “And there wasn’t much 20 years ago,” he continued. “Since what we know is probably the tip of the iceberg, to quantify that contribution [of environmental agents] is certainly to underestimate the total contribution of environmental agents.”

For instance, environmental pollutants and occupational exposures might contribute to many prostate cancers, said Jonathan M. Samet, M.D., an environmental pollution researcher at the Keck School of Medicine at the University of Southern California. “We have a very hard time identifying predictors of prostate cancer,” he said, adding that for “a number of [other] cancers,” much of the etiology is mysterious, and in some of these cases, genetics has been ruled out, leaving environment as the potential culprit.

**Early Exposures**

To support its contention that not enough is known to quantify the risk from environ-
mental contaminants, the President's Cancer Panel emphasized the potential power of exposures during key “windows of vulnerability” such as the prenatal period, early life, and puberty. “Environmental contaminants may have profound impact at these stages, and even prior to pregnancy, via the mother,” said Clapp. These agents could be acting through mechanisms of genetics, epigenetics, or endocrine disruption—or even chemical disruption of nucleosomes, the macromolecules that package the DNA, he said.

The dramatic and accidental proof of concept that exposures in utero could lead to cancer was the discovery that diethylstilbestrol, given to prevent miscarriage, increased the risk of vaginal cancers in daughters of women who took the drug.

A study of cord blood in the early 1980s first showed that even at this early stage in life, environmental contaminants are present. At that time, Frederica Perera, Dr.P.H., now a professor of environmental health sciences at Columbia University’s Mailman School of Public Health, began studying the role of polycyclic aromatic hydrocarbon (PAH)–DNA adducts, which are suspected carcinogens, in human cancer. Searching for pristine samples, she was shocked, she said, to find such adducts in cord blood. Since then, other contaminants have been found in cord blood, including pesticides, flame retardants, polychlorinated biphenyls, phthalates, and bisphenol A. Many are known or suspected carcinogens. Newborns and fetuses are at potentially greater risk because they lack the enzymes to dismantle these chemicals and repair the damage they cause.

In a series of studies that began in the 1990s, Perera and her colleagues documented the greater susceptibility of the fetus to carcinogenic PAHs, which are derived from combustion of fossil fuel and other organic material. They measured PAH–DNA adducts in mothers and newborns in two populations in New York City and one each in China and Europe. The levels of such adducts were roughly equal in mothers and their newborns, notwithstanding that the placenta has been shown experimentally to reduce fetal exposures to PAH by a factor of about 10. Perera said that although

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predicting individual risk on the basis of these adducts is impossible, they are red flags that indicate the need to reduce exposures.

Endocrine Disrupters
The panel also pointed to endocrine disrupters as another class of pollutant that may be adding to the cancer burden in ways that have not been quantified. Endocrine disrupters are fairly common chemicals with estrogen-like activities, which may mimic the effect that hormones have on promoting certain cancers, notably breast, prostate, and ovarian. The American Cancer Society’s Thun said that these “might initiate or promote breast cancer in people, throughout life, or at susceptible ages, or they might induce menarche [the onset of menstruation] earlier,” which is associated with a greater risk of breast cancer.

However, Thun added, “the story is by no means clear, partly because weak estrogens like tamoxifen and raloxifene reduce breast cancer risk by blocking the receptors and because the science of measuring estrogen-like activity of chemicals is still under development.” Others suggest that many environmental pollutants may be interacting synergistically or with other agents to cause cancer and that epidemiological studies overlook such interactions. But few examples of synergism have been documented epidemiologically, and even that between smoking and asbestos “is not as clear cut as some say,” said Samet. Like Samet, Siemiatycki thinks that such synergisms are not an important part of the underestimation he sees of environmental contaminants’ contribution to cancer. He has spent several decades developing methods for studying them, and he said that studies of single agents should pick up synergisms if the effect is strong.

The debate over links between environmental contaminants and cancer seems sure to continue, and data to resolve it are likely to be slow in coming. The National Children’s Study, now in the pilot phase, will recruit pregnant women with the goal of examining environmental influences on their children’s health and development from time in utero until age 21 years. But this study isn’t even designed to study cancers, Kelsey said, “although we will certainly get some nice clues.” He mentioned this study, he said, because it illustrates what the cancer community is up against in the quest to understand environmental cancers.

Although the President’s Cancer Panel is an advisory panel with no authority to implement recommendations, the report could influence legislation. “The cancer prevention advocacy community and the advocates for the Toxic Chemicals Safety Act . . . will undoubtedly use the President’s Cancer Panel report to support their work,” said Clapp. That bill, submitted by Congressmen Henry Waxman and Bobby Rush and Sen. Frank Lautenberg, would revise the Toxic Substances Control Act, the 1976 legislation that largely enables the Environmental Protection Agency to regulate such substances. Other stakeholders, both in and outside the United States, are similarly using the report, Clapp said.

It is through such efforts that any recommendation from the President’s Cancer Panel is implemented—or not.