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Histopathological changes in experimental free thyroid transplants

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Introduction

DISTRESSING dysphonia and disabling dysphagia may affect many patients with lingual and subhyoid thyroids. Many other pathological changes may complicate the thyroid tissue in these particular sites (Fish and Moore, 1963; Wertz, 1974). As these ecotopic thyroids are the only thyroid tissue in the body in 70–80 per cent of these cases (Emanuel *et al.*, 1976), many surgical procedures have been attempted to alleviate the patients' symptoms, at the same time preserving some thyroid tissue.

Undoubtedly, transplantation of the thyroid tissue with its intact blood supply forms the ideal surgical procedure which could be applied for this condition (Skolnik, 1963; Wertz, 1974; Emanuel *et al.*, 1976). However, the perfection of this procedure is not easily attained. As an alternative approach, free thyroid transplants have been tried at different receptor sites by different authors, with very variable degrees of success (Shafey and Longmire, 1967; Wertz, 1974).

It was therefore decided to transplant free thyroid tissue experimentally in dogs, in a new receptor site, by two different techniques, and to investigate the degree of survival of these implants as a first step for assessing its functional capabilities.

Materials and Methods

This work was carried out on adult dogs of both sexes, with an average weight of 9 kg. Anaesthesia was induced with thiopentone, 25 mg/kg mixed with 0·05 mg atropine sulphate, intraperitoneally. In each dog, total thyroidectomy was performed and one lobe was implanted subcutaneously in the scrotum or the labia majora. They were classified into two groups, A and B. In group A, the thyroid lobe was bisected and everted before transplantation, while in the other group it was implanted with its capsule intact. Fourteen dogs in each group were studied. Four dogs from either group were sacrificed at the end of the second and the fourth weeks, while the rest of the animals in both groups were sacrificed at the end of the sixth week. In each animal, the transplantation site was removed, fixed, dehydrated, cleared, embedded in paraffin and cut in 8 μ sections that were stained with haematoxylin and eosin. The general condition, weight, appetite and behaviour of each animal were observed.

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Results

The general condition of all the animals, in both groups, remained good and their appetite did not change. The average weight of the dogs in both groups also remained unchanged. The skin incision healed with first intention in all animals. At the end of the second week, in dogs of group A, there were early necrotic changes in the central part of the autograft. The acinar cells showed flaring of the borders, very hazy cytoplasmic components and necrotic nuclei (pyknosis, karyorrhexis and karyolysis). The colloid content was faintly-staining, fragmented and granular. The interacinar spaces were heavily infiltrated by neutrophils and macrophages which were seen to infiltrate the lumina of some acini. Thin-walled, congested vascular spaces could be detected all over the graft, particularly at the periphery of the necrotic area (Fig. 1). Surrounding the previously necrotic zone, there were surviving acini, with either faintly-staining or absent colloid. The lining epithelium of these acini was of the high cubical type (Fig. 2). At the end of the fourth week, the central parts of the autografts in group A showed almost complete absence of thyroid tissue, which was replaced by fibrous tissue (Fig. 3); while, at the periphery, there were many acini with moderately-stained colloid. Buds from the acinar epithelium were seen in the surrounding connective tissue, and this suggests regeneration and proliferation of the acinar cells (Figs. 4 & 5). The

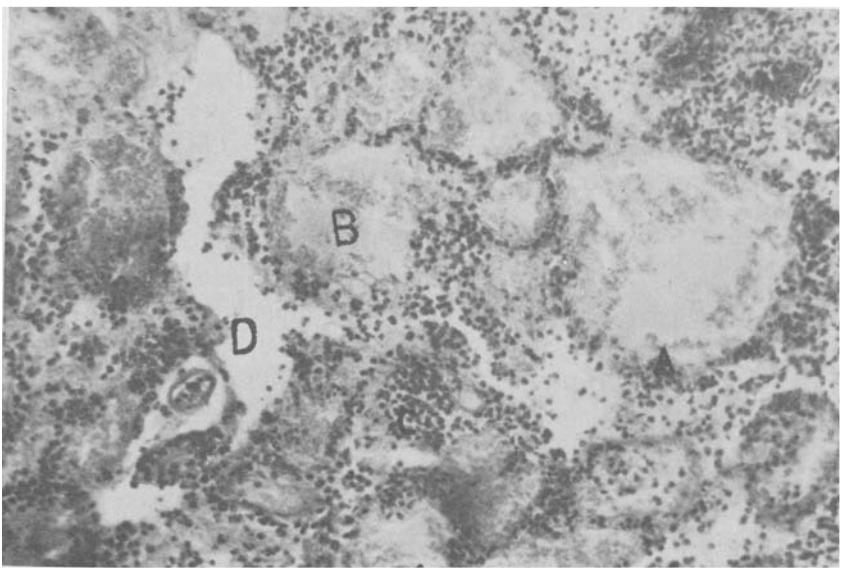


FIG. 1

A—Degenerating acinar cells.
B—Fragmented, granular colloid.
C—Neutrophils and macrophages around the acini.
D—Vascular spaces.

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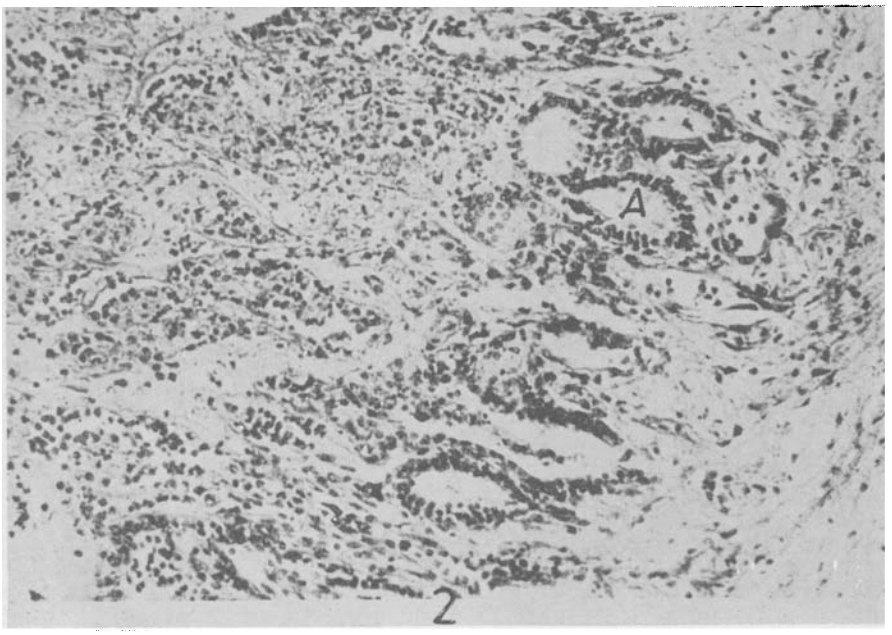


FIG. 2
A—Acini with high cubical epithelial lining.

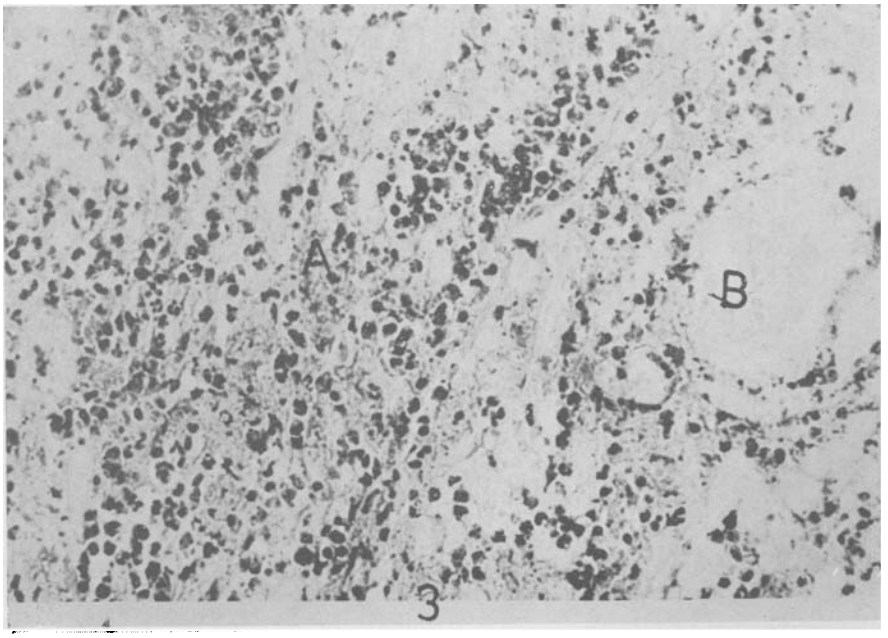


FIG. 3
A—Fibrosis with chronic inflammatory cell infiltration.
B—Residue of an acinus.

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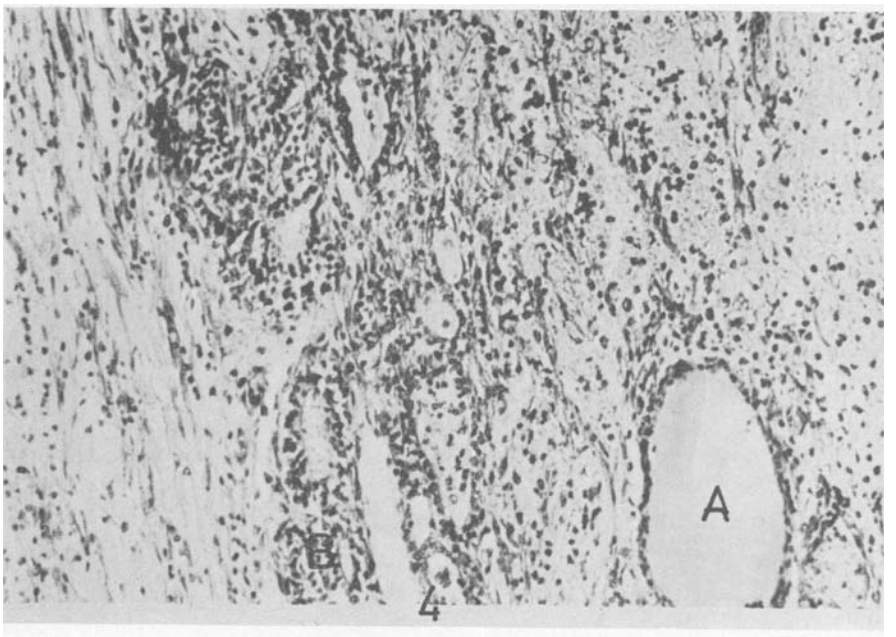


FIG. 4

A—Acinus with normally-stained thyroglobulin.
B—Buds from acini × 10×10.

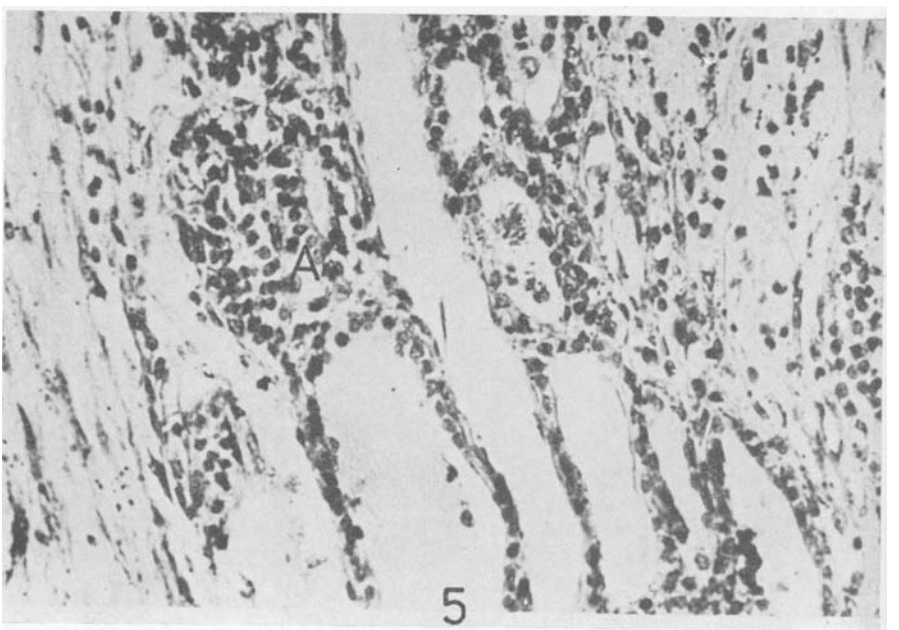


FIG. 5

A—Magnified buds × 10×20.

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peri-acinar connective tissue showed leucocytic infiltration. The central part of the grafted thyroid which was removed at the end of the sixth week showed complete fibrosis, with chronic inflammatory cellular infiltration and thin-walled blood spaces. The peripheral zone contained an increase of thyroid acini filled with normally-staining colloid. These acini were lined with flat cubical epithelium, and they were surrounded by fibrosis and chronic inflammatory cells (Fig. 6).

The autografts in group B which were examined at the end of the second week showed the same histopathological findings as those in Fig. 1, with a much denser infiltration by neutrophils and macrophages (Fig. 7). At the end of the fourth and sixth weeks, the grafts were replaced by fibrosis, which was seen to merge with the adjacent connective tissue. Very few scattered acini with faintly-staining colloid could be seen at the periphery of some grafts at the end of the fourth week. These acini were undetectable in the specimens which were removed from the animals in this group at the end of the sixth week (Fig. 8).

Figure 9 shows normal thyroid tissue from the unimplanted thyroid lobe.

In general, in all animals of group A, there was survival of thyroid acini, in irregular form, with normally-staining thyroglobulin at the periphery of the autografts. The autografted thyroid tissue in group B showed complete fibrous replacement in all animals at the end of the sixth week.

Discussion

Lingual and subhyoid thyroids have received prolonged and vigilant attention from many authors. Dysphagia and distressing dysphonia are present in many cases, in addition to the cosmetic troubles that are commonly associated with a subhyoid thyroid. There are more than 400 reported cases of this disease (Wertz, 1974). This type of ectopic thyroid is the only thyroid tissue in the body in 70–80 per cent of them (Emanuel *et al.*, 1976). Ulceration and hypertrophy frequently affect these thyroids, resulting in aggravation of symptoms already present. The hypertrophy is probably due to over-activity of TSH on this quantitatively deficient and marginally functioning thyroid tissue (Wertz, 1974). The excessive, prolonged action of TSH on the quantitatively deficient glandular tissue may explain the high incidence of carcinomatous changes, which occur in 6 per cent (Fish and Moore, 1963) of cases.

In humans, many surgical procedures have been attempted, to preserve the thyroid tissue and at the same time to alleviate the patients' symptoms. Skolnik (1963), Wertz (1974), and Emanuel *et al.* (1976) have shown that the ideal way to attain this goal is to transplant the tissue with its blood supply intact. However, this pedicled grafting needs long training and experience for its perfection, and the patency of the blood vessels can never be guaranteed after transplantation to the new receptor site. Free thyroid

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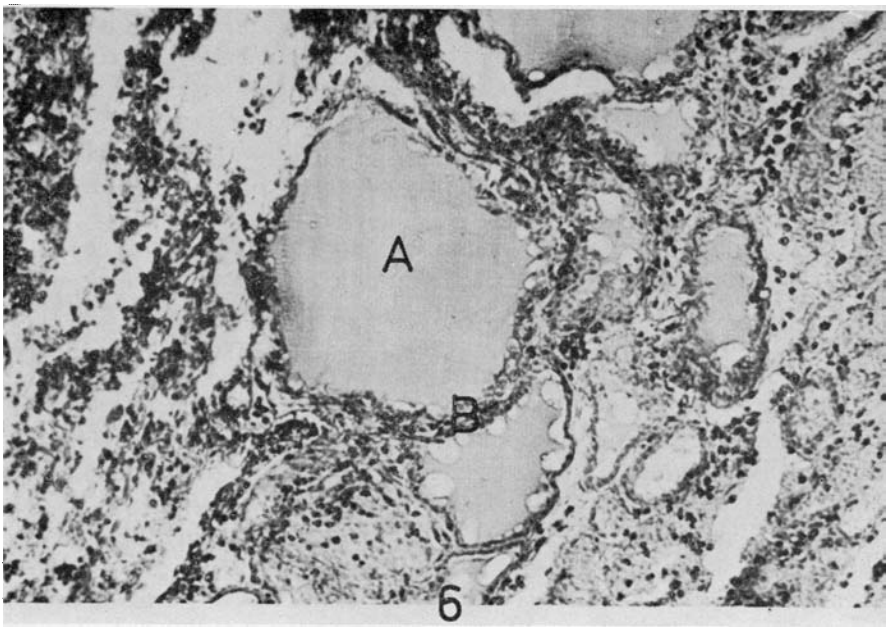


FIG. 6
A—Thyroid acini with normally-stained colloid.
B—Thick fibrous walls.

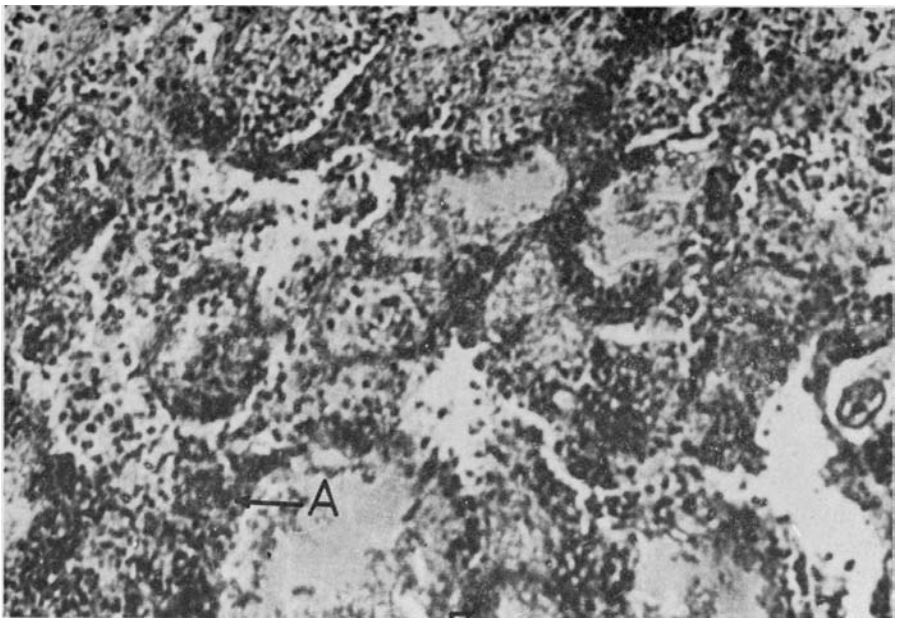


FIG. 7
A—Denser cellular infiltration as compared to Fig. 1.

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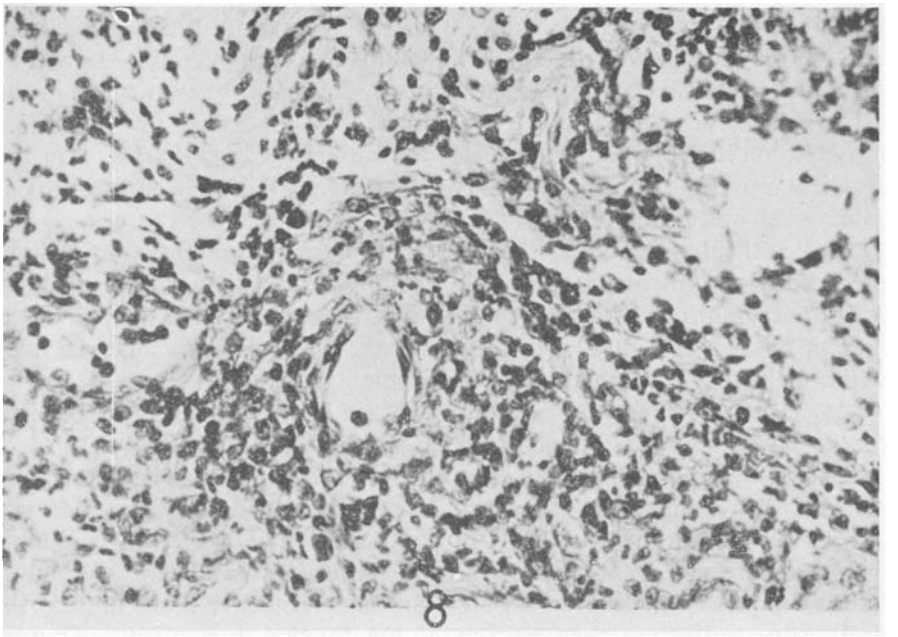


FIG. 8
Complete fibrous replacement of thyroid tissue.

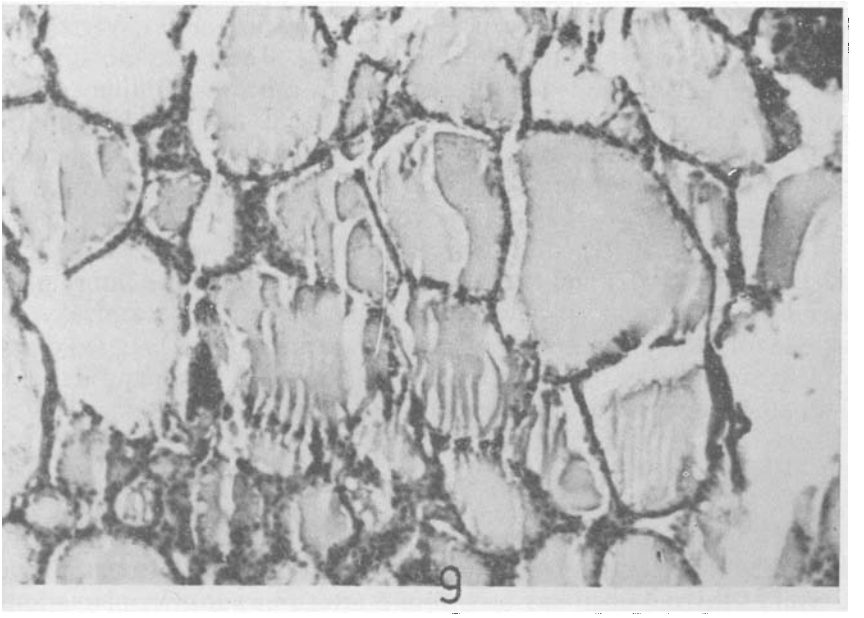


FIG. 9
Normal thyroid acini in dogs.

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autografts have also been studied by many workers at different receptor sites, as an alternative to pedicled grafting, with very variable degrees of success. Thyroid sheets have been autotransplanted subcutaneously in the neck (Rosen and Walfish, 1967; Long *et al.*, 1964), between the abdominal muscles, in the liver and on the pectoralis muscle (Swan, 1967), between the cervical muscles (Jain, 1969), and at different sites in a single patient (Steinwald and Muehrcke, 1970). Wertz (1974) defined the criteria for successful thyroid implants: they should have a life-time function without the need for supplementary thyroid hormones; and they should not produce functional or cosmetic troubles. This author reported that no single patient has yet met these criteria; however, a few patients have survived without thyroid supplement or undesirable hypertrophy.

In dogs, free thyroid autografting to the surfaces of muscles beneath the deep fascia have survived in all cases (Shafey and Longmire, 1967).

In the present study there has been a very acceptable survival of thyroid acini, with normally-staining thyroglobulin, particularly in the marginal zone, after free autoimplantation of the bisected and everted thyroid lobe, into a new receptor site, viz. scrotum or labia majora. There were many buds of acinar epithelium in the surrounding connective tissue around the graft, thus indicating regeneration of the thyroid acinar cells. Thyroid lobes which were implanted with their capsules intact did not show any surviving acini in any case. The surviving acini in the first group (A) acquired a relatively thick fibrous wall, which was surrounded by chronic inflammatory cells. This confirms the suggestion of many authors that free thyroid autografts should be transplanted in thin sheets (Wertz, 1974; Swan, 1967; Steinwald and Muehrcke, 1970). There was no difference between animals in the two groups as regards general condition, appetite, behaviour or average weight after the experiment, in spite of the contrast in survival rate of the thyroid acini in the two groups. Work is already in progress in our laboratory to assess the functional state of these free thyroid autografts.

The findings of this study have confirmed those reported by Shafey and Longmire (1967) and they show great promise for the future of free thyroid autotransplants in new receptor sites, not only for ectopic thyroids, but also for other purposes. The thyroid tissues should be exposed directly to their surrounding tissues, preferably in sheets, as a prerequisite for the histopathological survival of the acini.

Summary

Free thyroid autotransplants into new receptor sites have been tried in 28 dogs, by two different techniques. Good but irregular histopathological survival of thyroid acini has been found after free autotransplantation of bisected and everted thyroid lobes into the external genitalia of dogs. The results have been very encouraging and the functional assessment of these

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implants is essential; such work is already in progress in our laboratory. Our findings and their significance have been discussed.

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