EVENTS

PHARMACOLOGY SEMINAR

October 18, 1951

SOME ASPECTS OF THE APPLICATIONS OF CATIONIC EXCHANGE RESINS IN MEDICINE. By Evan W. McChesney, Senior Member Biology Division, Sterling-Winthrop Research Institute, Rensselaer, New York.

A recent and promising method for salt-depletion in the treatment of edema is the feeding of cationic exchange resins. These are compounds containing numerous acidic groups, which, in the presence of salts, may give up their hydrogen atoms and fix metallic ions. There are two principal types of cationic exchange resins, one a polymer of sulfonated vinyl and divinyl benzene, and the other a polymer of methacrylic acid and divinyl benzene. The former, a strong acid, gives up its hydrogen ions rapidly in exchange for metallic ions, whereas the latter, a weak carboxylic acid, reaches equilibrium in its exchange reaction only over a period of several days. The carboxylic acid polymer, however, has about twice the exchange capacity by weight. In spite of these differences, at physiological pH there is little difference in their behavior.

Some of the original enthusiasm for the use of resins in place of salt-free diets has waned. The amount of sodium absorbed by the resins in rats appears to be influenced by the level of sodium in the diet. On high intakes, only a portion of the intake is absorbed, whereas in salt-free diets, virtually no sodium is excreted via the resin. There is no adequate explanation for this phenomenon. The suggestion that the exchange takes place entirely in the stomach, before exposure to the salt-containing pancreatic secretions, does not hold, as the carboxylic polymers are inactive at the pH of the stomach.

Cationic exchange resins have affinities for ions other than sodium—in fact, the strength of affinity increases in this order: sodium, potassium, bivalent ions. Fecal analysis in rats indicates that some magnesium, very little calcium (probably due to the insoluble state of a large portion of the calcium in the gut), and an appreciable amount of potassium are removed by the resin. The problem of potassium depletion is successfully solved by using resins in which one mEq. of potassium per gram of resin has previously been substituted. Ammonium ion is also removed, but not amino nitrogen, thiamin, or riboflavin.

W. P. McN.

YALE MEDICAL SOCIETY

October 31, 1951

EXPERIENCES IN KOREA WITH MEDICAL CARE IN FORWARD AREAS. By Captain E. R. Hering, MC, U.S.N., Field Medical Service School, Camp Jejeune, North Carolina.

In November, 1950, after some fifty thousand Chinese troops attacked UN positions near the Chosen reservoir in Korea, forty medical officers handled six thousand casualties in six days. Four thousand of the men, of which two thousand were suffering from frostbite, walked to the rear in weather thirty degrees below zero. Such a military operation was possible because of the way in which the medical corps is organized. The fast moving chain of evacuation begins when an injured man is moved to a battalion aid station by a platoon aid man. After administration of plasma and/or whole
blood he is transferred to a collecting and clearing station for surgical procedures including attention to uncontrolled bleeding, damaged viscera, and chest wounds. Some miles to the rear he may be hospitalized or flown to distant general hospitals.

Civilian defense officials should profit from the vast military medical experiences in Korea. A realistic, well-organized system, centered around small, flexible installations rather than large, permanent hospitals will be of greatest value if our cities are attacked. Civilians must concentrate on casualty sorting, supply, purchasing, and transportation procedures as do the military. Certain aspects of public health and preventive medicine, including mass immunizations for tetanus, and the like, must not be neglected.

J. K. R.

PHARMACOLOGY SEMINAR
November 1, 1951

Physiological Disposition of Drugs Labelled with Radioactive Carbon. By Paul K. Smith, Ph.D., Professor and Chairman of the Department of Pharmacology, George Washington University School of Medicine, Washington, D. C.

Radioactive carbon, although it has a half-life of six thousand years, can be used safely in studying the mechanism of drug action because it is eliminated from the body within thirty days. Labelled salicylates were given to both experimental animals and humans. Chromatography and Craig's counter-current technique were used to isolate metabolites of the drugs. The metabolic products of salicylates separated by this technique were identical with those isolated previously by classical methods. The fates of purines and pyrimidines are being explored in a similar fashion.

J. P. G.

NATIONAL ACADEMY OF SCIENCES
Public Lecture
November 5, 1951

The Microstructure of Living Cells and Their Constituents. By Francis O. Schmitt, Massachusetts Institute of Technology, Cambridge, Massachusetts.

By application of special optical methods, such as polarized light microscopy, it is now possible to infer in the living cell the presence of structures of several hundred Å in size. With the electron microscope the mitochondrial membrane can be seen, while studies of its birefringence have led to an elucidation of its molecular structure. Chemical isolation studies implicate the mitochondria in the synthesis of ATP and show that the spatial relationships of the mitochondrial enzyme molecules are important in determining their characteristic activity.

Application of these techniques has led to many advances in the study of chromosomes, microsomes, and other cellular constituents. Electron microscopic shadowgraph techniques reveal much of crystalline structure, and X-ray diffraction patterns expose more and more of the intra-molecular configurations of proteins. Protein fractionation and electrophoretic studies are being used to investigate proteins and their activity in such cells as the cleaving sea urchin egg and the squid giant axon. Important discoveries will undoubtedly come from the increasing use of these last named techniques.
Collagen fibers and a non-naturally occurring fiber with a longer periodicity have been reproduced in vitro. The technique involves dissolving collagen fibers in acetic acid, passing the solution through a sintered glass filter and crystallizing the water-clear filtrate. This results in the deposition of very small, apparently unorganized fibers as seen through the electron microscope. Addition to the filtrate of a given quantity of salts, or a small amount of glycoprotein with subsequent crystallization, yields highly organized collagen fibers with the same periodicity as that seen in nature (i.e., 640 Å). Addition of larger amounts of glycoprotein results in the formation of the long-spaced fibers, which have a characteristic periodicity of their own. These observations suggest that the in vitro production of other cellular structures and, possibly, of entire cells may soon be accomplished.

J. M. Q.

PHARMACOLOGY SEMINAR
November 6, 1951

NEWER METHODS OF COLLECTING BLOOD FOR TRANSFUSION. By Edwin J. Cohn, Chairman, Division of Medical Sciences, Harvard University.

Processes for the fractionation of plasma have been considerably improved since the last war, so that the various protein fractions may now be isolated with very little change from the natural state. By the older methods, for example, concentrations of ethanol up to 18% and pH as low as 5 were required for the precipitation of albumin. The use of low concentrations of zinc, and in some cases cadmium and lead, significantly lowers the concentration of ethanol required and shifts the point of maximum insolubility toward the physiological range of pH. The metallo-protein complexes so formed are dissociable, and subsequent to separation the ions may be removed with exchange resins.

A machine for immediate fractionation of donated blood was demonstrated. Anticoagulants are not used. The blood is led directly from the vein through a column of exchange resin to remove platelets and calcium. It then passes into a continuous centrifuge, that separates red cells, white cells, and (quantitatively) plasma. Platelets may be eluted from the column, and the plasma may be treated directly for protein separation.

W. P. McN.

PHARMACOLOGY SEMINAR
November 8, 1951

THE ACTION OF FIBRILLATORY AND ANTIFIBRILLATORY DRUGS ON CARDIAC EXCITABILITY. By C. McC. Brooks, Professor and Chairman of the Department of Physiology and Pharmacology, State University of New York College of Medicine, New York City.

The practical and theoretical implications of the recovery phase of excitation have long interested students of the cardiac cycle. The speaker and his co-workers used the open chest of a cat or dog. The heart was driven at a constant rate by an artificial pace-maker, time being plotted as abscissae against thresholds determined by a testing stimulator. The resulting graphs reveal that recovery is not a process which continues at a constant rate of declining threshold, but is represented by a line which dips and rises during the general descent. Stimuli above the threshold ordinarily produce extrasystoles, but result in fibrillation at the dip phase. Extrasystoles may be induced even after a long latent period when the tissue is stimulated early in the T wave of the electrocardiogram. Further
study with this preparation shows that a rise in temperature or heart rate shortens recovery by influence on the absolute rather than the relative refractory period. The auricular effects of vagal stimulation are found to be: increased rate of conduction, shortened recovery period, and increased susceptibility to fibrillation.

Since these studies suggested differences in the chemical aspects of phases of recovery as well as in susceptibility to fibrillation, investigation of drug effects was undertaken. Quinidine does not, as one might expect, abolish the dips (corresponding to periods of maximum vulnerability to fibrillation) in the curve, but it does prolong both the relative and absolute refractory periods. Amarin (a drug similar to chloroform in its ability to render the heart vulnerable to epinephrine fibrillation), surprisingly enough, resembles quinidine with reference to electrical stimulation in that it increases the absolute refractory period. Such experiments suggest that electrical stimulation may operate by a different mechanism than chemical, and hence, "it may be possible to fibrillate the heart by more than one dysfunction." Other hypotheses were suggested, however: (1) that slowed conduction of one drug may allow two waves to exist on the heart at once, should a stimulating drug be added, or (2) that with augmentation of the origin of beats by one drug and shortening of refractory period by another, normal conduction might now be too slow to prevent the simultaneous existence of two waves. Thus "the normal processes are out of phase" permitting "the disorientation which is fibrillation."

O. L. K.