Medical Research Leading to the Acceptance of the Orthomolecular Approach

Roger J. Williams'!

In explanation of the title of this paper, it should be noted that medical research may properly be defined as investigators designed to throw light on how to achieve the objectives of medicine—the promotion of health and the prevention and treatment of disease. All of the work supported by the Clayton Foundation, with which I have been so closely associated for many years, has been medical research under this definition.

Mr. Benjamin Clayton's interest and his philanthropies have continuously been medically oriented, and when in 1940 he had an opportunity to support fundamental work designed to elucidate the nature of degenerative metabolic diseases including cancer, he was intrigued.

He realized that the diseases of greatest interest were baffling ones and that the proposed goals were long range. He was not dismayed. The Clayton Foundation Biochemical Institute was founded.

1 Clayton Foundation Biochemical Institute, Department of Chemistry, University of Texas, Austin, Texas 78712.

My own interests developed exactly along these lines for it was evident that long before any treatment methods for these baffling diseases could even be thought of, a large amount of fundamental understanding would have to be gained. Treatment or preventive measures would constitute a superstructure which must, however, be built upon a foundation of fundamental medical research. No one primarily interested in clinical applications could possibly do this long-range foundation building.

Without question, medical research on cancer, for example, had to start with explorations designed to find the roots of the disease. As long as the fundamental medical research remained undone, so long would definitive and successful work on cancer be delayed. Every expert in the field of medical research on cancer knows that this was and still is so.

The essential problem in cancer is that sometimes cells "go wild" and propagate uncontrollably with devastating effects. No one knew (or knows at present) precisely how or why this happens.

Common sense tells us, as it told Mr. Clayton, that it would be entirely futile to expect a worker, who knew nothing about the mechanisms involved, to repair a watch, radio, or electronic device. Likewise, no one could hope to accomplish anything with cancer unless he knew how living cells can be deranged, and in order to know this he would have to have a tremendous store of information and insight into how cells operate when they are healthy.

Productive medical research on cancer must build a foundation of knowledge as to how cellular machinery works when it is in order before it can hope to control the disorder which accompanies cancer. The central problem which confronted the Clayton Foundation Biochemical Institute at its inception was to gain intelligent answers to the question: "In what ways can cells become deranged?" Only when one has an idea as to all the ways cells can be deranged can he pick out those which are most likely to be involved in a particular disease. It should be noted that this fundamental question—"In what ways can cells be deranged?"—is one which needs to be answered as a foundation for the intelligent study of all diseases which have a cellular origin.

Finding comprehensive answers to this basic question is unbelievably complex because of the numerous entangled, complicating considerations which have to be taken into account.

To begin with, the cells which are capable of becoming deranged are microscopic in size and hence difficult to explore. They may be so small that billions of them could be lost in the machinery of the tiniest lady's watch. Furthermore, they differ enormously in size, in chemical composition, and in the functions they are built to perform. It is thus dangerous to think entirely in terms of "the cell" as though it were a uniform entity.

In spite of their microscopic size, each cell is more complicated than a single machine like a watch, dynamo, radio, or television set. Each cell resembles more closely a complete factory complex.

Every cell has its own power plant from which it derives its energy. The burning process from which energy is derived is a highly ordered, many-step process in which many different catalysts are involved. Each catalyst (enzyme) is protein in nature and is made up of hundreds of amino acids (and often vitamins) put together in exactly the right way. The power plant makes it possible for every cell to be highly dynamic. Something is happening every microsecond. Complex chemical transformations—filtering, ultrafiltering, emulsifying, dispersion, aggregating, absorption, adsorption —are continually in progress. Tearing down, building up, and repairing are constantly going on.

Cells have their own ways of designing and making blueprints; "printing" and duplicating are very much in evidence. Cells also have their own versions of assembly lines. They have transportation systems; sorting, pumping, and streaming; and molecules riding piggy-back on others are common processes. Intricate mechanisms, including feedbacks, are used by cells to regulate their numerous activities.

Cells have communication systems-messages and messengers. They have the equivalent of both an intercom system and devices for sending and receiving messages to and from the outside. Electrical activities are continually manifest.

Cells are equipped with sewage and disposal systems. They even have in effect pollution-control mechanisms whereby toxic molecules are converted into others which are relatively harmless. The crucial need to recognize and become acquainted with the intricacies of cell machinery rests on the fact that each part of the mechanism is subject to disorder, in which case the entire activity of the cell may be seriously impaired.

In metabolic diseases, all sorts of derangements can take place, and there is little hope of control unless the mechanisms are recognized and to a degree understood.

Recognition of the particular areas which require attention in an attack on any disease involving cellular metabolism.

leads us to consider another phase of cellular activity.

Cells are not only complicated like entire factory complexes, but they are capable of building new factory complexes which may duplicate the original. Even this understates the potentialities of living cells. In biological differentiation, factory complexes are built successively and eventually become very different indeed from the original parent factory. A better understanding of this whole process of cell propagation is essential for an attack on the cancer problem because cancer development is intimately associated with the production of new cells. If a particular cell were to take on metabolic characteristics like those of cancer, but was unable to propagate new cells, no harm would come. It is only cells which propagate wildly that produce cancerous growths.

Because propagation is involved, medical research on cancer must of necessity be very much concerned with the genesis of new cells and how this process may become disordered. A whole field of science—molecular biology—has developed in the last decade or two and is primarily concerned with the mechanisms involved in cell replication. That phase of virology which has to do with cancer viruses is intimately concerned with the same process.

A highly important phase of "molecular biology" has to do with the fundamental details of protein structure and particularly how proteins are built and how the process is controlled. If no proteins are built, no new cells can be produced.

A large volume of fundamental work was done and continues to be done in the Clayton Foundation Biochemical Institute. In a short history of this institute (1966) there is presented a bibliography of 700 papers emanating from this group of investigators (Williams, 1966). Many of these papers had to do with the structure and functioning of what we call "B vitamins" in cellular metabolism.

The cellular approach to biological problems was a natural outgrowth of my attention to those aspects of yeast cell metabolism which had to be recognized in connection with the discovery and isolation of pantothenic acid (Williams et al., 1933, 1938, 1939; Weinstock et al., 1939; Williams, 1939).

Coupled with this broad cellular approach there developed in our laboratories an intense interest in what came to be known as biochemical individuality. A forerunner of this interest were numerous observations the culminative effect of which was to make me realize that the "normal" or "average" organism is a scientific artifact—only a statistical abstraction—and could not be taken very seriously by those whose primary interest involved real diseases afflicting real people. Medical research may involve basic fundamentals, but it must eventually, if it is to be effective, be concerned with application.

One aspect of biochemical individuality has to do with nutritional needs, and it became evident to us that each individual animal and human being probably has a distinctive pattern of nutritional needs. The list of needed nutrients may be the same for every member of the human family, but the relative amounts needed may be distinctive for each individual for genetic reasons.

In 1950 we published the first detailed exposition of the genetotrophic concept (Williams, 1950). This carries the idea that certain individuals may be prone to a particular disease because their nutritional needs are unusual, and these are not satisfied by the diet they consume. According to this fundamental idea, if the vulnerable individual is continuously supplied with the nutrient or nutrients which he does not get enough of in his diet, the disease will vanish.

It is obvious that what was originally a hypothesis needed to be backed up by substantial evidence before it could be accepted as worthy of serious attention. Many pertinent questions needed to be asked and answered before this concept could be applied to the prevention and cure of disease. How distinctive indeed are the nutritional requirements of human individuals for the numerous nutrients they require? How do problems of digestion, absorption, transport, and distribution enter into the problem? Is it possible, physiologically, that certain nutrients may have to be administered in massive doses in order that the individual get enough of what he needs? If so, for what particular nutrients does this hold and why?

Partial answers to these questions have come from many studies, but more complete answers are desperately needed. In 1956 I published a book, **Biochemical Individuality,** which sought to cover the evidence in support of the genetotrophic idea which was available at that time (Williams, 1956).

In 1967 my book, **You Are Extraordinary,** was published which sought to bring to popular attention the whole concept of biological individuality and its importance to human life (Williams, 1967).

In 1971, **Nutrition Against Disease** was published (Williams, 1971). Its central theme is that the quality of the food we consume determines the adequacy or inadequacy of what Claude Bernard called the milieu interieur of our bodies, and that this internal environment is crucial to human health. It is postulated that if this internal environment can be brought into line with individual human needs all manner of diseases can be prevented. To use Pauling's apt designation, this is "Orthomolecular medicine." Fortunately many medical men, including psychiatrists, on the basis of their own extensive work have come to the same basic idea

The Orthomolecular approach to psychiatry, as set forth by Pauling in his classical paper in **Science** in 1968, is in its infancy, but it is a lusty infant; there is not the slightest doubt in my mind that it will develop in a phenomenal way. I am sure that mistakes will be made in this area—all infants make mistakes—and it would be unfortunate if the success of the movement should be judged on the basis of any particular application. I firmly believe that the Orthomolecular approach to psychiatry and to medicine has a perfectly sound biological base, and that this approach cannot fail to be highly productive. Questioning whether it will be effective or not is almost equivalent to asking, "Is the environment of one's body cells important?"

I am convinced that other members of the medical profession will eventually join with a veteran physician who wrote me with respect to **Nutrition Against Disease,** "I have gone over this book fairly carefully and it seems to me that your position is unassailable."

REFERENCES

WILLIAMS, Roger J.: "The Clayton Foundation Biochemical Institute: A Short History." (Available from the Clayton Foundation Biochemical Institute, The University ot Texas, Austin, Texas.) 1966.

WILLIAMS, Roger J., LYMAN, CM., GOODYEAR, G.H., TRUESDAIL, J.H., and HOLADAY, D.: "Pantothenic Acid, A Growth Determinant of Universal Biological Occurrence." J. Am. Chem. Soc. 55, 2912-27, 1933.

WILLIAMS, Roger J., TRUESDAIL, J.H., WEINSTOCK, H.H., Jr., ROHRMANN, £., LYMAN, CM., and McBURNEY, C.H.: "Pantothenic Acid. II. Its Concentration and Purification from Liver." J. Am. Chem. Soc, 60, 2719-23, 1938.

WILLIAMS, Roger J., WEINSTOCK, H.H., Jr., ROHRMANN, E., TRUESDAIL, J.H., MITCHELL, H.K., and MEYER, C.E.: "Pantothenic Acid. III. Analysis and Determination of Constituent Groups." J. Am. Chem. Soc. 61, 454-7, 1939.

WEINSTOCK, H.H., Jr., MITCHELL, H.K., PRATT, E.F., and WILLIAMS, Roger J.: "Pantothenic Acid. IV. Formation of Beta-Alanine by Cleavage." J. Am. Chem. Soc. 61, 1421-5, 1939.

WILLIAMS, Roger J.: "Pantothenic Acid-A Vitamin." Science 89, 486, Mav. 1939.

WILLIAMS, Roger J.: "Concept of Genetotrophic Diseases." Nutrition Review 8, 9, 257-260, September, 1950.

WILLIAMS, Roger J.: Biochemical Individuality. New York, John Wiley and Sons, Inc., 1956.

WILLIAMS, Roger J.: You Are Extraordinary. New York, Random House, 1967.

WILLIAMS, Roger J.: Nutrition Against Disease. New York, Pitman Publ., 1971.