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LETTERS

Cause and effect?

Like the statistical methods it uses, the field of epidemiology is relatively young. The study of disease incidence, distribution, and control in populations has helped squelch incipient plagues, tag new pathogens, flag toxic substances, and clear paths to healthy living. But epidemiology may have tested the limits of its powers, as indicated by "growing pains" of controversy. When does a research result warrant a headline? Or a new regulation? What constitutes a real risk to health? Such questions—of value and judgment as well as technique—are discussed here by some of the field's top practitioners in response to a 14 July Special News Report.

The Discipline of Epidemiology

In the Special News Report "Epidemiology faces its limits" (14 July, p. 164), Gary Taubes assembles a series of quotations from ourselves and others about potential methodologic pitfalls in epidemiologic studies that might leave readers with the misimpression that evidence based on epidemiologic findings is not usually credible.

A problem does exist with general media reports about single scientific studies. Such reports often herald new results without describing the scientific context, which can create unnecessary fear and confusion. However, this is more an abuse of epidemiologic evidence than a problem with epidemiologic research. Taubes seems to perpetuate this confusion by listing several media reports of published findings and telling the reader "you be the judge" (p. 156) when proper judging is impossible without substantial additional information. In any scientific field, findings of individual studies are usually not considered seriously until confirmed by others. Also, in epidemiology, as in any other scientific field, more powerful studies need to be conducted to evaluate smaller effects, where sources of bias may be especially problematic. Often, doing so will require large and long-term prospective studies with repeated measures of exposure based on both questionnaires and biological measurements; a substantial number of such studies have commenced over the last 15 years.

Taubes did not emphasize that what we do know about the prevention of cancer and cardiovascular disease has derived largely from epidemiologic findings. This knowledge includes not just the many adverse effects of cigarette smoking, but also the relation of overweight to many diseases, the benefits of increased physical activity for cardiovascular disease, the effects of many occupational exposures (such as benzene and asbestos), the relation of exogenous postmenopausal estrogens to cancer of the uterus, the relation of sunlight to all forms of skin cancer, the relation of ionizing radiation to many cancers, the adverse effects of many pharmacologic agents (for example, DES and thalidomide), and the protective effects of high intake of fruits and vegetables against many cancers.

Epidemiology has also provided important reassurance that many aspects of daily life are *not* major risk factors. For example, the relation between coffee consumption and coronary heart disease may not be completely settled, but the danger is minimal: The uncertainty is whether as much as five cups per day is a weak risk factor or not a risk factor at all (*1*). Fear of saccharin carcinogenicity engendered by studies in rats was quelled by epidemiologic research. Furthermore, epidemiologic studies have provided clear evidence that the incidence of several other forms of cancer, including ovarian cancer, is lessened as a consequence of using birth control pills.

If we wish to continue our progress in understanding the importance of lifestyle and environmental risk factors, we have little choice but to monitor the occurrence of illness of persons who have and have not been exposed to such factors. As Bruce Ames, a molecular biologist at the University of California, has noted (*2*), advances in other biological sciences can greatly add to the power of epidemiologic studies, but cannot replace them.

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References

1. S. Greenland, *Epidemiology* **4**, 366 (1993).
2. B. N. Ames, *Science* **221**, 1256 (1983).

Taubes's report is insightful and useful for epidemiologists and nonepidemiologists alike. However, I have two objections, one of them of personal nature, the other more general.

Taubes writes that I have expressed the view that only a fourfold risk should be taken seriously. This is correct, but only when the finding stands in a biological vacuum or has little or no biomedical credibility. We all take seriously small relative risks when there is a credible hypothesis in the background. Nobody disputes that the prevalence of boys at birth is higher than that of girls (an excess of 3%), that men have a 30% higher rate of death compared to women of the same age, or that fatality in a car accident is higher when the car is smaller.

The more general issue is that Taubes has omitted a consideration that is of paramount importance in any scientific argument. Epidemiology should be evaluated *in comparison to other disciplines* that serve the same objective, that is, to identify the causes of human disease and facilitate their prevention. Among these disciplines, only epidemiology can document causation without concern about dose-extrapolation or species vabiability and with built-in accounting for potential modifiers.

It could be said for epidemiology, with respect to disease etiology and prevention, what is frequently said about democracy as a system of government: They both have many problems and weaknesses, but they still represent the best available approach for the achievement of their respective objectives.

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Taubes's excellent article about the proliferation of health-related messages to the public, and in particular the role of the popular press in their promulgation, misses one factor driving this process. Research institutions are eager to have the results of health risk factor studies performed in their laboratories appear in prominent newspapers and news magazines. This is so because individual philanthropists like almost nothing better than to support institutions whose research efforts have appeared on

page one of, say, the *New York Times*. With the deceleration in government funds available for research and the concomitant increased dependence on private, and especially individual, funding sources, there will likely be an acceleration of these sorts of articles appearing in the popular press. It would generate far less confusion if they were just left in the scientific literature.

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The limits of epidemiology for environmental studies are well covered by Taubes. Genetic epidemiology is quite a different story. Clustering of cancer in families has led to the recognition of tumor suppressor genes by Alfred G. Knudson Jr. through study of retinoblastoma in childhood (*1*). These genes have since been found in other cancers of children and some of the commonest cancers of adults. Epidemiologic identification of the diverse familial cancers that cluster in Li-Fraumeni syndrome led to laboratory research that has furthered understanding the role of the *p53* gene in carcinogenesis (*2*). New clues to the origins of neoplasia are also coming from laboratory studies based on cancer clusters in heritable disorders, such as ataxia-telangiectasia (*3*). Genetic epidemiology should not suffer guilt by association with the downside of its environmental counterpart.

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References

1. A. G. Knudson Jr., *Proc. Natl. Acad. Sci. U.S.A.* **68**, 820 (1971).
2. D. Malkin *et al.*, *Science* **250**, 1233 (1990).
3. K. Savitsky *et al.*, *ibid.* **268**, 1749 (1995).

When critics of epidemiology pay homage at the altar of the randomized clinical trial, such trials are made to sound only moderately troublesome compared to observational studies, when in fact they are often absolutely impractical or absolutely unethical. Examples include randomizing women to method of birth control and individuals to diet.

For such research, observational studies are the only recourse if you want to work with humans. The future and power of epidemiology rest not with simply self-reported data, but with combining such information with molecular data on susceptibility. In this way, risk measurements reflect characteristics of both host and environment and make targeting prevention strategies rational. The challenge will be to use these host factors, such as genetic data, in a socially acceptable and nonpunitive fashion. Then epidemiology will provide truly meaningful and relevant estimates of risk.

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Most of the epidemiology of multifactorial diseases fails a test of method, due to absent experimental randomization and unachievable control of biases and confounders. In general, it also fails the ultimate test of predictivity, as large randomized experiments designed to verify major observational inferences have been thoroughly disappointing (*1*). Now, a resounding admission of impotence threatens our survival and demands remedial measures.

As other professionals have done, epidemiologists could establish a code of good practice, spelling out optimal standards of hypothesis formulation, study design, and conduct. Structural uncertainties should limit heuristic causal inferences to relative risk or odds ratio values above 3 or 4, as Trichopoulos (quoted in the article by

Taubes) and others before him have concluded (2). Although still short of assuring verification, this last provision would link with *de minimis* considerations of ongoing regulatory reform.

Epidemiologist have no choice but to warrant their credibility. We owe it to society and to the young entering the profession, who need to know honestly whether they can make a difference. Too much of epidemiology has become predictable advocacy without secure philosophical foundations. A code of good epidemiologic practice would be a beginning, perhaps after some soul-searching about the morality of provoking public anxieties and policies based on essentially unverifiable conjectures.

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References

1. M. Susser, *Epidemiol. Rev.* **7**, 147 (1985); L. Werko, *Acta Med. Scand.* **221**, 323 (1987); MRFIT Group, *J. Am. Med. Assoc.* **263**, 1795 (1990).
2. N. E. Breslow and N. E. Day, *Statistical Methods in Cancer Research, vol. 1, The Analysis of Case-Control Studies* (International Agency for Research on Cancer. Publ. No. 32, Lyon, France, 1980); K. J. Rothman, in *Cancer Epidemiology and Prevention*, D. Schottenfeld and J. F. Fraumeni, Eds. (Saunders, Philadelphia, PA, 1982), pp. 15–22; E. L. Wynder, *Prev. Med.* **16**, 139 (1987).

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Glass Ceiling: Bump, Bump

We were struck by the excess of males among those quoted in Taubes's news article of 14 July: 25 men versus 2 women. The Society for Epidemiologic Research, the primary professional organization of epidemiologists in the United States, has a membership, as of 1993, of 1194 men and 1009 women. The latter include senior faculty, department chairs, and a dean of a school of public health. Prominent female epidemiologists are located in most of the institutions where those who were interviewed work. Many of the studies cited in the news report had women as first authors. Women epidemiologists deserve more of a voice in *Science*.

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As evolutionary biologists, we were excited and interested to see the "Frontiers in biology: Ecology" special section in the 21 July issue (pp. 313–360). As women scientists, we were disappointed that in the first two articles only one of the more than 30 ecologists mentioned or quoted was a woman. From this representation it is difficult to tell that ecology is a field where, in 1992, 36% of the graduating Ph.D.'s were women and where four of the last nine Ecological Society of America presidents were women. We know "a good woman is hard to find," but really. . . .

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Plasma Physics and Fusion Research

James Glanz's otherwise excellent article about the National Research Council's (NRC's) panel report on the state of plasma physics and fusion research (News, 14 July, p. 153) does not treat what may be the most intractable part of the history of the subject: the degree to which the perspectives, procedures, and dominant personalities of the field have been selected by the Department of Energy (DOE) and its ancestors (the Energy Research and Development Administration and the Atomic Energy Commission), on the basis of an agenda that was not solidly rooted in anything scientific. Our style did not emerge from any traditional academic process, but rather a political and economic one.

Every branch of physics older than plasma physics developed its habits, interests, and formative experiences in the rough-and-tumble atmospheres of university seminars for several years before they became of interest to newspapers or government agencies. Collegial ideas about how and on what to work were allowed to develop to some extent independently of the funding required to support them. From day one, with only the briefest of interludes in the 1960s, plasma physics has had its priorities arranged by managers in the government who, while well meaning, were essentially unacquainted with the subject at a working research level. The subject, under their tutelage, began to speak with one voice in public about 20 years earlier than it was appropriate to do so. In selling Congress and the *New York Times* on the tokamak as the cure for energy shortages in the early 1970s, the field committed itself to a way of life in which its public image and its annual funding struggles in Congress assumed more importance than any scientific issue that could ever come up. To a large degree, we are still functioning in this mode.

A technical point, largely unappreciated, is the extent to which plasmas at the temperatures we now operate at are experimentally undiagnosed. Information about spatial and temporal profiles of such internal plasma variables as the magnetic field, the current density, the velocity field, and the electric field is largely lacking. Stories about the internal dynamical behavior of confined plasmas are easy to make up, hard to dispute, and at this stage virtually impossible to demonstrate. It is largely unappreciated that the DOE in its wisdom went around for years turning off every plasma experiment that was cool enough to diagnose, on the grounds that those temperatures "were not of thermonuclear interest." Only lately has it been possible to hear respectable doubts expressed that this was a wise thing to have done. Many groups perished then and were not heard from again.

If the NRC or anybody else can turn the situation around, then more power to them. But it would be a mistake to think that it is obvious how to do this. Even very good people who have spent a lifetime adapting themselves to unwise agency policies not of their making and being rewarded for it are not likely, in middle age, suddenly to start biting the coins and questioning the wisdom of what they have been doing for the last few decades. What plasma physics needs more than anything is a long period of benign neglect, during which it is modestly but reliably funded, insulated from agency-directed campaigns and from congressional feasts and famines, and allowed to go through the scientific maturation that has heretofore been denied it. When we are ready to build a fusion reactor, you will know it; it won't be a matter of lobbying or image-making.

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Restoring Prince William Sound

I am concerned that the article "Marine center is lightning rod in dispute over restoration" by Lisa Busch (News & Comment, 14 July, p. 159) will leave readers with the impression that the decision of the *Exxon Valdez* Oil Spill Trustee Council to support the Alaska Sealife Center is divisive, widely opposed, and leaves residents of Prince William Sound with incomplete restoration. The article does not mention that the Trustee Council has spent tens of millions of dollars to improve other aspects of pink salmon and Pacific herring management in Prince William Sound, including more than $9 million to support the Sound Ecosystem Assessment, based at the Prince William Sound Science Center in Cordova, which is investigating the causes of annual