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26 August 1971
Access to Data

Early this year Washington University undertook a project under my direction, with the aim of reviewing some of the crucial data linking smoking to disease. Ten distinguished scientists, from as many leading universities and laboratories, agreed to provide guidance and to advise us on how to set up conditions that would assure a fair, unbiased, and authoritative review of the data. An invitation was also extended to E. Cuyler Hammond, of the American Cancer Society, to meet with this panel. He was given assurances of all possible safeguards in the use of his data. Hammond's reply was a flat refusal on the grounds that he had promised the thousands of volunteer workers who had collected the data for his large prospective studies that the material would be used only by the American Cancer Society for research purposes. This refusal followed an earlier refusal by Hammond and Oscar Auerbach of a public review of data from their smoking dog experiment (1).

Ever since his first survey of smokers and nonsmokers was made in 1952, the methods by which Hammond obtained and analyzed data have been thoughtfully criticized by some of the world's outstanding statisticians and scientists. The problems created by their objections were never adequately dealt with. Yet, there are disturbing possibilities that the association between smoking and lung cancer, presented with such conviction by Hammond, is a by-product of biased sampling methods (of particular methods that may result in what has been described as the "Berkson" fallacy). There is an equally disturbing possibility that much of the relationship between smoking and lung cancer in Hammond's data may actually be an expression of occupational exposures hidden within these data and not brought out by his analysis. As Hammond continues to produce publication after publication based on these same data, many anomalies of the population studied become apparent. In few measures or observations does this study population resemble the makeup of the population of this country. It is becoming increasingly unclear who really is represented by that sample collected by volunteers of the American Cancer Society.

This series of events has serious implications for American science, particularly in the fuzzy area where science affects public health matters. The refusals of these key investigators to make their data available for public review threaten one of the basic tenets of science in a free society. As often before, the question arises, Can science exist unless its actions are kept public? Unfortunately, and again as often before, the question of the credibility of claims based on secret data arises over an extremely unpopular issue.

It is obvious that we cannot, as a community of scientists, examine in detail the data collected by each individual member. It is also equally clear that testimony of experts very often must be accepted. However, as a practical procedure, published results and testimony have meaning only because we assume that, in the event the need arises, the actual data on which the investigator or the expert bases his conclusions are open to inspection. Otherwise, the claims of investigators or the testimony of experts completely lose their credence. Perhaps the matter was stated most succinctly by Bertrand Russell in his discussion of the limitations of the scientific method: "... it is clearly impossible that each of us should verify the facts of geography; but it is important that the opportunity for verification should exist, and that its occasional necessity should be recognized" (2). The transactions of the scientific community must be conducted in public. This tenet is deeply engrained in the process of scientific inquiry. It limits any prior commitments scientists can make that would prevent access to data on which they base published claims or results or that compel them to suppress their findings. This is certainly no less true when data are collected with the help of public participation and public funds. The fundamental pillar on which science rests is the accessibility of information, observations, and data. I quote, for instance, the AAAS Committee on Science in the Promotion of Human Welfare: "Science gets at the truth by a continuous process of self-examination which remedies omissions and corrects errors. This process requires free disclosure of results, general dissemination of findings, interpretations, conclusions, and widespread verification and criticism of results and conclusions" (3). Data on which scientific claims are based must be public in the sense that they are available for review. Conversely,
can one give credence to any widely disseminated claims based on observations which are kept secret or confined? This question is especially pressing in instances where long-range research plans and public actions affecting many individuals have to be based on scientific inference. To give credence to reports based on privileged data is to destroy the validity of the scientific method.

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References

Education in Chemistry

In the current employment market one can view with indifference our failure to interest Black and other minority students in entering degree programs in the sciences, but one cannot be indifferent to their ability to handle the science prerequisites for medical school or related professional training. Last September a conference was held at the University of Illinois at Chicago Circle to consider how these matters affect education in chemistry. The conference devoted a major part of its deliberations to background problems that affect education in any of the sciences, among them the particular educational problems of various categories of underprepared students.

Two large-scale development projects designed to prepare such students for academically oriented education were described. Remedial programs in communication skills, mathematics, and background science were presented, as well as descriptions of supportive programs in chemistry that are now offered to underprepared students in ten institutions.

The conference did not produce definitive answers to any of the problems to which discussion was directed. It did produce some promising results—particularly a list of characteristics for successful programs for underprepared students and the encouragement and enthusiasm which derive from talking with others deeply involved in the same difficult problems. Although the conference was particularly devoted to education in chemistry, the discussion of background deficiencies in academic preparation and of the self-image of the educationally disadvantaged is applicable to underprepared students in any college major program. An 80-page report of the conference has recently been published. It may be ordered by sending a remittance of $3 a copy to Stipes Publishing Company, 10 Chester Street, Champaign, Illinois 61820.

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National Parks

Houston's recommendations in "Ecosystems of National Parks" (14 May, p. 648) would represent significant advancements in the management concepts of the National Park Service and, if fully implemented on a national scale in our parks, would do much to enhance their natural settings.

Cessation of "control" for pests such as the mountain pine beetle, use of fire to maintain certain vegetation types, limiting angling, and continuous monitoring of ungulate populations to assess their impact on vegetation represent significant changes in National Park Service policy, which was formerly similar to that of the more commercial Forest Service.

As Houston points out, many of the management problems within the national parks (usually blamed on park officials) have been caused by changes occurring outside park boundaries and the fact that the parks have not included all of the historic winter ranges of some ungulate populations, such as the elk range in the Yellowstone Valley near Yellowstone National Park and the area south of Jackson Hole near Grand Teton National Park.

The prohibition of sprawling new camping and trailer grounds and the possible elimination of some existing facilities, particularly in Yellowstone Park, also represent a radical departure from past National Park Service policy, which emphasized the need to accommodate as many people as possible, in the vain hope of obtaining more funds from a sparing Congress. Houston's proposals are far-reaching and deserve top priority from the National Park Service.

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The release of vasoactive materials (histamine and serotonin) from mast cells and platelets is an important factor for deposition. These vasoactive amines increase the permeability of the blood vessels, which then permit the passage of soluble complexes. Whether or not the latter become entrapped depends on their size: complexes smaller than 19S “pass,” while larger ones are deposited. Administration of antihistamines or vasoactive material affects complex deposition in the expected manner: antihistamines decrease deposition, vasoactive material enhances the process.

P. M. Henson, also from Scripps, investigated the interaction of neutrophils and immune complexes in experimental animals. Here ICD falls into two classes: (i) those like arteritis which require large numbers of neutrophils and (ii) those like glomerulonephritis in which the role of the neutrophils is less clear. Henson simulated the in vivo situation in models in which (i) the immune complex was anchored to a Micropore filter, which represented a surface that could not undergo phagocytosis, and (ii) the immune complex was either “free” or fixed to antibody and complement. In model (i), the degranulation was observed toward the exterior of the cell. In model (ii), however, when the complexes were phagocytized, degranulation was observed into the phagocytic vacuola, and enzymes appeared in the surrounding medium.

According to H. J. Muller-Eberhard (Scripps), complement participates in ICD via two different mechanisms. In the first, the complement products accumulate on the surface of the target cell and cause its destruction, either directly, by cytolsis, or indirectly, by phagocytosis. The second mechanism involves freely circulating complement components (anaphylatoxins and leukotactic factors) which act on effector cells such as granulocytes.

Leukotactic factors consisting of complement-related products were found by P. A. Ward (Armed Forces Institute of Pathology) in soluble tissue extracts of vasculitis lesions and in synovial fluid from patients with RA. Similar materials were, however, also found in synovial fluids from patients with inflammatory, nonrheumatic arthritis and in extracts of experimentally infarcted myocardium. Chemotactic factors—mostly related to the C5 and C6 components of human complement—were also found in RA joints by N. J. Zvaifler (University of California, San Diego) who showed that these were produced locally by an enzyme found in more than half of the rheumatic fluids examined.

The role of chemical mediators (K. F. Austen, Robert B. Brigham Hospital, Boston) is also undergoing revision. Recent evidence (infusion of large amounts of mast cells which did not induce a massive allergic reaction, and failure of antihistamines to affect all symptoms in such a well-defined allergic disease as asthma) indicates that histamine is by no means the only chemical mediator involved. One of the factors that is currently being considered is the cellular level of cyclic AMP which seems to control the antigen-induced release of both histamine and the slow-reacting substance of anaphylaxis (SRS-A). β-Adrenergic agents and methylxanthines, which increase the level of cyclic AMP, are inhibitory, whereas β-adrenergic blocking agents, like propanol, which decrease the cellular levels of cyclic AMP, enhance the antigen-induced release of the mediators.

The localized acute inflammatory reaction noted in ICD has long been associated with the appearance of large numbers of polymorphonuclear leukocytes at the site of inflammation (N. J. Zvaifler and Gerald Weissmann, New York University). Weissmann showed that the immune complexes themselves trigger the release of enzymes from human polymorphonuclear leukocytes. The release is selective: lysosomal enzymes (β-glucuronidase, acid phosphatase) are released, cytoplasmic lactate dehydrogenase is not. (Such a selective release was confirmed by Henson with human and rabbit neutrophils.)

R. J. Winchester (Rockefeller) described unusual complexes containing γ-globulin which were found in the serum and joint fluid of patients with rheumatoid arthritis. The exact nature of these complexes remains unknown, but those in the joint fluid can activate and fix complement, and they appear to play a role in initiating the characteristic inflammation of the joints. Zvaifler presented related observations on the local synthesis of γ-globulin by synovial tissue. There was considerable discussion of the possible stimulus involved in this local production of antibodies and the local formation of immune complexes.

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