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READ BEFORE THE SCIENTIFIC SESSION

PRESIDENTIAL ADDRESS

BIOLOGICAL BEACHHEADS

By THOMAS FRANCIS, JR.

In the past year a group of nations of divergent ideologies, through coordinated and exhausting effort, has succeeded in applying control measures to a disease which had been increasing in scope and virulence so as to reach epidemic proportions in the world politic. A few experienced political epidemiologists had recognized the danger early and pointed out the threat, but the majority relied upon our isolation and quarantine regulations to meet it. Various placebos were tried. It was not, however, until an open focus appeared on our own flank that we really rose to action. The emergency demanded highly concentrated authority, enormous expenditures and the drafting of men from all activities into one great effort. By amazing combinations of land, sea and air power, beachheads were established and a *cordon sanitaire* formed. From these points the further advances were made which finally disrupted the essential reservoirs to a point of ineffectiveness, and the epidemic subsided.

Like all other epidemic diseases, however, it survives in foci to which must be applied all conceivable specific and environmental control measures in order to prevent a resurgence. This is the foremost problem of the day and, unless effectively approached, reduces our other hopes for advancement to sheer vapor.

No people can pass through such experiences without receiving a deep imprint upon its philosophy. The influence extends beyond the social and political fields, hence, it is not surprising that the patterns which were developed under military exigencies should be proposed as those which would function effectively in the establishment of biological beachheads.

The trends are seen in the current discussions of national legislation in support of research. One group has urged action similar to the methods used in the atomic bomb research project. It apparently visualizes a higher echelon of master minds which plans, organizes and directs—busily splitting its mental 235 in an effort to set up a chain reaction in the low grade cerebral pitchblende of a large body of workers. Research workers are human tools—the important thing is to know what job they are good for and how to use them. The impression is promoted that the mass attack will settle problems of disease quickly and finally. Another proposal accepts the desirability of increased funds for scientific endeavor from federal appropriations to be distributed by a body of scientists with a minimum of governmental direction—but nonetheless an organization administered through the federal government.

There is general agreement that it is highly desirable

to encourage more men of ability to enter the different fields of scientific investigation. Moreover, if these men can develop sufficient common interest to study certain problems with different disciplines and different points of view, to share experiences and trade ideas, it is clearly advantageous. The past five years have furnished numerous examples of men giving up their individual preferences to join in a coordinated effort designed to test a lead or to give their abilities to continued, tedious studies, even though disagreeing with the major plan. Furthermore, in most problems a stage is reached where it is profitable and strategic to concentrate upon an organized study which can test under controlled conditions the validity and applicability of experimental observations. This quantitative approach would seem to be most useful when the stage of application is reached. But whether the concept of coordinated study can be expanded indefinitely is open to considerable doubt.

Disease is a complex biological problem and while much has been learned concerning certain mechanisms at play and the reagents involved, I believe it is fair to say that the intimate details of but few of them are really known. Nor, with possibly a few exceptions, is it clear how a clinical case of disease actually begins. While we have reached the atomic age in the physical sciences, biologically we are still in the molecular stage. Experimental work is primarily qualitative in its approach. It constitutes the advance intelligence, the scientific G-2, seeking to gather data on which biological beachheads can be established. It requires judgment in evaluating and correlating small bits of information and in deciding which areas are most vulnerable to attack. It must not allow rumor in the form of uncontrolled observations, or premature interpretation to be mistaken for fact. "The experimental method," said Claude Bernard, "is the scientific method which proclaims freedom of mind and of thought." It does not submit to authority, but draws from within itself an impersonal authority which dominates science. Original thinking and observation do not derive from conformity with accepted opinion.

How best can a national research foundation serve to promote these ends and at the same time preserve spontaneity and freedom of action? Certainly, not through another atomic bomb project. Perhaps the greatest reservations concerning the desirability of a national agency lie in skepticism as to the spirit in which it will function. Administrative principles of a large organization tend to be founded on orthodoxy. There should be as little display of central authority and direction as

can possibly be got along with. Care should be taken to avoid the setting up of favored programs of research to the exclusion or disadvantage of other less prominent fields of activity; this procedure could lead to lobbying and pressure groups who would work to promote special interests. Moreover, programs incline inevitably to seek the application. One might, with a certain sincerity, suggest the motto "A pogrom on programs." The current tendency to give support only to well defined projects should be minimized, and encouragement given both to extended work in a broad field which offers many opportunities, and to dabbling in a narrow field where the next move is obscure. Gilding of the lily should not become the major scientific objective; the simplicity of observation should not give way to the glamorous phrase; the seat of influence must not replace the work bench in determining the direction of investigation. A national foundation must be free of political domination by either the professional or the scientific politician. If undertaken it must be inaugurated on a sufficiently sympathetic basis that it shall not have to justify itself in terms of the first few years' results, nor concern itself too greatly with detailed evaluations of the progress which is being made. The concept which flows through the Bush report of general research funds largely administered through university channels to meet their own needs, and to take advantage of their own resources, seems of all the most desirable, because it returns the opportunity and the responsibility for initiation and support of research to its proper place. Moreover, it would probably result in a great reduction in incidence of that occupational disease of the experimentalist, a divergent strabismus developed from trying to keep one eye on his work and the other on the source of funds.

There is a need to increase the positions and the environments in which men can work continuously upon problems in which they themselves are interested. The current system contrives to drive men from research since the positions to which they can advance furnish frustration rather than fruition of their research interests. The generation of ideas and new information should constitute sufficient warrant for their support without detailed pleading before a dispensing board.

There is a need to promote the investigation of disease as a broad problem in biology. Too often the pre-clinical years of the medical curriculum are urged to emphasize clinical application rather than biological implications. Greater latitude for thought and work in these latter channels will undoubtedly extend the boundaries of clinical investigation.

There is little doubt that if more men who could be interested in the investigation of disease problems were found, given the opportunity to develop, provided facilities and *time*—for thought and work, afforded reasonable incomes and opportunity to advance, all in an atmosphere of scientific freedom, progress in medicine might well be more rapid. This is the manner in which increased funds can be most effectively employed.

In the original formation of a federal organization for the support of scientific research, which now seems im-

minent, it will be the responsibility of members of this and other research societies to see that the personnel and the philosophy upon which they act are truly representative of the best scientific thought. Otherwise it is we, not they, who will have lost the beachhead. Failure will not only be harmful to *research*, but will destroy a great opportunity science has had to project the honesty and objectivity of the scientific outlook into a world of social confusions and warped emotions.

A Comparison Between Infectious Hepatitis and Serum Jaundice in Experimentally Infected Human Volunteers.
By W. PAUL HAVENS, JR., New Haven, Conn.

Although the exact relationship between *infectious hepatitis* and *homologous serum jaundice* is not understood, experiments in the transmission of these two conditions to human volunteers have revealed certain information which assists in making a distinction between them.

The causative viruses of both diseases are filtrable, resistant to a temperature of 56° C. for 30 minutes, and may be transmitted to human volunteers in serial passage, producing a clinical disease in man which resembles catarrhal jaundice.

In contrast to these similarities are certain differences which include route of infection, length of incubation period, and period of infectivity.

Our strain of *infectious hepatitis* virus produces disease in human volunteers following parenteral inoculation or ingestion, with incubation periods ranging from 15 to 34 days. Virus is demonstrable in both blood and stool during the acute phase but not in the incubation or convalescent periods. Homologous immunity is present in these patients.

Our strain of *homologous serum jaundice* is infectious when inoculated parenterally with incubation periods ranging from 56 to 134 days. It is demonstrable in the blood of inoculated subjects one-third and three-fourths way through the long incubation period and during the acute phase of disease, but not 1 month after onset. Apparently it is not present in the stool of patients, nor is it infectious when ingested. Patients convalescent 6 months from infection with this strain are not immune to experimental infection with our strain of *infectious hepatitis* virus.

A Study of the Urinary Coproporphyrin in Hepatitis and Cirrhosis. By C. J. WATSON, Minneapolis, Minn.

In this study the total coproporphyrin in the 24-hour urine was determined in 154 cases. This series included 60 cases of infectious hepatitis; 45 cases of cirrhosis of the liver of various types; 17 cases of jaundice due to extrahepatic biliary obstruction; 1 case of carbon tetrachloride poisoning with jaundice; 1 case of jaundice due to sulfanilamide. The relative percentage of the type 1 and 3 coproporphyrin isomers was determined by means of differential precipitation of the esters in 30 per cent acetone, as described by Schwartz, Hawkinson, and Watson. Normal human urine has been found to contain from 65 to 90 per cent of the type 1 isomer. The normal range for the total coproporphyrin in 24 hours