EVENTS

PHARMACOLOGY SEMINAR
December 6, 1951

The life-span of white blood cells measured with radioactive phosphorus. By D. L. Kline, Department of Physiological Chemistry, Yale University.

Researchers widely disagree on the length of life of the white blood cells. Studies thus far are really measurements of the replacement time of destroyed or removed white cells by an animal. In vitro and in vivo work with radioactive phosphorus (P³²) indicates that the isotope is incorporated into the DNA of the nucleus only at the time of formation of the cell. Once in the nucleus, the phosphorus is held there for the life of the cell and not exchanged.

In this study the isotope was administered orally to humans, and blood samples were drawn at intervals and analyzed for DNA P³². A curve, showing the isotopic concentration in the white blood cells plotted against time, was similar in shape to that which had been obtained by Shemin and Rittenberg using N¹⁵ labeled red blood cells. The P³² concentration rose slowly for four to five days, sharply climbed, maintained a plateau from the 6th to the 10th day, and fell off in an S shape.

The random disappearance of an isotope follows the form of a log curve. If DNA P³² had been exchanged during the study, the resultant would have been the typical log curve; this did not occur. Mathematical analysis of the curve indicates that labeled white blood cells disappear from body circulation about 13.3 days after administering the isotope. Since the cells did not appear in large quantities until four to five days after giving the P³², it is possible that they remained at the site of formation for that time.

This method does not distinguish between the types of white blood cells. It appears that the life span of their major components is not a matter of hours, but of days—approximately two weeks.

J. K. R.

YALE MEDICAL SOCIETY
January 9, 1952

Dye intermediates as potential carcinogens: clinical and laboratory studies with benzidine. By J. Wister Meigs and Louis J. Sciarini.

Although not considered to be true carcinogens, benzidine and its derivatives may produce cancer at the base of the urinary bladder after prolonged exposure. Since it is possible that these substances or their metabolites appear in the urine and so give rise to cancer, metabolites of these dyes are being investigated for carcinogenic activity. Feeding experiments are being conducted on both mice and dogs. Further studies on industrial workers have shown that benzidine penetrates the skin as well as the respiratory epithelium; therefore, daily showers and changes of underclothing are recommended for workers exposed to these potentially hazardous substances.

V. S. G.

Influence of hypothalamic lesions upon food intake. By Bal K. Anand and John R. Brobeck.

The hypothalamus has been further implicated as a regulatory and integrative region by the demonstration of a “feeding center” in the lateral
hypothalamic region of the diencephalon of the rat. Marked differences in food intake were observed in a series of 94 female rats as a result of lesions placed in various regions of the hypothalamus. Using the Horsley-Clarke apparatus and electric coagulation, bilateral lesions in the medial hypothalamus at the lateral aspect of the ventromedial nucleus produced obesity due to hyperphagia. Overnight food consumption of as much as 40 gm. resulted in extreme cases. Unilateral lesions in this region were ineffective in producing hyperphagia.

As a result of inadvertent bilateral lesions extending well into both lateral hypothalamic regions, a definite hypophagia resulted to the extent that the rats would starve to death despite ad libitum feeding conditions. By systematically producing small, selective lesions, the location of the feeding center was determined. The relationship between the ventromedial nucleus and the lateral “feeding center” was determined by creating lesions selectively in these regions. A unilateral “feeding center” lesion did not affect the hyperphagia of the animal previously given bilateral ventromedial nucleus lesions. If this lateral lesion was inflicted on both sides, immediate cessation of food intake resulted. Thus, the ventromedial nucleus may be regulatory of the “feeding center,” as evidenced by the lack of inhibition of eating habits when this nucleus was bilaterally destroyed. It seems that eating may be a reflex facilitated by higher centers.

DONALD DEAN DAVIS

Familial Coincidence of Sickling and Thalassemia. By David H. Clement.

A seven-year-old boy, who became extremely ill requiring transfusions, digitalization, and oxygen therapy, and who recovered and remained well for the past two years, showed evidence of sickle cell and Mediterranean anemias. A careful investigation of family history found the sickle cell trait in the father and paternal grandfather and thalassemia minor in his mother and maternal grandmother. The patient is homozygous for neither trait; he is heterozygous for both traits and as such demonstrated the minor forms of both diseases.

Clinical laboratory tests for sickle cell anemia should be made on all patients whose ancestry centers geographically along the northern Mediterranean coast. For accurate results, tests should be conducted with appropriate reducing agents such as ascorbic acid or sodium bisulphite.

In this patient it may be assumed that the diseases are additive, but their precise pathogenesis is obscure.

J. K. R.

TOXICOLOGY SEMINAR

January 14, 1952

The Tribulations of the Industrial Toxicologist. By D. D. Irish, Biochemical Research Laboratory, Dow Chemical Company, Midland, Michigan.

The work done in the speaker’s laboratory has its theoretical basis in comparative biochemistry, i.e., the assumption that every species of living organism has some biochemical difference from every other and therefore that any organism can be eliminated in the presence of any other. Practically, the problem is to discover the toxicological agent that will effect this end at least to a useable degree in that the agent should be able to destroy or at least control the destructive organisms while avoiding injury to man and to most organisms beneficial to man. The scope of the investigations
conducted is extensive, covering insect, plant, microbial, and animal toxicology.

Some of the chief problems involved in this work were discussed. There is the primary problem of insuring the safe use of a product which involves, apart from basic research on toxicity, co-operation with medical and production personnel, and with the sales department in attempts at educating the public in proper use of the material. There is also the very practical problem of having to screen large numbers of new chemicals with relatively few personnel.

Finally, specific cases were discussed where toxicity studies had presented some unusual features relevant to the aforementioned problems. Briefly touched on were studies of styrene, carbon tetrachloride, alkyl halides, silicone compounds, ethylene oxide, and ethylene imine.

R. G.

YALE MEDICAL SOCIETY
Woodward Lecture
January 16, 1952

AUSTRALIAN STUDIES ON TWO MOSQUITO-BORNE VIRUS DISEASES: RABBIT MYXOMATOSIS AND MURRAY VALLEY ENCEPHALITIS. By Sir Macfarlane Burnet, Director, Walter and Eliza Hall Institute for Medical Research, Melbourne, Australia.

In 1951 the Australian government experimentally released the rabbit myxoma virus as a possible means of controlling the excessive rabbit population. In the same year there appeared numerous cases of an often fatal human encephalitis in the Murray Valley, where the rabbit epidemic also was at its peak. A suspected connection between the two diseases initiated the research the results of which Sir Macfarlane presented. These results, however, show that two different viruses account for the two diseases, with one important epidemiological similarity. Both are spread by mosquitoes; hence the similar distribution along the river valleys and also the identical seasonal incidence of the diseases. Rabbit myxomatosis has previously been described in Brazil, and further work showed that it is specific for the rabbit (it can, however, be grown on the chorioallantoic membrane of the chick embryo). Seemingly, the disease belongs to the pox group, its virus being similar to vaccinia.

Murray Valley encephalitis, in contrast, belongs to the group of arthropod-borne encephalitides, being not unlike Japanese B and St. Louis encephalitis. Its range of infectivity in animals is identical with that of Japanese B, but it is serologically different. It is believed to be identical with the Australian X-disease, of which two epidemics are known to have occurred in 1917 and in 1918. The seasonal incidence and age distribution of X-disease and Murray Valley encephalitis are almost identical. The reactivation of this disease probably was due to the fact that 1951 was an especially good "mosquito-year" and to some upset having occurred in the bird-mosquito-bird cycle, to which the virus is usually restricted.

N. A. H.

CARDIOVASCULAR STUDY UNIT
January 23, 1952

EXPERIMENTAL ASPECTS OF HYPERTENSION. By Ephraim Schorr, Professor of Medicine, Cornell University School of Medicine, New York, New York.
VEM and VDM are part of the humoral mechanisms responsible for the control of the capillary bed. They exert no direct effect, but seem to act by respectively increasing or decreasing the sensitivity of the precapillary sphincters to epinephrine. Assay for these substances is done on the mesenteric capillaries of the rat, by using serial dilutions of the sera of substances to be tested. Similarly, the conjunctival vessels of man have been used, under direct microscopic observation. VDM has been identified by Dr. Schorr chemically; it is the iron-storing ferritin. This substance itself is stored in the inactive form, and when released by the liver, spleen, or muscle its -SH groups are freed and thus it becomes physiologically active. This process is anaerobic, while the inactivation, which can occur in the liver alone, requires the presence of oxygen. VEM in contrast is produced as well as inactivated by the kidney alone, being also restricted to anaerobic production and aerobic breakdown.

The relation of these substances to hypertension has been studied in Goldblatt animals. In the stage of rising blood-pressure the VEM is far in excess of VDM; however, when the latter reaches an equivalent level, the blood pressure stops rising. A great increase in the number and size of capillaries accompanies this process. DOCA-produced hypertension does not seem to involve this pathway, since no changes can be demonstrated in the VEM-VDM system or in the capillary bed.

N. A. H.