Marino, California: Studies of the genetic effects of ultra-high frequency irradiation.

APPRENTICE SEAMAN ELLSWORTH CHARLES DOUGHERTY, specialist training program, Navy; research fellow in zoology, University of California, Berkeley: Studies of the comparative morphology of the parasitic nematodes of the suborder *Strongylina*.

Four fellowships were awarded to Canadian scholars, including two in science, as follows:

DR. ROGER YATE STANIER, penicillin production manager for Merck and Company Ltd., Montreal: Studies on the nature, relationships and biological activities of bacteria, particularly of the myxobacteria.

DR. JOHANNES F. K. HOLTFRETER, department of genetics, McGill University: Investigations of the causal factors involved in the embryonic development of vertebrates. This is the second Guggenheim fellowship awarded to Dr. Holtfreter.

SPECIAL ARTICLES

THE STRUCTURE, FUNCTION AND INHIBITORY ACTION OF PORPHYRINS[1]

Hemophilus influenzae requires hematin for growth. It is unable to synthesize it from ordinary culture media. This fact may be utilized in a study of the function of hematin-like compounds. The results obtained throw some light on the synthesis, action and specificity of various porphyrin compounds. Hoagland and Ward[2] have recently used this organism as an assay method for the second growth factor, coenzyme I, required by this organism. We have utilized their bacteriological procedures in this study.

Hematin is the iron compound of protoporphyrin, which is characterized by its vinyl side chains. Iron-free protoporphyrin supports the growth of *H. influenzae* as well as does hematin,[3] and a positive peroxidase test on organisms grown for several passages on protoporphyrin is evidence for the fact that iron has been inserted into the protoporphyrin ring by the bacillus. Other iron-free porphyrins which contain no vinyl groups, such as hematoporphyrin, mesoporphyrin and coproporphyrin, will not support the growth of the organism. However, the iron compounds of some of these porphyrins, for example, iron mesoporphyrin, will support growth. Therefore it appears that the organism, although it is able to utilize for growth various iron porphyrins, is able to insert iron only into protoporphyrin and that the vinyl groups are required for this operation. The vinyl groups are essential in another respect, namely, for the reduction of nitrate to nitrite. The organisms are able to reduce nitrate in the presence of hemin or of protoporphyrin, but no nitrate is reduced in the presence of other iron porphyrins. Multiplication of the bacillus is unaffected by this inability to reduce nitrate.

Furthermore, some of the iron-free porphyrins actually inhibit the growth-promoting faculty of hematin, protoporphyrin, or other iron porphyrins, which support growth. There is a competitive inhibition between the iron-free porphyrins lacking vinyl groups and the iron porphyrins, over a range of concentrations that is limited by the low solubilities of these compounds. For example, ten molecules of hematoporphyrin inhibit entirely the growth-promoting influence of one molecule of iron protoporphyrin. We regard this fact as evidence for the competition of the various porphyrins for the combination with the specific proteins of the heme enzymes.

There is evidence suggesting that the combination between the specific protein and the porphyrin takes place by the interaction of the ionized propionic acid side chains of the porphyrin, probably with basic groups of the protein. Iron protoporphyrin and protoporphyrin which normally promote growth of *H. influenzae* do not do so if their propionic acid groups are esterified. Also the porphyrins which may act as inhibitors do not inhibit if their propionic acid groups are esterified.

The iron porphyrin proteins are the catalysts which make oxygen available to the organism. If an organism were to produce a porphyrin into which iron could not be inserted this porphyrin could compete with iron porphyrins for the combination with the specific proteins which go to make up the heme enzymes. Such a porphyrin would thus be a natural inhibitor, and in a sense a regulator governing the degree of anaerobic versus aerobic metabolism. A porphyrin of ubiquitous distribution that might function in this manner is coproporphyrin. If the facts derived from *H. influenzae* can be carried over to other organisms, then coproporphyrin under certain conditions might function as a regulator for the rate of oxygen consumption by the cell.

A detailed report on the action of porphyrins on other bacteria and also the effect of metalloporphyrins other than the iron-containing ones, will be published in the near future. We wish to take this opportunity to express our gratefulness to Dr. Leonor Michaelis for his continued interest and advice in these studies.

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[1] From the Laboratories of The Rockefeller Institute for Medical Research, New York.

[2] C. L. Hoagland and S. M. Ward, *Jour. Biol. Chem.*, 146: 115, 1942.

[3] M. Lwoff, *Ann. Inst. Pasteur* 51: 707, 1933.