

Draft

THE POSSIBILITIES FOR FURTHER PROGRESS
IN MEDICINE THROUGH RESEARCH

By LINUS PAULING

When I was born, in 1901, the electron had been discovered, but the atomic nucleus had not. In 1912 Rutherford reported his experiments on the scattering of alpha particles, and his interpretation of them as showing that the mass of an atom is for the most part concentrated into a very small particle, carrying a positive electric charge [—] _^ the nucleus of the atom, about which the electrons move. Most chemists were confident that the structural formulas that they wrote for chemical substances bore a close relation to the actual arrangement of the atoms in the molecule, relative to one another, but there was little expectation that in a decade or two it would become possible to determine the structures of molecules and crystals with great accuracy.

The first measurements of inter^{atomic} distances were made by W. H. and W. L. Bragg, by application of their method of determining the structure of crystals by X-ray diffraction. This method was soon supplemented by others: ^{the} _^ analysis of band spectra, the electron-diffraction technique for gas molecules, and so on. By 1940 precise structural information had been gathered for hundreds of gas molecules and hundreds of crystals.

It then became possible to ask significant questions about the molecular structure ^{of the human body} _^ and the molecular basis of disease and of therapeutic ~~methods~~ treatments. A few of these questions have been answered. We have begun to talk about molecular biology and molecular medicine, and to have the feeling that biology and

medicine are just at the beginning of ^a ~~the~~ period of extraordinary development, a Golden Age similar to that through which physics and chemistry have passed during the last seventy years.

Even though powerful methods of experimental investigation have been developed during recent decades, we must recognize that the problem of determining the molecular structure of the human ^{body} is an extremely difficult one, and that progress may be slow. I may illustrate this point by mentioning the substance that constitutes a larger fraction of the human body than any other substance -- the substance water. We know a great deal about the isolated water molecules; we know that the average distance between the center of the oxygen atom and the center of each of the two hydrogen atoms is $0.965 \overset{\circ}{\text{A}}$, and that the H-O-H bond angle has the value $104^{\circ} 31'$. Also, we know the detailed structure of ice. But the water molecules in the human body are not present as isolated water molecules or as ice; they are present as liquid water, containing various substances in solution. We are still largely ignorant about the structure of liquid water and the structure of aqueous solutions in general. We shall continue to have difficulty in understanding the nature of physiological processes so long as we have not solved the problem of the nature of liquid water and of its solutions. A most striking development of recent years has been the increase in our knowledge about the structure of proteins and of ^{nucleic} ~~amino~~ acids. A number of diseases are now known to result from a gene mutation that leads to the substitution of a single amino-acid residue for another in a polypeptide chain of some protein in the human body. For example, in the disease sickle-cell anemia it is known that the two beta chains

of the hemoglobin molecule (rather than the two alpha chains) carry the abnormality, that the abnormality is in the sixth position from the free amino end of the beta chain (which contains 146 amino-acid residues), and that it involves the introduction in this position of a valine residue, ~~in this position,~~ ^{there} in place of the glutamate residue that is found in normal adult human hemoglobin. Moreover, rapid progress is being made in the attack on the problem of the nature of the genetic code, and it is likely that within a year or two it will be possible to say just what substitution of one nucleotide for another in the polynucleotide constituting the gene for the synthesis of the beta chain of hemoglobin has taken place during the mutation from normal to sickle-cell hemoglobin.

We can be confident that ^{in one or two decades} similar information will become available for hundreds of diseases, and that this information will in the course of time lead to improved methods of prevention and treatment.

There is, moreover, the possibility of a great improvement along another line -- the understanding and control of mental disease. I estimate that there is a strong hereditary factor in 80% of the cases of mental disease. There is, of course, also in many cases a significant environmental factor. A human being may sometimes have a hereditary nature such that he can withstand great environmental stress, whereas for other human beings the ^{hereditary} hereditary character is such that even the minimum amount of environmental stress is enough to cause serious mental disease. About half the hospital beds in the United States are occupied by mental patients.

About 10% of the American people spend some time during their lives in a mental hospital. I believe that through research on the molecular basis of mental disease it will be possible to decrease its incidence significantly.

One way to attack the problem of mental disease is to carry on research on the structure and function of the brain. I believe that it will be possible, perhaps within twenty years, to determine the nature of the electric oscillations in the brain that constitute consciousness and ephemeral memory, the nature of the material pattern in the brain that constitutes permanent memory, and the nature of the interactions between the electric oscillations and the material pattern. I believe that it will be possible to discover the important molecules involved in the process of thinking, to determine their structure, and in the course of time to discover what the molecular abnormalities are that lead to mental deficiency and to mental illness. Molecular biology and molecular medicine are new fields of science that can be greatly developed for the benefit of mankind.

The young man or woman who is now attending medical school and preparing to be a physician is faced with a problem that will be with him throughout his life. The nature of medical practice is going to change, more and more, during the next few decades, as the result of discoveries that are made about the human body, the vectors of disease, and the molecular basis of drug action. It will be important that the physician understands these changes that are brought about by the new discoveries. To prepare himself to follow the progress of medical research in the future, the student of medicine can do nothing better than to

participate in research himself. I am accordingly pleased that I can be associated with some of the University of Toronto medical students who have been carrying on research and are publishing ~~XXXXX~~ accounts of their work in the Research Issue of the University of Toronto Medical Journal.

Linus Pauling