

based on different rates of the bell were tested first, with the result that it required 200 positive tests intermixed with 96 negative tests before any sign of regularity occurred in the correct responses to the negative conditioned stimuli. In the first 8 sessions of testing after the operations practically all of the positive tests were correct and nearly all of the negative tests were positive and incorrect. The greatest number of correct negative tests came during the first test session, when 3 out of 12 were correct, the first, second, and fourth. Had the results of the early negative tests been listed as true negative conditioned reflexes, and only a few tests been made, this dog might have been reported as retaining its ability to make correct differential responses in spite of its extirpated cortex.

Another typical example of an external inhibition reflex may be cited from a dog which had acquired correct conditioned differential responses with all the routine analysers before the operation, but which after pre-frontal lobectomy and bilateral removal of large portions of the association cortex (all projection centers except optic were intact) was unable to acquire correct conditioned differential responses with either set of general cutaneous analysers. In some 700 tests after operation practically all of the positive tests were correct and a large proportion of the

negative conditioned tests were positive responses and incorrect. There were, however, 1 or 2 correct negative tests during each day's session, and these could be explained as the result of external inhibition since in these tests there was inhibition of respiration and other movements. The entire picture of every daily session of tests after the operations was one of inability of the dog to make correct differential responses.

That these two negative reflexes are really different is indicated by the following observations: (1) The negative reflex from external inhibition occurs in normal dogs long before there are any signs of correct conditioned differential responses. (2) They may appear in dogs after varying amounts of association cortex have been removed, when correct conditioned differential negative reflexes cannot be executed. (3) The external inhibition reflex is more than mere cessation of nervous activity, for respiration is inhibited and a restless animal becomes quiet. This reflex is apparently simpler than the negative conditioned response and may involve fewer neurons.

These early sporadic inhibitory reflexes have not been observed in all our dogs during the process of acquiring correct conditioned differential responses, but when they do occur it is important that they are recognized.

14352 P

Development of Cirrhosis in the Liver of Dogs Deprived of Both Pituitary and Thyroid Glands.*

I. L. CHAIKOFF, C. ENTENMAN, J. F. RINEHART, AND F. L. REICHERT.

From the Divisions of Physiology (Berkeley) and Pathology (San Francisco) of the University of California Medical School, and the Laboratory of Experimental Surgery, Stanford University School of Medicine, San Francisco.

It was shown recently that the concentration of all lipid constituents (total fatty acids, phospholipids, free and esterified cholesterol) is greatly increased in the blood of the hypophysectomized-thyroidectomized dog.¹ The

present report deals with the condition of the livers of such animals.

The livers of 9 dogs were examined at intervals of 70 to 419 days after they had been deprived of both pituitary and thyroid glands. The completeness of hypophysectomy in all dogs was established at necropsy. A fatty infiltration of the liver was observed in 8 of them. The livers of 6 contained abnormal

* Aided by a grant from the Christine Breon Fund for Medical Research.

¹ Entenman, C., Chaikoff, I. L., and Reichert, F. L., *Endocrinology*, 1942, **30**, 802.

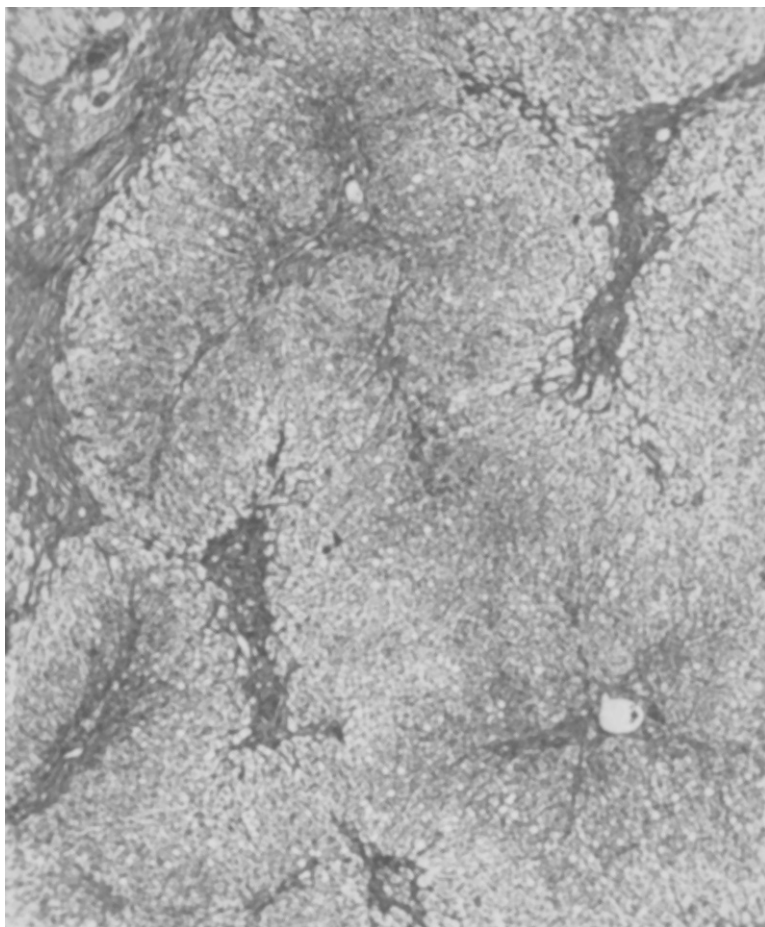


Fig. 1.

Microphotograph of section of liver of dog HT8. Stain, hematoxylin and eosin. Magnification, 73.

amounts of fibrous tissue; all degrees of cirrhosis from early to advanced portal cirrhosis were found. The diet received by these dogs was adequate with respect to calories, proteins, salts, and vitamins and not high in fat. The details of the diet have been recorded elsewhere.¹

A section from a typical liver (dog HT8) is shown in Fig. 1. Excessive amounts of fat are present in the liver cells. The fat is distributed in both large and small droplets. There is a well developed cirrhosis with excessive amounts of fibrous connective tissue in the portal spaces. Fine ramifications of connective tissue radiate outward from the portal areas, in some instances connecting one area

with another.

The high fat content (11 to 52%; average 21%) found in the livers of the hypophysectomized-thyroidectomized dogs is in keeping with previous reports from these laboratories in which it was shown that a fatty infiltration precedes the formation of fibrous tissue in the liver of the dog.^{2,3} Cirrhosis of the liver was not observed in dogs subjected to thyroidectomy alone but in these animals the fat content of the liver did not exceed 11%.

² Chaikoff, I. L., Connor, C. L., and Biskind, G. R., *Am. J. Path.*, 1938, **14**, 101.

³ Chaikoff, I. L., Eichorn, K. B., Connor, C. L., and Entenman, C., *Am. J. Path.*, 1943, **19**, 9.