

Testimony of Lester Breslow, M.D., M.P.H.*
for U.S. Senate Subcommittee on Health
on Basic Issues in Biomedical Research

17 June 1976

Mr. Chairman and members of the Subcommittee:

My name is Lester Breslow. I appreciate the invitation to appear before the Subcommittee on the present topic. Now, Dean of the UCLA School of Public Health, my work over the past 30 years has included health research, especially epidemiological studies of chronic disease; and service as President of the American Public Health Association, the International Epidemiological Association and the Association of Schools of Public Health. At present I am a member of the Institute of Medicine of the National Academy of Sciences.

Today, however, I am appearing as an individual--not as a representative of the University of California or any other organization.

Public Law 93-352 (1974) established a President's Biomedical Research Panel to:

- "(1) review and assess
- (2) identify and make recommendations with respect to policy issues concerning the subject and content of, and
- (3) identify and make recommendations with respect to policy issues concerning the organization and operation of biomedical and behavioral research conducted and supported under programs of the National Institutes of Health and the National Institutes of Mental Health."

* Dean, School of Public Health, UCLA.

The Panel has now submitted its report in the form of Report of the President's Biomedical Research Panel, U.S. Department of Health, Education, and Welfare, DHEW Publication No. (OS) 76-500, April 30, 1974; and Appendices A-D.

That report outlines the highly productive biomedical and behavioral research effort in which the United States can take great pride. It refers to the remarkable science base of our nation as "an indispensable national resource," and "the only sound basis for learning how to prevent and control disease." Mentioned also is the "restrained elation" of the panel consultants who sense that "the successes of the last three decades portend an acceleration in the pace of discovery in the immediate and the distant future."

The Report continues that "The primary mission of the NIH, as constituted today, is fostering, supporting and conducting laboratory and clinical research to increase our understanding of life processes and the etiology, treatment, and prevention of diseases In addition to its basic mission, the NIH must explore applications of new knowledge that are effective in health care and must assist in disseminating this new knowledge to appropriate groups. The degree to which the NIH engages in these 'transfer' functions and the problem of resource allocation for these activities as distinct from basic research functions has raised troublesome and complex issues in the science community, in the NIH, in the DHEW, and in the Congress."

"The continuum from the development of new knowledge to the application of such knowledge in health care includes a number of steps:

1. discovery, through research, of new knowledge and the relating of new knowledge to the existing base;
2. translation of new knowledge, through applied research, into new technology and strategy for movement of discovery into health care;
3. validation of new technology through clinical trials;
4. determination of the safety and efficacy of new technology for widespread dissemination through demonstration projects;
5. education of the professional community in proper use of the new technology and of the lay community on the nature of these developments; and
6. skillful and balanced application of the new developments to the population.

"Until recently, the primary mission of the NIH encompassed the first three steps mentioned above. Within the past several years, however, public organizations and members of the Congress have increasingly expressed concern about the impact of research on particular disease problems. Simultaneously, the public tended to focus on the responsibility of the government to take the lead in accomplishing the last three steps. The public insistence that the Congress proceed with these activities forced a search for the proper federal agency to manage programs for hastening the movement of discovery into general clinical application. Repeatedly, the Congress has selected the NIH to manage these programs and the NIH has therefore faced a series of new demands on its organization and resources.

"The congressional authorizations in 1971 and 1972 for high-priority programs in cancer and heart disease greatly expanded the scope of the NIH in the fields of knowledge application and dissemination and moved it closer to conducting clinical service programs. This has led to differences of opinion regarding the proper role of the NIH. Many in the science community prefer that the NIH revert to a 'pure' research institution. Others within this same community and elsewhere feel that this new responsibility is appropriate and that the mission of the NIH encompasses knowledge applications in the interest of improving health care and public well-being."

I should like to focus on two aspects of the Panel's report.

One is the notion, common in the biomedical research community which the Panel reflects, that essentially the only means of understanding how to prevent and otherwise control disease and to maintain health is through laboratory and clinical research.

The second idea is that the biomedical research community should be concerned only with the development of new knowledge and technology, and should bear no responsibility for the development of means for applying that knowledge and technology; the lag between the development and availability of technology, and widespread use is said to be "beyond the control of the research community." Further, "Knowledge application and dissemination activities and clinical trials should be staffed and funded by resources dedicated solely to these purposes and should not compete with research budgets."

The first of those notions is, in the words on the cigarette package, "dangerous to your health"; the second poses a sharp policy question for the Congress and the Administration.

Means of Developing Knowledge to Prevent and Control Disease

Laboratory and clinical research do constitute important means of gaining knowledge about how to control disease, including how to prevent it. Especially in the development of vaccines against communicable diseases and drugs for treatment of several diseases, as the Report indicates, biomedical research in the sense of the Report has made tremendous contributions. However, it is important to note that many fruits of such research, for example, poliomyelitis vaccine, can safely be made generally available to the population only after epidemiologically controlled field trials. The large-scale test of poliomyelitis vaccine directed by epidemiologist Thomas Francis was an essential link in the chain of work by several individuals that assured prompt delivery of the means of preventing poliomyelitis to the millions of Americans who benefitted thereby. Most procedures in preventive medicine are subjected to such field trials before wide-spread use.

Incidentally, it would be desirable that procedures widely used in curative medicine be tested in the same kind of epidemiologically controlled trials. That would help to curtail the adoption and use of many drugs and other alleged curative procedures of extremely dubious merit. It would also help to reduce the cost of medical care and to avoid harmful side-effects. With the spiralling of medical technology derived from biomedical research, we have unfortunately tended to adopt procedures that seem promising and then look backward after they have been used for

a while to determine whether enough damage has occurred to require abandoning them. The Panel notes that "such premature acceptance can pose just as serious a threat to the nation's health as any real delay in making new and proven technologies available." The point deserves emphasis.

Perhaps even more important to health in an adverse way is the notion, unfortunately perpetuated in the Report, that advances in prevention and control of disease have come essentially only through laboratory and clinical research. The history of disease prevention and control shows that notion to be false.

A few examples may be useful.

Means for preventing cholera were discovered by epidemiological investigation--years before Pasteur established the germ theory of disease and decades before the bacillus of cholera, the causative agent, was discovered. John Snow in London in 1854 found that drinking Thames river water polluted by human intestinal discharges was causing the then-raging epidemic of cholera. He made that discovery in a classic epidemiological study which demonstrated that the occurrence of cholera in households served by water taken from the Thames below the city, polluted with raw sewage, was 14 times greater than the occurrence of the disease in households served by water taken above the city. That finding provided the way to prevent cholera and other epidemic intestinal infections: avoid drinking sewage-polluted water. Subsequent discovery of the specific microbic agents and other means of avoiding their damage were refinements, but the basic preventive measure was established by an epidemiologic investigation.

Means for preventing scurvy and beri-beri, major scourges of days gone by, were also discovered by epidemiological investigation--unguided by knowledge of vitamins. These diseases were only later found to be results of specific chemical dietary deficiencies (avitaminoses). In the 18th century James Lind in another classical epidemiological study found that epidemic scurvy among British sailors was due to lack of fresh food; and that it could be prevented by small amounts of citrus fruit. British sailors have since been called "limeys" because their shipboard diet after Lind included a compulsory ration of limes or lime juice. In the 19th century Dr. Takaki, a Japanese doctor who had worked in the British navy, discovered by an epidemiological experiment involving two ships, that about two-thirds of the men eating the traditional Japanese white rice diet developed beri-beri whereas only a handful of those on a ship with a British navy diet developed the disease (and they were later found to have actually kept to the white rice diet). Takaki wrongly attributed the condition to something in the white rice rather than to something absent from it, but it was still clear--regardless of the mechanism--that a diet restricted to white rice caused beri-beri.

Only in the 20th century did science yield vitamins, the absence of which caused certain disease states. Even after the first vitamin (thiamine) was discovered, it was a "shoe-leather" epidemiologist, Joseph Goldberger, who found how to prevent pellagra. The latter is a nutrition-deficiency condition common during the early part of this century in the rural south. Goldberger did not accept the prevalent notion that pellagra was a microbic disease and he correctly identified the cause to be the absence of something present in milk or meat. Again the epidemiological approach demonstrated how to prevent a disease (pellagra) years before the biochemical process was understood.

Epidemiological investigation of cholera and other intestinal diseases provided a scientific clue to the existence of germs, and epidemiological investigations of scurvy, beri-beri and pellagra provided a scientific clue to the existence of vitamins whose absence causes those diseases. It is important to note that it was possible to prevent the diseases before we knew about germs and vitamins.

To take a more recent example, means for preventing 90% or more of the lung cancer that occurs in the United States was also discovered by epidemiological investigation--and we still don't know the mechanism by which cigarette smoking causes lung cancer. It may be observed that discovering the means for preventing lung cancer does not translate immediately into control of the disease. Stopping cigarette smoking is not easy for many people--just as it was not easy to stop pollution of water to control cholera, or to establish a diet to prevent pellagra in the southern states of this country. Incidentally we are making some headway in the case of cigarette smoking; while unfortunately more youngsters are smoking cigarettes, adults are giving up the habit. Cigarette smoking is becoming a "kid" phenomenon.

The main point to be derived from these examples--cholera; scurvy, beri-beri and pellagra; and lung cancer, and many more could be cited from history--is that epidemiological research cannot infrequently show how to control disease before the biologic mechanisms are known. It is a fair estimate that we now seem as close to understanding how to control in large part the major fatal diseases of our time, cancer and coronary heart disease, through further epidemiological studies as through research into the biologic mechanisms of these diseases.

Obviously this is not to suggest that we should abandon biomedical research that may lead to control of such diseases. It is intended to emphasize, however, the almost exclusive concern with laboratory and clinical research in the Report of the President's Biomedical Research Panel (Appendix A does acknowledge some role for epidemiology and preventive medicine). The overwhelming emphasis on the findings of traditional biomedical research as "the only sound basis" for disease prevention and control does not reflect the actual history of disease prevention and control.

If the Congress wishes to advance means for disease prevention and control, I would suggest either commissioning a study of how to accomplish that purpose; or, perhaps more appropriately and certainly more quickly, drawing upon the several recent studies of that subject. The Panel report gives a distorted view of the matter. If examined more fully in the light of history and actual influence on disease control, epidemiological studies will be found relatively more important in relation to laboratory and clinical research than the Report indicates. Also it will be found, I believe, that epidemiology has been relatively starved in the world of health science.

Development of Means for Applying Knowledge and Technology in Disease Prevention and Control.

It is clear that Congress intends to advance the development of means for applying knowledge and technology in disease prevention and technology in disease prevention and control. As noted in the Report of the Panel, "congressional authorizations in 1971 and 1972 for high-priority programs in cancer and heart disease" called for more than "pure" research. Congressional hearings since that time have included

querying of administrators concerning their response to these authorizations and the accompanying appropriations. It must be said that NIH has moved only ambiguously and with considerable resistance beyond step 1 and the first part of step 2 in the continuum outlined by the Panel. Efforts to go as far as step 4, demonstration projects, have in the case of cancer encountered especially severe resistance from the biomedical research community. That resistance has had substantial impact on the National Cancer Institute although the Director and his staff in Cancer Control have energetically attempted to carry out the intent of Congress.

Attention should be directed, in this connection, to two sentences in the Panel's report: "The primary role of the NIH should continue to be that of conducting and supporting laboratory and clinical research attuned to the search for new knowledge and, given adequate resources, of conducting and supporting clinical trials, selected demonstrations, and selected educational programs Knowledge application and dissemination activities and clinical trials should be staffed and funded by resources dedicated solely to these purposes and should not compete with research budgets."

That highlights the issue: In view of the antipathy in the biomedical research community toward proceeding beyond step 1 and the first part of step 2 in the continuum of knowledge development and application outlined by the Panel; and in view of the powerful influence of that biomedical research community as the essential constituency of NIH, should the Congress further entrust NIH with responsibility for developing means for applying knowledge and technology in disease prevention and control?

Before suggesting ways that issue might be approached, it may be helpful to discuss briefly the question of whether that endeavor is important. Is Congress correct that it is necessary to support application?

Throughout the Panel's Report one finds the implication that application of knowledge to control disease is increasingly automatic and that perhaps the most the Federal government should undertake in this regard is "facilitating the involvement of commercial effort (and) mitigating the inhibiting influence of the requirements of the regulatory agencies." For anyone familiar with the history of occupational health endeavor in this country, an important aspect of disease prevention and control based on scientific knowledge, or with the history of the development and promotion of drugs in this country, that is a rather strange suggestion.

In considering whether supporting applications of disease-preventive knowledge and technology is important, one can examine actual experience with various means of disease control and prevention developed during the past several decades. Take, for example, the cytologic test (Papanicolaou smear) for cancer of the cervix. The technology of that test and effective surgery for the disease were well established and their usefulness demonstrated as early as 1943. Yet for the next 15 years more than 10,000 women in the United States died on the average each year--in retrospect, unnecessarily prematurely--because of our failure to apply the available means for preventing the deaths. By the late 1950's, 15 years after these means were known, the test had been applied to less than half the adult women in the country and least of all to poor women who were well known to be most affected by the disease. Another 15 years were to pass, and more than an additional 100,000 women were to die unnecessarily of cervix cancer, before the test was given even once to three-fourths of the women in the country; and still those at greatest risk of the disease were the most neglected.

In just one disease, then, cervix cancer, our failure in what the sophisticates call "technology transfer" resulted in more than a quarter-

million deaths. That is a fair-sized "epidemic." Stretched out over several decades it does not impact on the public consciousness as would, say, an epidemic of influenza that took a quarter-million lives. But the nature of the major diseases of our day is long-term, both for the individual and for society. Cervix cancer is only one example. Many more could be cited.

Where should the Congress place responsibility for doing what we can and should do as a nation to avoid such tragedies, due to our failure to test systematically and promote application of proven measures for the control of disease?

At least three options are available. One is to continue placing that responsibility on NIH. Another is to place it in some other present agency of HEW. The third is to establish some new agency.

In selecting among these three, and possibly other options, consideration needs to be given to several aspects of the problem, including:

1. Clear definition of the mission, especially differentiation from biomedical research as it has developed in this country; and emphasis on epidemiological studies and controlled field trials.
2. Establishment of a coherent staff and leadership dedicated to the mission, not bits and pieces scattered through NIH and other agencies of the Federal government.
3. Sufficient budget, including present allocations scattered through NIH and elsewhere in the Federal health agencies.
4. Development of a substantial partnership with those outside the Federal government, especially in state and local government, voluntary health agencies and many elements of the health professions.

5. Careful oversight by the Congress.

With attention to these criteria in deciding upon the next step in disease prevention and control, the United States could move ahead rapidly in this field.

I would be pleased to answer any questions I can.