

# AUTOTRANSPLANTATION AND HOMO- TRANSPLANTATION

OF THE THYROID GLAND USING THE THYROID CAPSULE AS THE SEAT  
OF TRANSPLANTATION \*

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Having under our care a large number of cretins in whom cessation of the thyroid feeding leads rapidly to a recurrence of myxedema with its train of symptoms, we were led to undertake the following experimental work on autotransplantation and homotransplantation of the thyroid gland in the hope of obtaining sufficient positive results to warrant clinical operative interference. The following experimental operations are presented as a preliminary report.

## AUTOTRANSPLANTATION

We have found that the autotransplants of the thyroid gland into the thyroid capsule was successful in all our cases, corroborating the work of other investigators in autotransplantation.

We have studied three such cases of multiple autotransplantation.

## HOMOTRANSPLANTATION

The homotransplantation of the thyroid gland in animals is of great importance, and yet it has been unsuccessful up to the present time. Success in this form of transplant work would be a great step in solving the question of homotransplantation in general. The tendency of nearly all the workers, especially Manley and Marine,<sup>1</sup> von Eiselberg,<sup>2</sup> Payr,<sup>3</sup> Hesselberg,<sup>4</sup> Salzer,<sup>5</sup> Sermann<sup>6</sup> and Enderlen,<sup>7</sup> has been to

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1. Manley, O. T., and Marine, David: The Transplantation of Ductless Glands, with Reference to Ferments and Function, Jour. Am. Med. Assn., 1916, **67**, 260.

2. Von Eiselberg: Transplantation of Thyroid and Parathyroid Gland, Arch. f. klin. Chir., 1914, **106**, 1.

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4. Hesselberg, Cora: A Comparison of Autoplastic and Homeoplastic Transplantation of Thyroid Tissue in the Guinea-Pig, Jour. Exper. Med., 1915, No. 21, p. 164.

5. Salzer, H.: A Contribution to the Transplantation of the Thyroid Gland, Arch. f. klin. Chir., 1909, **89**, 861.

6. Sermann, Chava: About a New Method of the Transplantation of the Thyroid Gland, Deutsch. Ztschr. f. Chir., 1908, **96**, 440.

7. Enderlen: Experiments on the Transplantation of the Thyroid Gland in the Abdominal Cavity of Cats and Dogs, Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1898, **3**, 474.

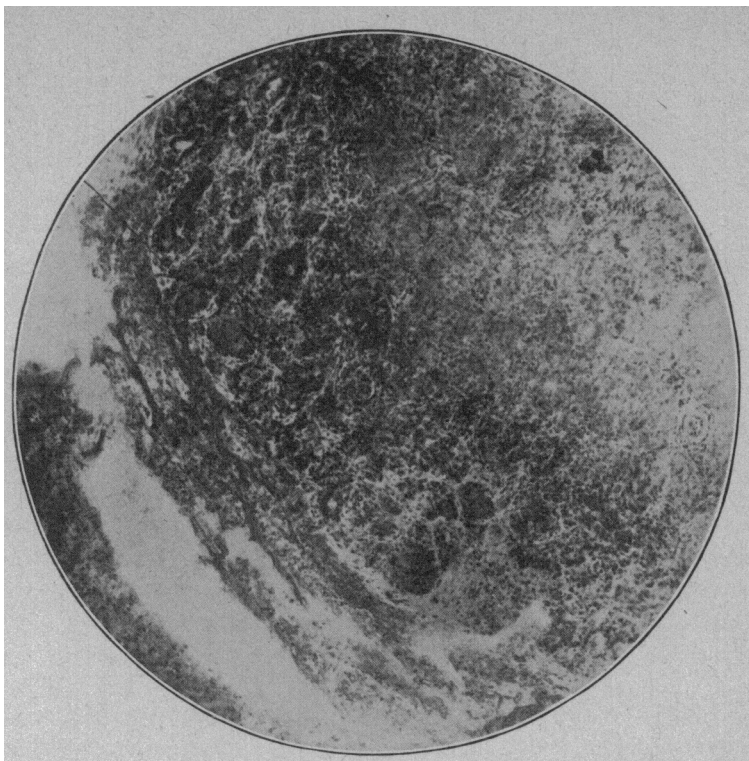


Fig. 1.—Autotransplant into loose areolar tissue in the neighborhood of the thyroid gland, twenty-five days after operation; magnification 15 diameters.

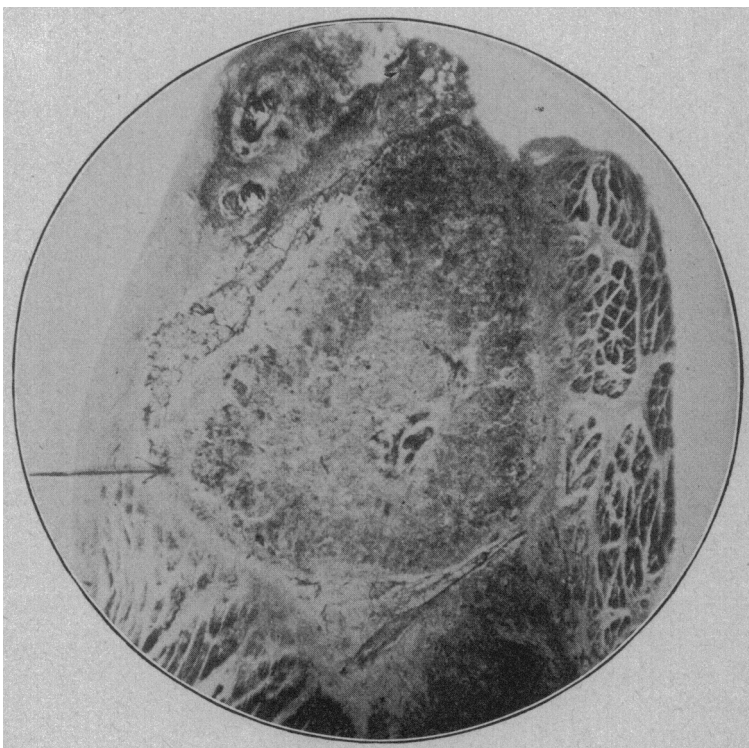


Fig. 2.—Same as Figure 1, magnification 60 diameters.

transplant the thyroid gland into some other portion of the body than into its normal location. Considering the highly specialized function of the organs of internal secretion, it seemed to us that the normal location was the best for definite functional reasons and therefore it seemed logical to us that we should attempt to transplant the organ in so far as possible at the seat of its normal blood supply.

We believe some of the important factors involved in a consideration of the normal position of this organ are, as follows:

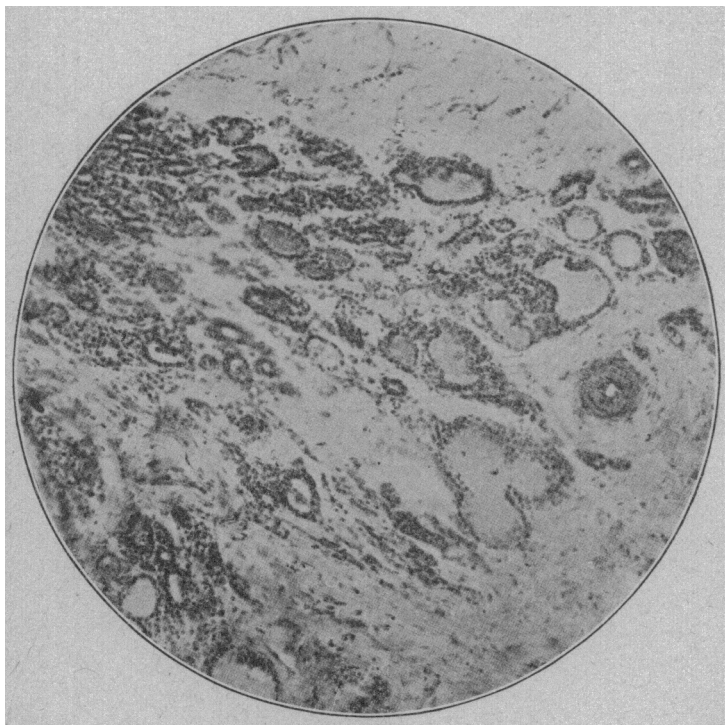


Fig. 3.—Autotransplant into capsule of thyroid gland, sixty days after operation; magnification 230 diameters.

1. The relation of the blood pressure and the size of the blood vessels nourishing this highly specialized organ must have an important bearing on the osmotic pressure of the blood and lymph as well as on the cellular structure of this particular organ, and consequently on its physiology.

2. It would appear that the chemistry of the tissue surrounding the thyroid transplant in intracapsular transplantation ought to be more adapted to its growth than would be the chemical reaction in foreign surroundings.

3. The secretion and iodine content of the remnants of the thyroid fragments within the capsule may be a factor in the retardation of the reaction between host and transplant in a manner similar to the results as shown by Marine, and Manley and Lenhart<sup>8</sup> in their iodine feeding of the host before the transplantation.

A considerable amount of experimental work has been done which, we believe, is conclusive proof that the quantity of secretion of the thyroid gland is regulated by stimuli reaching it through the circulation. Manley and Marine make the following statement in regard to their functional results in autotransplantation:

Inasmuch as such transplanted thyroid tissue undergoes all the morphologic variations associated with growth and function that are observed in nontransplanted thyroid tissue, and inasmuch as transplanted thyroid tissue shows the same reaction with iodine and the same storage of iodine as nontransplanted thyroid, we believe that this is sufficient evidence that such transplants may grow, involute or function equally as well as nontransplanted thyroid gland.

The above quoted experiments lead us to the same conclusions as these authors, to the effect that specific nerves, whether secretory or regulatory, are not necessary for normal growth or functional activity of the thyroid gland.

#### TECHNIC

The next important point in this series of transplants was the preservation of the normal blood supply of the thyroid gland of the host. We attempted to do all our transplant work without cutting off any portion of the blood supply to the gland. This was accomplished by placing our transplants into the thyroid capsule without ligation of any of the vessels supplying the thyroid gland. We accomplished this by splitting the thyroid capsule and removing part, or in some cases practically all of the thyroid tissue. During this time the assistant secured both poles of the thyroid gland between the thumb and index fingers, in this way controlling the hemorrhage without severely traumatizing the intima of the large blood vessels and at the same time establishing a soft thrombus. At the end of eight to ten minutes we found that there was practically no bleeding, and we were ready to insert our transplant into its new bed formed by the thyroid capsule. We believe that the avoiding of injury by clamps and ligatures applied to the vessels supplying the thyroid of the host is of great importance to the transplants. Necropsy showed a complete restoration of the circulation through these vessels in every case examined.

In almost all of the operations we avoided getting the sutures near

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8. Marine, David, and Lenhart, C. H.: On the Effects of the Administration or the Withholding of Iodine Containing Compounds in Normal, Colloid or Actively Hyperplastic Thyroids of Dogs, *THE ARCHIVES INT. MED.*, 1909, **3**, 66; *ibid.*, **4**, 253; *ibid.*, **4**, 440.

the transplanted portion in our closure of the capsule, for it is well known that any foreign body will cause a local leukocytic reaction and connective tissue hyperplasia about such a foreign body; therefore, our sutures were placed either in the capsule or the surrounding connective tissue as far from the transplant as was possible.

We used dogs and guinea-pigs as experimental animals, and performed three autotransplants and thirty-one homotransplants, twenty-seven of these being done on dogs and four on guinea-pigs, applying the above technic in the hope of producing successful results.



Fig. 4.—Homotransplant in puppy 6 weeks old, necropsy 120 days after operation; magnification 60 diameters.

After doing three autotransplants and fourteen homotransplants, using the foregoing operative technic but without paying any attention to the age and familial relationship of the experimental animals or to the type of gland as seen in the individual animals (and it should be remembered that the thyroids of dogs are subject to great histologic variation), we found that the homotransplants had practically disappeared within twenty to thirty days, with the exception of two cases, in which small islands of thyroid tissue remained as isolated areas surrounded by connective tissue. These latter were not of such size as

to offer any considerable encouragement as to the feasibility in human subjects.

We can corroborate the work of Cora Hesselberg, who describes these homotransplants as a degeneration and necrosis in the central portion of the transplant, with an infiltration of leukocytes, lymphocytes and connective tissue cells, which takes place in a varying degree in various animals, depending on the reaction that exists between the host and the tissue used for transplantation.

Believing that age, familial and histologic variations might be important factors in accounting for the failures with the technic given

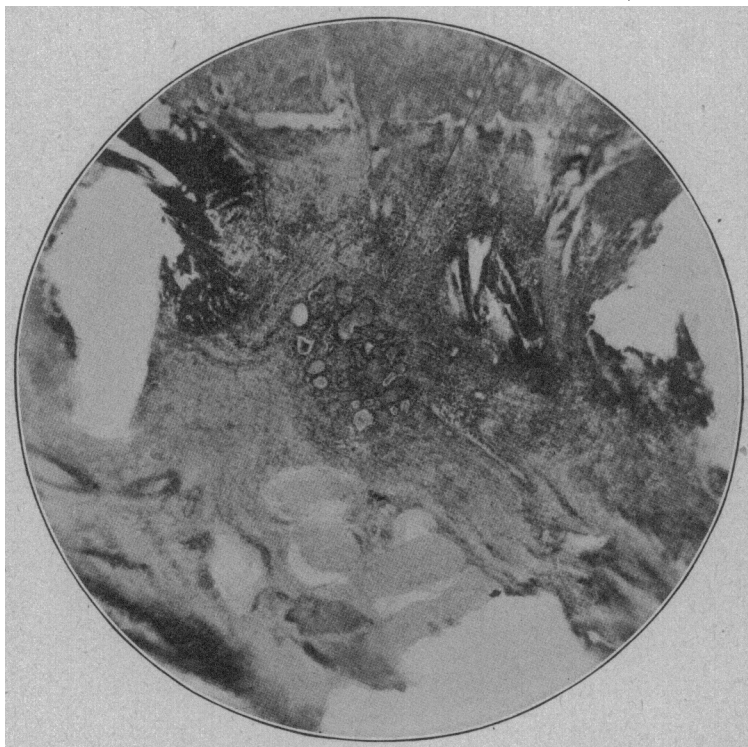


Fig. 5.—Homotransplant in puppy 7 weeks old, necropsy seventh day following operation; magnification 45 diameters.

above, we resorted to the use of young puppies of the same litter, aged from 2 to 6 weeks. We operated on eight puppies, using in each case those from the same litter. Seven of these puppies survived and were necropsied 7, 8, 19, 25, 60, 60 and 120 days, respectively, after the operation. In four of these we obtained living homotransplants, which can be described as follows:

There were small, isolated areas of thyroid alveoli, surrounded by new connective tissue or the capsule of the thyroid gland.

Many of the alveoli were seemingly normal in size. The cells were high and cuboidal in shape. Their nuclei stained well and the arrangement of the alveoli was normal. Many of the alveoli were filled with colloid material.

Dog 23 (Fig. 4), a female puppy, which was 6 weeks old when operated on, nursed its mother for several days following the operation and necropsy was performed 120 days after the operation. The transplant in this case was taken from a male puppy of the same litter. The surviving islands of thyroid tissue were embedded in areolar connective

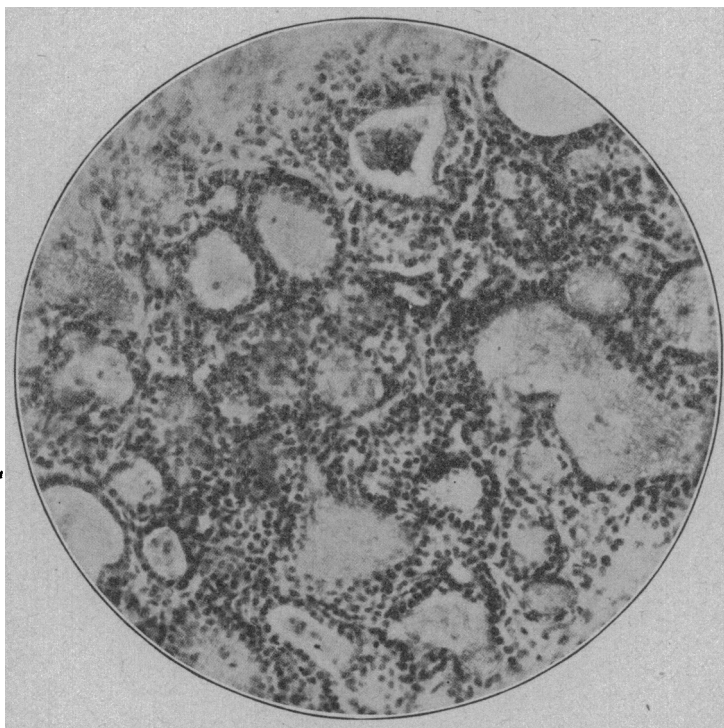


Fig. 6.—Same as Figure 5, magnification 230 diameters.

tissue, which was well organized with the remainder of the thyroid and connective tissue of the capsule proper.

Dog 24, a puppy, aged 7 weeks, was brought to necropsy on the seventh day following operation. The transplant had been taken from another puppy of the same litter (Figs. 5 and 6). There was a large area of transplant which showed quite marked degenerative changes and invasion of leukocytes and lymphocytes. At one side of this transplant there seemed to be a well-defined area of fairly normal-appearing thyroid tissue, which had the typical form of alveoli, filled with colloid material. The cells themselves were somewhat flattened, but the nuclei

stained very clearly and distinctly. This transplant showed changes similar to those seen in Dog 25, with the exception that there was not so much living thyroid in evidence.

Dog 25 (Figs. 7 and 8), a puppy, aged 7 weeks, of the same litter as Dog 24, from which the transplants were taken, was brought to necropsy on the eighth day. The transplanted thyroid showed a considerable hemorrhage, but not a great deal of infiltration of leukocytes and lymphocytes. There was a large part of this transplant which

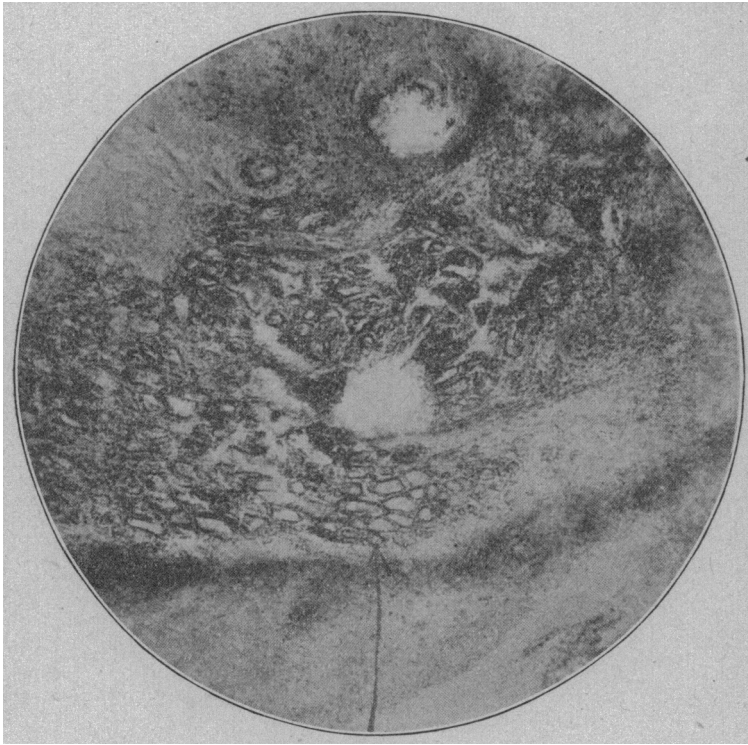


Fig. 7.—Homotransplant in puppy 7 weeks old, necropsy eight days after operation; magnification 50 diameters.

appeared almost normal. The alveoli of the living tissue were well arranged. Some of these alveoli were filled with colloid material. The nuclei stained well, but the cells were slightly flattened. Around the periphery of this transplant there was a large infiltration of leukocytes and lymphocytes. We believe that this thyroid transplant was living and well organized, but showed degenerative changes which were marked by the small alveoli and the flattening of the cells.

Dog 18, a puppy, aged 4 weeks (Fig. 9), was brought to necropsy sixty days after operation. A pocket had been made in the gland with-

out removing any of the capsule, and a piece of thyroid 1 by 2 by 4 mm. from a pup of the same litter had been planted into the capsule, which had been closed without suturing through the transplant. At necropsy the transplant showed some degenerative changes, some hemorrhagic areas, and some lymphoid and leukocytic infiltration, but there were many small, isolated areas of thyroid tissue, which, however, had lost their alveolar arrangement. There were a few alveoli present in this mass which showed a small amount of colloid. The thyroid cells in this mass stained perfectly and the nuclei were very distinct. This area lay just beneath the suture line.

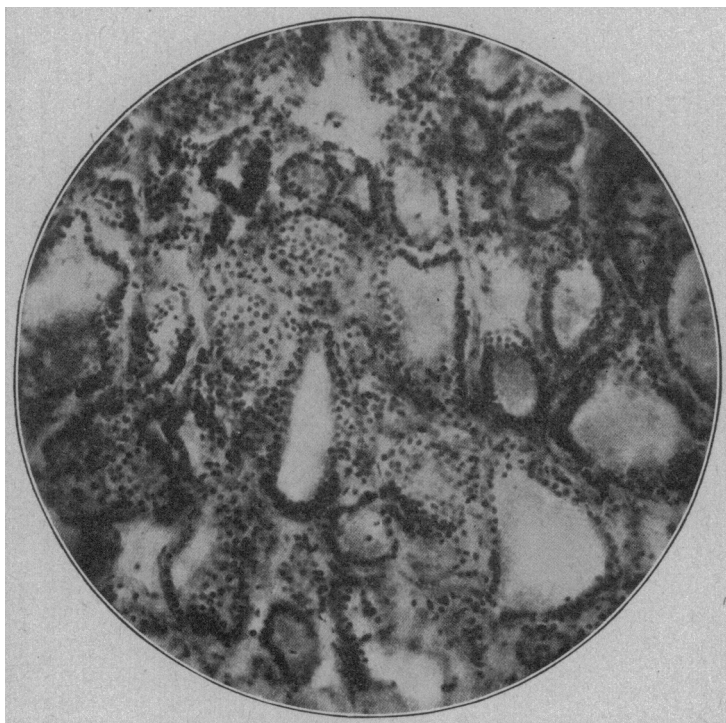


Fig. 8.—Same as Figure 7, magnification 230 diameters.

In the other three no such positive result was demonstrable. In two of these dogs, Puppies 16 and 17, the transplant was destroyed in sectioning the tissues.

In the four puppies described which were operated on with tissues taken from puppies of the same litter there seemed to be less destructive reaction between the host and the tissue transplanted into the thyroid gland than in the older dogs from different litters, and therefore these transplants survived in a manner similar to that seen in autotransplantation, but with much smaller islands of living tissue. The

results shown in Figs. 5, 6, 7 and 8 may be open to question because of the short time between operation and necropsy, seven and eight days, respectively. However, we have based our conclusions on the well-preserved sections of tissues as shown in photomicrographs.

#### TRANSPLANTATION AFTER REPEATED PRELIMINARY TRANSFUSION

We cross-transfused several animals over a period of several weeks, giving from two to four injections at intervals of one week, using from 40 to 100 c.c. of freshly drawn citrated blood from each animal, which

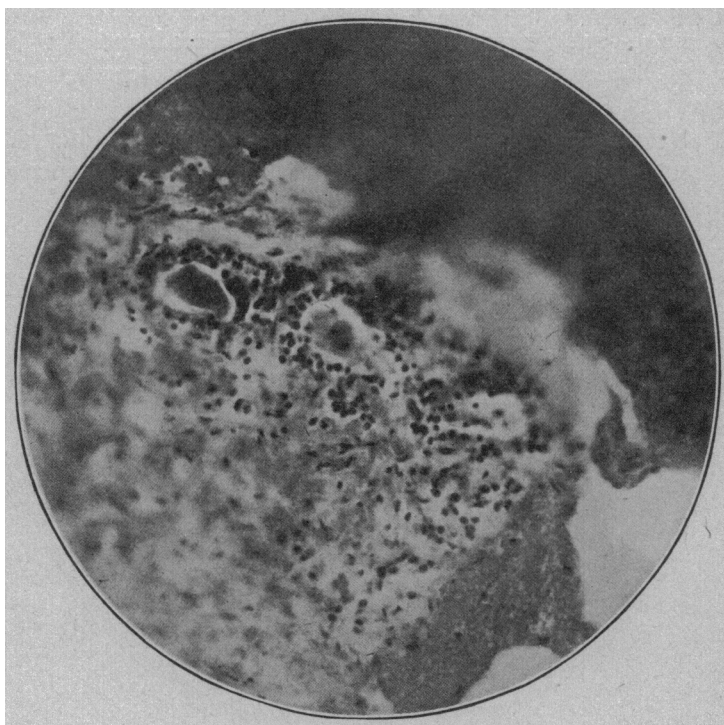


Fig. 9.—Homotransplant in puppy 4 weeks old, necropsy sixty days after operation; magnification 230 diameters.

was rapidly injected intravenously. Following this preparation, we cross-transplanted the thyroid glands, in each instance using the thyroid capsule as the seat of the transplant. Tests were made for the production of isohemolysins and iso-agglutinins in the two sets of dogs operated on, following two preparatory transfusions in one set and three in another set of dogs, but none were found.

We obtained the same results as Lexer and Morris, namely, this seemed to increase the reaction between the host and the transplanted tissue and thereby hastened the destruction of our transplants. It seems

to us, therefore, that to prepare the animal for transplantation would mean to prepare the blood and tissues in such a way that a leukopenia rather than a leukocytosis would be produced in the region of the transplant. To produce this seems to be the stumbling block in the efficiency of the homotransplant work.

#### CONCLUSIONS

We believe that the transplantation of autotransplants and homotransplants of highly specialized organs into the region normally occupied by these tissues is worthy of further trial.

We believe there should be a minimum disturbance of the blood supply in the region in which the transplant is placed, and that foreign bodies, such as suture material, should not come into contact with the transplant.

The varying degree to which a homotransplant takes depends on the amount of reaction between the host and the tissue transplanted, and so far we have found no means either in the blood or in the thyroid gland itself by which we could determine the factor which produces this different condition in the various animals.

A familial relationship and probably the early age of the animals on which operation was performed were important factors in our results.

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