The strictly pharmacological studies reported by S. Loewe record for the first time a full account of the biological control work associated with the chemical identification and synthesis of active compounds as carried out at the University of Illinois and the Bureau of Narcotics Laboratory. This highly successful example of teamwork has furnished new starting points for future inquiries. Some valuable drugs may subsequently be developed from findings of this sort and the problem deserves further study beyond the obviously unpromising attempt to use marihuana compounds in alleviating the withdrawal symptoms of morphine addiction.

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DEPARTMENT OF PHARMACOLOGY,
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# REPORTS

## GUGGENHEIM FELLOWSHIP AWARDS

THE award of ninety-six fellowships and $230,000 to the recipients is announced by the John Simon Guggenheim Memorial Foundation. Forty-one of the newly appointed fellows received their awards under the plan for post-service fellowships available to Americans who are engaged directly in the war effort in the Army, Navy and civilian war agencies. Their fellowships will be held for their use after they are discharged from service. The foundation will make another series of appointments to post-service fellowships in June.

DR. SAMUEL HERRICK, assistant professor of astronomy, University of California, Los Angeles, will carry on studies of navigation. He will investigate its present and prospective methods and instruments and the effect of the introduction of rocket propulsion.

DR. PAUL ERDÖS, mathematician, Ann Arbor, Michigan, will carry out research on polynomials and approximation of continuous functions by polynomials.

Biological studies will be carried on by the following fellows:

DR. CARLOS EUGENIO CHARDON, director of the Institute of Tropical Agriculture, Mayagüez, Puerto Rico: The completion of a historical study of the great naturalists who worked in Latin America. From 1931 to 1935 Dr. Chardon was chancellor of the University of Puerto Rico, and he has acted as agricultural adviser to several Latin American countries.

DR. DENIS LLEWELLYN FOX, associate professor of marine biochemistry, Scripps Institution, La Jolla, Calif. The preparation of a monograph on the physical, biological and biochemical features of the structural colors and pigments of animals.

DR. KENNETH WILLARD COOPER, assistant professor of biology, Princeton University: Studies of the mechanism of sex chromosome conjunction during meiosis in male *Drosophila*.

DR. AARON J. SHARP, associate professor of botany, University of Tennessee: Studies of the correlations between the plants of the Southern Appalachians and the temperate floras of the mountains and highlands of Mexico and Central America. This is the second Guggenheim Fellowship awarded to Dr. Sharp, who is now working in Mexico.

DR. DAMON BOYNTON, associate professor of pomology, Cornell University: A study of ion competition as a factor affecting the inorganic nutrition of plants, with particular reference to potassium-magnesium and nitrogen-phosphorus relationships in fruit trees.

DR. THEODORE C. SCHNEIRLA, associate professor of psychology, New York University, and associate curator of animal behavior, American Museum of Natural History: Studies of the relationship between instinct and learning in insect psychology. Dr. Schneirla is now in Tehuantepec, Mexico, where he is studying the behavior of colonies of army ants. This is the second Guggenheim fellowship awarded to Dr. Schneirla.

Awards of fellowships for postwar work in science were made to:

DR. JOHN WILLIAM CALKIN, professor of mathematics, Illinois Institute of Technology, Chicago; now doing war work in Office of Naval Operations, Washington, D. C.: Mathematical studies of the operational theory of boundary value problems and the application of this theory to differential equations.

DR. EDWIN HEWITT, operations analyst, Army Air Forces; formerly instructor in mathematics, Harvard University: Mathematical studies in the field of topology.

DR. LEO LEROY BERANEK, director of research on sound, Harvard University; now engaged upon war research under the Office of Scientific Research and Development: Research in the field of acoustics and design of acoustical materials.

DR. CHANDLER MCCUSKEY BROOKS, associate professor of physiology, the Johns Hopkins School of Medicine; now engaged upon war research under the Office of Scientific Research and Development: A study of the comparative physiology of the nervous and the neuro-endocrine systems.

DR. SEYMOUR STANLEY COHEN, biochemist at the University of Pennsylvania; now engaged upon war research under the Office of Scientific Research and Development: A study of methods of virus and rickettsial cultivation suitable for and preliminary to investigation of biochemical aspects of the host-virus relationship, with special reference to nucleic acid metabolism.

DR. DEAN STANLEY TARBELL, assistant professor of organic chemistry, University of Rochester; now engaged upon war research under the Office of Scientific Research and Development: A study of the synthesis of colchicine and other organic compounds of biological interest.

LIEUTENANT EDWARD NOVITSKI, Army; geneticist, San

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.

S. GRANICK
H. GILDER

[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.