

physectomized rats there was no significant difference in the average molecular weight between the 2 groups, although the animals on the carbohydrate diet had liver fat with the highest molecular weight of the 4 groups. These animals also had the least amount of fat in the liver. The difference may be due to this being largely a residuum of phospholipid.

Summary. On a high fat diet the glycogen content of the liver was originally lower than on a high carbohydrate diet, but it did not disappear so rapidly from the liver. Hypophysectomized rats had less liver fat and more body fat than controls on the same caloric intake of a given diet. They showed the same conserving action of the fat diet on glycogen. The molecular weight of the liver fatty acids of the control rats on a high carbohydrate diet was significantly lower than those of the 3 other groups.

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Response of Bone Marrow in AKH and RFI Mice to Nucleic Acid.*

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Furth and his associates¹ and MacDowell and Richter² and others have shown that a leukemia similar to the human disease occurs spontaneously in mice, and that by inbreeding of selected individuals the percentage incidence of the condition may be increased to as high as 80%. Furth has developed two strains known as the Akh and the Rfi. The Akh strain carries lymphoid leukemia, and 60% to 80% of all animals which live to be 8 months of age suffer from the disease. The Rfi strain carries myeloid leukemia, and in somewhat older mice from 1% to 2% develop this variety of leukemia. This preliminary report is concerned with attempts to demonstrate additional constitutional differences between these two strains of mice. The most logical approach appeared to be some test of the response of the bone marrow to stimulation. Menkin³ showed that

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¹ *Am. J. Cancer*, 1937, **31**, 276.

² *Cancer Probl. Symposium*, September, 1937, 42-44.

³ Menkin, V., *Am. J. Path.*, 1940, **16**, 13.

sterile inflammatory exudates produced in the pleural cavity by the injection of turpentine contained a substance that provoked leukocytosis when injected into other animals.

Pleural exudates were collected according to the directions of Menkin, and the globulins were precipitated by half-saturated ammonium sulfate. Injections of from 20 to 50 mg of this material caused a leukocytosis of from 18 to 40 thousand in Akh mice and a leukopenia of 6 to 10 thousand in Rfi mice, if the blood counts were made 4 hours after the injection. The average normal white blood count was 11,500 in the Rfi, 12,400 in the Akh. Further chemical study showed that the active principle was precipitated by dilute acids and by ethyl alcohol. It, therefore, seemed possible that the activity was due to some substance associated with the nucleoproteins. Accordingly, 10 to 15 mg of thymonucleic acid were injected intraperitoneally into the 2 strains of mice. The results were essentially the same as those obtained with the exudate. The average white blood cell count after 4 hours in Akh mice was 32,150 and in Rfi mice 9,900. A similar but less striking response was secured with yeast nucleic acid, that is, a leukocytosis in the Akh animals and no change or slight leukocytosis in the Rfi animals.

The above results are based entirely on determinations made 4 hours after the injection of the stimulatory substance. More complete investigation over a 20-hour period showed that the Rfi animals which at the end of 4, 6, and 8 hours had a leukopenia, developed a leukocytosis at the fourteenth and eighteenth hour. Thus the 2 animals both responded with a leukocytosis, immediate in the case of the Akh animal and delayed in the Rfi animal. As a point of further investigation it seemed possible that this difference was due to a difference in the ability of the two strains to hydrolyze the nucleic acid and liberate the actual substance producing the leukocytosis. Thymonucleic acid was digested with duodenal mucosa at a pH of 8.5 for 24 hours. This digest gave an immediate leukocytosis in both strains. Similarly, the two pure chemical substances, adenine and guanine, in 25 mg amounts, produced a leukocytosis in both strains. It should, however, be pointed out that 4 of the 20 animals injected with adenine and guanine gave no leukocytosis.

With this information regarding the effect of the split products of nucleic acid, it became desirable to study the relative amount of the nuclease enzymes in the blood and tissues. These experiments were carried out by determination of the amount of inorganic phosphate liberated from 100 mg of thymonucleic acid at a pH of 7.4 during the course of incubation for 2½ hours. There was no dif-

ference in the amount of enzyme in the liver, but preliminary experiments with blood and with the spleen indicated that almost twice as much inorganic phosphate was liberated in experiments with Akh animals as with Rfi animals.

Finally it is worthy of note that the leukocytosis produced in the Akh strain is primarily a segmented-cell type of response. A typical hemogram four hours after the injection of thymonucleic acid was: lymphocytes, 13; monocytes, 1; segs, 63; stabs, 14; juveniles, 5; eosinophiles, 2; and basket cells, 2.

It should be emphasized that the experiments deal with the response of the bone marrow, while the type of leukemia in the Akh animal is lymphoid. We have not been able as yet to establish any connection between the type of response and the subsequent development of leukemia, in a given animal, but experiments along this line are under way.

Summary. By comparison of the response of the bone marrow to the injection of nucleic acid and its split products a difference has been demonstrated between two strains of mice, Akh and Rfi, the former of which carries lymphoid leukemia and the latter myeloid leukemia.

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Promin in Treatment of Experimental Tuberculosis.

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Promin* is the sodium salt of p,p'-diaminodiphenylsulfone-N,N'- — (dextrose sulfonate).

Greedy, MacLaren, and Lucas¹ reported that promin is effective in streptococcus infections in mice. Feldman, Hinshaw, and Moses² reported that it exerts an impressively beneficial effect on the course of experimental tuberculosis in guinea pigs, even when^{3, 4} treatment

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¹ Greedy, P. H., MacLaren, D. B., and Lucas, C. C., *Can. Med. Assn. J.*, 1939, **40**, 319.

² Feldman, W. H., Hinshaw, H. C., and Moses, H. E., *Proc. Staff Meet. Mayo Clin.*, 1940, **15**, 695.

³ Feldman, W. H., Hinshaw, H. C., and Moses, H. E., *Ibid.*, 1941, **16**, 187.

⁴ Hinshaw, H. C., and Feldman, W. H., *J. A. M. A.*, 1941, **117**, 1066.