

The pigeon was number 3 of the series reported by me in 1921.⁷ It was a full grown pigeon, recovered quickly from the operation, and remained healthy and in good condition throughout the 49 days of study.

A microscopic study of the brain by means of serial sections prepared by Mr. Martin W. Schmidt, using the Krause method, was made by Dr. Albert Kuntz. A small residue of apparently living cerebrum was found distributed in three different regions. Two of the regions were contralateral duplicates of each other, located on the mid-ventral surface of the cerebrum, just anterior to the anterior plane of the optic chiasma; and each averaged roughly 1.5 mm. wide, 2.5 mm. high, and 2 mm. long. These regions revealed some good cerebral tissue, with some medullated fibers and neuroglia, apparently in good condition. They also showed in parts, evidences of degeneration and infiltration. The third region was roughly globular in shape, about 1.5 mm. in diameter, and, cut by the frontal plane of the optic chiasma. It lay near the ventral surface of the cerebrum, about 4 mm. from the sagittal fissure. In it there was evidence of degeneration. There were no medullated fibers present. "Holes" showed where cells had been absorbed, and the cells remaining were scattered. The brain stem showed a large blood clot in its center with necrotic tissue around it.

¹ Flourens, P., *Recherches expérimentales sur les propriétés et les fonctions du système nerveux*, Paris, 1842.

² McKendrick, F. J., *Recent Researches on the Nervous System*, Edinburgh, 1874.

³ Ferrier, David, *The Functions of the Brain*, London, 1876.

⁴ Vulpian, E. F. A., *Leçons sur la physiol. du système nerveux*, Paris, 1866.

⁵ Schrader, M. E. G., *Pflüger's Arch. f. ges. Physiol.*, 1889.

⁶ Howell, *Textbook of Physiology*, Sept., 1927.

⁷ Shaklee, A. O., *Am. J. Physiol.*, 1921, lv, 65.

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The Thyroid in Infections and Toxemias.

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The work of Baumann,¹ who demonstrated in 1895 that the thyroid gland contained iodine, and of Oswald,² who a few years later isolated thyro-globulin and the nucleoproteins, contained the

basic facts upon which the modern advancements in prevention and treatment of goiter have been dependent.

We have observed, as has been noted by others, that the normal histological picture in animals, especially the dog, is somewhat variable. In a series of experiments upon dogs, we undertook to produce pathological changes in the thyroid and noted marked changes, many of which were of the hyperplastic type, after production of certain kinds of infections and toxemias. The thyroid glands of laboratory animals which succumbed to peritonitis, pneumonia, etc., most of which were secondary to an operation, were removed and analyzed for iodine content after a small piece was removed for microscopical section. Careful weights of the glands were obtained, making deductions for the pieces removed for section, and iodine determinations made according to the method of Hunter,³ as modified by Kendall.⁴ Peritonitis was also produced by ligation of the appendix and its mesentery, and empyemata produced by injection of streptococci and staphylococci into the pleural cavity. Sections of the thyroid were also removed from animals suffering from intestinal obstruction and severe subcutaneous infections produced by the injection of fecal material. In practically all animals, which were killed by either of the methods mentioned above, the iodine content of the thyroid gland was found to be diminished, and a quite constant destruction of acinal cells noted, with an accompanying attempt at hyperplasia.

In 7 dogs which were killed by the methods mentioned above, the iodine content was compared to that of 7 control dogs of equal weight which were kept and fed under the same circumstances as the dogs which died from infection produced by operations, etc. Analyses revealed 0.147 mg. iodine per kilo of body weight in the thyroids of the dogs with infection and 0.382 mg. per kilo body weight in the thyroids of the healthy control dogs. In other words, the thyroid gland of the healthy animals contained slightly more than twice the amount of iodine which was contained in dogs with infection. The weights of the thyroids, however, varied in a reverse manner. There was 0.294 gm. thyroid tissue per kilo of body weight in the dogs with infection, whereas the healthy control animals had only 0.191 gm. thyroid tissue per kilo of body weight.

There is a gross relation of the amount of colloid to the amount of iodine found by analysis, but instances were encountered when this relation was by no means exact. Many of the thyroids in the dogs which succumbed to infection were so cellular as to be absolutely free from any visible colloid, but were found to have 50 to 60% as much iodine as the thyroid in a normal dog of equal weight.

Apparently, the thyroid cells contain a substance which holds iodine in chemical combination within the cell.

The increase in size seems best accounted for by a hyperplasia. One might expect edema to be an important factor, but, as a matter of fact, very little evidence of edema is seen in the microscopical sections. The microscopical picture of the glands, removed from the animals with infections, varies. There are certain characteristics, however, which are quite constant. A desquamation of the acinal cells into the alveoli with disintegration of the protoplasm, is a constant finding. The cells remaining intact lose their cuboidal shape and become columnar in type. In many cases there is a heaping of acinal cells with papillary ingrowths into the alveoli, in a manner which can scarcely be differentiated from an exophthalmic goiter as found in human beings. Loss of colloid is also universal. This occurs in certain areas, about the section, and resembles the distribution of colloid as seen in a thyroid gland of a patient with a toxic goiter, to whom iodine has been given. In the latter case, however, the colloid is reappearing instead of disappearing.

In a series of thyroids removed at autopsy by Dr. S. M. Gray, a large percentage were decidedly abnormal. These abnormal glands were usually encountered in patients who succumbed to infections. They revealed the pathological changes, including desquamation, hyperplasia, loss of colloid and increased scar formation, which are seen in animals. The thyroid of one patient presented areas which were characteristic of early changes as seen in exophthalmic goiter, adenoma, and thyroiditis.

A lack of iodine in the food or drinking water had previously been assigned as a cause of epidemics of goiter. However, McCarrison⁵ cites an instance, with other data, where the cause and control of endemic goiter had no relation to the amount of iodine in the drinking water. The discovery by Oswald,⁶ that the thyroid gland of a patient with exophthalmic goiter contains less iodine per gram of weight than does the normal gland is pointed evidence that there is a relation between iodine metabolism, and toxic goiter. Marine and Lenhart⁷ claimed a constant relationship between the iodine content and the structure of the gland. The fact, however, that the total amount of iodine in a normal gland and one from a patient suffering from exophthalmic goiter is about equal, suggests that there are other factors, probably more important than the iodine metabolism or deficiency in the production of goiter.

An inconstant swelling of the neck during the course of certain infectious diseases including measles, scarlet fever, typhoid fever, etc., has been recognized for years and emphasized by Garnier.⁸

Roger and Garnier,⁹ as well as McCarrison¹⁰ have reported pathological changes in animals following certain infections and toxemias. McCarrison¹¹ has recently observed that the histological structure of a normal thyroid gland (of rats) can be altered by feeding unbalanced diets.

Summary. All of the data presented in this article point strongly to the fact that the thyroid gland takes an active part in the mechanisms combatting diseases of the body in general. Especially does this seem true in acute infections and fevers. This active relation is not surprising, when we consider the part played by the thyroid in the metabolism of the body. Lesions in the thyroid have been produced by infections and toxic means which strongly resemble the microscopical pictures seen in exophthalmic goiter and toxic adenoma as seen in the human. Since the iodine content of the gland is reduced so markedly during acute infectious processes, experimentally, it seems logical to assume that administration of iodine to patients with infectious processes, especially of the acute type, might be beneficial. We are not yet prepared to state what the action of iodine in such cases might be, and we, therefore, are in no position either to advocate it or to state what might be considered safe dosages in such conditions.

¹ Baumann, E., *Z. für physiol. Chemie*, 1896, xxi, 318 and 481; 1896, xxii, 1.

² Oswald, A., Strassburg, 1900; *Princip. Biochem. Centralb.*, 1902-1903, i.

³ Hunter, A., *J. Biol. Chem.*, 1910, vii, 321.

⁴ Kendall, E. C., *J. Biol. Chem.*, 1914, xix, 250.

⁵ McCarrison, R., *Brit. Med. J.*, 1927, i, 94.

⁶ Oswald, A., *Virchow's Arch.*, 1902, clix, 444.

⁷ Marine, D., and Lenhart, C. H., *Arch. Int. Med.*, 1909, iv, 440. *Ibid.*, 1911, vii, 506.

⁸ Garnier, M., *Le glande thyroïde dans les maladies infectieuses*. Paris, 1899.

⁹ Roger, H., and Garnier, M., *Compt. rend. Soc. de biol.*, 1898, l, 890. *Presse Médicale*, Paris, 1899, i, 181.

¹⁰ McCarrison, R., *Lancet*, 1927, i, 916.

¹¹ McCarrison, R., *The Thyroid Gland*. London, 1917.