SURGERY AND PATHOLOGY

OF THE

THYROID AND PARATHYROID GLANDS

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WITH 57 ILLUSTRATIONS IN THE TEXT AND 40 FULL-PAGE PLATES,
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TO

DR. CHARLES H. MAYO,

IN RECOGNITION OF HIS SPLENDID WORK IN THE DEVELOPMENT OF THYROID SURGERY IN AMERICA,

THIS VOLUME IS DEDICATED BY

THE AUTHORS.

PREFACE.

The great interest that surgeons and pathologists are experiencing in the study and treatment of diseases of the thyroid and parathyroid glands seems to justify the production of the present volume, which has been planned to bring to the practitioner of surgery and medicine the result of a study of the work of those who have given much time to the development of this special field. It also includes the clinical and technical personal experience in the surgical treatment of a large number of patients suffering from diseases of the thyroid gland which have come under the care of the senior author during the past twenty years. It has seemed proper to give special emphasis to details which have practical value in the diagnosis and treatment of exophthalmic goitre, because in this matter this book will probably have its greatest field of usefulness.

In the chapter on thyroid pathology the attempt has been made to simplify as much as possible our understanding of goitre. A basis for a clinical and pathological correlation of the symptoms and morphological changes in the thyroid gland in exophthalmic goitre has been offered by Dr. Louis B. Wilson, and we have taken full advantage of his excellent study of the subject. We are also indebted to Dr. Wilson for several illustrations which accompany the text. The organization of surgical clinics has made possible, by the proper relationship of surgeon, internist and pathologist, not only the most satisfactory treatment, but also the most advanced pathological study of this disease that we are able to offer at the present time.

An apology for the compilation of the main facts regarding the parathyroid glandules here presented is not necessary. These vital organs have been too long neglected, both in medical text books and in medical teaching. Most students have never seen the parathyroid glandules, and there is no text book that devotes more than a brief paragraph to these bodies—organs that are necessary for the maintenance of life. In fact, until the excellent chapters of Dr. George Dock appeared in Osler's Modern Medicine even the more exhaustive books had practically disregarded these glandules.

The author of this section of the book wishes to express his indebtedness to Professor Ludwig Pick, Director of the Pathological Institute, Friedrichshain, Berlin, for assistance and stimulation which has led to the accomplishment of much of the original work by the author that is included in these chapters.

The section of the book on the thyroid gland, with the exception of the chapter on pathology, is written by the senior author; this chapter and the section on the parathyroid glandules are by the junior author.

A. J. Ochsner.
R. L. Thompson.

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PART I.

CHAPTER I.

THE SURGICAL CONSIDERATION OF THE THYROID GLAND.

INTRODUCTION.

The first decade of the present century has added the treatment of the diseases of the thyroid gland to the surgical side of our art. This applies more especially to that form of disease which had been most discouraging heretofore, and which now is one of the most satisfactory conditions in the field of major surgery—namely, the disease generally known in America as exophthalmic goitre.

Although the diagnosis is practically never difficult at the time at which these patients come into the care of the surgeon, still it has seemed to be of great importance to discuss extensively the diagnosis and differential diagnosis, and with this the history, etiology, symptomatology and physical findings.

The treatment, after-treatment and prognosis will be considered in detail, and special care will be taken in making clear the points in the technic that seem of importance in making the operative treatment safe and the results immediately and ultimately successful.

In the search for support for the various ideas incorporated in this volume in the literature of the subject there have been encountered in the original and in abstracts and references nearly twelve hundred monographs, articles and case reports, less than ten per cent. of these being surgical.

It would be quite useless to enumerate these and many others which a further search of the literature would reveal, and consequently only those have been added to the bibliography that have aided very materially in the development of the surgical side of the subject.

HISTORY.

The surgical history of the diseases of the thyroid gland is extremely meager before the last quarter of the past century, when the remarkable work of Theodor Kocher attracted the attention of the entire surgical world by his practical demonstration—first in a few, then in hundreds and later in thousands of cases—that thyroidectomy, if performed skillfully, is not the extremely dangerous operation that the earlier surgeons had pictured.

He eliminated the principal dangers—namely, those from anæsthesia, sepsis, hæmorrhage, shock, hyperthyroidism, cachexia strumipriva, injury to the recurrent laryngeal nerve and injury to the parathyroid glands—and gave us relatively an exceedingly safe surgical procedure. In many of these features, and especially in many of the details, much important support came from other sources.

Moebius supplied a most important element for the rational surgical treatment of the important class of exophthalmic goitre by his logical and convincing studies, which made it clear that in this disease there is absorption of an excessive amount of substance secreted by a diseased gland, which enters the general circulation through the lymphatic system.

This important element will be referred to at length at the proper place. In connection with this part of the history of this subject it is proper to state that Rehn pointed out just a quarter of a century ago the splendid effect of surgical treatment on exophthalmic goitre, and Tillaux had pointed out similar results four years earlier in the year 1880, although he had no definite theory by which he could explain the great benefit obtained by excision of the gland. There can be no doubt, however, that the surgical treatment of exophthalmic goitre resulted directly from the surgical work of Kocher in simple goitre and the pathological and physiological explanation of Moebius.

In this as in most other instances, the benefit of operative treatment of exophthalmic goitre was first observed accidentally in cases in which the goitre was removed, not to cure this disease, but to relieve pressure or deformity.

To the development of the technic much has been added by the work of Dr. C. H. Mayo, of this country, who has the largest personal experience in the treatment of exophthalmic goitre at the present time.

The subject of exophthalmic goitre in its clinical aspect dates back much further than the entire subject does in the surgical aspect. As early as 1786, more than one and a quarter centuries ago, Parry described this disease clearly, and in the year 1800 an Italian physician of the name of Flajani described a disease much less clearly which undoubtedly represented the same condition. In the year 1828 Adelmann directed attention to the goitre heart.

In the year 1835 Graves described this disease in his lectures, which were published in book form eight years later—hence the name of Graves' disease. This description was so clear that it was accepted as typical by English speaking physicians throughout the world.

In 1840 v. Basedow described this disease in Germany, and since then it has been known as morbus Basedowii, although the term was not formally adopted until 1858, following the suggestion of Hirsch.

From the standpoint of symptomatology and diagnosis the observations of Charcot in 1856, those of v. Graefe in 1864, those of Stellwag in 1865, those of Marie, beginning in 1856 and continuing for a period of forty years, seem to be of special importance, and will be considered fully in the discussion of that portion of our subject. In 1873 Gull described myxœdema. In 1882 Kocher established the fact that this condition can be brought about regularly by removing the entire thyroid gland—hence his introduction of the term cachexia strumipriva. The most important historical data regarding this portion of our subject, however, seems to be that Moebius was able in 1886 to permanently establish the fact that exophthalmic goitre is a "form of poisoning of the body through a diseased activity of the thyroid gland," and not a disease due to some primary lesion of the central nervous system, especially the medulla oblongata; neither a disease due to a pathological condition of the sympathetic nervous system, nor a form of hysteria. It is a disease due to a pathological development in the thyroid gland itself. From the surgical standpoint the correctness of this theory had already been proven by the cure of many patients suffering from this disease whenever the diseased gland has been removed. There are two publications, one published in France by Tillaux in 1880 and the other in Germany by Rehn in 1884, which seem of specially great historical interest. The establishment of technic which ensures safe and permanent surgical treatment belongs to our contemporary surgeons.

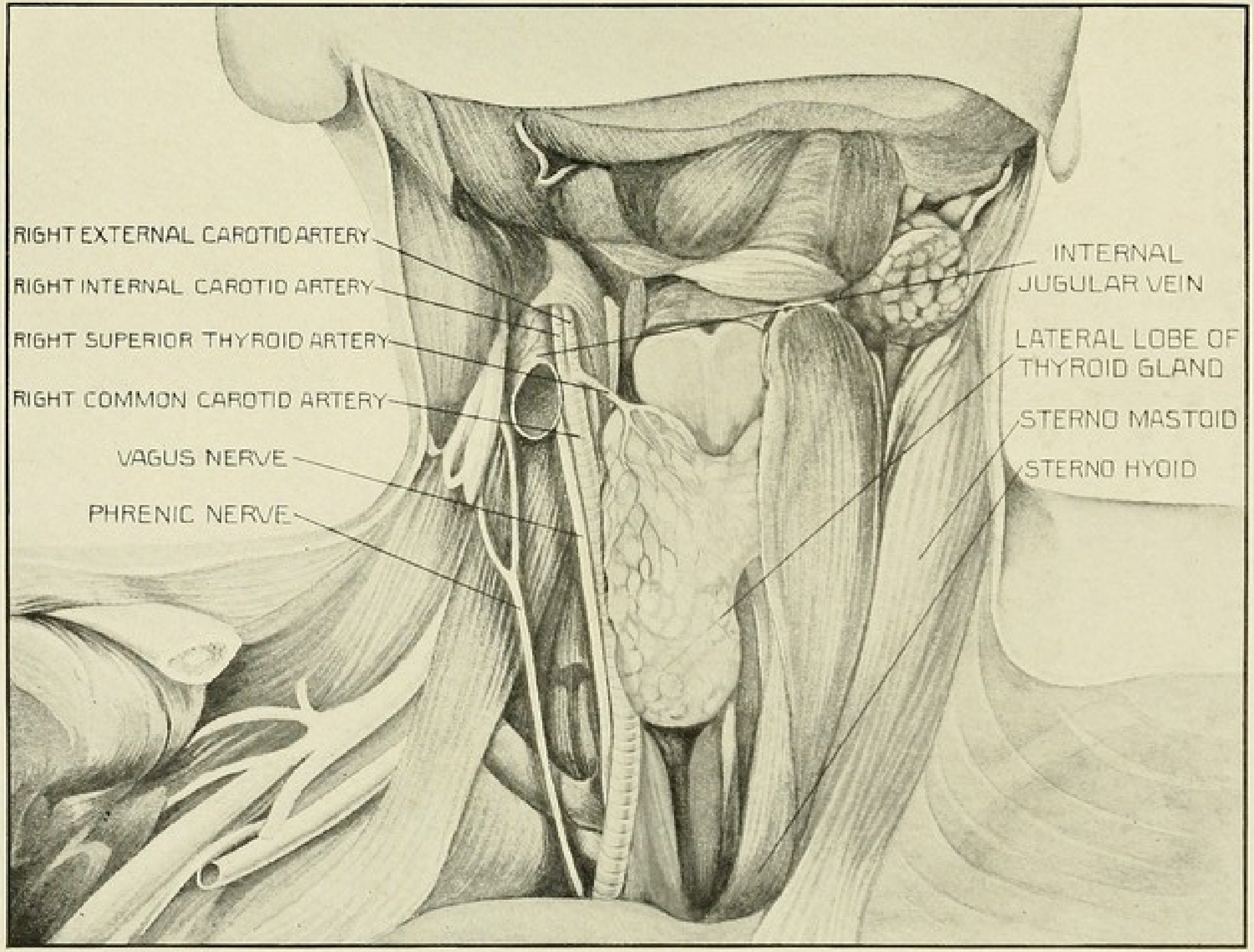
CHAPTER II.

THE PATHOLOGY OF THE THYROID GLAND.

The function of the thyroid gland is to furnish an internal secretion, which is not only important, but indispensable, for the building up and maintenance of the organism. A lack of this material leads to nutritional disturbances (myxœdema or cachexia), and its overproduction to nervous phenomena (exophthalmic goitre). Therefore, in a study of this organ we are most interested in the conditions which give rise to a diminution, an increase, or a perversion of this important function.

A new field for study was offered in the experimental problems that suggested themselves in connection with thyroid function, which was opened by the discovery of Kocher and of Reverdin, that extirpation of the thyroid was followed by severe cachexia. At first these experiments were complicated by a lack of knowledge of the parathyroid glands, but that subject has now been made clear by a more exact study of the latter organs, which will be discussed in other chapters. Then came the observation of the efficacy of mouth administered thyroid extracts as a substitute for the gland itself, and then the discovery that the thyroid possessed a marked power of regeneration when transplanted—sufficient, indeed, to act permanently for a removed or diseased organ.

PLATE I



VIEW OF THE NECK, SHOWING IMPORTANT STRUCTURES ENCOUNTERED IN OPERATIONS ON THE THYROID GLAND.

Our knowledge of hyperthyroidism has been increased by the ability to study glands removed at various stages of Graves' disease, but the complicated phenomena that occur in connection with the reaction of thyroid diseases on the organism as a whole still offer a rich field for investigation that may well lead us into a consideration, not only of cretinism and exophthalmic goitre, but also of such conditions as certain neuroses, psychoses and dermatoses, rickets and osteomalacia, obesity, and allied conditions.

Anatomy. The thyroid gland consists of two lateral lobes, connected by a narrow strip called the isthmus. Each lateral lobe is somewhat pyramidal in form, and possesses an antero-external, inner and posterior surface. These surfaces come together, forming the apex, over the upper posterior part of the body. The lower end of the lateral lobe is thick and rounded. The isthmus usually crosses the second and third rings of the trachea. It varies in size, and is sometimes absent. A projection may extend up from either the isthmus or one of the lateral lobes, which is known as the pyramidal process of the gland. The inner surface of the lateral lobes lies against the trachea, the cricoid cartilage and the lower part of the thyroid cartilage, and reaches back to the œsophagus.

Considerable variation is found in the gross blood supply of the thyroid gland. In general, however, we find the superior thyroid artery approaching the gland at the upper pole, and the inferior thyroid artery approaching from beneath the gland. These main arteries (superior and inferior thyroid) run along the margin of the gland and form anastomoses, which vary considerably in different thyroids (as has been described in detail by Landström). Branching of the large arteries is mostly upon the surface of the gland; only smaller branches penetrate the tissue. Small arteries pass between the lobules, and give off branches which supply the lobule; these, in turn, divide to supply the individual follicles. The follicular arteries end in a capillary network. The

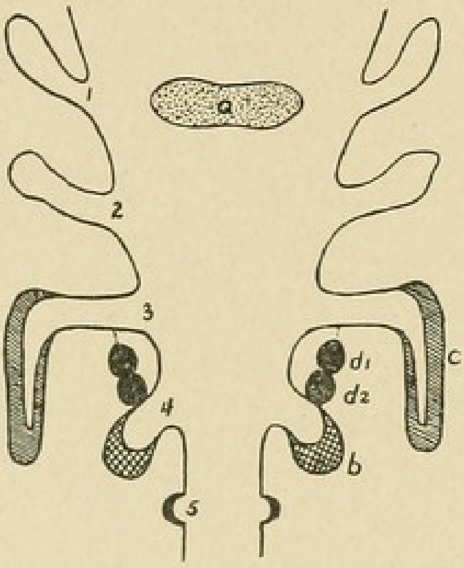


Fig. 1. Scheme showing the origin of the different branchial epithelial bodies. 1, 2, 3, 4, 5, branchial grooves. a, median thyroid. b, lateral thyroids. c, thymus. d1, outer parathyroids. d2, inner parathyroids. 5, rudimentary parathyroid of Getzowa. (Modified from Aschoff.)

veins follow the same course as the arteries to the surface of the gland. They are rich in anastomoses.

The lymph spaces in the thyroid are found outside the capillary network which surrounds each follicle. They connect with larger trunks which run between the lobules into still larger ones between the lobes, and, following the course of the blood vessels, finally form a rich lymphatic network beneath the capsule of the gland. The further lymphatic drainage is usually described as following out the blood vessels, one trunk passing upward and the other passing downward.

The thyroid gland arises from a median unpaired evagination of the epithelium of the front wall of the throat in the vicinity of the second visceral arch. This detaches itself from its place of origin and wanders down the neck, to merge finally with the second points of origin, which are from the epithelium of the fourth visceral cleft, and which wander upward somewhat and form a portion of the lateral thyroid bodies.

At first the proliferating cell masses form a network of solid cords, which later become separated into round masses, with a lumen. The cells arrange themselves as a lining to the lumen, which finally becomes somewhat enlarged and, through secretion of the cells, filled with colloid. These mature, rounded, closed spaces are called follicles. In the adult thyroid the epithelial cells lining the follicles may be columnar, cuboidal, or flat. The colloid varies in amount and staining reaction, as will be described later on. The follicles are surrounded by connective tissue, carrying blood and lymphatic vessels, as has been described. The capsule, as well as the lobular partitions of the gland, is made up of dense connective tissue.

Between the follicles, especially in the new born, one finds frequently rests of fœtal tissue, appearing in strands and small masses. It is from these cells that the so-called fœtal adenoma are supposed to arise.

Abnormalities of Development. Either a part of the thyroid or the whole gland may be lacking. The pyramid or the isthmus not infrequently presents unusual forms, or there may be complete lack of development of these parts, as well as absence of one of the lateral lobes. Aplasia, or complete absence of the thyroid gland, gives rise to sporadic cretinism or congenital myxœdema, in contradistinction to the endemic variety found in certain regions, in which the gland, present at birth, later undergoes atrophy.

Accessory thyroid nodules are frequently found, sometimes lateral to the thyroid, but more commonly in the neighborhood of the hyoid bone, or they may be below the gland as far down as the aortic arch, behind the sternum. Rarely they are found within the larynx or trachea. The accessory thyroids are of the same histologic structure as the thyroid gland itself; goitre and tumors may develop from them, just as from the main gland.

Failure of closure of the thyroglossal duct may give rise to cysts, fistulæ or tumor formation.

Circulatory Disturbances. The thyroid gland has an extremely rich blood supply—so rich, in fact, that when its vessels are overfilled (hyperæmia) the gland may be notably increased in size. This great development of blood vessels which the gland possesses, combined with its proximity to the larger neck vessels, caused some of the older authors to believe that the thyroid was a sort of safety valve for regulating the circulation of the brain.

Of more interest is the physiologic active hyperæmia of the gland, which stands in close relationship to the genital organs, especially of the female. A visible enlargement of the gland may occur in connection with menstruation, during pregnancy, after coitus, and especially after defloration. Cases have also been reported where a distinct goitre was

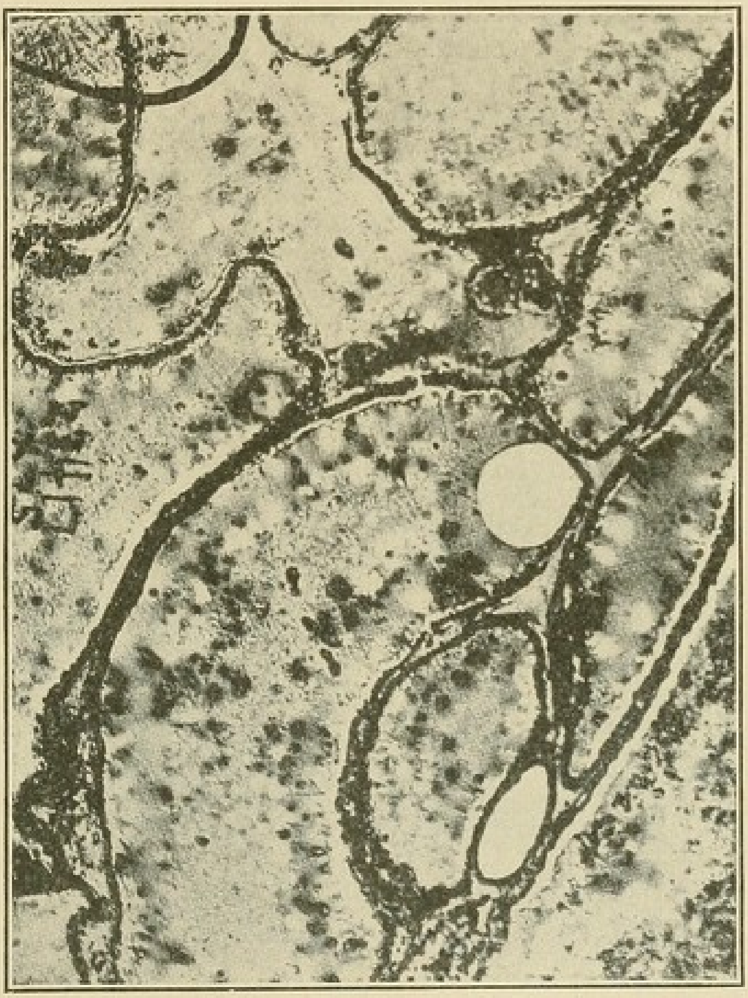


Fig. 2. Old, simple, diffuse, symptomless goitre. Epithelium degenerated and the distended follicles filled with thick, stainable colloid. Calcareous degeneration in places. (Louis B. Wilson.)

present during the period of conception, which subsided with the beginning again of menstruation. This sexual hyperæmia of the thyroid is so constant that in certain southern countries zealous mothers measure the neck of the bride before and after the marriage night.

Hæmorrhage is more frequently found in goitre than in the normal thyroid, although any trauma of the thyroid may result in hæmorrhage into the acini or into the stroma of the gland.

Infarction and embolism of the thyroid can be practically disregarded owing to the free anastomoses in this organ.

Passive congestion of the thyroid may occur, but it rarely causes changes of importance. Destruction of the blood supply of the gland, as by ligation of the thyroid arteries, leads to atrophy of the thyroid. This ligation of the thyroid arteries was first practiced for the treatment of goitre by Wölfler in 1886. The possibility of leaving in the neck a beginning malignant growth instead of a simple goitre was an objection urged at once by von Bergmann against this operation.

Inflammation. Primary acute inflammation of the thyroid gland (thyroiditis) is almost never seen. Acute inflammation of a goitrous gland may be occasionally observed. In general septicæmia, with involvement of various organs, the thyroid is rarely included, as it is one of the most resistant of all the tissues. However, in connection with certain infectious diseases, acute inflammation of the thyroid has been described. So we find an occasional rare case of thyroiditis reported following such infections as puerperal fever, influenza, typhoid fever, diphtheria, erysipelas, orchitis, acute articular rheumatism and similar infections.

These acute inflammations, when they do occur, are usually purulent. Pus accumulation (abscess) is found in the majority of these cases. Rupture of the abscess and healing by cicatrization may occur, or simple resolution may take place. Sometimes abscesses may rupture into the trachea, œsophagus or mediastinum, causing death.

Gangrene as a result of acute infection has occurred, but such an outcome is extremely rare. Perhaps seven or eight such cases have been reported. Also sufficiently rare to be of interest are the few cases where thyroid destruction by acute inflammation has been sufficient to cause symptoms of myxœdema.

Chronic Inflammation. Chronic interstitial thyroiditis may be found in very young individuals (primary infantile atrophy) or in older individuals without giving rise to any symptoms of hypothyroidism. In such cases the gland is diminished in size and the parenchyma is replaced to a greater or less extent by connective tissue.

The atrophy of old age is to be distinguished from the sclerosis due to a chronic inflammatory process, although the increase in stroma and decrease in colloid and epithelial elements gives practically the same histologic picture.

The thyroid has been found atrophic in scleroderma (Hektoen) and in icthyosis (Moore and Warfield).

Tuberculosis. Tuberculosis of the thyroid is a comparatively rare finding, but careful search of the gland will sometimes reveal tubercular foci in connection with cases of wide-spread general tuberculosis, especially acute miliary tuberculosis. Fraenkel found the thyroid involved six times in fifty cases, the lesions usually appearing as miliary tubercles, although rarely a large caseous nodule was found.

The tubercles arise in the interstitial tissue between the follicles. The latter are compressed, stellate at times, with their walls pressed together, and their content and lining epithelium degenerated or lost altogether.

Ruppanner has recently described, in addition to

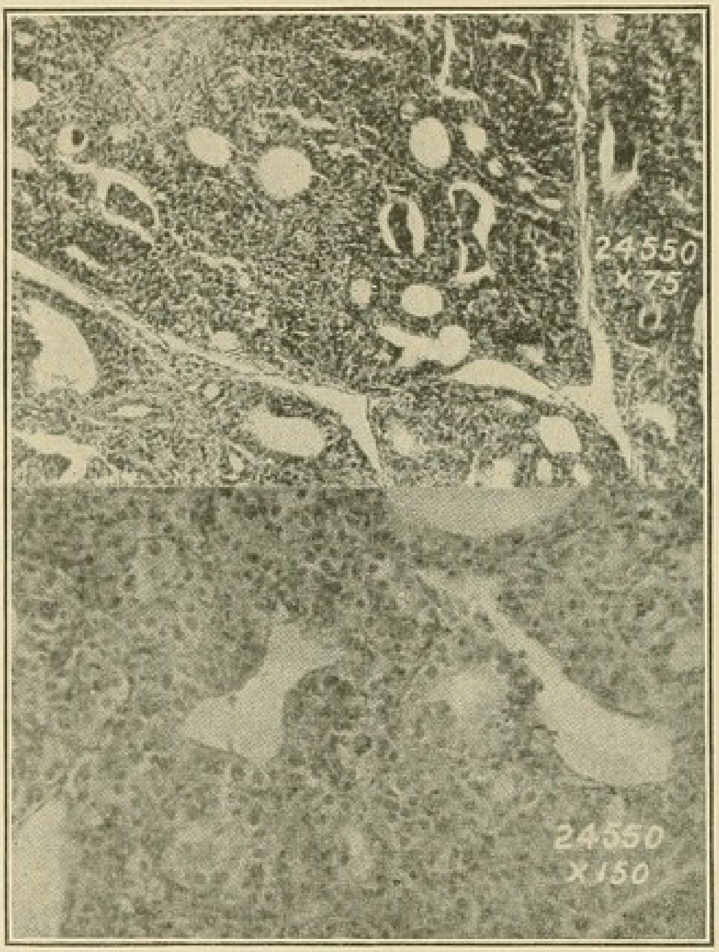


Fig. 3. Very early, mild Graves' disease. Sections show small intra-alveolar parenchyma increase, with small amount of thin secretion. (Louis B. Wilson.)

the interstitial form, an intrafollicular tubercular process in the thyroid, and also differentiates between miliary and chronic tuberculosis of the gland.

Syphilis. Syphilis of the thyroid gland is much more rare at the present day than it was formerly.

Practically the only instances seen now are in connection with visceral syphilis of infants, in which the thyroid may show pea-sized, or smaller, gummatous nodules, grayish red or grayish yellow in color, with typical microscopic structure, such as new formation of connective tissue, with lymphoid and plasma cell infiltration and destruction of parenchyma, but showing less tendency to necrosis than the tubercular nodules.

Certain cases of general thyroid enlargement in connection with tertiary syphilis have been reported, which disappeared under syphilitic treatment, but recurred with the other symptoms on discontinuance of the treatment.

Degeneration and Infiltration. While various forms of degeneration may occur in the normal thyroid, these processes are much more frequently met with in goitre, and are sometimes so marked as to give the title of the degeneration to the goitre—e. g., "calcified goitre," a term that is lacking in the true significance of the process.

Slight parenchymatous changes have been described in connection with acute infectious diseases, but the thyroid is so variant in its histology that it is difficult to state when such changes are actually present. Thus Torri described hypersecretion of colloid and new formation of epithelium, which goes on to progressive changes if the disease is long continued, in connection with acute infections.

Hyaline degeneration is of little importance, and fatty change is rarely observed, save in degenerated areas, especially of goitres. The epithelium of the thyroid normally contains some fat (Erdheim).

Calcification, and at times ossification, is seen, particularly in old age. In goitre, calcified areas are very common. Old cyst walls may be completely infiltrated with lime salts.

Amyloid infiltration may be found in connection with cases of amyloidosis, but is much less often present in the thyroid than in the liver, spleen and other parenchymatous organs. It is found, when present, deposited in the walls of the arteries and in the stroma of the gland.

Hypothyroidism. Lack of thyroid function, as brought about by congenital defect or degeneration, or removal of the thyroid gland, is followed or accompanied by certain disturbances, the most common of which are swelling of the subcutaneous tissues, falling of the nails and hair, stupidity, idiocy and skeletal disturbances. The various cases that come under this head lend themselves to the following classification (Ewald).

1.—Endemic Cretinism, a chronic disease found in regions where goitre is endemic, manifesting itself through skeletal deformity, skin and subcutaneous tissue changes, lack of genital development, diminution in intellect and sense function. Such cases show changes in the thyroid gland, consisting of partial or complete degeneration, which may be either atrophic or goitrous in its inception, or, as Getzowa has described, cases are found in which atrophic areas and goitrous degenerated nodules alternate in the same gland.

2.—Sporadic Cretinism, a similar condition to the above, due to congenital absence of the thyroid gland (thyroaplasia).

3.—Infantile myxœdema, due to acquired loss or perversion of thyroid function in the early years of life, and therefore showing greater or less severity of symptoms, according to the amount of functional disturbance of the gland. Under this head may be included the abortive cases of myxœdema (myxœdeme fruste).

4.—Adult myxœdema, a spontaneous hypo, or athyreosis of adults. In these cases the thyroid gland is usually diminished in size and atrophic, pale yellowish white in color, firm in consistence. Microscopically the parenchyma is replaced by dense fibrous tissue. Degenerated epithelial cell nests, small cysts containing fat and cholesterin, and areas of lymphoid and plasma cell infiltration may be found. In addition to the changes in the thyroid, peculiar changes are found in the corium (thickening and fracture of the connective tissue fibres, infiltration with gelatinous like material).

5.—Operative myxœdema (cachexia strumipriva or thyropriva), a condition due to the operative (complete) removal of a goitre or the normal thyroid gland. This latter condition has been fully discussed in the chapters on the parathyroid glands.

Hypertrophy (Goitre). Although we can not always make a sharp distinction between new growth, in the tumor sense, and hypertrophy, especially in the circumscribed forms as they occur in the thyroid gland, still the ordinary goitre (struma) probably best lends itself to the above classification.

We recognize two main forms of hypertrophy or simple goitre: 1, diffuse; 2, nodular.

In diffuse goitre we have a uniform enlargement of the thyroid gland, or perhaps one lobe of the gland is frequently considerably more enlarged than the other, but presents no circumscribed nodules differing in structure from the rest of the lobe. Occasionally, however, a more rapidly proliferating area may be encountered in such a thyroid than is shown in the adjoining tissue, but such areas are not sharply bounded.

This diffuse type of hypertrophy may show itself in two forms: (a) Colloid goitre. In this type the amount of colloid is so greatly increased that the follicles of the gland are often greatly dilated, and the epithelium lining the same more or less flattened, or finally completely destroyed, by the pressure of the increased colloid content. The septa between neighboring follicles may be broken through by strong pressure and subsequently absorbed. If sufficient dilatation and confluence of follicles is brought about by this process, we can finally have the appearance of considerable sized cysts (cystic colloid goitre).

(b). Parenchymatous goitre. This type of hypertrophy consists of a glandular proliferation that is more in the order of a new formation in the tumor sense. Solid cell masses and cords, together with connective tissue, form follicles much in the same manner as they are built up in the fœtal thyroid. The colloid content is usually scant, or may be altogether lacking. The epithelium lining the follicles may be cylindric, and sometimes forms papillary projections into the lumina of the follicles. By enlargement of the follicles and continued papillary ingrowth into the same, we may have a variation of type, which has been designated papillary cystic goitre.

These two types of diffuse goitre just described are widely different in regard to their clinical significance. In the first type (a) the functioning epithe-

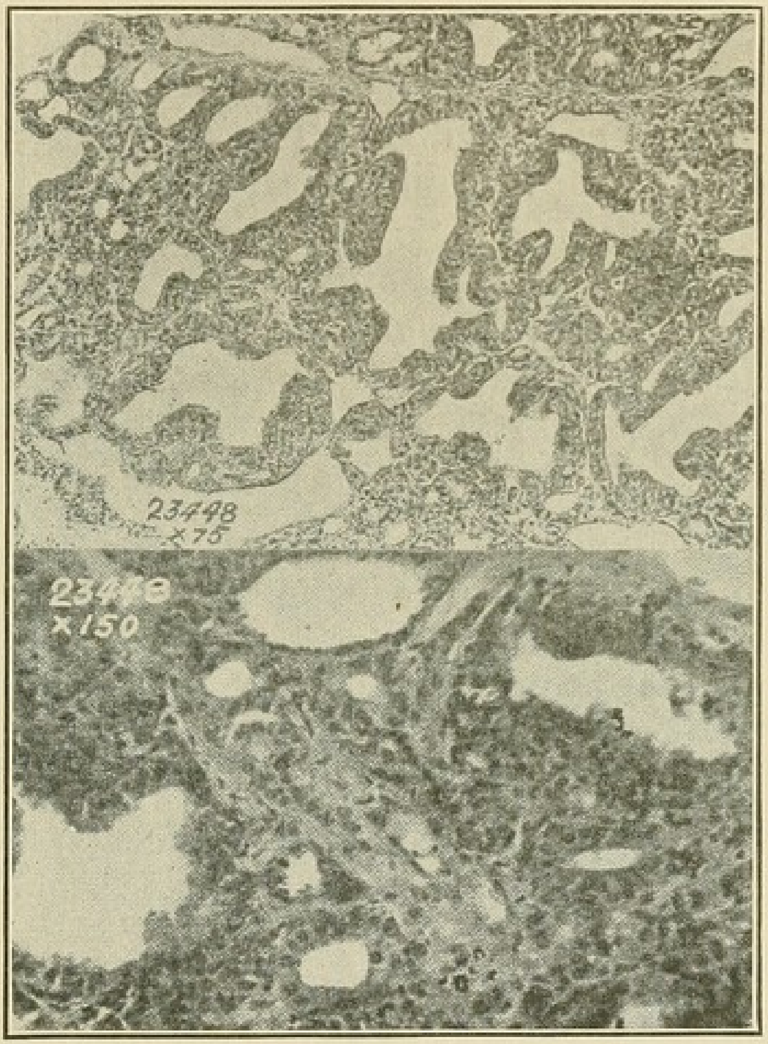


Fig. 4. Acute stage of Graves' disease. Sections show increased alveolar parenchyma, papillae formation, and a large amount of non-staining secretion. (Louis B. Wilson.)

lium of the gland is more or less completely destroyed and the colloid usually non-absorbable; therefore such goitres are not associated with hyperthyroidism. In the second type (b), on the contrary, we have an increased amount of functioning tissue, and it is from such goitres that hyperthyroidism (Graves' disease) arises.

Marine and Lenhart have shown that in the dog one can carry a thyroid gland through a variety of stages of goitre. By partial removal of a thyroid, for example, one may produce an active hyperplasia, as was originally shown by Halsted. This hyperplastic type of gland may be reduced to a simple colloid type by the administration of iodine. By means of partial removals, together with withholding and giving iodine, one may follow the process of reversion of a hyperplasia to colloid, produce again a second hyperplasia, and finally obtain a secondary reversion to colloid in the same animal. It is interesting to note that these authors find that an actively proliferating thyroid (hyperplasia) may revert to a pure colloid goitre within a month.

Nodular goitre is characterized by the occurrence in the thyroid gland of circumscribed nodules, varying in number and size, between which either normal or completely degenerated or atrophic thyroid tissue appears. Even the smallest (microscopic) nodules show a distinct connective tissue capsule. The nodules may present the typical picture described under colloid goitre, or may be of the parenchymatous type. Sometimes in the same gland nodules of both types may appear. In these nodules various degenerative processes are frequently encountered, such as hyaline and fatty change. A nodule may undergo complete connective tissue transformation (fibrous goitre), or lime salts may be deposited in the same (calcified goitre). Through breaking down and absorption of the content of such nodules, cysts may frequently arise, which through hæmorrhage may show a red brown or deeper brown colored content. A combination of these various degenerative processes in the same nodule gives rise to the multicolored appearance frequently seen on fresh section of the same.

Still another variation of the nodular form of goitre is to be found in the so-called fœtal adenoma

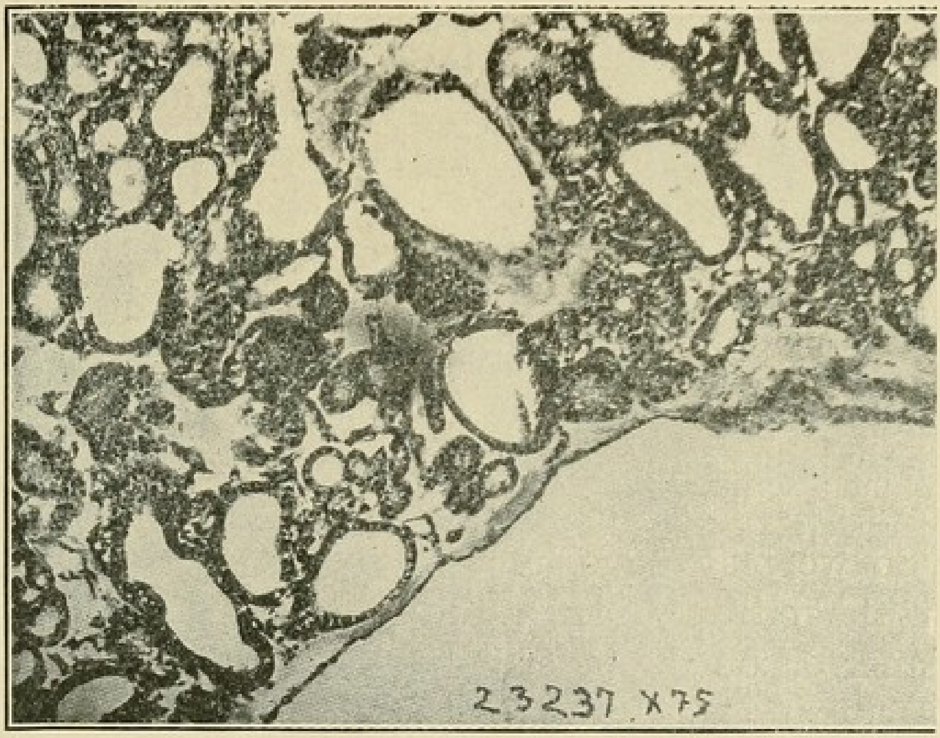


Fig. 5. Fœtal adenoma of the thyroid, with acini in various stages of development and edge of a large cyst. (Louis B. Wilson.)

of the thyroid, which consists of encapsuled nodules made up of cells corresponding to the undifferentiated cell rests of embryonal thyroid. The development of these latter nodules may in certain instances give rise to hyperthyroidism.

Hyperthyroidism (Graves' Disease, Basedow's Disease, Exophthalmic Goitre). In connection with certain types of thyroid hypertrophy (parenchymatous goitre, papillary cystic goitre, and sometimes fœtal adenoma of the thyroid, according to the classification of MacCarty), we have, in addition to the struma, the appearance of certain phenomena, such as exophthalmos,[1] heart palpitation, tremor of the hands, and nervous symptoms, especially of vasomotor type, in varying degrees of prominence. Autopsies on such individuals show, in addition to the changes in the thyroid, usually dilatation of the heart, more or less wide-spread fatty muscle atrophy, parenchymatous myocarditis, and frequently a persistent thymus and splenic enlargement.

It is in the hyperactive thyroid that we seek an explanation for these symptoms, and the recent work of Dr. Louis B. Wilson has shown that there is a definite parallel between the increased amount of functioning tissue and absorbable secretion in the thyroid gland and the degree of severity of the symptoms.

So we may have hyperthyroidism result from a simple goitre by increase in function of the thyroid gland; or, on the other hand, by continued activity, degenerative changes may appear in the functioning cells, and blocking of the lymphatic drainage take place, so that, provided the patient lives long enough, a case of hyperthyroidism can return to a simple goitre. In such cases, however, the heart

(1) If we take for granted hyperthyroidism as the cause of exophthalmos, we are still considerably in doubt as to how the action is brought about. The phenomenon can not rest on so simple an explanation as increased fatty tissue, congestion or edema within the orbit. Muscular spasm, sympathetic irritation, vasomotor congestion and what not have been assumed. A mechanical basis for its occurrence has been offered by Landstroem, who has recently described a new muscle within the orbit. This muscle, which consists of a cylindric band of smooth muscle fibres, has its origin in the orbital septum and its insertion into the equator bulbi. The cone-like insertion is sufficient to pull the eyeball forward and produce exophthalmos under the sympathetic irritation which is assumed as a result of the hyperthyroidism.

and nervous symptom may persist as a result of the previous over action of the thyroid for a considerable time after the thyroid has become quiescent. It is in such cases that Wilson has warned against operative interference.

The thyroid gland itself in hyperthyroidism while usually increased in size is not necessarily always large, it is firm in consistence, and decidedly vascular, especially in acute cases.

Microscopically the important change is the parenchyma increase which may appear within the alveoli as a cellular increase in a single layer, or there may be a reduplication of layers. In many instances this cellular increase is brought about by infolding of the alveolar wall, or papillæ formation within the alveoli. In a second type of case there is an actual increase in the number of alveoli (adenoma type). The acute cases also show a considerable amount of thin, non-eosin staining secretion). The more chronic cases show degenerative changes consisting of desquamation of the alveolar epithelium and denser staining of the secretion.

Wilson has been able to classify the pathological findings in this condition very closely with the clinical symptoms. Eighty per cent. of his cases showed a remarkable parallel between the pathologic finding in the thyroid gland and the condition of the patient. According as to whether the cases were acute, and mild, moderate or severe, there was a rising increase of functional activity as shown by increased parenchyma and increased absorbable secretion in the thyroid gland. Cases that had been severe but with remission of symptoms at the time of examination showed microscopically beginning degeneration. Cases that had been severe but that had reduced themselves to the residual stage where only heart and nervous symptoms persisted as a result of the previous intoxication, showed histologically more or less complete degeneration in the thyroid gland.

The extent of the pathological process in the thyroid is not always to be brought in line with the

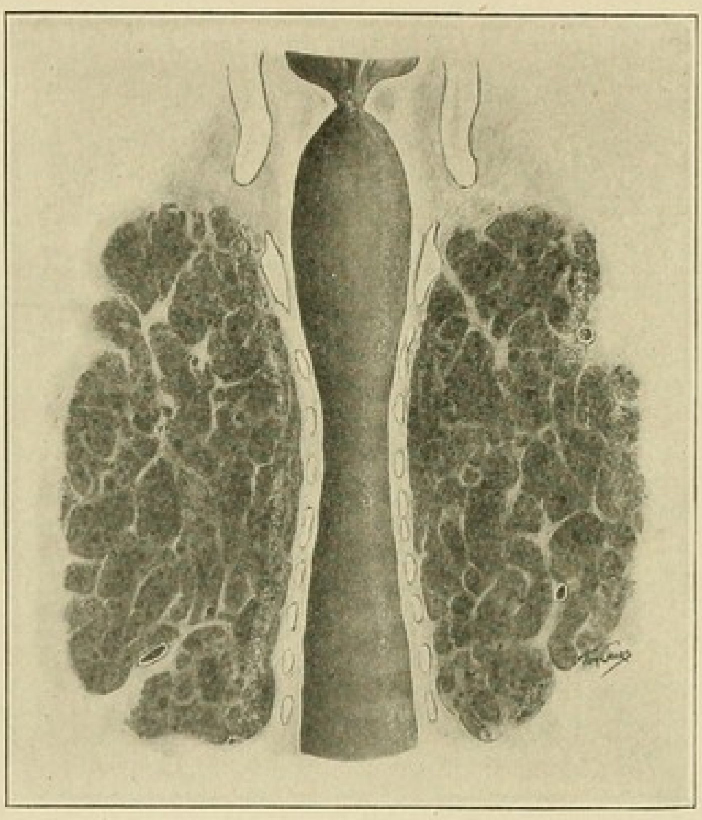


Fig. 6. Showing lateral compression of the trachea by a large goitre.

severity of the symptoms, however, as the patient's ability to neutralize the increased secretion has to be taken into account.

Tumors. Simple histoid growths, such as fibroma, chondroma, osteoma, etc., may be found in the thyroid gland and show no peculiarities worthy of note in this situation. More complicated structures, including teratoma in which all three germ layers are present, have been found in the gland.

Sarcoma. Primary sarcoma of the thyroid is very rare; less than a hundred authentic cases have been reported. Most of these cases have appeared in the middle years of life, and have been found more frequently in women than in men. They have also been found more often in an already goiterous gland than in the normal thyroid.

Histologically these growths may be of almost any sarcoma type, although the round cell and spindle cell varieties are most frequently met with. Giant cell and osteoplastic growths have been described, as well as tumors classified as perithelioma and endothelioma.

The sarcomatous cell growth is infiltrative in type, rarely encapsulated, and sometimes so completely destroys the gland that no recognizable thyroid tissue can be found. These tumors may become so large as to cause dangerous pressure symptoms. Metastasis from such growths may take place by both blood and lymph channels.

Carcinoma. Primary malignant epithelial new growths are also rare in the thyroid gland. Less than one per cent of all carcinoma has its origin in this location; moreover, the disease is more common in goiterous regions, as cancer develops oftener in struma than in the normal thyroid. The interesting work of L. Pick on carcinoma of the trout has emphasized the coincidence of goitre and carcinoma. The growth is usually of the medullary type, soft in consistence, scant in connective tissue, and according to its blood content, gray white to dark red in color. Areas showing degeneration and haemorrhages are frequent. Owing to lack of encapsulation the growth may penetrate the trachea or the skin by direct extension. Frequently there is growth directly into the thyroid veins or their branches, emboli from which lead to wide-spread metastases.

At times the structure of these malignant growths bears a close resemblance to actively proliferating goitre, or even to normal thyroid gland, so that histological differentiation as to malignancy is extremely difficult, or at times impossible; the metastatic nodules in the lungs, liver, bone, etc., for instance, corresponding almost identically with normal thyroid gland.

Adenocarcinoma types, with widening of the gland follicles and papillary ingrowths may sometimes appear so that a so called papillary cystocarcinoma is formed.

In addition to metastasis through direct ingrowth into the veins and subsequent vascular embolism, the lymphatics may be invaded. As a rule greatly enlarged neighboring lymph nodes accompany these growths. The lungs are the most favorable site for metastasis; more rarely other internal organs are included.

Bone metastases are especially to be noted in connection with these malignant thyroid tumors, which apparently find a most suitable opportunity for growth in bone marrow. This favorable influence of bone marrow on thyroid proliferation is borne out by the fact that such a situation is best adapted to successful thyroid transplantation.

A rare but interesting form of tumor is a malignant growth found usually in bone which may metastasize to other organs, but which possesses the typical structure of normal thyroid gland or of simple goitre. Such tumors are made up of typical follicles filled with iodine containing colloid. The thyroid gland in such cases may be free from any tumor growth. Fabris has reported such a case, which was diagnosed Pott's disease, but at autopsy the vertebra were found to be filled with a tumor growth corresponding histologically with thyroid tissue.

Mixed tumors of the thyroid which have been occasionally observed, i. e., growths apparently of both connective tissue and epithelial origin—sarco-carcinoma—are best explained by the experimental tumors of Ehrlich and Apolant.

Two such cases have been reported by Teacher, and a case of Schmorl's is distinctly of this type. In the latter case an adenoma of the thyroid was removed at operation. After a time the tumor recurred and this examination showed carcinoma and sarcoma in about equal amount. Finally the patient died from metastases, which presented, histologically, the structure of pure spindle cell sarcoma.

CHAPTER III.

DIAGNOSIS.

The diagnosis of goitre in itself is exceedingly simple because of the definite location of the thyroid gland and its attachment to the trachea which causes it to move upwards with the larynx during the act of swallowing. Normally the form of the thyroid gland is quite regular as shown in our anatomical illustrations and whenever there is a uniform enlargement ot the gland, the larger it becomes the easier it is to make the diagnosis. This uniform enlargement of the gland is, however, not the rule and usually the distortion increases with the extent of enlargement. There seems to be no definite rule as to the number of lobes that are to be involved when the enlargement has once begun to become apparent. It is, however, more common to find the middle lobe and one lateral lobe enlarged than to find both lateral lobes affected with the middle lobe in a normal condition. Most commonly one lateral lobe is greatly enlarged, the middle lobe considerably and the other lateral lobe but slightly.

The differential diagnosis may sometimes be somewhat difficult between goitre and branchial cyst but the latter is usually more uniform. There is usually distinct fluctuation present in the latter condition and the normal thyroid gland can be felt usually below the branchial cyst.

Enlarged lymph nodes due to leukæmia or pseudo-leukæmia are definitely composed of separate more or less spherical glands which are arranged along the anterior or posterior border of the sterno-cleido-mastoid muscle, or in the vicinity of the submaxillary, salivary or the parotid glands.

Moreover, the first nodules usually appear high up in the neck and not in the region of the thyroid gland.

Diffuse or dissecting lipoma of the neck is likely to begin on the posterior surface of the neck and to progress downwards and forward.

Lymphosarcoma may occur at any point in the neck usually in front of the sterno-cleido-mastoid muscle. It is only slightly movable, if at all, and neither this nor the preceding two forms of enlargement move up and down with the larynx at deglutition.

Carcinoma in the lymph nodes of the neck will not be mistaken for goitre upon careful examination because the former is always secondary to carcinoma of the mouth, pharynx, nose, scalp, parotid gland or ear or some other tissue.

Occasionally the primary tumor is very small and in this way it may be overlooked, but even in this case the masses do not rise and fall with the larynx, and the normal gland can usually be outlined in its proper position by making a careful examination. The surgeon is rarely called upon to treat simple goitre until it has advanced to a considerable size so that the growth is a source of annoyance to the patient because of the deformity it produces, or because of the fact that the pressure from the tumor interferes with respiration or deglutition. Occasionally these symptoms exist in cases in which inspection does not reveal an enlargement of the thyroid gland but upon deglutition a tumor will be seen to rise from under the upper end of the sternum. In these cases there is a marked enlargement downward of a portion of the middle lobe which presses forward against the sternum and backward against the trachea. In a few instances I have encountered such a lobe projecting inward and downward from the lower end of one of the lateral lobes extending quite behind the upper end of the sternum and giving rise to severe obstruction to respiration.

THE DIAGNOSIS OF EXOPHTHALMIC GOITRE.

There is no disease in which familiarity through repeated contact is of greater aid in making a diagnosis than in exophthalmic goitre. The earlier observers like Parry, Graves, Basedow, Desmarres and Trousseau placed especial stress upon two elements contained in the name exophthalmos and goitre to which the symptom—which later became the most important of all—tachycardia was soon added. Later many other symptoms which will be described in detail were added from time to time, but we must bear in mind that in England the description of the disease by Parry and Graves, in Germany by von Basedow, in France by Charcot and Trousseau, and in Italy by Flajani had thoroughly established this as a distinct disease before any of the following symptoms had been shown to be present in exophthalmic goitre. Recently it has been claimed by several clinicians that a diagnosis of this disease can and must be made in case tachycardia is present which cannot be explained upon any other pathological theory in any given case especially if several of the other symptoms, but neither exophthalmos nor goitre are present. When either of these two symptoms is present with tachycardia all authorities agree on the diagnosis.

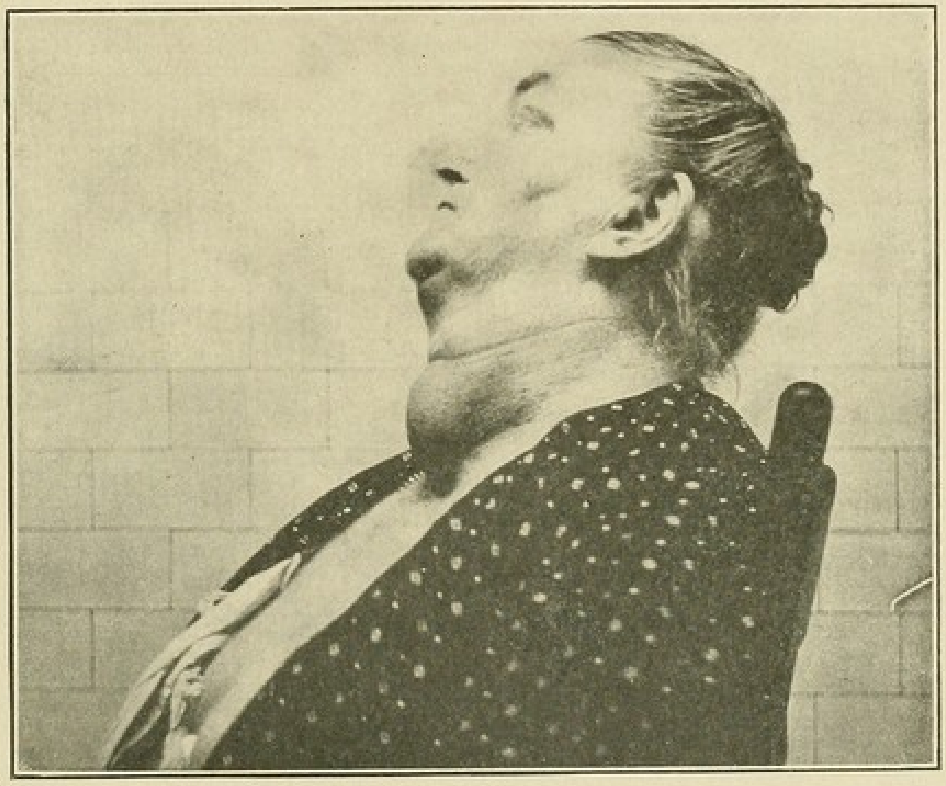


Fig. 7. Exophthalmic goitre, lateral view of neck, showing moderate enlargement of thyroid gland.

This has given rise to a serious objection to the term exophthalmic goitre because it was argued that a disease with a description name should at least in part conform with this description.

Since the disease has been definitely accepted as a condition, due according to Moebius to an increased pathological activity of the thyroid gland, those who have most carefully studied the specimens removed by operation have always been able to find some portion of the gland with the typical pathological structure of the thyroid gland even in cases in which from external examination the pressure of a goitre could not be definitely demonstrated. In my own cases it was always possible to demonstrate even in the gross specimen some portion that showed the presence of hypertrophy and histologically every case showed typical tissue in some portion. It is true that there is often a marked discrepancy between the extent of the goitre and the degree of tachicardia, tremor, muscular weakness and other symptoms. When one bears in mind, however, that very minute quantities of any one of a number of active drugs with which we are familiar when introduced into the circulation produce exceedingly violent symptoms it is easy to understand how the secretion from a very small portion of diseased tissue in the thyroid gland may produce all of the symptoms of this disease. All of these symptoms may be intermittent. There may be a marked difference in the size of the thyroid gland from week to week, the eyes may be so prominent one day that they will attract attention at once at one time and a few weeks later this symptom may be scarcely perceptible. In the same manner the pulse may vary from eighty to one hundred and sixty beats per minute, although it rarely remains under one hundred during the entire day.

In these cases there seems to be a discharge into the circulation of a considerable quantity of the poison at intervals. This may be brought about by mental or by physical influences.

I have known severe sorrow over the death of some member of the family, excitement over a fire, a sudden fright, overwork, both physical or mental, anxiety and fatigue during a political campaign, excitement in social life and many other similar conditions to give rise to severe, sometimes fatal exacerbations of this condition.

In each case it has seemed as though the patient could not quite return to the condition in which he was before the last exacerbation and although the next attack might not be more severe than the previous one still its effect upon the patient seemed at least somewhat more severe.

MINOR SYMPTOMS.

Before enumerating the minor symptoms of exophthalmic goitre it will be well once more to insist upon the fact that in the presence of tachycardia together with even the slightest degree of exophthalmos or enlargement of the thyroid gland, a positive diagnosis of exophthalmic goitre can always be made.

In some instances the changes in the thyroid gland may be so slight that only some insignificant irregularity may be noticed, still upon excision of this portion of the gland the pathological condition is so typical that there can be no doubt regarding the correctness of the diagnosis when the histological examination has been made. I am so persistent in impressing this fact because this is really the only class of cases which is likely to be overlooked by the clinician who has seen only a small number of well developed typical cases while these cases are regularly overlooked by those who must depend upon description of the disease for a basis upon which to make a diagnosis.

Fortunately for the patient one or more of the following symptoms will be found in almost every case so that the diagnosis can be further supported.

At this point it may be well to direct attention to the fact that cases are frequently encountered in which other conditions may readily be mistaken for a tachycardia. These conditions are always due to other causes.

Of these the excessive use of nicotin especially in cigarette smokers is the most common cause at the present time. Myocarditis due to chronic alcoholism is another condition which is still more misleading because the alcoholic tremor is almost identical with the tremor of exophthalmic goitre to be described among the minor symptoms.

Habitual users of the various coal tar preparations form another class which may mislead the clinician in making his diagnosis. The habitual use of a number of other drugs like strychnine, cocaine, quinine and chloral must be borne in mind in making a diagnosis. Similarly severe anaemia, or marked obesity, or the depression following severe illness, or unusual mental or physicial exertion especially when long continued and accompanied with loss of sleep may give rise to a condition of the heart which may lead to a mistaken diagnosis. Great sorrow, severe fright, long continued worry especially when accompanied with insomnia, exposure to great heat and in fact any condition which severely affects the nervous and circulatory system may cause a condition of the heart's action which may easily be mistaken for the tachycardia of exophthalmic goitre. This condition is frequently present after persons have experienced injuries during railroad wrecks.

It is well to bear these facts in mind especially because any one of these conditions may be the ex-

Fig. 8. Exophthalmic goitre; thyroid gland only moderately enlarged.

citing cause of an attack of exophthalmic goitre. Moebius has reasoned this out in the following manner: Many patients may possess thyroid glands that are slightly pathological so that there is a slight degree of overproduction of normal or possibly abnormal secretion which, however, is either not absorbed or if it is absorbed the quantity is so limited that it does not make any appreciable impression upon the tissues of the body and especially the tissues of the heart.

The patient may consequently live in an apparently normal condition until there is a severe depression due to one of the conditions mentioned above whereupon the effect of the thyroid poisoning is felt sufficiently to give definite symptoms, first of tachycardia and later of other typical conditions and then the presence of exophthalmic goitre is established. This thyroid poisoning added to the other conditions may be sufficient to make the disease permanent or it may subdue as the bad results of the acute shock to the general system subside because the amount of thyroid poisoning may not be sufficient even after such an exacerbation to produce typical symptoms.

It is plain, of course, that such cases must be guarded against a repetition of acute strains of all kinds as the resistance against thyroid poisoning as has been said above is reduced with each successive exacerbation.

Another theory may be mentioned at this point namely that there may be an actual increase in the secretion due to the strain which has temporarily been placed upon the nervous and circulatory systems by any one of the conditions mentioned above. Until some one can determine by actual measurement the isolated poisonous substance in the circulation in patients suffering from exophthalmic goitre it seems unlikely that the correctness of this theory will or can be proven although there is much in the course taken by the disease that speaks in favor of the hypothesis.

For the sake of clearness and brevity the minor symptoms will be first enumerated and then discussed separately.

LIST OF MINOR SYMPTOMS.

1—Tremor; 2—Muscular weakness; 3—Nervous excitability; 4—Mental deficiency; 5—Vertigo; 6—Graefe's sign; 7—Stellwag's sign; 8—Moebius' sign; 9—Paroxysmal dyspnœa;

10—Intermittent vomiting without apparent exciting cause.

11—Intermittent diarrhœa without apparent exciting cause.

12—Intermittent sweating without apparent exciting cause.

13—Intermittent mental depression without apparent exciting cause.

14—Increase of gravity of symptoms upon psychic excitation.

15—Increase of gravity upon mental fatigue.

16—Increase of gravity upon physical fatigue.

17—Increase of gravity upon administration of thyroid extract.

18—Increase of gravity upon administration of iodine.

19—Emaciation in advanced cases.

20—Anæmia in advanced cases.

21—Increased lymphocytosis, decreased polymorphonuclear leucocytosis.

22—Oedema of upper and lower eyelids, later of feet.

23—Visible pulsations in goitre.

24—Discoloration of skin especially about nipples and orifices.

Any one or any group of these symptoms may be prominent early in the course of the disease. They rarely precede the presence of tachycardia but frequently the appearance of exophthalmos or marked enlargement of the gland and frequently several of these symptoms have developed to a marked degree before either exophthalmos or enlargement of the thyroid gland can be demonstrated.

It is in these latter cases in which a thorough knowledge of an acquaintance with these symptoms is of especial importance in making a diagnosis. They should always be carefully noted in all cases in which the three major conditions, tachycardia, exophthalmos and enlargement of the gland are present in order that the relation of these conditions may be recognized when found associated only with tachycardia.

1—**Tremor.** The most important minor symptom which can be recognized in all advanced cases is muscular tremor. This was first associated with the disease by Charcot and later by his pupils notably by Marie. The similarity between the tremor of chronic alcoholism and that of exophthalmic goitre further supports the theory of Moebius that the disease is due to a condition of poisoning through toxic substances circulating in the blood and affecting the tissues directly. The symptoms can be most easily elicited by having the patient extend an arm at right angles with his body or by standing upon one leg and flexing the other thigh with the knee extended. The latter test is of course too severe for advanced cases. Accurate measurements have been made to determine the number of contractions per second, according to Marie, from 8 to 9 oscillations take place per second.

Although there seems to be much uniformity in the frequency of the oscillations there is a great difference in their severity. In many patients it is

Fig. 9. Lateral view of large goitre weighing seven pounds giving rise to severe discomfort because of its weight and because of the direct pressure upon the trachea which caused marked obstruction to breathing. It also forced the patient to hold her head in a most uncomfortable position.

this tremor that first causes them to consult the physician, consequently it is necessary to bear the relation between this symptom and exophthalmic goitre constantly in mind in order not to overlook it and make a wrong diagnosis. In many cases the tremor remains permanently after it has once appeared while in others it may be present at times with varying degrees of severity only to disappear and reappear again at intervals. Sometimes the tremor is so marked that a look at the patient from a distance will convince the trained observer that the patient presents this symptom to an extent which will make it necessary only to establish one or two other symptoms to confirm the diagnosis of exophthalmic goitre, while in other cases the most painstaking examination may barely enable the most acute observer to establish the presence of this symptom. Whenever the symptom is present in any given case it will usually appear in a more marked form whenever there is an exacerbation of the disease from any other cause.

This symptom may be confined to the upper or to the upper and lower extremities or it may effect all of the muscles of the body so that one can feel it by placing the hand upon any portion of the patient's body. It has been observed in most of the voluntary muscles. Tremor of the eyes is not uncommon, but not nearly so common as in the extremities.

It may be so severe that it may become difficult for the patient to do any kind of accurate work with the hands or even to walk with comfort. The tremor in the hands seems to differ from that observed in paralysis agitans in that there is no especial motion of the fingers but rather a wavelike motion or oscillation of the separate muscle fibres rather than a contraction of any muscle as a whole. This condition is entirely different from a condition of muscular spasms or cramps described by Mackenzie.

In my own observation the tremor has been exceedingly common in exophthalmic goitre patients while distinct cramps have occurred only in a very small proportion of cases. In quite a proportion of patients who have suffered from exophthalmic goitre for a considerable period the presence of mild contractions reminding one of incipient chorea may be observed. These contractions seem to affect especially the head and sometimes also the upper extremities. Since we are familiar with the fact that removal of all of the parathyroid glands invariably results in tetany some authors have attributed the spasmodic contractions just described to a diseased condition of the parathyroid glands. It has been suggested that this condition of the parathyroid glands may be due to the effect upon these glands exercised by the pathological thyroid secretion circulating in the blood in exophthalmic goitre, it being supposed that these glands may have been rendered incapable of performing their physiological functions precisely as the muscle fibres have become incapacitated by direct contact with the same poison.

2—**Muscular Weakness.** In advanced cases of exophthalmic goitre there is always muscular weakness. This may show itself simply in the fact that the patient becomes fatigued more readily than normal, or it may become so serious that the muscles will give out suddenly and the patient may lose complete control of certain muscle groups unexpectedly and may suddenly drop things held in the hand or it may affect the lower extremities so that the patient suddenly falls to the ground because his legs give way. This condition has been called paraparesis. It may be only temporary or it may begin in a mild form and increase in severity. Many patients first notice this condition when they find that it is no longer possible for them to change from the sitting to the standing position without lifting the weight of the body with the arms. Conversely they find in changing from the standing to the sitting posture that unless they steady themselves with their arms they will suddenly drop down into the seat while they had expected to lower the body gradually.

This condition must, of course, not be confounded with similar symptoms which are frequently present in patients suffering from hysteria.

This weakness seems to be due to a condition of the muscle tissue itself caused by the poisoning of this tissue by the thyroid secretion in the blood.

Although this symptom is usually present quite late in the course of the disease still it has occasionally been the first to attract the attention of the physician.

It is likely that the same condition affecting the muscles of the orbit has much to do with producing the symptoms of exophthalmos as well as the symptoms to be described later as Graefe's, Stellwag's and Moebius symptoms. Since Landström has given us a more perfect knowledge of the muscles of the orbit it seems certain that the exophthalmos is due especially to the weakness of an unstriped cylinder-formed muscle which had formerly been overlooked both by anatomists and clinicians as well as by pathologists.

This muscle is under the control of the cervical sympathetic plexus The weakness may be uniform throughout the muscles of the body or it may be selective affecting only certain muscles, those in the orbit being affected more often than any of the others. In rare cases the muscles of one side of the body may be affected alone but it is likely that in these cases there are other definite complications like cerebral hæmorrhage or circumscribed cerebral anæmia or it may be due to hysteria.

In connection with the symptoms of exophthalmos it must, of course, be borne in mind that aside from weakness in the muscles which ordinarily keep the eyeball in place there are other conditions like engorgement of veins which aid in pushing the eyeballs forward.

There is quite an opportunity for theorizing concerning the relation of the weakened condition of various groups of muscles to other secondary conditions. The digestive disturbances may be accounted for by the weakened condition of the muscles of the stomach and intestinal walls. The same explanation may be applied to the diarrhœas. It seems, however, scarcely necessary to discuss all of these theories in the present work. It is quite possible that the digestive disturbances are quite as much dependent upon the direct effect which the thyroid poison in the circulation has upon the glands secreting digestive ferments as upon the condition of the muscles of the alimentary canal.

Although the effects of this poison can be most readily demonstrated in the muscular system still it is not at all likely that any of the other tissues are less seriously affected, and it would consequently not be correct were we to attribute the effects which this disease has upon the digestive apparatus entirely to the impaired muscles of the walls of stomach and intestines.

3—**Nervous Excitability.** From the first observations to the present time the presence of great nervous excitability has been noticed as one of the symptoms almost invariably present in some

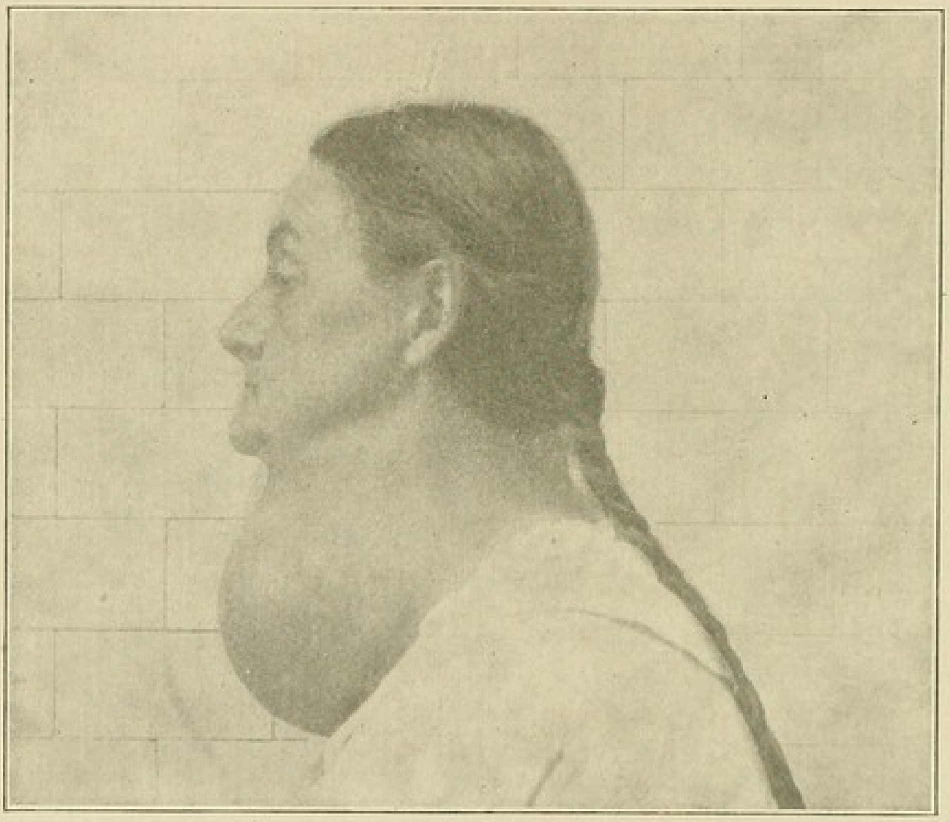


Fig. 10. Shows the same patient as Fig. 9 the enlarged gland overhanging its base to a marked degree.

form. In fact it was the presence of marked nervous symptoms which caused the greatest amount of opposition against a separate classification of this disease, especially in the French Academy. It was pointed out constantly, that the most marked symptoms of this disease were identical with those characterizing hysteria. At this point a symptom dwelt upon especially by Martin B. Tinker should be emphasized. He points to the fact that these patients frequently complain of a symptom which could readily be mistaken for typical globus hystericus and which has often even at the present time caused careful observers to make a diagnosis of hysteria in patients suffering from unquestionable exophthalmic goitre.

In many of these cases there may be but a very small central lobe which acts in the form of a ball valve and interferes with the patient's breathing and occasionally even with the swallowing of food, or the lateral lobes may have prolongations at their external borders which may be directed backward and inward around the posterior surface of the trachea, and this may cause a compression of the latter tube and thus cause difficulty in breathing. Or again, the middle lobe may have an enlargement on its lower border which may be permanently located behind the upper end of the sternum or it may take this position only when the patient's tissues are in a relaxed condition during sleep. I have had one of these patients come to me with a diagnosis of cardiac asthma whose attacks came on regularly at night after the patient had fallen asleep but which would not occur in case the patient would remain awake for any reason. Many of these patients wander from one sanitorium to another because their symptoms of neurasthenia or hysteria are so marked that the presence of exophthalmic goitre is entirely overlooked.

The fact that the disease comes on so often to a marked degree directly after some severe mental, emotional, or physical strain has served still further to obstruct the diagnosis. It seems, however, that we must agree with Moebius that this simply indicates an increase in the abnormal secretion at a time when there was a decrease in resistance. Or it may mean a decrease in resistance in a case that was able to overcome a slight increase so long as there was no abnormal strain.

I am thus explicit at this point because it is here that most errors are made in diagnosis. In the beginning of the disease these patients are especially likely to be moody. They fear something they cannot explain, they are joyous or depressed or they may change from one of these conditions to the other without cause and often without the ability of ascribing their mental or emotional condition even to an imaginary cause.

Many attempts have been made to make differential tests by the use of electricity which have been exceedingly interesting to those engaged in this research but as the results are entirely speculative, and unreliable from a practical standpoint, it will not be best to give them any space in this volume.

It is of course plain that there must be a marked increase in the power of the skin as a conductor in patients in whom profuse sweating is one of the marked symptoms but it can hardly be considered of much value to make tests requiring such great technical skill to diagnose cases with symptoms so pronounced that they can readily be recognized with the unaided senses.

4—**Mental Deficiency.** In a proportion of these cases the first symptom noted is some form of mental deficiency. In some instances this may take one form, in others quite the opposite. Some of these patients suffer markedly from melancholia while others are in a constant state of exhilaration, some become quiet and thoughtful while others talk incessantly. In a number of instances these patients first consult their physicians because they cannot live in peace with the other members of the family. In only a few instances have I encountered these patients with definite illusions or hallucinations but it is likely that the proportion of such patients encountered in the neurological practice must be much larger than in a surgical practice.

It is of course important to bear in mind that an insane person may acquire exophthalmic goitre independently of his insanity and *vice versa* that a patient suffering from exophthalmic goitre may become insane although in the latter case one would naturally be likely to consider the former condition responsible for the latter. On the other hand insanity and exophthalmos may both be due to increased intracranial pressure especially if this is caused by the presence of a tumor.

5—**Vertigo.** This symptom is not present with any regularity and it has appeared to me to be due largely to the anæmia in these cases and also that in many cases what appears to be vertigo is in fact only a condition of unsteadiness due to general weakness of the muscles which come into use in locomotion.

The symptom is not of great diagnostic importance in itself. Personally, I have never encountered it in any case not sufficiently far advanced to make a diagnosis possible long before this symptom made its appearance.

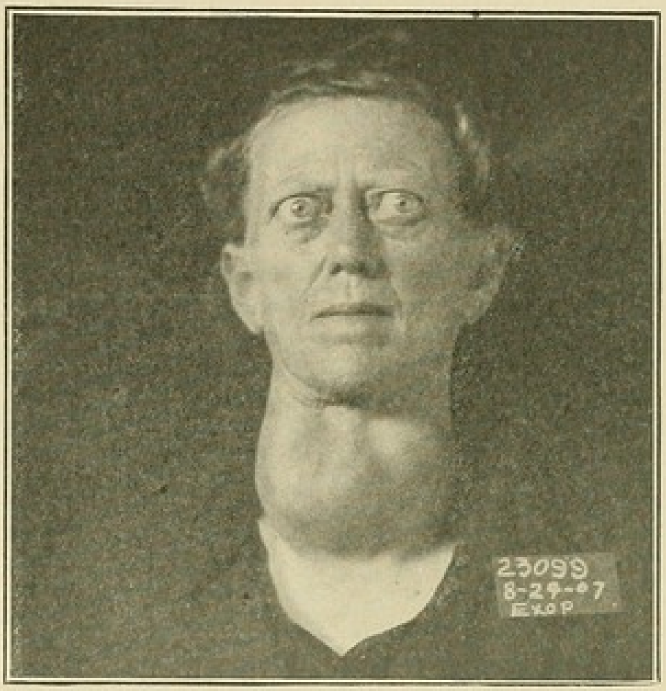


Fig. 11. Exophthalmic goitre with very prominent exophthalmos, the eyes protruding nearly to the point of dislocation. All lobes of the thyroid gland are markedly enlarged especially the right lobe. (By the courtesy of Louis B. Wilson.)

6—**Graefe's Sign.** In the year 1864, v. Graefe described a definite symptom which had been described independently eight years before by Desmarres in France but neither author seems to have known of the fact that the symptom had been recognized by the other.

The former's name has been attached to this symptom because of his long continued interest shown in this subject resulting in the publication of several excellent articles and because he was one of the greatest leaders in his specialty in his day.

The symptom can be readily recognized even in relatively mild cases but its absence does not warrant a negative diagnosis in the individual.

In directing the eye downward, the lower margin of the upper eyelid does not follow the line of vision normally but lags behind or follows in an irregular spastic manner. This clear cut symptom is of real value in making the diagnosis.

It should always be elicited when present. It is probably due to the weakness of the eye muscles due to the poisoning caused by the hyperthyroidism. Landström attributes this symptom also to the diseased condition of the muscle he has described.

The same explanation will apply to the condition elicited by the tests used to demonstrate Stellwag's sign and the sign of Moebius, so it will not be necessary to refer to it again.

Undoubtedly there are differences in the inherent conditions of these various muscles not only in different individuals but also between the various groups of muscles in the same individual which will account for the variations in the results of these various tests.

7—**Stellwag's Sign.** In close relation to Graefe's sign we must place that first described by Stellwag in 1869. This consits in the fact that especially in cases suffering from marked exophthalmos there is a retraction of the upper eyelid and at the same time the lid remains much more stationary than it does under normal conditions. There is also a marked decrease in the frequency of winking.

8—**Moebius' Sign.** In 1895, Moebius pointed out the fact that in many cases of exophthalmic goitre there is an insufficiency of convergence. If the patient is directed to look at the ceiling and then suddenly at his own nose it will be found that only one eye will be directed toward the nose and the other may take any other direction although it usually maintains its axis fairly parallel with the eye that is directed toward the nose. This symptom may also be elicited by having the patient fix an object with his eyes at a distance of several yards then by gradually approaching the face a point will be reached at which only one eye will continue to fix the object. The other eye will cease to see the object. There will be no double vision but the patient will feel a certain degree of strain during this experiment.

There is no definite distance from the eyes at which the convergence will cease and the distance is not constant in the same patient at different times.

There does not seem to be any definite relation between the degree of exophthalmos and the deficiency indicated by the test.

This test is not positive in all cases of exophthalmic goitre but it can be elicited in a majority of these cases.

9—**Paroxysmal Dyspnoea—Bryson's Symptom.** In close relation also with the symptoms just described we must place that of paroxysmal dyspnœa, because it is undoubtedly also dependent largely upon the effect which the thyroid poisoning has had upon the muscles of respiration.

It is important not to overlook the fact that the dyspnœa may in reality be due to the pressure upon the trachea by the enlarged thyroid gland referred to above. Neither must the anæmia and the weakness of the heart be lost sight of in the consideration of this subject. It is likely that in most cases all of these conditions or several of them may act together. then there may be a further exacerbation at times due to a dilatation of the stomach which is not uncommon and which would naturally cause more disturbance in these than in other patients.

Late in the course of the disease, a form of dyspnœa occurs which is not paroxysmal in character because it is entirely due to the œdema of the lungs.

10—**Intermittent Conditions Without Apparent Exciting Cause.** There are several conditions which come and go intermittently which may be considered together. They may all occur in the same patient at the same time or at different times, or they may occur but once or twice but there is this peculiarity that it does not seem possible to determine a satisfactory exciting cause for their occurrence.

These conditions are vomiting, diarrhœa, sweating often over circumscribed portions of the surface of the body, and mental depression, all intermittent. In many cases there seems to be a general exacerbation of the disease whenever one or more of these symptoms appear.

During these times the thyroid gland is sometimes engorged to a condition which has been aptly compared with a lactating breast as compared with the same organ during its inactive stage. That there is an increase in the local blood supply during periods of exacerbation there can be no doubt.

So far as the gastrointestinal symptoms are concerned it is likely that the involuntary muscles suffer quite as much in the walls of the stomach and intestines as do the heart muscles and the muscles in the extremities, and this would readily account for any disturbances in this part of the body .The mental depression has been attributed to the direct effect of the hyperthyroidism upon the tissues of the brain.

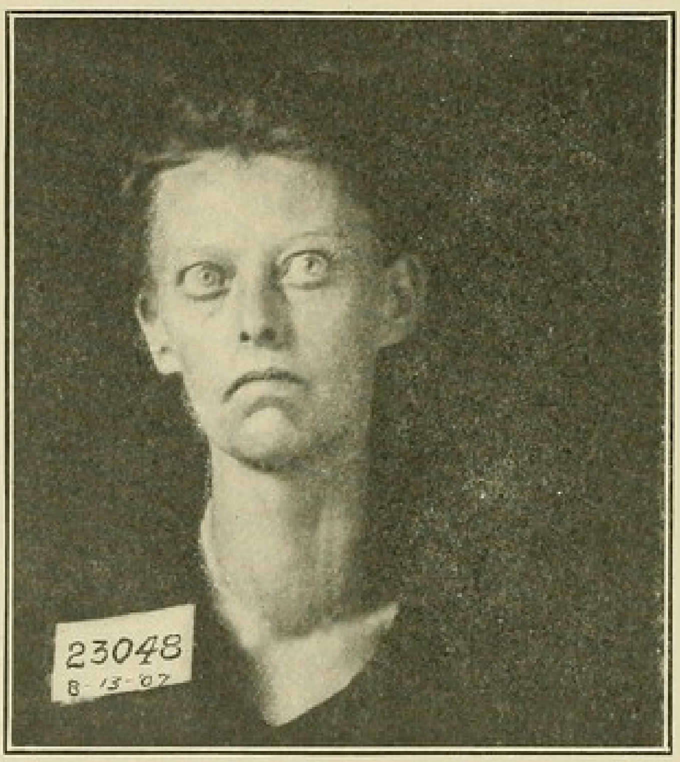


Fig. 12. Exophthalmic goitre with the goitre scarcely perceptible but the exophthalmos quite marked but not nearly so prominent as Fig. 11. (By courtesy of Louis B. Wilson.)

The erratic sweating reminds one very forcibly of hysteria and this symptom has frequently been brought forward in support of the neurotic origin of the disease. It seems, however, not unreasonable to suppose that notwithstanding the fact that satisfactory nerve lesions cannot be demonstrated still so general a poison is likely to have some effect directly upon the nerve tissues and that certain branches will be more affected than others. The actual pathological findings in the nervous system have been fully described in the chapters on pathology. In connection with the condition of intermittent mental depression without apparent exciting cause, it is proper to refer to epiliptiform seizures which frequently have been reported. There is no reason why true epilepsy should not complicate exophthalmic goitre but there are cases in which the cortical irritation is undoubtedly directly due to the thyroid poison. It is often difficult to distinguish between these paroxysms and those due to hysteria which also frequently complicates exophthalmic goitre.

Here again it is necessary to establish the existence of exophthalmic goitre because a mistaken diagnosis might readily give rise to an endless amount of harm to the patient. Undoubtedly, many cases diagnosed as hysteria which are actually suffering from exophthalmic goitre have been made much worse by extended travel, mountain climbing, social diversions, vigorous hydrotherapeutic treatment or by the various other methods often employed in the treatment of patients suffering from hysteria. I have personally encountered a number of these instances.

11—**Conditions Increasing Gravity of Disease.** A number of conditions regularly serve to increase the gravity of exophthalmic goitre sometimes to an alarming or even to a fatal extent, and it is consequently important that these should be pointed out with especial emphasis. This is true especially because some of these conditions are employed in the treatment of neurasthenia or hysteria and others in the treatment of simple goitre.

Psychic excitation is extremely harmful. In many instances every symptom is increased with enormous rapidity so that the patient loses ground to a marked extent from day to day and a week or a month may change the case from a hopeful to a hopeless condition. I have repeatedly observed such decline. It seems in these cases as though the blood were rapidly filled with a most active poison. Mental and physical exhaustion bring the same results only in a less violent form. In a number of cases in which the condition was mistaken for neurasthenia and consequently treated by vigorous exercise and mental diversion and social excitement, I have seen these patients become worse rapidly only to improve upon the substitution of absolute rest.

In order to impress this fact more acutely, I will give an abstract of the history of a case under treatment at the present time. A business man, 34 years of age, who had severely overworked for a number of years began to lose a pound in weight each day for a period of ten weeks, he also became severely nervous. Being exceedingly powerful and weighing 240 pounds, he did not pay much attention to the loss of weight and strength which he attributed to the fact that he had worked from seven in the morning until one o'clock the following morning during this time. When he began to suffer from dyspnœa he consulted his physician who prescribed a diet, out-door exercise and tonics, and a few weeks later a trip in the mountains at an elevation of over 10,000 feet with long rides on horseback over mountain trails. The case proved on examination to be a typical exophthalmic goitre. It is plain that the trip would have been extremely harmful if not worse.

The administration of thyroid extract is sure to have a harmful influence upon these patients although there may be a decrease in the size of the goitre. The decrease in the size of the goitre is especially likely to occur in patients who have suffered from simple goitre for some time before the occurrence of exophthalmic goitre. Recently, I have examined a maiden lady of thirty-six years who came for relief of gastric ulcer. She had carried a simple goitre for a number of years without any discomfort. Eight months ago she began to suffer from tachycardia and at the same time her eyes began to bulge forward. She also lost rapidly in strength. Two months ago she began to suffer from intermittent nausea, pain in the region of the stomach, occasional diarrhœa, profuse sweating, dysmenorrhea. All of these conditions were attributed by her and her physician to a gastralgia and as the symptoms were increased, to ulcer of the stomach.

The patient directed the physician's attention to the presence of the goitre, but the latter was so thoroughly engrossed in the care of the stomach that he gave only incidentally some slight attention to the goitre by prescribing thyroid extract internally and an iodine ointment for external use. Notwithstanding the most painstaking attention to the stomach the patient has lost over three pounds each week for the last eight weeks. She is now exceedingly anæmic and weak, her pulse beats 136 times per minute and she has all of the typical symptoms of exophthalmic goitre described above. This case is not at all isolated. I simply describe it because it was so typical in every respect.

What I have said of thyroid extract applies to a somewhat slighter extent to the use of iodine in the treatment of exophthalmic goitre. The use of iodine in any form always makes them worse.

Emaciation and Anaemia. In advanced cases emaciation and anæmia are practically always present but it will hardly be necessary to discuss these symptoms because they are plainly secondary to the malnutrition which is caused by the condition of the gastrointestinal tract described above.

We have confirmed the findings of Kocher in the examination of the blood that there is an increased lymphocytosis and a decreased leucocytosis but in itself the blood examination cannot determine the diagnosis, it can at most confirm a diagnosis which has already been made from a study of the symptoms described above.

Kocher reports careful blood examinations in fifty-eight cases in which he found the number of lymphocytes increased while the polynuclear forms were diminished. The total number of leucocytes was normal or rather below normal. The increase in lymphocytes was sometimes absolute but more commonly relative. In early cases and in those that have improved under treatment there is usually no increase of lymphocytes.

Conditions Occasionally Present. There are some other conditions which seem of little importance because they are present only in a very small proportion of cases, but as they are likely to direct the attention of the physician away from the correct diagnosis it seems proper to give them a limited amount of space at this point. Their presence or absence should not affect the diagnosis of exophthalmic goitre but it is important that their presence be not used to introduce doubt into the correctness of a positive diagnosis.

Discoloration of the Skin. In some cases there is a marked degree of darkening of the skin especially in the portions exposed to light or to the irritation of certain portions of the clothing like garters and waistbands.

The mucous membrane is either entirely free or only very slightly affected. In the face the most marked portion is around the eyes.

The areas about the nipples and the axillary spaces, the lower portion of the abdomen and the inner surface of the thighs are usually darker than the remaining portion of the body. Theoretically it may be supposed that this condition is due to the effect of the thyroid poison upon the suprarenal glands which seems reasonable although it will require much careful study to prove or disprove this theory because it is not likely that the pathological material can be obtained in a sufficiently fresh condition in a considerable number of these cases to bring about positive results.

The pigmentation changes with the severity of the conditions and disappears almost entirely after operation if this treatment has been successful in removing the typical symptoms of the disease.

These patients are likely to be mistaken for cases of Addison's disease. It is plain that such a mis-

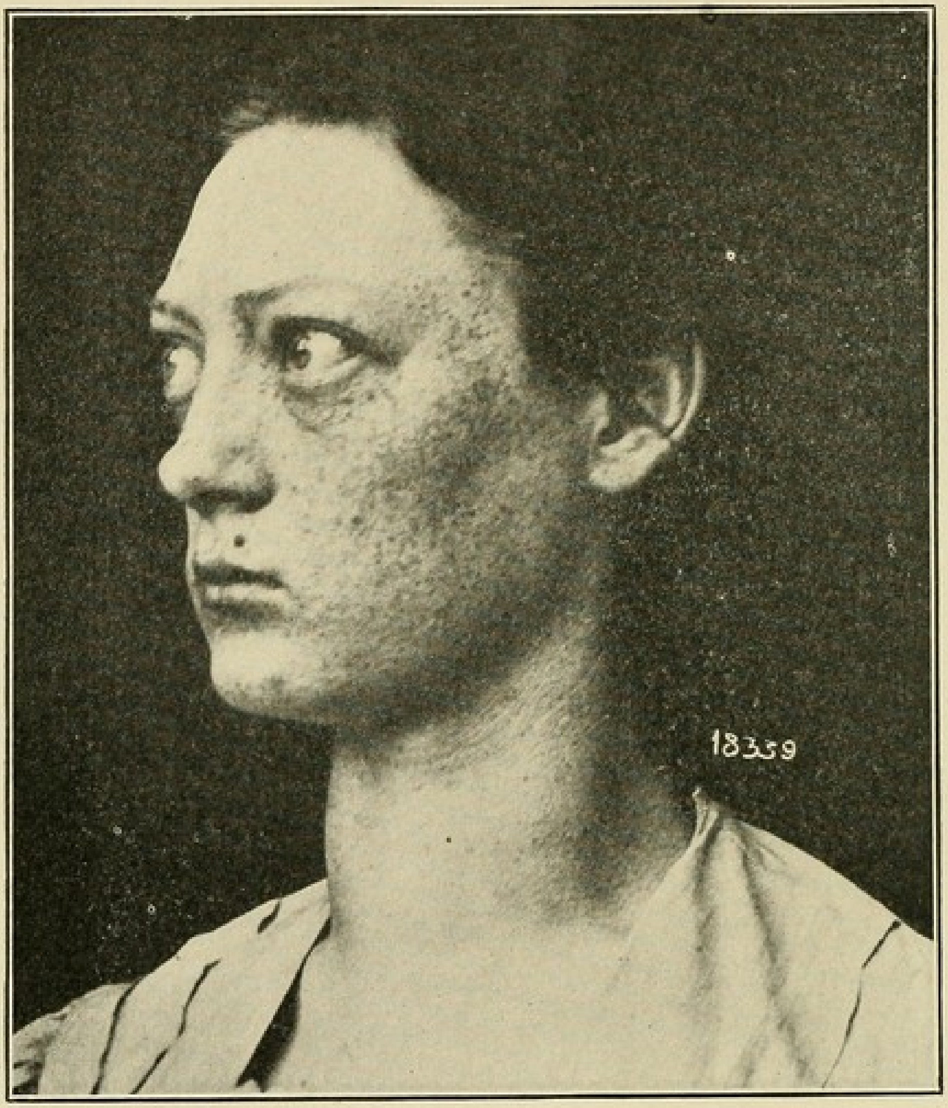


Fig. 13. Profile of exophthalmic goitre with but a slight goitre but fairly marked exophthalmos. (By courtesy of Louis B. Wilson.)

take would probably prove fatal to the patient unless corrected before the degenerative changes had advanced to a hopeless condition.

There is, of course, no reason why Addison's disease should not occasionally complicate exophthalmic goitre, but one should always exclude the latter disease carefully in every case in which the presence of pigmentation may suggest the presence of Addison's disease because in this way valuable time for treatment of the hyperthyroidism may not be lost. It is possible that the pigmentation may be due in these cases to the effect of the thyroid poison upon the suprarenal glands.

Erythema. This condition although not common should be borne in mind because it is likely to occur early in the disease and thus cause the physician's attention to be directed away from the correct diagnosis unless he is familiar with the fact that it occurs as a complication of exophthalmic goitre.

Blushing. Occasionally patients suffering from exophthalmic goitre are annoyed by the fact that the slightest mental excitement causes them to blush violently, a symptom which is less uncommon in young women who are suffering from this disease early in its course before marked anæmia has appeared.

Urticaria. In some instances urticaria may occur either spontaneously or upon external irritation. In some instances only one form of irritation will bring about this condition while in others it may be brought about by many forms of external irritation.

Circumscribed Oedema. In a considerable proportion of patients suffering from exophthalmic goitre circumscribed œdema may be observed. This condition may remain for days or weeks or it may appear suddenly and disappear again within a few hours. It may reappear in the same location or at any other point or it may disappear permanently. This condition can be differentiated from anasarca by the fact that it is not influenced by the position of the part of the body affected and that it is not symmetrical.

It is undoubtedly related in some way with myxœdema although the histological sections of tissue which have been removed from these circumscribed areas are quite different from similar sections made in cases suffering from myxœdema. The tissue in the former is thickened because of the presence of water, in the latter because of the infiltration with a mucoid substance.

Myxoedema has been observed in some cases in connection with exophthalmic goitre although the presence of this condition would indicate an absence of activity of the thyroid gland while as has been repeatedly stated exophthalmic goitre represents an increase in thyroid activity. This apparent discrepancy in theories has been explained by the supposition that on the one hand the thyroid gland has lost its ability to perform its normal physiological function, while on the other hand a portion of the gland is still active in producing abnormal secretion which when forced into the circulation gives rise to more or less typical exophthalmic goitre. It is most important to bear in mind these conditions because this will enable the physician to recommend treatment which is likely to correct both conditions. The treatment indicated for the relief of exophthalmic goitre in these cases must consist in the removal of that portion of the thyroid gland containing the nodules secreting the substance which causes the disease, or the double ligation and section of the superior, inferior, and anterior thyroid veins. Then the myxœdema must be relieved by administering thyroid extract. Were the thyroid extract

Fig. 14. Exophthalmic goitre, very early stage, neither the goitre nor exophthalmos well marked. (By courtesy of Louis B. Wilson.)

administered before the removal of the diseased portion of the thyroid gland, the tachycardia and the other symptoms of exophthalmic goitre would increase probably to a fatal extent. On the other hand were the thyroid gland removed without the subsequent use of thyroid extract, there would undoubtedly result an increase in the severity of the myxœdema. In these cases it would be reasonable to remove the diseased thyroid gland and simultaneously transplant normal thyroid gland from another person.

Scleroderma. This condition has frequently been observed. Singer believes that there is a definite relation between the condition of the thyroid gland and scleroderma not only in cases in which it has been incidentally observed in connection with goitre but also in all cases in which the patient is suffering from scleroderma independently.

Alopecia. In a number of cases, either circumscribed or general, baldness has occurred as a complication of exophthalmic goitre and in other cases there has been a loss of eyebrows, eyelashes, axillary and pubic hair. The beard seems affected less frequently than other portions of the body.

Atrophy of the Mammary Glands. There seems to be a marked shrinkage of the mammary glands early in the course of exophthalmic goitre before the effect upon the patient's general condition is sufficient to produce so marked a local effect. This seems to be coincident with a depression in the sexual vigor of these patients. This condition does not preclude pregnancy, although it is much more common to encounter patients in whom exophthalmic goitre has developed during the period of pregnancy or lactation than those in whom pregnancy has occurred during the existence of exophthalmic goitre.

A circumscribed œdema of one or both breasts may be mistaken for a hypertrophy but the condition is the same as though it occurred in any other portion of the body.

Enlargement of Lymph Nodes. In operating for the removal of portions of the thyroid gland one frequently encounters enlarged lymph nodes. It is doubtful if these have any definite relation to the disease. It is important not to mistake them for parathyroid glands. Confounding them with aberrant thyroid glands is of no importance because the removal of the latter is immaterial.

Enlargement of Thymus Gland. Practically, the fact is important that this gland is enlarged in a considerable proportion of cases. At autopsies in patients succumbing to exophthalmic goitre the upper margin of the thymus gland has frequently been found to touch the lower end of the thyroid, or in other instances enlarged lymph nodes have been found between the two. In the cases that died after thyroidectomy Capelle found persistency of the thymus gland in 79 per cent. It is possible that there is a lower death rate in cases in which the thymus gland has disappeared because in statistics taken without reference to operative treatment the number of persistent thymus glands is always considerably lower. Von Houseman found a persistent thymus in each of four out of eight cases. If this theory should become established, it would of course become necessary to find some way of determining the presence or absence of a persistent thymus gland before undertaking the operation.

In its presence it would then become proper to make the operation according to a plan which will be described fully under surgical treatment which would materially reduce the severity of the operation, possibly at the risk of being less uniformly effective. This would have a tendency to leave a safe margin of resistance in this particular class of cases.

Osteomalacia. This condition is mentioned by many authors all of whom seem to be convinced that there is some relation between it and thyroid disease. Clinically I cannot discuss this condition from personal observation. This may be a coincidence or it may indicate that the condition is quite as rare in those suffering from exophthalmic goitre as it is in others or the condition of the bones may not have been determined with a sufficient degree of accuracy in my cases.

In a number of cases of fracture in which union failed to take place promptly we have administered thyroid extract but it is impossible to determine positively whether this remedy definitely influenced the healing of these fractures.

General Appearance of Patients Suffering from Exophthalmic Goitre. Patients suffering from simple goitre need not be especially described because the condition is so apparent that it will require no especial description to enable even the least experienced physician to recognize the condition. The following illustrations, Fig. 7 and Fig. 8, will be introduced simply for the purpose of comparison. As regards the size of the swelling, it may be so small as to be scarcely perceptible and it may be necessary to palpate the neck in order to discover any abnormal condition or again in case the growth is retrosternal it may become necessary to have the patient go through the act of swallowing in order to make the enlargement apparent when it rises with the remaining portions of the thyroid gland which may not be enlarged.

From this size it may vary in other cases to an enormous proportion. Fig. 9 and Fig. 10 illustrate one of these cases in which the gland when removed weighed six pounds and fourteen ounces after the blood had drained away.

The growth may be sessile with a broad base as shown in Fig. 9 or it may be narrower at the base with its greatest portion projecting down over the chest, or it may arise from one lobe and be pedunculated. In fact the swelling may take upon itself a large variety of forms and the size may vary enormously. It is surprising how large a goitre a patient will occasionally carry about without seeking relief from surgical interference. This was true especially in the portions of Switzerland in which goitres are endemic before Kocher popularized the operation of thyroidectomy. In some instances the growth becomes so large that the patient has to improvise a form of bandage which contains a pouch in front into which the goitre fits and a broad band behind to be buttoned around the neck so that the weight of the tumor is supported partly from the back of the neck instead of pulling entirely on the front. Fortunately for the patients the old fear of operation no longer exists and consequently relief is usually obtained before so advanced a condition has developed.

In exophthalmic goitre the size of the goitre is rarely an important feature although occasionally one encounters large goitres in connection with this disease. The striking feature in the appearance of these patients is the prominence of the eyes which may vary from a scarcely perceptible prominence to an actual protrusion which may be so marked that

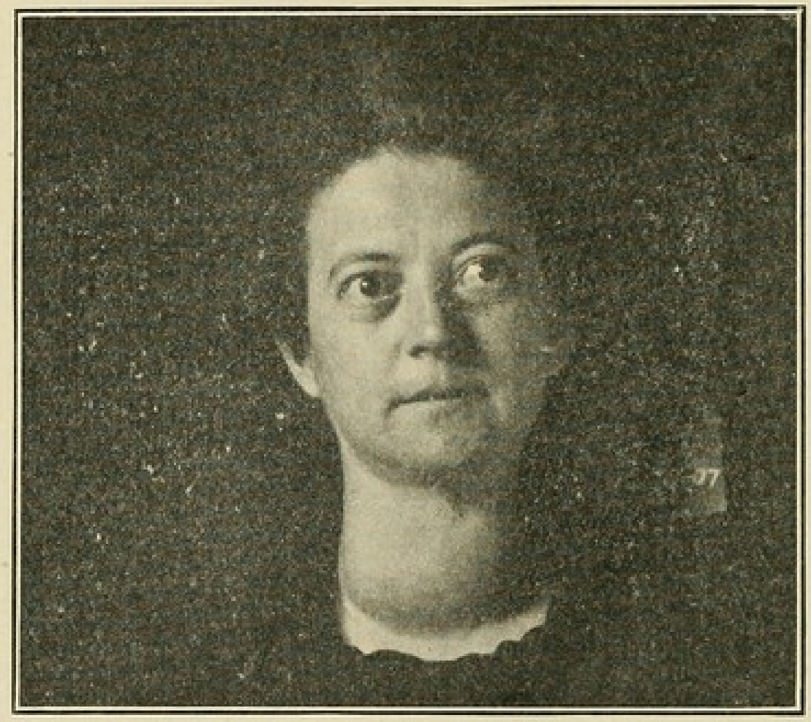


Fig. 15. Exophthalmic goitre. The exophthalmos and the goitre well marked. (By courtesy of Louis B. Wilson.)

the eyeball may actually be dislocated from its socket so that it hangs down upon the cheek.

I have personally encountered but one case in which the condition was so extreme but many cases have been reported and I have encountered a number of cases that approached this condition. Fig.

11 approaches this degree of protrusion. In this case the goitre itself is of considerable size while in Fig. 12 we have quite a marked protrusion of the eyes while the enlargement of the thyroid is scarcely perceptible from a distance. The same is true in Fig. 13 in which the condition is shown in profile.

.Figures 14, 15, 16, show various degrees of protrusion but in cases like these there is no difficulty in recognizing the condition. It is in cases like the one shown in Fig. 17 in which neither the exophthalmos nor the goitre is prominent that the condition is likely to be overlooked.

Complications. Aside from the complications which have been mentioned in connection with the discussion of the major, minor, and incidental symptoms exophthalmic goitre may be complicated with all diseases which a person can acquire who is not suffering from the condition and conversely aside from the fact that a patient with slight resistance is more likely to suffer from diseases in general, it may be said that a patient suffering from exophthalmic goitre is no more likely to suffer from any complication than any normal person.

Contagious and infectious diseases have not been mentioned frequently in connection with this disease but this may be accounted for by the fact that these patients are not likely to be exposed to contagion or infection. An exception should be noted in the fact that relatively a considerable number of these cases suffer from tuberculosis.

. All other diseases have been mentioned but it is clearly not necessary to enumerate these separately.

It is, however, exceedingly important to bear in mind the fact that the presence of any other disease does not exclude the possibility of its complication with exophthalmic goitre and also that this is a grave complication at all times and one that will require especial attention. An example of the importance of this element will become apparent upon studying the report of Gautiers, of Geneva, who found that symptoms of exophthalmic goitre frequently develop in apparently latent cases upon the administration of iodide of potassium. The use of this drug is of course especially contraindicated together with the use of thyroid extract in cases which were suffering primarily from simple goitre but in whom exophthalmic goitre developed later.

CHAPTER IV.

NON-SURGICAL TREATMENT.

Treatment of Simple Goitre. Although this book should properly not reach beyond the surgical side of this question, it seems important to bear in mind that all forms of non-traumatic and non-malignant diseases of the thyroid gland are primarily medical.

There is so convenient an opportunity for the surgeon of falling into an error in logic at this point because he comes in constant contact only with those cases that have failed to respond to internal treatment that it may appear to him from his own experience that internal treatment always fails to cure goitre because it has always failed in all of the cases that have come under his professional care. As a matter of fact, a much larger proportion of cases never consult a surgeon because they recover spontaneously or they are cured by internal, dietetic, and hygienic treatment. For this reason it seems important to give some attention to this feature before directing attention to the means offered by surgery for the relief of thyroid disease.

The fact that practically all cases which come to the surgeon for relief of thyroid disease have wasted much time by subjecting themselves to the ineffective efforts of the internist, neurologist or the various electrical and other specialists might readily be construed to mean that all of these methods are useless and that the patients should be at once referred to the surgeon for operative treatment. This conclusion would, however, be quite as wrong as it would be for an internist to conclude that because the few cases he has referred to a surgeon have died following the operation, therefore surgical treatment is always contraindicated.

The facts are as follows: More than one-half of all cases of goitre will recover under careful dietetic, hygienic and medicinal treatment which must consist in drinking an abundance of good water which can always be obtained in regions where goitre is endemic by distilling it, by carefully regulating the diet, by correcting the conditions of ventilation in homes and especially in sleeping rooms, by insisting upon an abundance of sleep and upon an absence of excitement and of mental and of physical fatigue.

So far the treatment refers as well to simple as to exophthalmic goitre.

In simple goitre the application of a non-irritating absorbable iodine ointment to the neck seems to be of considerable benefit. Internally general tonics are of undoubted value and from 3 to 5 grains of a reliable thyroid extract given from three to six times daily seems to have a specific value.

It should be borne in mind that many of the preparations of the thyroid gland in the market are perfectly inert because these have been deprived of their active elements by some faulty process in the manufacture. It is consequently important to use only tested products.

In case of simple goitres that do not yield upon the treatment just outlined it is well to inject directly into the substance of the gland ninety drops of a five per cent. aqueous solution of pure carbolic acid, a method introduced and practiced for many years by Professor Moses Gunn. It is important to prepare this solution carefully by mixing the carbolic acid with boiling water because when mixed with cold water small globules of the strong acid may continue to float in the solution and these will cauterize the tissues with which they come in contact. This treatment is to be repeated once each week. When more than one lobe of the gland is involved the different lobes should be injected at successive treatments, until all of them have been so treated when two or three of the lobes may be injected at each treatment. If the patient shows marked vertigo or if the urine becomes dark and cloudy the quantity injected should be reduced. It is, however, but rarely necessary to reduce the quantity. In order to determine the fact that the injection is actually made into the gland, the patient should go through the effort of swallowing before the contents of the syringe has been discharged after the needle has been plunged into the enlarged gland. If the needle is in the proper position the syringe will rise with the act of swallowing. It is well for the patient to lie down for a few moments after the injection has been made because there is frequently a little vertigo directly after the solution has been injected into the gland. During the administration of many hundreds of these injections, I have never seen any harmful effects.

In cases which can be cured by this method, there is usually a marked improvement by the time the patient has received from six to ten injections. In the meantime the treatment with tonics, thyroid extract and hygienic and dietetic methods should be continued. In many cases in which the latter treatment alone without the injections made no impression the patients have recovered fully after this

Fig. 16. Exophthalmic goitre. Both exophthalmos and goitre are sufficiently advanced to be easily recognizable but cases of this degree are very frequently overlooked.

treatment was added. It seems important to insist upon the use of distilled or pure spring water in all patients who continue to live in the vicinity in which they acquired the goitre.

In simple goitre in regions where this disease is not endemic fully fifty per cent. of all cases will recover by the use of hygienic, dietetic and medicinal treatment and more than one-half of the remaining cases will recover if the injection treatment is added to the other treatment. The remaining twenty-five per cent. will resist every form of treatment except excision which will be considered later. In countries where goitre is endemic these methods seem less useful probably because it is so much more difficult to eliminate the exciting cause. Electricity has been employed in the form of x-ray exposure and by the application of practically every form of this agent, Undoubted improvement has been noted in patients subjected to this form of treatment but it is difficult to determine just how much can properly be attributed to the action of the electricity and how much should be attributed to the benefits from concurrent diet, hygiene and medication.

The cases that do not yield to any of these forms of treatment should then properly be considered surgical in character and should receive relief through operative interference provided the patient suffers because of the presence of the deformity or because of obstruction to breathing or swallowing or discomfort from pressure either because of the location or the size of the goitre.

That there is a certain proportion of cases of simple goitre which will not yield to any form of non-surgical treatment there can be no doubt and it is this class of cases that come under the observation of the surgeon after all other means have been tried and which gives him the impression that none but surgical treatment is indicated for the relief of patients suffering from goitre unless he is in a position to observe the much larger proportion of cases also which never come to his department because non-surgical treatment has eliminated them. The varieties of non-exophthalmic goitres which are most likely to yield to non-surgical treatment will be considered further with the discussion of the pathology of goitre.

The reason for discussing the medical treatment so briefly is of course apparent but I wish to be emphatic in stating that all non-malignant and non-traumatic diseases of the thyroid gland should first be considered medically because with the rise of thyroid surgery it would otherwise be certain that many patients would be subjected to operative treatment quite unnecessarily. More than one-half of all the patients who have come to me for examination during the past twenty years have recovered promptly upon the use of non-surgical treatment and the proportion of cases that are curable without operation coming to the surgeon for advice must necessarily be much smaller than that coming to the internist for the same purpose. It is doubtful whether one could come upon some permanency of cure following the non-surgical treatment of these cases in countries where goitre is endemic.

That the results of non-surgical treatment are permanent where they are primarily effective in this vicinity, I have had an abundance of opportunity to confirm, because I had the care of many of these cases while serving as the assistant of Prof. Moses Gunn, who introduced the carbolic acid treatment, and I have followed many of these cases for a period of twenty-five years. It would be interesting to follow these cases statistically in some of the great internal clinics but I have failed to encounter any important records. It seems that no one has followed these cases after their recovery for the purpose of reliable statistics to compare with the results obtained in cases treated surgically.

Non-Surgical Treatment of Exophthalmic Goitre. The use of rest especially as well as other hygienic and dietetic measures applies even to a greater extent to the non-surgical treatment of exophthalmic goitre than to the treatment of simple goitre. There are, however, two very distinct differences. It is far more important that these cases be subjected to early surgical treatment in case the non-surgical treatment proves futile than is the case with simple goitre. In exophthalmic goitre prolonged non-surgical treatment in cases in which there is no improvement always results in serious degenerative changes. These progress to a point at which surgical treatment is no longer possible because the patient's power of resistance has been dissipated to a hopeless degree so that a fatal result must be expected after an operation. Or the patient may still have a sufficient degree of resistance to recover from the operation which may serve to stop the progress of the disease so that there is no further degeneration of any of the tissues which suffered as a result of the thyroid poisoning before the operation, but the degree of degeneration may have advanced so far that the power of recuperation may be entirely or almost entirely lost. Such cases may continue to live for many years following the removal of the diseased gland without any increase in symptoms which would indicate that the thyroid poisoning is still active but they will remain weak. If they are dependent upon their own efforts for their support they invariably become public charges. If they have independent means they are usually extremely unhappy because they are not able to follow the pursuits or pleasures which they enjoyed during their lives before acquiring exophthalmic goitre. Even if surgical treatment is employed early there is usually not a complete recovery according to the investiga-

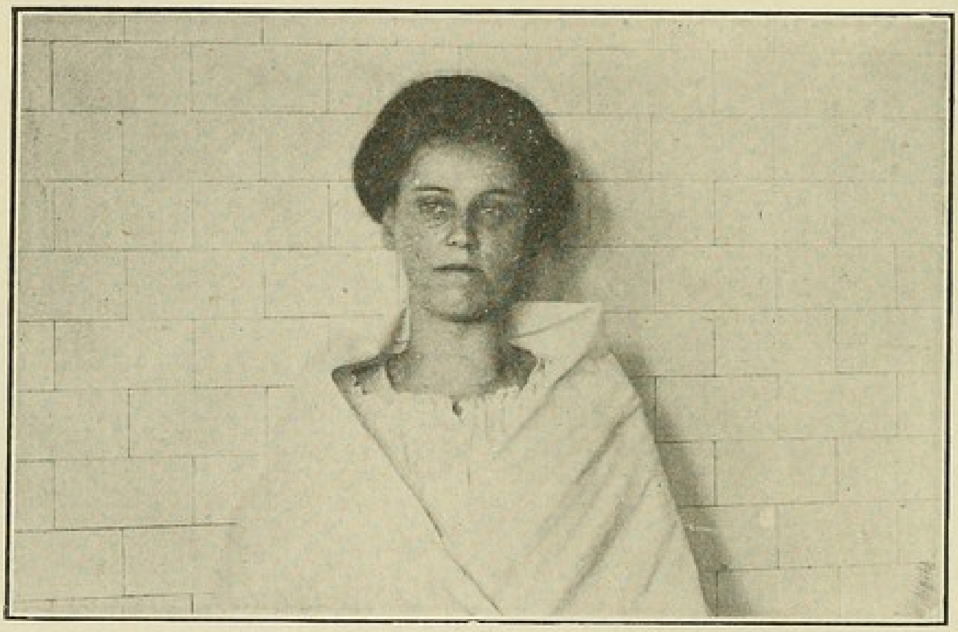


Fig. 17. Represents a case of exophthalmic goitre in which both the exophthalmos and the goitre are so slight that they will usually not be discovered until the diagnosis is suggested by the presence of other symptoms like tachycardia, tremor or muscular weakness.

tions of Landström. Although the patients may be apparently quite well a careful examination of the heart will usually demonstrate at least a slight defect.

Treatment. Rest is the most important element in the treatment of exophthalmic goitre and in the after-treatment following operations, and it should be borne in mind that this refers quite as much to mental and emotional as to physical rest.

The mental condition of these patients often causes them to become intensely interested in social or religious affairs or in other matters such as literature or music. I have encountered an instance in which the patient, a delicate woman, became almost insanely interested in card playing. The particular subject in which these patients waste their energies is probably largely accidental and due to environment but it is equally harmful and must be stopped without making too severe an impression upon the patient's emotions. In post operative cases this is plainly much easier of accomplishment than in cases that have not been operated. That it is of the very greatest importance to secure rest for these patients there can, however, be no doubt. This must be insisted upon for many months after the patient has apparently recovered without regard to the mode of treatment that has been employed in any given case.

Such patients should be guarded as much as possible against severe sudden or continued strains that can be avoided but that must be accepted in the life of other persons. This would apply especially to pregnancy which has resulted in a large proportion of abortions according to Schmauch and in the death of a considerable number of mothers, although according to Charcot, the surviving mothers are likely to recover from the exophthalmic goitre.

Specific Medication. In a condition which is clearly due to a definite poison circulating in the blood, the treatment must logically consist either in removing the source of the poison, thyroidectomy, or in the introduction of some medium which will make this poison harmless after it has been introduced. A number of attempts have been made to find a substance which will have a neutralizing effect upon this poison. Moebius has introduced the serum of thyroidectomized goats known as "antithyroidin," which is administered internally in doses of from 20 to 60 drops every eight to twelve hours at first regularly and later at intervals of several days. Much stress has been laid upon giving a meat free diet consisting mainly of vegetables, fruits, eggs and milk and that the use of table salt be reduced to a minimum.

Beebe and Rogers have prepared and administered a serum which in early cases has given good results when used in connection with rest, hygiene and proper diet. This serum seems to be of especially great value in acute cases with very severe symptoms.

Forschheimer highly recommends the use of hydrobromate of quinia in doses of five grains, administered four times daily in gelatine coated pills, either with or without the addition of one grain of ergotin. He has usually observed improvement within 48 hours after beginning this treatment, which he continues until the patient is normal. He has observed cures within three months from the beginning of the treatment while in one case he continued the treatment uninterruptedly for a period of three years. The patient recovered without experiencing any harmful effects from the use of the remedy. In case a patient does not improve from the use of the quinine hydrobromate in forty-eight hours he adds one grain of ergotin to each dose.

He has observed the following effects of this treatment: 1. The tachycardia disappears. 2. The thyroid gland diminishes in size. 3. The tremor and the exophthalmos diminishes and later disappears. The first change usually takes place within 48 hours after beginning the treatment which must be continued until all symptoms have disappeared. In nine out of twelve patients of fully developed cases the treatment was entirely successful, the failures were in the very violent forms primarily or in foudroyant relapsing cases. In forty-five cases of all varieties of severity treated by this method there were five failures.

A large number of other drugs have been recommended and discarded which cannot be discussed. Kocher has used sodium phosphate with the hope of stimulating elimination.

It seems reasonable to hope that at some time a remedy may be introduced which will thoroughly neutralize the thyroid poison in the blood. It is possible that in favorable cases this is accomplished by the hydrobromate of quinia.

In the meantime it will be necessary to remove the cause in a large proportion of these cases by performing thyroidectomy.

Iodine. For many years the internal and external use of various forms of iodine as well as the hypodermic injections into the enlarged thyroid gland in simple hypertrophy has obtained so fixed a position in the minds of practitioners of medicine that it has been difficult to impress upon them the fact that in exophthalmic goitre this remedy is almost always certain to do harm although it may cause the goitre to decrease in size. The manner in which patients become worse is by an increase of the hyperthyroidism and with this the increase in all of the important symptoms of exophthalmic goitre but especially the heart symptoms.

Lanz, and many of his followers, have claimed constant improvement in patients who lived largely on milk from thyroidectomized goats. This would virtually represent another form of serum therapy. Many other observers have reported improvement from the use of a liberal diet of milk either alone or with other food.

Thymus gland has been given in the hope of obtaining in this manner a kind of antibody. The results do not seem to have been encouraging.

Strophanthus, belladonna and arsenic are mentioned by most authors but discredited by more. Reliable statistics are lacking with all of these.

Thyroidectomy. General Considerations: Within a quarter of a century this operation has changed its position entirely in the minds of the surgical profession. At the beginning of this period, it was looked upon as one of the most dangerous of all major operations and at the end of this short space of time, we look upon it as one of the safest of major operations. This change is due largely to the skill and genius of Professor Kocher whose enormous experience enabled him early to speak with authority upon this subject, pointing out methods, recognizing dangers, simplifying technic and in thyroidectomy for exophthalmic goitre pointing out the importance of operations in repeated stages doing at any one time only as much as the individual patient under consideration could safely bear.

His views have been supported on all sides by surgeons whose wide experience has insured excellent surgical judgment.

Dangers of Thyroidectomy. The following dangers of thyroidectomy should not be overlooked 1, anæsthesia; 2, shock; 3, hæmorrhage; 4, hyperthyroidism; 5, infection; 6, recurrent laryngeal nerve injury; 7, injury to parathyroid glands; 8, air embolism; 9, collapse of trachea and consequent asphyxia.

CHAPTER V.

ANAESTHESIA.

Accidents from anæsthesia have not been uncommon during operations upon the thyroid gland. There are several reasons why this should be the case. In many of these cases respiration has been impaired for a considerable period of time before the operation so that even during sleep the patient has felt the necessity of being prepared for emergencies of asphyxiation so that the sleep has become habitually light. Under deep anæsthesia the patient is no longer able to use his muscles to guard against this difficulty and before the anæsthetist notices anything wrong the patient may be in serious trouble. Moreover, the operation is at a point where the anæsthetist can readily watch the work of the surgeon unless some precaution is used to prevent this and consequently the administration of the anæsthetic may not receive as close attention as is proper. Again, especially in cases of exophthalmic goitre the heart has suffered very severely as a result of the disease and consequently the toxic effect of the anæsthetic is more serious than in other cases. The manipulations in form of pressure and traction upon the trachea and larynx often increase the flow and accumulation of mucus which interferes with respiration. Many authors, especially Landstrom, consider general anæsthesia the greatest danger in operations, especially for the relief of exophthalmic goitre and they consequently insist upon operating only under local anæsthesia. Moebius on the other hand thinks that the harm done the sensitive nervous system of these patients is much greater than the harm of a carefully administered anæsthetic. Crile also points out the fact that mental excitement greatly increases all symptoms and that consequently local anæsthesia should not be practiced.

Remedies Against Dangers from Anaesthesia. In many cases it is wise to give the patient a hypodermatic injection of one-quarter of a grain of morphia and one one-hundredth of a grain of atropine half an hour before operation.

There are two methods which may be employed to prevent difficulties from this source.

1. Local anæsthesia. In order to use local anæsthesia successfully it is necessary to have a number of hypodermic syringes which can be sterilized and which are in good working condition. The solution to be used should be freshly prepared and should of course be sterile.

All preparations should be made quietly and with as little annoyance or excitement as possible for the patient.

Unless the patient's confidence can be gained before the administration of the local anæsthetic is begun, it is much better not to attempt it because the patient will imagine that she is suffering and this will be of almost as much harm to her as actual pain. It is consequently especially important if local anæsthesia is employed in operations for exophthalmic goitre that this condition be achieved. This is very largely a personal matter. Many surgeons have the full confidence of their patients in all of their undertakings and for them it is not a difficult matter to employ this method.

Moreover, in institutions in which many of these operations are performed patients encourage each other and the new arrivals are impressed with the fact that it is really a very simple matter and when they have once become convinced of this fact, it is an easy matter to carry out any plan.

Choice of Anaesthetic. Cocain in one per cent. solution has been used in many cases or to this may be added one-half per cent. of adrenalin chloride (1 to 1000). This is preferred by many surgeons because it reduces the amount of oozing of blood from the wound surface during the operation. Landstrom condemns the use of adrenalin because he has observed severe hæmorrhage after its effect upon the tissues had worn off.

A two per cent. solution of novacain has been recommended by others and again others recommend the use of a one-half per cent. solution of beucaine which is a synthetic preparation which does not degenerate upon boiling. If adrenalin is used in connection with this preparation, however, it must be added after boiling has been completed. The addition of adrenalin chloride to beucaine makes the anæsthesia last from four to eight times longer than beucaine alone which is active for about fifteen minutes.

All of these substances should be dissolved in normal salt solution; eight parts of sodium chloride in 1000 parts of distilled water, sterilized by boiling.

A syringe armed with a fine needle filled with any one of the above solutions is employed. The needle is inserted into the skin at any point along the proposed line of incision, enough of the solution is forced into the skin to form a bleb one c. m. in diameter. Then the needle is pushed on into the skin along the proposed line of incision

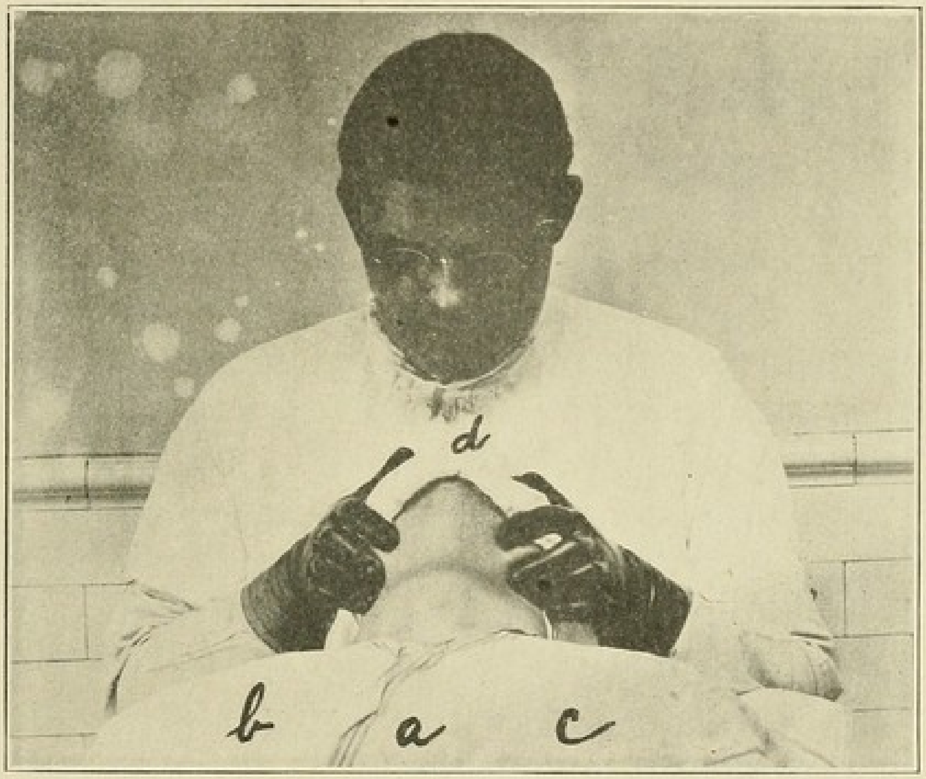


Fig. 18. Anterior view of patient already anaesthetized and in position for operation with the head elevated, the towels a, b, c in place, also pad of eight thicknesses of gauze placed over mouth and nose to prevent patient from breathing or coughing into her own wound. The assistant is holding the jaw upward and extending the neck.

and more of the fluid is forced into the skin until the entire line of incision forms a continuous row of blebs from one to two c. m. in width. A small puncture is now made in the line of incision with a large sharp needle, a Hagedorn being preferred, or a fine, sharp narrow-bladed scalpel, and now the sharp needle of the syringe is exchanged for a long, blunt needle with an opening on the side near its distal end.

This needle is introduced through the needle puncture and passed upwards along the inner border of the sterno-mastoid muscle and a small amount of the fluid is forced into the tissues along the course of the needle. With a little practice it is possible to anæsthetize the tissues so thoroughly that there is absolutely no pain upon making the skin incision and this will give the patient much confidence so that if the remainder of the operation is carried out with a sufficient amount of gentleness, the amount of suffering will be at least bearable and will soon be forgotten after the operation is completed.

It is this enforced gentleness in the manipulation of the tissues during the operation which is really of the greatest value to the patient because the patient cannot and will not submit to the violent manipulations which the surgeon might inflict upon the tissues were the patient under the influence of a general anæsthesia. Surgeons who are habitually violent in their technic will undoubtedly have better results if they make their thyroidectomies under local anæsthesia.

The operation may also be performed under local anæsthesia by means of Schleich's infiltration with very weak solutions but the tissues appear so unnatural as a result of this infiltration that the difficulties are greatly increased.

Moreover, the wounds seem to be much more painful after the effect of this local anæsthesia has disappeared than after operations performed under general anæsthesia.

For several years the fact that Kocher had performed so large a number of thyroidectomies with local anæsthesia and that others notably Landstrom had attributed a large proportion of the mortality following this operation to the use of general anæsthesia has caused many of the more recent authors to treat the question of anæsthesia in these cases as settled in favor of local anæsthesia. The following facts should, however, not be overlooked; first, that real harm is done to the patient by the mental strain due to undergoing an operation without being unconscious as pointed out, particularly by Crile, and Moebius, and second, the fact that in Mayos' Clinic and in Crile's and in my own, general anæsthesia has been practiced in a much larger number of cases of thyroidectomy than local anæsthesia has been employed in any other clinic with the exception of Kocher's, and that we have had a mortality quite as low as the lowest that has been recorded in the clinics where local anæsthesia is being practiced. Of course, it should be borne in mind that careless general anæsthetization must be absolutely condemned in these cases. I would also add that probably no general anæsthetic except ether and that only when given by the drop method, is at all safe in exophthalmic goitre. It may be an advantage to precede the administration of ether by the hypodermatic administration of one-fourth of a grain of morphine and one one-hundredth of a grain of atropine.

Ether Anaesthesia. It has been found that all patients not suffering from asphyxia at the time of operation do well if ether is administered in the folling manner:

After protecting the patient's eyes by the application of a piece of guttapercha tissue covered externally with a thick layer of cotton, an ordinary wire mask such as is usually employed in the administration of chloroform, is covered with four to six layers of gauze or two layers of rather thick stockinette material. This is placed over the patient's nose and mouth, then the anæsthetist begins to count and requests the patient to repeat the numbers after him slowly. The anæsthetist repeats some number with three figures slowly, after the patient has repeated this number the anæsthetist repeats the next number either upwards or downwards and the patient again repeats this. This plan is continued until the patient has been very thoroughly anæsthetized, the ether being dropped slowly but constantly upon this mask. By using this open mask there is never any danger of asphyxiation. By following this particular plan of counting, the patient's attention will be fixed upon the anæsthetist's voice. While the anæsthetist repeats the next number of three figures the patient has sufficient time to thoroughly fill his lungs by taking a deep inspiration. He does this unconsciously and unintentionally in the preparation for repeating the next number. While he repeats this number of three figures he unintentionally exhales fully and is in condition again to fill his lungs thoroughly by the next inspiration. Ordinarily this will result in from eight to twelve inspirations per minute.

The regularity and monotony of the performance has an excellent effect upon the patient's nervous system and in presence of a rapid pulse there is usually a marked improvement in the character of the pulse by the time the anæsthesia has been completed. In fact we have observed a marked difference in cases in which this method was employed and in those in which the patient was directed to count independently from one upwards. The patient should always be completely anæsthetized before she is disturbed by washing the field of operation preparatory to beginning the operation. If the patient is disturbed before full anæsthesia has been reached, a stage of excitement is likely to be caused which will necessitate the use of a much larger amount of the anæsthetic before full anæsthesia has been reached.

After the patient is fully anæsthetized, the neck which has been carefully prepared the previous evening is again washed with alcohol. A piece of gauze saturated with alcohol is placed over the neck, the towels and sheets separating the field of operation together with a considerable portion of the surrounding area from the remaining surface of the body are then adjusted. This requires but a few moments, during which time the administration of the ether is continued.

Whenever everything is ready for the operation to begin the ether mask is removed and a pad composed of eight layers of sterile gauze is placed transversely across the face thoroughly covering nose and mouth and preventing the patient from breathing or coughing into her own wound.

The lower end of the table is now depressed from an angle of 30 degrees to 45 degrees so that the patient is in the inverted Trendelenburg position. This results in a sufficient cerebral anæmia so that the operation can be readily completed without the administration of any additional anæsthetic. This position has the further advantage of reducing the hemorrhage to quite a marked extent. In order to keep the respiration unobstructed an assistant lifts the lower jaw forward so that the lower incisor teeth become engaged in front of the upper ones. At the same time he holds the gauze pad in place as shown in Fig. 19, so that there can be no infection from the mouth or nose. A small pillow placed under the patient's shoulders causes the anterior surface of the neck to become prominent and the traction by the assistant exaggerates this at the same time that it facilitates the patient's breathing.

There are several very distinct advantages in administering the anæsthetic in this manner. 1. The patient is relieved of all nervous and mental irritation and depression. 2. The amount of anæsthetic required is exceedingly small. 3. The heart's action improves under this form of administration of ether. 4. The administration of anæsthetic having ceased before the operation is started, the surgeon can concentrate his entire attention upon the operation itself. 5. There is no possibility of infection from mouth or nose or by the anæsthetist during the operation. 6. The patient exhales so much of the ether taken before the operation is completed that nausea and vomiting practically never occur. 7. Upon lowering the head at the completion of the operation the patient awakens fully almost immediately. 8. It is usually possible to give these patients sips of hot water to drink shortly after the operation which is an advantage after operation for exophthalmic goitre. 9. These patients do not inspire mucous which is often very troublesome when the anæsthetic is continued throughout the operation. 10. They are able to sit up at once when they return from the

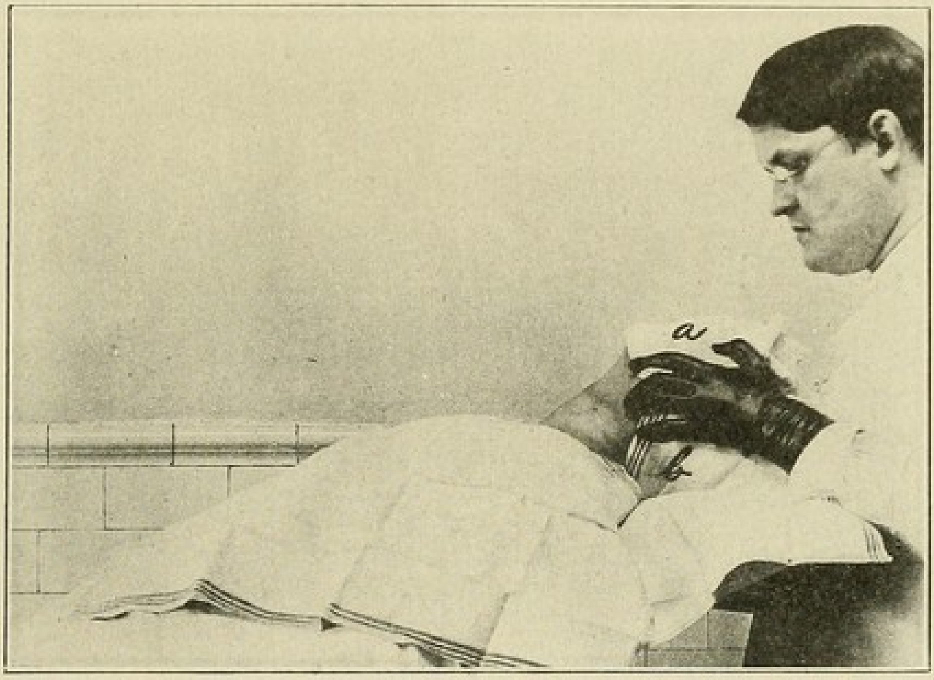


Fig. 19. Lateral view of patient anaesthetized and in position to begin operation. A pillow has been placed under the shoulders in order to extend the neck. The assistant holds the jaw forward, extends the neck and holds the gauze pad covering the patient's mouth and nose. The patient's hair is carefully covered by a towel (b) and the body is covered completely with a sterile sheet and towels, only the neck being exposed.

operating room which still further protects them against bronchitis and pneumonia.

It seems important to be thus explicit because when these details are carried out one of the greatest difficulties in the way of thyroidectomy for the relief of exophthalmic goitre is eliminated in a very safe and simple manner. One point must be insisted upon which might readily be overlooked, the task of lifting the patient's jaw forward must be entrusted to a reliable, intelligent and trained assistant and not to any one who may accidentally be available and is unfit for any other duty. In one instance, I have observed an almost fatal asphyxia because this assistant relaxed his hold upon the lower jaw after the gland had already been removed. This permitted the tongue to fall back into the pharynx and to obstruct the respiration completely. The surgeon did not know this had happened until he noticed a deep cyanosis in the flap. Then he immediately drew forward the tongue, lowered the head of the table and performed artificial respiration. Fortunately the patient had not advanced in her disease to the stage of advanced myocarditis, a condition so commonly found in connection with exophthalmic goitre and consequently the patient recovered which would have been quite unlikely in a more advanced case.

Rectal Anaesthesia. The advantages of this method must be apparent if further experience does not show harmful effects.

The following advantages are claimed for the method by those who have employed it.

1. The amount of ether employed is very much smaller than by the inhalation method.

2. There is no stage of excitation.

3. There is no irritation of the respiratory mucous membranes.

4. The anæsthetist does not approach the field of operation.

5. Besides being out of the way he also is unable to infect the wound.

6. The patient awakens almost at once after the anæsthetic is stopped.

7. There is said to be less nausea and vomiting probably because the patient has not swallowed quantities of mucous saturated with ether.

8. There is no depressing effect upon the heart.

It is, however, to be remembered that all of these advantages are also obtained if the method is employed which has just been described of thoroughly anæsthetizing the patient by the inhalation method and then stopping the anæsthetic and elevating the head during the operation.

Method of Application. It is most important that the colon be empty at the time of administration of ether by rectum, because the presence of fæces will prevent the rapid absorption of ether and the openings in the tube through which the ether fumes are introduced, may become clogged and thus the introduction in sufficient quantities may be prevented.

In order to secure an empty colon, two ounces of castor oil, preferably in beer foam, should be given twenty-four hours before the operation, twelve hours later the patient should receive a large cleansing enema of soap suds and normal salt solution and the latter should be repeated three hours before the operation. In the meantime, no food should be given except broths and gruels in order that there may not be any fresh accumulation.

Technic. The patient is placed upon the table the surface of the neck thoroughly prepared and then covered with a piece of sterile gauze saturated with alcohol. The hair is covered and a gauze pad is placed across the mouth and nose as described in Fig. 19, in fact the preliminary preparation is identical with that employed if the operation is to be performed under ether anæsthesia by inspiration. An assistant also draws the lower jaw forward as described above, and holds it in that position throughout the operation.

An ordinary soft rubber rectal tube with an opening at the end is then introduced into the rectum slowly a distance of eight or ten inches. The tube should be thoroughly lubricated in order to prevent annoyance by friction. The gas contained in the rectum is thus permitted to escape in order to facilitate the absorption of ether. The rectal tube is then attached to the tube through which the ether fumes are pumped into the rectum. The colon is then slowly filled with ether fumes and then the rectal tube is once more disconnected in order that the remaining intestinal gas which was not evacuated primarily may escape. This procedure may be repeated several times, care being taken that the ether fumes are not injected too rapidly for fear of causing too great distension or irritation. At first some gas may escape along the side of the rectal tube but this can soon be prevented by injecting only just enough gas to fill the colon. There may be slight colicky pains at first but the patient will soon become accustomed to the sensation. If the castor oil and the enema have acted satisfactorily, there will be no annoyance from defecation or clogging of the rectal tube. The full anæsthesia will occur in from five to fifteen minutes and the operation can be performed with the consumption of from one to three ounces of ether. When the operation is completed to the point of suturing the external wound, the apparatus is detached from the rectal tube and the accumulated gas in the colon will be permitted to escape. If the patient is slightly conscious of the application of the skin sutures, the consequent deep breathing will facilitate the excretion of most of the ether contained in the blood through the expired air. It also facilitates the expulsion of any ether fumes which may still remain in the colon. This can be further facilitated by making gentle abdominal massage.

The patient must be observed throughout the period of administration with the same care as when ether is given through the respiratory tract. Cyanosis will almost never occur if the lower jaw is held forward as indicated in Fig. 19. The pulse and respiration will indicate the progress of the anæsthesia. It is rarely necessary to disconnect the rectal tube from the apparatus and to make abdominal massage to force the ether fumes out of the rectum during the operation, but in case of necessity this could be readily done. If the head is elevated after the operation is begun almost no anæsthetic will be required during the actual progress of the operation.

Apparatus. Various forms of retainers have been invented for producing the ether fumes utilized in this form of anæsthesia. A simple deep bottle constructed on the general plan of wash bottles used in chemical laboratories seem to suffice perfectly preferably mounted on a stand which can easily be moved without breaking the bottle or its attachments. The bottle contains a rubber stopper with two holes one of which contains a glass tube whose lower end is even with the stopper and whose upper end is attached to a rubber tube which at its other end contains a glass tube for attachment to the rectal tube. The other hole contains a glass tube with bulb-shaped lower end containing many small perforations and reaching to the bottom of the bottle. The upper end of this tube projects through the upper surface of the rubber stopper a sufficient distance to permit the attachment of a rubber tube the other end of which is attached to a bulb with which air can be forced into the bottle. The bottle should be at least thirty centimeters deep so that the air can be forced through a considerable column of ether. The bottle is filled with ether to a point five c. m. from the lower surface of the cork, the upper portion of the bottle being left as a gas space.

This bottle should be immersed in a vessel containing water at a temperature of from 80° to 100° F. according to various clinicians the boiling point of ether being 98.6 F. A thermometer placed in the water is to be added and a stop-cork at the lower part will make it possible to remove the water when the temperature has become too low.

According to another method which has also been frequently used and apparently with equally satisfactory results the arrangement for blowing through the ether is dispensed with; a simple flask being employed containing a rubber cork fitted with a glass tube whose lower end is even with the lower end of the rubber stopper. To the upper end of this a glass tube is attached which in turn is attached to the rectal tube by means of an intervening glass tube. Some surgeons prefer to have this attachment made by means of an intervening rubber tube which is fitted with a stopcork so that the flow of the ether fumes may be interrupted at any time.

The flask containing the ether is then immersed in a waterbath at a temperature of 105° F. which will cause ether to evaporate with sufficient rapidity to bring about the anæsthesia. In case the amount evaporated is not sufficient the temperature may be increased. If the evaporation is too rapid, the flask may be raised out of the waterbath either partly or completely until it again becomes desirable to increase the amount of ether fumes.

The method is so simple that any one who has seen it applied once can readily administer ether in this way, but it seems worth while to be explicit in the description of this method because it has not as yet received practical application to a sufficient extent to become familiar by demonstration. By substituting a good sized thermos bottle for the container of the warm water, with a rubber cork that fits closely around the upper end of the bottle containing the ether, the apparatus can be still further improved because the water will then maintain a fairly uniform temperature throughout the operation and the slight decrease in temperature will be rather an advantage than a disadvantage.

Spinal Anaesthesia. A few enthusiasts have described methods by which spinal anæsthesia may be employed in thyroid operations. It is plain that no one whose judgment has not been impaired by the desire to accomplish that which is unusual would expose a patient already so severely handicapped to the direct application of cocaine to the upper portion of the spinal cord. I simply mention this method to express the opinion that it should never be employed in these cases.

High Spinal Anaesthesia by the use of Stovaine and Neutral Sulphate of Strychnine. During the past eighteen months Prof. Thomas Jonnesco has tried high spinal analgesia for many different operations upon the head and neck in more than 150 cases without any fatality and without any serious after effect. It therefore seems proper to describe this method, although it does not seem wise at the present moment to recommend it in operations for goitre as the experience is still limited.

The following directions are taken from Prof. Jonnesco's article in the British Medical Journal:

The Preparation of the Solution. The solution must be made at the time when the operation is to be performed as follows: The necessary quantity of stovaine is introduced into a glass tube provided with an india rubber stopper, and sterilized in the autoclave. The substance need not be sterilized since it is itself antiseptic, and some of its properties would be destroyed by heat.

The strychnine solution is made by dissolving 5 c. c. of neutral strychnine sulphate in 100 grams of sterilized (not distilled) water in a glass-stoppered bottle previously sterilized; 1 c. c. of the solution will contain 5 mg. As the strychnine takes some time to dissolve, it is better to prepare this solution a little before the time when it has to be used. With an ordinary Pravaz syringe provided with a needle for lumbar puncture, 1 c. c. of the solution of strychnine is drawn up and is injected into the tube containing the dose of stovaine judged to be necessary for the puncture about to be made. The tube is corked again, and shaken, and the salts are dissolved. The same syringe is then filled with the contents of the tube and is held with a sterilized compress and removed from the needle while the puncture is being made; 3 c. c. of stovaine is the usual dose for adults.

Upper Dorsal Puncture. Upper dorsal puncture between the first and second dorsal vertebrae is easily performed; the landmark is the vertebra prominens with the visible and tangible protuberances of the spinous processes of the second and third dorsal vertebrae. When the patient's head is strongly flexed, so that the chin touches the sternum, the protuberances are very marked, and the spaces they bound are enlarged. The patient being placed in this position, the surgeon marks with the forefinger of his left hand the space between the first and second dorsal vertebrae, and the needle, held between the finger and thumb of the right hand, is pushed in, following the upper border of the spinous process of the second dorsal vertebra.

The Injection. As soon as the escape of cerebrospinal fluid renders it certain that the arachnoid space has been entered, its further loss should be stopped, for I am convinced that the escape of more than a certain quantity of fluid is rather harmful than useful. The loss of too much fluid (1) may cause signs of faintness, pallor of the face, sweating, etc.; and (2) by suddenly diminishing the quantity of cerebro-spinal fluid may cause too rapid diffusion of the anaesthetic, which is undesirable and may be mischievous. As soon, then, as a few drops of fluid escape, the needle is closed with the forefinger of the left hand, while with the right the syringe filled with the anaesthetic mixture is adapted to the needle. The liquid must be slowly injected so as not to produce an undue impact upon the spinal cord.

Position of Patient after Injection. "The position to be assumed by the patient after the injection, so as to ensure analgesia of the region to be operated upon, is a cardinal point, for by attention to it we can favor the distribution of the liquid in the desired direction. If with the higher dorsal injection it is desired to obtain analgesia of the head and neck, the patient is made to lie on his back if the operation is to be on the throat, the head should be a little raised; if on the face or skull, he should lie horizontally; if on the upper limb or thorax bent slightly forward. If after four or five minutes the analgesia of the head or of the neck is not complete, the patient's head should be lowered below the level of the body for three or four minutes."

Morphin and Hyoscin. A number of surgeons have administered from one-sixth to one-third of a grain of morphin with one one-hundredth of a grain of hyocin hypodermically from twenty· to forty minutes before beginning the administration of ether in order to reduce the quantity of the latter drug required.

In the same manner one one-hundredth of a grain of atropin has been combined with the morphin for the same purpose. There is no doubt but that both of these combinations will reduce the amount of ether required, but whether this advantage is sufficient to balance the disadvantage of subjecting these patients to the effect of these powerful drugs does not seem clear.

CHAPTER VI.

DANGERS OF OPERATION.

Shock. Until Billroth and Kocher demonstrated the fact that shock can be very largely eliminated from this operation, the surgical profession laid great stress upon this element and this fear has caused many surgeons, even to the beginning of the present century, to hesitate before recommending this operation to their patients. Kocher's statistics and his daily demonstrations to surgeons from all parts of the world, and again the results of his many disciples, have served to dispel this fear. In America, the work of C. H. Mayo has served especially to bring about similar results more particularly in the surgery dealing with exophthalmic goitre. If the surgeon proceeds systematically with a thorough knowledge of the regional anatomy to be encountered in this operation, if he is reasonably skillful so that he can complete the operation in a comparatively short time, if he has the ability of working without unreasonably traumatizing the tissues and if he is careful to secure the vessels before they are severed in order to minimize the loss of blood, then he need not fear the element of shock. To this should be added good judgment in selecting the proper time for operation especially in exophthalmic goitre.

Haemorrhage. In connection with prevention of haemorrhage we are again indebted to Kocher for the greatest progress. He pointed out the importance of keeping the field free from blood and demonstrated a method with the use of his director and his reliable hæmostatic forceps by means of which this could be very readily accomplished. These will be discussed and illustrated in connection with the technical description of the operations.

It is important to bear in mind that the veins are usually dilated to many times the normal size and that consequently great care must be exercised because a tear in the walls of one of these vessels will result in the loss of a considerable amount of blood. Moreover, it is not only the loss of the blood that is to be deplored but the fact that the field of operation is obscured and consequently the progress of the operation is retarded and successive vessels to be grasped may be overlooked causing unnecessary hæmorrhage. Besides this, Kocher claims that the blood itself in these cases has a considerable degree of toxicity so that the patients whose wound surfaces have been free from blood make a better recovery than those in whom the surfaces have been drenched with blood. Of course, excessive hæmorrhage always increases the shock in three ways: 1, by prolonging the operation; 2, by increasing the amount of manipulation and 3, by the loss of blood itself.

Hyperthyroidism. Whoever has operated frequently for the removal of thyroid glands must have become impressed with the real danger to the patient from postoperative hyperthyroidism due either to the absorption of thyroid secretion pressed out of the gland and into the circulation during the operation or of thyroid secretion or toxic blood absorbed from the wound surface. It seems that all surgeons who have operated for many years can recall numerous instances from the early cases while their later experience has been relatively free from this complication. Moreover, a number of surgeons have reported a greater number of patients suffering from hyperthyroidism while they operated under ether or chloroform anæsthesia, than after changing to local anæsthesia. It seems clear that under local anæsthesia what might be called violent surgery is not possible, because the patient would not submit to it while awake even though the tissues might be numbed to a considerable extent by the use of local anæsthetics. It is often difficult, when the patient is thoroughly anæsthetized, to conduct every step of the operation not only the part accomplished by the surgeon but that carried out by the assistants without unduly traumatizing the tissues.

In this connection it may be well to refer to the value of drainage for from one to three days after the operation. There is usually a considerable amount of oozing of blood and serum and where a layer of the posterior portion of the gland is left in place to protect the recurrent laryngeal nerve and the parathyroid glands there is always some thyroid secretion that exudes into the wound and it seems well to insist upon making some provision which will rapidly carry these fluids beyond the absorbing surfaces. I have seen violent hyperthyroidism in two of my own cases in which it had seemed unnecessary to provide for free drainage. I am confident that in both of these cases this calamity might have been prevented by the use of free drainage to be described later.

Above all things it seems important to be gentle in the manipulation of the thyroid gland itself.

Injury to Parathyroid Glands. A study of the discussion of the parathyroid glands in the later chapters of this book convinces the reader that injury of these glands must not occur during operations upon the thyroid gland. In the early days of thyroidectomy these injuries were numerous as shown by the statistics already quoted. As soon as the importance of these glands was generally recognized these calamities virtually disappeared because as will be shown in connection with the discussion of the surgical anatomy involved, it is an exceedingly simple matter to avoid injuring these important structures. In the meantime it is, however, important always to bear in mind the fact that this is really a vital organ from the standpoint of the clinical surgeon and that nothing can be more important than a careful study of all that is known about this structure. The anatomical position of these glands made their removal almost certain during the early operations because they are so intimately attached to the posterior surface of the capsule of the thyroid gland, but it is this very fact which has made it so easy to preserve these glands since their importance has been recognized. That these glands can be restored by transplantation has been demonstrated many times in animals and von Eiselsberg, who reports one successful case in the human patient, thinks that it is justifiable to take a gland from a donor only when one can be certain that he has three other healthy glands or virtually only in cases operated for cyst of one lobe of the thyroid gland. Pool also reports a most interesting case and discusses the subject thoroughly.

Infection. In preantiseptic days this was the most feared of all complications because an infection usually resulted in a septic mediastinitis which in turn proved fatal to the patient. The infection could readily extend along the vessels of the neck into the mediastinal space.

Since the introduction of aseptic surgery this danger has practically disappeared in the hands of surgeons who are otherwise qualified to undertake the operative treatment of goitre. At the present time hospitals in which such operations are performed are so perfectly equipped and assistants and nurses are so thoroughly trained that infections from implements, instruments, sponges, dressings and the hands of operator or assistants or nurses is almost impossible.

There are two sources which are always present which cannot be so absolutely eliminated unless especial stress is laid upon certain precautions and unless the attention of everyone is especially directed to these details. I refer to the difficulty of protecting the patient against infection from her own mouth and nose and the difficulty one often experiences in keeping the surrounding areas together with the ears and hair of the patient thoroughly covered throughout the operation to prevent infecting something by contact with these parts and later bringing the infected object in contact with the wound.

Unless an intelligent assistant is especially entrusted with keeping mouth and nose covered throughout the operation and unless this is his only duty with the possible addition of keeping the lower jaw forward it may easily happen that the patient may cough or breathe infectious matter into her own wound. As difficult as it may seem to protect the patient against incidental contact infection so easy it becomes when all details have been systematically arranged.

It is not at all important that these details be uniform in the work of different surgeons but it is exceedingly important for each surgeon to develop some satisfactory system which is regularly carried out in all of his operations upon the thyroid gland.

Injury to the Parathyroid Glands and the Recurrent Laryngeal Nerve. This danger is especially enumerated only because in the early operations upon the thyroid gland it was not at all uncommon, which will be readily understood when we come to consider the surgical anatomy involved. Fortunately the same precautions which serve to protect the parathyroid glands will serve to prevent the injury to the recurrent laryngeal nerve.

The injury may occur by cutting the nerve at the point at which it passes between the posterior surface of the thyroid gland and the trachea; or it may be caused by crushing with hæmostatic forceps in attempting to grasp the inferior thyroid vessels or their branches. What has been said regarding prevention of hæmorrhage should be repeated here. If all the vessels are caught before they are severed the field of operation will not be obscured and other structures will not be injured. As a result of this injury, there is a paralysis of the vocal cord on one side which is, of course, a serious matter.

Air Embolism. The thinness of the vein walls makes air embolism quite unlikely although it must of course be borne in mind in connection with this as with all other operations which are performed in the vicinity of the large veins of the neck. If the precautions mentioned in connection with the methods advised for prevention of hæmorrhage are carried out there is still less likelihood of the occurrence of this accident.

Air embolism occurs only when a considerable quantity of air enters a vein at one time. Usually this occurs when the vein walls are cut and the incision is held open either artificially as by means of forceps or by surrounding non-elastic structures as in case the vein is surrounded by lymph nodes which have been invaded by carcinoma or infected by tuberculosis. As these conditions are almost never present in cases in which operations upon the thyroid gland are indicated this complication must be extremely rare in connection with thyroid operations.

Collapse of the Trachea. Almost every surgeon who has frequently operated for the removal of diseased thyroid glands has encountered cases in which the trachea has collapsed as soon as it has lost its support due to its attachment to the thyroid gland. The cartilages of the trachea may become exceedingly soft and pliable or they may practically disappear as a result of pressure atrophy caused by the enlarged thyroid gland. The patient then shows immediately symptoms of asphyxia. The more violent the efforts at inspiration the more complete will be the obstruction because the anterior wall of the trachea is drawn into the lumen of this tube like a valve and the further it is drawn in the more completely will the valve close the lumen of the tube. If the surface of the wound has been kept fairly free from blood one can easily see the anterior wall drawn in but if there is much blood on the surface of the wound it may not be possible to recognize the condition by direct inspection. In that case it may be confounded with sudden collapse of the patient or if an anæsthetic has been administered throughout the operation the difficulty may be attributed to the anæsthetic; of course, the usual methods of restoring the patient for collapse due to anæsthesia will be quite useless and in the meantime the asphyxia with the weak condition of the patient may result in a fatal ending. Again, it may occur that a large middle lobe may have been lodged behind the sternum and when the latter lobe has been severed from its attachments posteriorly and externally, but is still attached to the middle lobe internally, the traction made may carry the middle lobe upward sufficiently to make severe pressure upon the trachea just behind the upper end of the sternum and this in turn may give rise to asphyxia which may be mistaken for the same condition due to collapse of the trachea. In order to avoid unfortunate results of collapse of the trachea it is best to keep in readiness a reliable mouth gag and intubation apparatus. If this cannot be employed it is well to insert two sharp tenaculae into the collapsed portion of the trachea and to draw the latter forward.

If this succeeds in giving relief an apparatus must be arranged which will maintain the anterior tracheal wall in this position. If this is not possible a longitudinal incision should be made as in ordinary tracheotomy and a tube, which should always be kept in readiness, should be inserted. If no tracheotomy tube is available it will be an easy matter to make some contrivance which will keep the incision open so air can enter freely.

This opening should be covered with four thicknesses of sterile gauze in order to prevent infection which might easily result in pneumonia. If an intubation has been used this should be removed on the fifth day in order to reduce as much as possible the injury done by the intralaryngeal pressure of the tube. If the breathing is not free after the tube has been removed it is well to replace the latter for two or three days when the same experiment should be repeated.

CHAPTER VII.

INDICATIONS FOR OPERATION ON THE THYROID GLAND.

Indications for Operative Treatment. Primarily the indication for operative treatment of simple goitre must be: 1, inability to relieve the condition by non-surgical means; 2, distress from pressure upon the trachea; 3, pressure upon the trachea and the œsophagus; 4, pain from pressure; 5, unsightly deformity; 6, discomfort due to the weight of the enlarged gland; 7, increasing symptoms of exophthalmic goitre also not yielding to non-surgical treatment.

1. As has been stated before a very large proportion of all patients suffering from non-malignant diseases of the thyroid gland can undoubtedly be relieved by non-surgical treatment provided this is applied systematically and continued for a considerable period of time after the patient has apparently recovered. Hygienic and dietetic and medicinal treatment should consequently be systematically employed in each case at its beginning and only after failing after these methods have been carefully employed should the surgical treatment be resorted to and then only if the disease has produced conditions that would warrant the undertaking of an operation requiring a considerable amount of skill and experience.

In many cases there is so marked a degree of pressure upon the trachea that the patient cannot breathe with any comfort. This may be constant or it may only occur when the patient is in the recumbent position. This may be due to a general pressure from all of the lobes or the middle lobe may contain a circumscribed mass which may press directly upon the trachea and may act like a ball valve applied to the outside of the tracheal tube frequently causing the softening of one or more of the tracheal cartilages. This is more commonly due to pressure from a portion of the middle lobe projecting downward behind the sternum. In one instance the patient, a young woman, was unconscious as a result of asphyxia caused by the condition just described, when I was called to give her relief. Her condition was so serious that I at once proceeded to secure local anæsthesia by injecting one per cent. of cocaine solution into the skin. The operation was performed immediately with the greatest possible speed, with the patient in this unconscious asphyxiated condition. No air seemed to pass in either direction past this obstruction until traction was made upon the right lobe which had been freed from its attachments when suddenly a prolongation downward from the middle lobe came up from its location behind the sternum. Immediately the patient inhaled deeply and a moment later she spoke of the remarkable relief she experienced.

In a number of other instances I have observed a similar condition to a less marked extent. This has been observed and described by many other clinicians and is certainly well worth bearing in mind as a strong indication for surgical treatment.

In other instances an acute inflammatory enlargement may have the same effect only usually to a more marked and also to a more dangerous extent because of the œdematous condition of the surrounding tissues.

Here again the course of the disease will indicate the treatment that should be chosen. If the condition shows a tendency to subside under non-surgical treatment the latter should be postponed but if the opposite is the case incision of the gland is indicated. If a circumscribed abscess is present simple incision will cause the condition to subside. If the inflammatory condition has resulted in a diffuse inflammation it may become necessary to remove one lateral or one lateral end and the median lobe. In this case it will become necessary to perform the operation presently to be described, but great care must be taken not to disturb the tissues low down in the neck in order to prevent infection of the mediastinum and very free drainage must be provided for.

The abscess of the thyroid gland may be located directly underneath the anterior capsule of the gland when it will be reached easily by making an incision parallel with and along the inner border of the sternomastoid muscle over the most prominent portion of the swelling. The incision must be carried through the skin, superficial-fascia, platysma and through the capsule of the gland. If the abscess is in the superficial portion of the gland all of the tissues underneath the skin and frequently even the skin will be found to be œdematous but if it is in the deep portion of the gland the first œdema may not be encountered until the capsule of the gland has been reached. In one instance I have been compelled to advance more than one half the distance through the gland before pus was reached.

The patient, a woman, twenty-six years of age, who had previously been quite normal suddenly experienced severe pain in the region of the right lobe of her thyroid gland. When seen a few hours later there was a slight amount of redness and very slight swelling. The right lobe of the gland was exceedingly tender but there seemed to be no grave symptoms. Six hours later severe symptoms of asphyxia appeared so that she was at once sent to the hospital for immediate operation. During a two mile ride symptoms subsided and the operation was postponed as there was only slight difficulty in breathing. The temperature which had reached 103° F. remained below 100° F. the leucocytosis reached 26000 and the general appearance of the patient indicated the presence of a considerable degree of sepsis. On the eleventh day after the beginning of the attack the patient consented to an incision under local anæsthesia with 1 per cent. cocaine solution. The first pus was reached after more than one-half of the thickness of the thyroid gland had been penetrated. Then a necrotic area 3 c. m. wide by 2 c. m. and 5 c. m. deep was exposed, filled with thick yellow pus and necrotic gland tissue.

One interesting feature in this case was the occurrence of severe syncope which recurred several times each day during the fourth and sixth days after the beginning of the attack and previous to the operation. These attacks were probably due to absorption from the substance of the necrotic thyroid gland together with pressure upon the trachea due to the abscess and to pressure from the surrounding codema. After carefully swabbing out the cavity of the abscess and inserting a gauze drain the patient recovered quite as readily as other cases in which the abscesses were located more superficially.

Indication for Operation in Exophthalmic Goitre. Aside from the indications just described in connection with the treatment of simple goitre the following indications should be borne in mind in connection with the treatment of exophthalmic goitre.

Whenever improvement in these cases from hygienic, dietetic and medicinal treatment together with rest is only of temporary duration then operative treatment is strongly indicated because in these cases the prognosis is usually most excellent if the surgical treatment is employed before the patient has suffered too many recurrences, while the fatal conclusion is usually only a matter of a relatively short time depending upon the frequency and severity of the attack if non-surgical treatment is continued. Moreover, the recovery after surgical treatment will be much more perfect if the operation is performed before the heart and other organs have suffered severely by these recurrent floodings of the circulation with thyroid poison. In simple goitre it is not of much importance except, of course, in the presence of asphyxia, but in exophthalmic goitre the element of time is very important.

Indication for Operation in Malignant Growths of the Thyroid Gland. The indications for the removal of thyroid glands containing a malignant growth is the same as in malignant growths in other organs. So long as the growth seems to be confined to the gland so that it seems reasonably safe to suppose that it will be possible to prevent a recurrence by removing the entire growth, the indication is, of course, absolute. I have never encountered this condition except in cases in which the malignancy was diagnosed incidentally during the microscopic examination of portions of glands removed for other reasons.

It is doubtful whether a thyroid gland with all lobes involved in a malignant growth can ever be removed while the tumor is still so completely confined to the gland that a recurrence can be prevented. If the tumor is confined to one lobe this is possible. In these cases it is doubtful whether it will be proper to remove the entire thyroid gland only preserving the parathyroids or whether one lobe or only the upper portion of one lateral lobe should be left in order to prevent myxœdema.

When we come to discuss the operative technic it will be shown that the remarkable arrangement of the blood vessels of the thyroid gland is to be taken into consideration in this as in all other operations upon this organ. Every portion of each lobe seems to be connected vascularly with every portion of the other lobes, hence, it seems doubtful whether any portion may be left safely when any other portion is involved in a malignant growth.

In removing the entire gland, however, we are certain to cause myxoedema unless accessory glands are present or unless this condition is prevented by transplanting normal thyroid gland into the body or by constantly feeding thyroid glands or thyroid extract.

All of these facts indicate that the results to be expected are not satisfactory. On the other hand, malignant growths of the thyroid gland may progress with great rapidity and destroy the life of the patient in a few months or they may cause little distress for a number of years. I have personally encountered both forms. I would consequently say that in case it seems possible to make a radical operation when the patient consults the physician, an operation should be performed at once. If it is not possible to do this, then the operation should be performed only if it becomes necessary in order to give relief from pain or asphyxia.

The technic of the operation to be performed will be discussed in another chapter.

According to Salzer the transplantation of the thyroid glands is so likely to be successful into patients who have been entirely deprived of their thyroid glands that it seems reasonable to suggest the removal of the entire gland and the simultaneous transplantation of one lobe from another patient. The transplantation is simple and accompanied with so little shock that it can easily be accomplished at the same time at which the complete thyroidectomy is performed for the removal of the malignant growth.

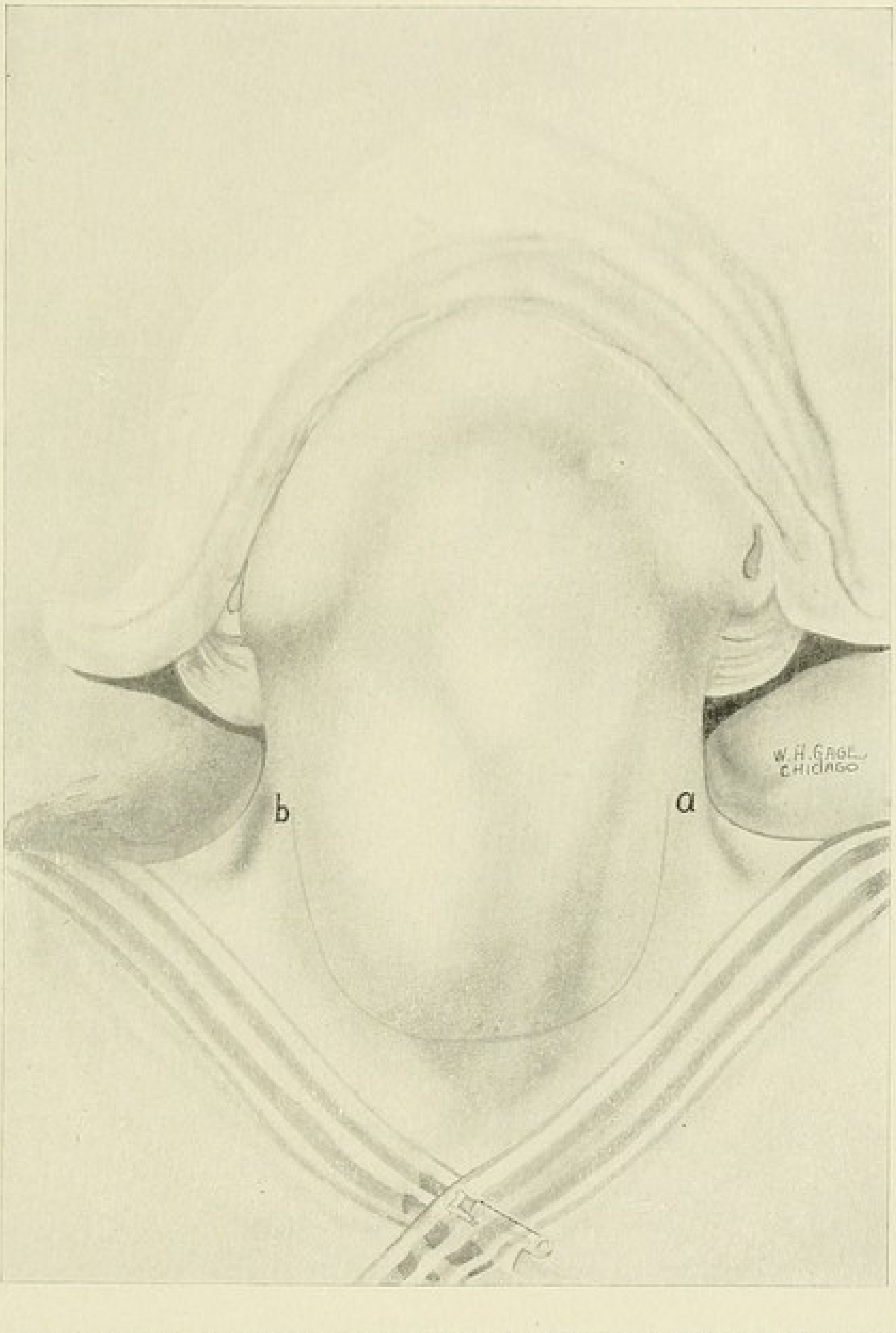
CHAPTER VIII.

THYROIDECTOMY.

In describing the technic of this operation only those methods will be chosen which I have found reliable. In none of them is there any important feature which is original with me. Every part of every operation to be described has been practiced by other surgeons and has in most instances been described in books or articles in scientific journals. Most of the important features were developed and practiced by Kocher although many of them have been modified in minor details by others. I make this statement at this point in order not to give the impression that because I may be unduly emphatic or enthusiastic in the discussion of certain features that, therefore, these may be my original methods. None of them are my methods except by adoption but all have been thoroughly tested by me in many cases. Those who have faith in my surgical judgment in selecting, adapting and accepting the methods of others may follow these methods with confidence.

Incision. It is important to bear in mind the fact that in operations upon the thyroid gland the incision must be so planned that it will result not only in a proper exposure of the tissues to be manipulated during the operation but also to result in little or no deformity after healing has taken place. It is very important to secure free access to the tissues to be

PLATE II



HORSE SHOE INCISION, BEING THE TRANSVERSE COLLAR INCISION OF KOCHER EXTENDED UPWARDS AT EACH END ALONG THE ANTERIOR BORDER OF THE STERNO-MASTOID MUSCLE TO (A) AND (B).

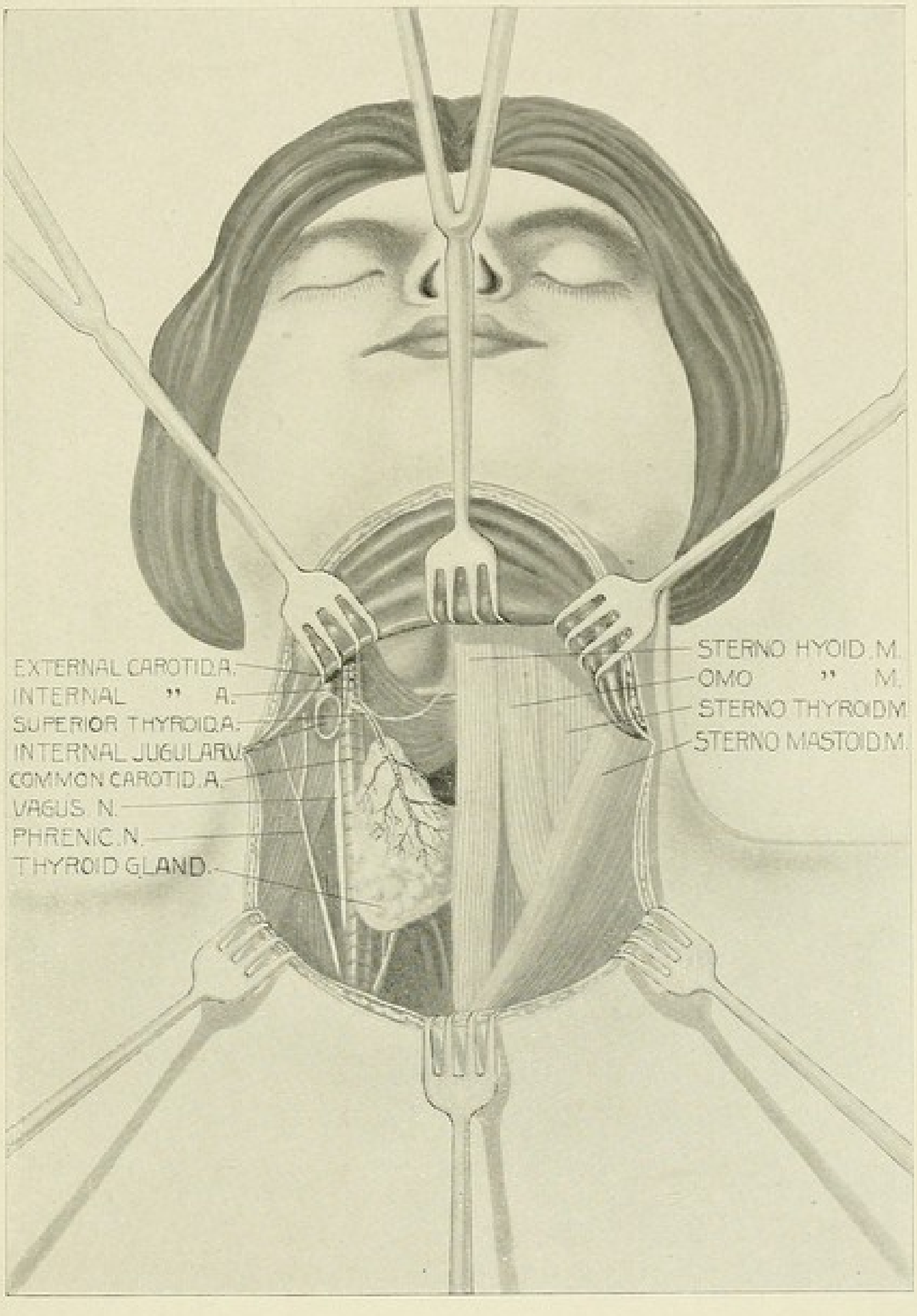
manipulated during the operation because as will be seen later there are various important structures which must be protected during the operation.

Moreover, it is important not to traumatize the tissues of the thyroid gland itself for fear of producing hyperthyroidism. It is also important to have a clear view of the field of operation in order to reduce the loss of blood to a minimum because aside from the loss of blood itself there seems to be a certain amount of harm done to the patient if the wound surfaces are severely saturated with blood during the operation, because according to Kocher there is a certain amount of specific toxicity in the blood in these cases. The total amount of traumatism to the tissues is greatly reduced if an ample incision gives free access to all tissues to be manipulated. This is even of greater importance if the operation is performed under local than under general anæsthesia, because the skin is most easily rendered painless, hence a large incision causes no more immediate pain than a small incision, while the pain of the remaining steps of the operation is proportionate with the amount of trauma and that is less with an ample than with a small incision.

As all of the muscles of the neck are arranged in pairs, it is plain that every incision which is not symmetrical as regards the muscles of the neck must result in a considerable amount of deformity because in these cases aside from the almost imperceptible deformity which is due to the line of incision itself all of the deformity resulting from thyroid operations is due to differences in the muscles on both sides of the neck which can, of course, be avoided if the muscles on both sides are always treated exactly alike. This, however, is possible if the inverted horseshoe incision, Plate 2, is employed, which was introduced by Kocher and called by him "the collar incision."

This incision begins at a point a little above the level of the most prominent portion of the larynx and the anterior border of the sterno-cleido mastoid muscle, it extends downward and makes a regular curve across the lower border of the thyroid gland two to three c. m. above the upper margin of the sternum. It then ascends to a corresponding point on the opposite side of the neck making a perfectly uniform symmetrical line. This incision may be varied in length and in the distance of separation of the vertical incisions according to the necessities of the case, but aside from these variations no other incision is required for the removal of any portion of the thyroid gland. Many other incisions have been described all of them taking the anterior edge of the sterno-cleido mastoid muscles as a guide, but I am thoroughly convinced that except for the opening of abscesses none of these incisions will be so satisfactory as the one just described, because none of them give so perfect an approach to the field of operation and each one leaves a greater amount of deformity. It is plain, of course, that in many cases it will not be necessary to make the incision nearly so long as shown in Plate 2. If the tumor is confined to the middle lobe it may be necessary to make an incision which would cover no more than the middle one-third of this incision. But even

PLATE III



ANATOMICAL DISSECTION THROUGH USUAL INCISION EMPLOYED IN MAKING THYROIDECTOMY, EXHIBITING STRUCTURES TO BE CONSIDERED DURING THE OPERATION.

in this case the curve should be quite as symmetrical and the tissues underneath should be treated precisely the same on both sides of the center of the incision. Some of the most troublesome little tumors are located precisely at this point or at the very lowest portion of one of the lateral lobes, and in these cases it is well not to permit any asymmetry in the skin incision because an avoidable postoperative deformity is equally annoying to the surgeon and to the patient.

The incision is carried through the skin, superficial fascia and platysma myoides muscle and all of these tissues are reflected upwards together as shown in Plate 3, leaving the entire field of operation thoroughly exposed. In case the operation is performed under local anæsthesia the tissues at the upper angle of the wound should be thoroughly infiltrated with the anæsthetizing solution by passing a blunt needle attached to a hypodermic syringe filled with this solution along the anterior and posterior surfaces of the sterno-cleido-mastoid muscles on both sides and also into the deep tissues along the lateral wings of the thyroid cartilage. As the blunt needle enters these various spaces the anæsthetizing fluid is slowly injected and again as the needle is withdrawn, the quantity injected being in inverse proportion to the strength of the solution employed. This may be done before the primary incision is made by first cocainizing the skin, then making small punctures with a sharp scalpel opposite the upper extremities of the proposed incision and then passing the blunt needle through these openings. It is well to wait five minutes before commencing the operation.

Having exposed our field of operation we will consider the anatomical structures to be dealt with and to be protected during the operation. These we have illustrated from dissections on the cadaver adjusted to the various steps of the operation. In our illustrations it has been necessary to exaggerate the condition somewhat in order to secure clearness, but all of these exaggerations were made in keeping with the actual tissues of the neck. For instance, when the sterno thyroid muscles are exposed in the operation they are covered with fascia, but if this were left in place our illustrations would not be more effective than are photographs made during this stage of the operation while if represented as showing the exposed muscle fibres the reader obtains a much clearer idea of the conditions.

Anatomical Consideration. The following tissues must be borne in mind throughout the operation in order to accomplish the work with the greatest possible facility in the shortest time with the least trauma, and without injury to any important structures and with the prospect of the best possible cosmetic results.

The gland itself is normally quite small weighing only from 30 to 60 gms. It is somewhat smaller in women than in men and larger relatively in infancy than in adult life.

The diseased gland may be but slightly larger than the normal gland, sometimes not exceeding 100 g. while it may be many times this size. The largest gland I have personally removed weighed 3,584 g. after the blood had been drained out of it.

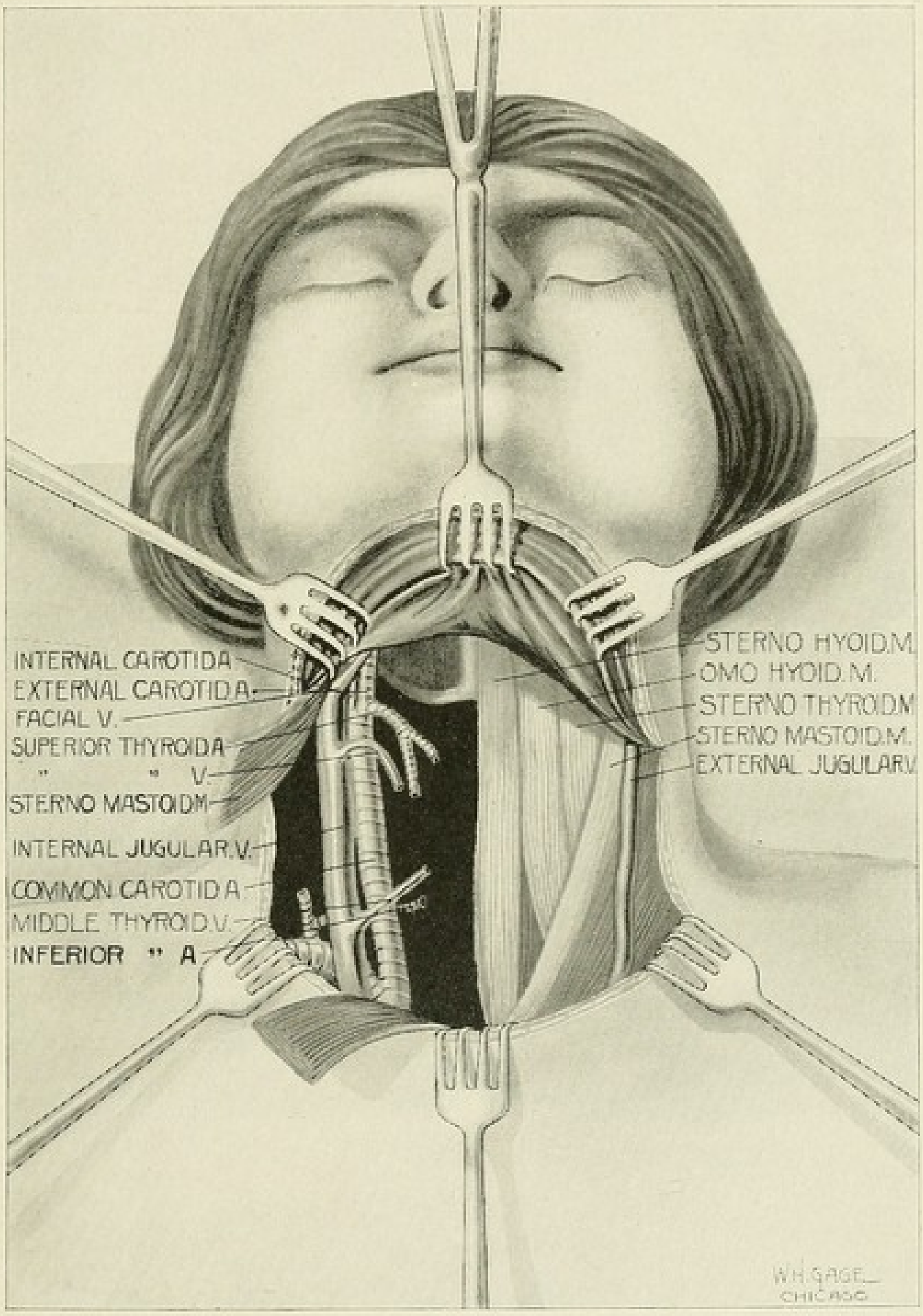
This would make the gland about one hundred times the normal weight.

In considering the location of the gland itself in relation to the surrounding structures we must consequently bear in mind not only the normal position and the normal relations, but also conditions which are the results of the change in form of the gland due to irregularities caused by the pathological condition present. In many instances abnormal adhesions are found caused by the previous treatment with injections into the gland and the surrounding tissues or to adhesions caused by the presence of infection at some previous time. Plate 3 represents a dissection which was made through an exposure such as one obtains by making the collar incision shown in Plate 2. It has seemed better to represent this through the same incision that we use in making a thyroidectomy than through the ordinary incision employed in the dissecting room, because in this way we have obtained not only the normal relation of the various structures but also the relation of these structures to the wound as it appears in the actual operation. There is the difference of having freed the muscles of their fascia and having carefully exposed all of the other structures, which is neither necessary nor desirable in the actual operation, but which seems necessary in order to impress sufficiently the relative positions of the various structures which must be constantly borne in mind during the progress of the operation. What has been said regarding the method of producing Plate 3 applies also to Plates 4 and 5.

On the right hand side we have the tissues as they appear after the flap has been dissected up together with the platysma myoides muscle. Of these muscles the sterno-cleido-mastoid muscle will be borne in mind prominently throughout the operation because it serves as a guide to almost every important step taken as will be seen later on in the discussion of the technic. The other three muscles are treated as one structure technically throughout the various operations. When displaced by retractors these muscles are always manipulated as one object. When severed for the purpose of exposing structures they are again treated as one structure and not being freed of the fascia covering these tissues the operator never distinguishes them as separate muscles. On the left side they have been removed entirely in order to expose the underlying structures so that they could be drawn distinctly and accurately. In the operation itself the attachment of these muscles with the underlying structures is only disturbed so far as the portion of the gland is concerned which is to be removed, all of the other attachments remain intact. So long as the surgeon knows precisely where these important structures are located it is quite unnecessary to expose them by dissection in order to protect them against injury, but it is of the greatest importance primarily to know where these various structures are located and secondarily to carry out the steps which are necessary to prevent injury which will be fully described later.

The thyroid gland itself can always be recognized readily by its lobulated surfaces. It is an exceedingly vascular body. In the living body it has a characteristic purple color which readily distinguishes it from all surrounding structures. The

PLATE IV



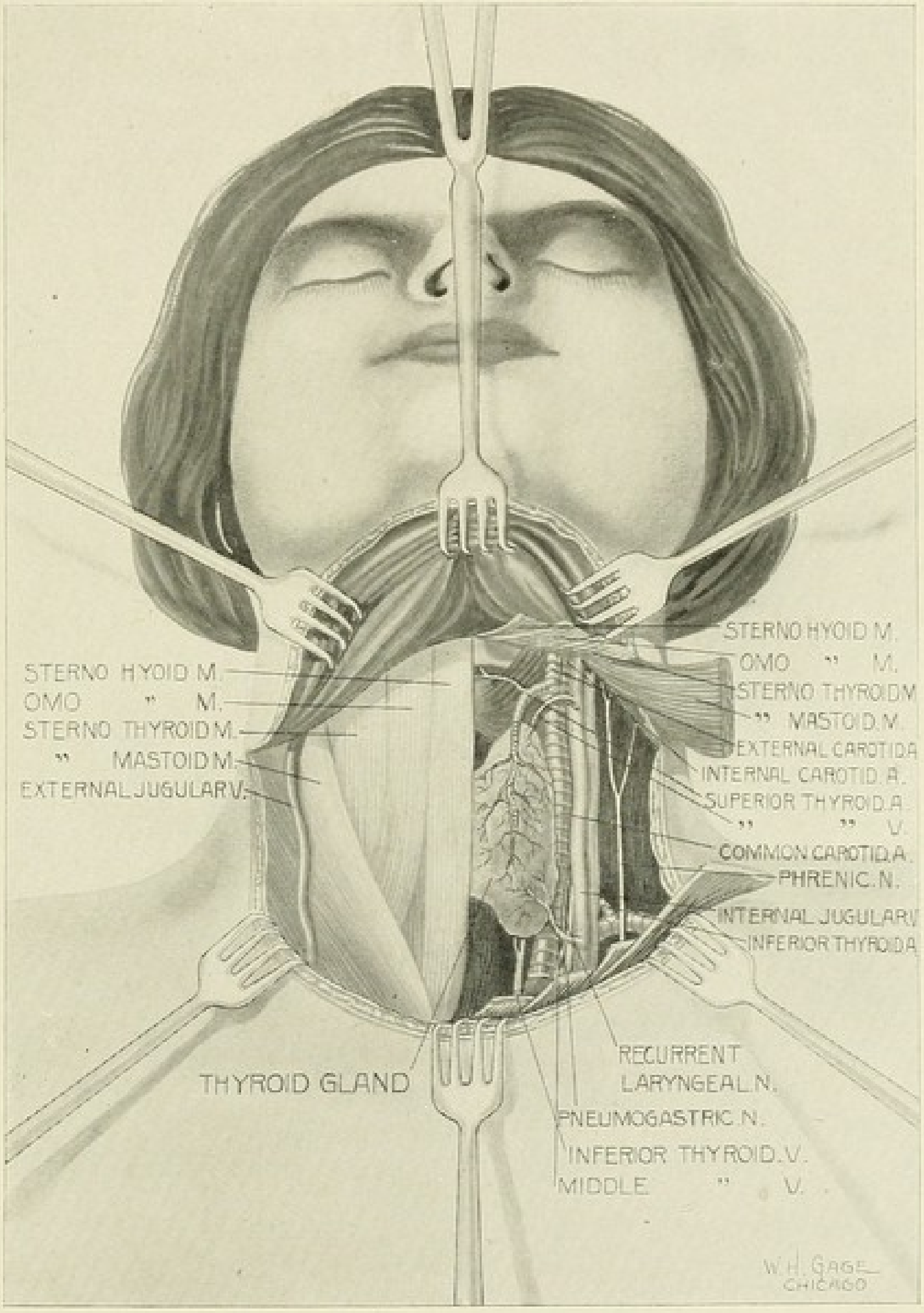
THE SAME AS PLATE III, WITH THE RIGHT LOBE OF THE THYROID GLAND REMOVED IN ORDER TO BRING OUT THE REMAINING STRUCTURES.

branches of the superior thyroid artery and vein cover the upper portion of the gland and over the surface of the lower portion a network of veins communicating with both the inferior and the superior thyroid veins can always be distinguished. These veins are especially prominent in cases of exophthalmic goitre but they can always be seen even when there is little or no enlargement of the gland. In order to make the drawing more distinct only the superior thyroid artery is shown in this drawing, the internal jugular vein and its branches having been dissected away in order to show the important deep structures. The superior thyroid artery can always be distinguished during the operation although its origin from the external carotid artery is but rarely exposed during the operation and the internal carotid artery which is also shown in Plate 3 should not be exposed together with the internal jugular vein when the surgeon lifts one of the lobes of the gland out of its bed. The vagus nerve is exposed occasionally during the operation especially when there are enlargements from the lateral surface of the lateral lobe. Very rarely the phrenic nerve is exposed under similar conditions. At the lower end of this drawing on the left side a thin white line represents the recurrent laryngeal nerve. As will be seen later it is not necessary to expose this nerve during the operation, but in this instance it was exposed for a short distance because of the general dissection which was employed to expose the other structures which have just been described.

In Plate 4 the internal jugular vein has been left in place and the lobe of the thyroid gland has been entirely removed not as it would be removed during an operation but for the purpose of showing the blood supply of the gland which must be considered during every operation upon this gland as the most important factor. On the right hand side, the drawing represents the same structures as Plate 3 with the addition of the external jugular vein which may, however, be disregarded technically during the operation. Usually it is possible to make the incision internally to this vein but when it is not possible to do this, the latter is simply caught between two pairs of forceps and ligated. The superior thyroid vein is usually located somewhat closer to the superior thyroid artery than shown in this illustration so that very commonly it is possible to ligate the artery and the vein with the same ligature when making thyroidectomy. In this dissection the muscles represented on the right side have all been removed on the left side with the exception of the sterno-cleido-mastoid which has been reflected.

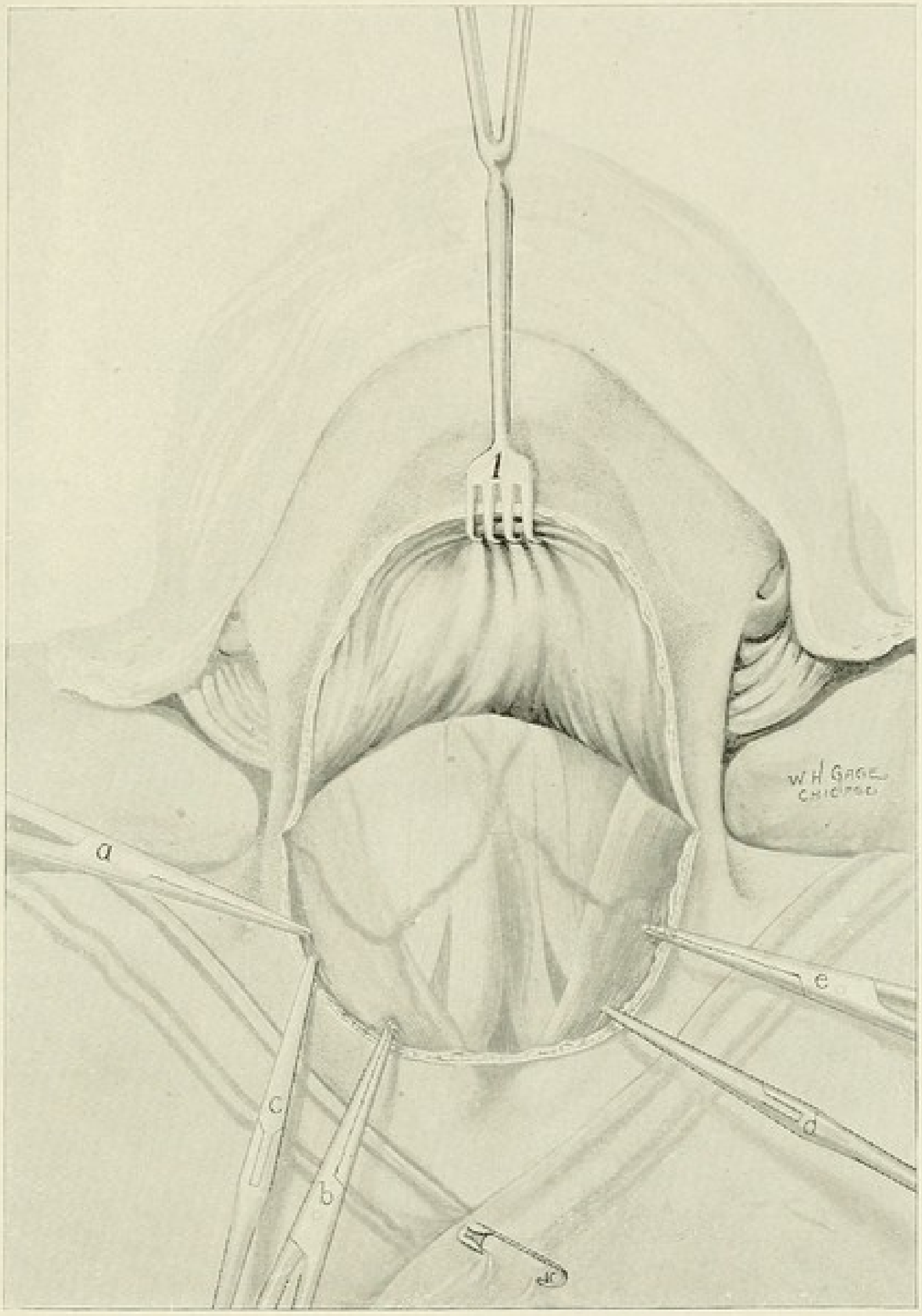
In Plate 5 we have represented the structures in a somewhat more diagramatic form in order to give a more general impression of the tissues to be borne in mind. On the left side all of the muscles shown in Plates 3 and 4, on the right side are in place together with the external jugular vein, while on the right side all of the muscles have been reflected so as to expose virtually all of the tissues which are to be considered in the subsequent technic. Most of these structures have already been mentioned in connection with Plates 3 and 4 but it seems worth while to consider them all together in their mutual relations to the external wound. In practice one is but rarely

PLATE V



ANATOMICAL DRAWING, SOMEWHAT DIAGRAMMATIC, SHOWING THE MUSCLES IN PLACE ON THE RIGHT SIDE AND ALL OF THE OTHER ANATOMICAL STRUCTURES TO BE CONSIDERED IN PLACE ON THE LEFT SIDE.

PLATE VI



INCISION FOR THYROIDECTOMY, WITH SKIN SUPERFICIAL FASCIA AND PLATYSMA RETRACTED UPWARD AND HELD OUT OF THE WAY WITH RETRACTOR (I). HAEMOSTATS ON SEVERED VESSELS AND SHADOWS SHOWING LARGE BRANCHES OF ANTERIOR JUGULAR VEIN.

called upon to operate in cases in which the relative size of the thyroid gland and the other structures is as it is shown in this figure, which is approximately as it exists in the normal conditions, but this will show how the different structures appear normally and then one can judge the changes from the amount of deformity encountered in each individual case. The enlarged portion of the gland usually simply displaces the various structures by lateral pressure but occasionally these structures are overlapped by some projection from the gland. There is, of course, an infinite variety of these displacements so that it would be useless to describe the individual forms which have been or may be encountered. These drawings may be recommended for careful study, and may be verified in the cadaver with profit before attempting the operation. As the condition is very similar in the cat and in the dog it is wise to operate upon these animals before attempting to perform the operation upon the human patient.

When one has once become practically familiar with the anatomical structures just described, the technic which follows will acquire a much less complicated aspect from that which one would obtain without this familiarity. Although it is true that most of the danger to the patient comes from the fact that operations upon the thyroid gland are performed upon patients who would not be good subjects for any operation, still the local conditions are such that the danger from the operation will be greatly increased unless the surgeon is perfectly familiar with the structures described in Plates 4 and

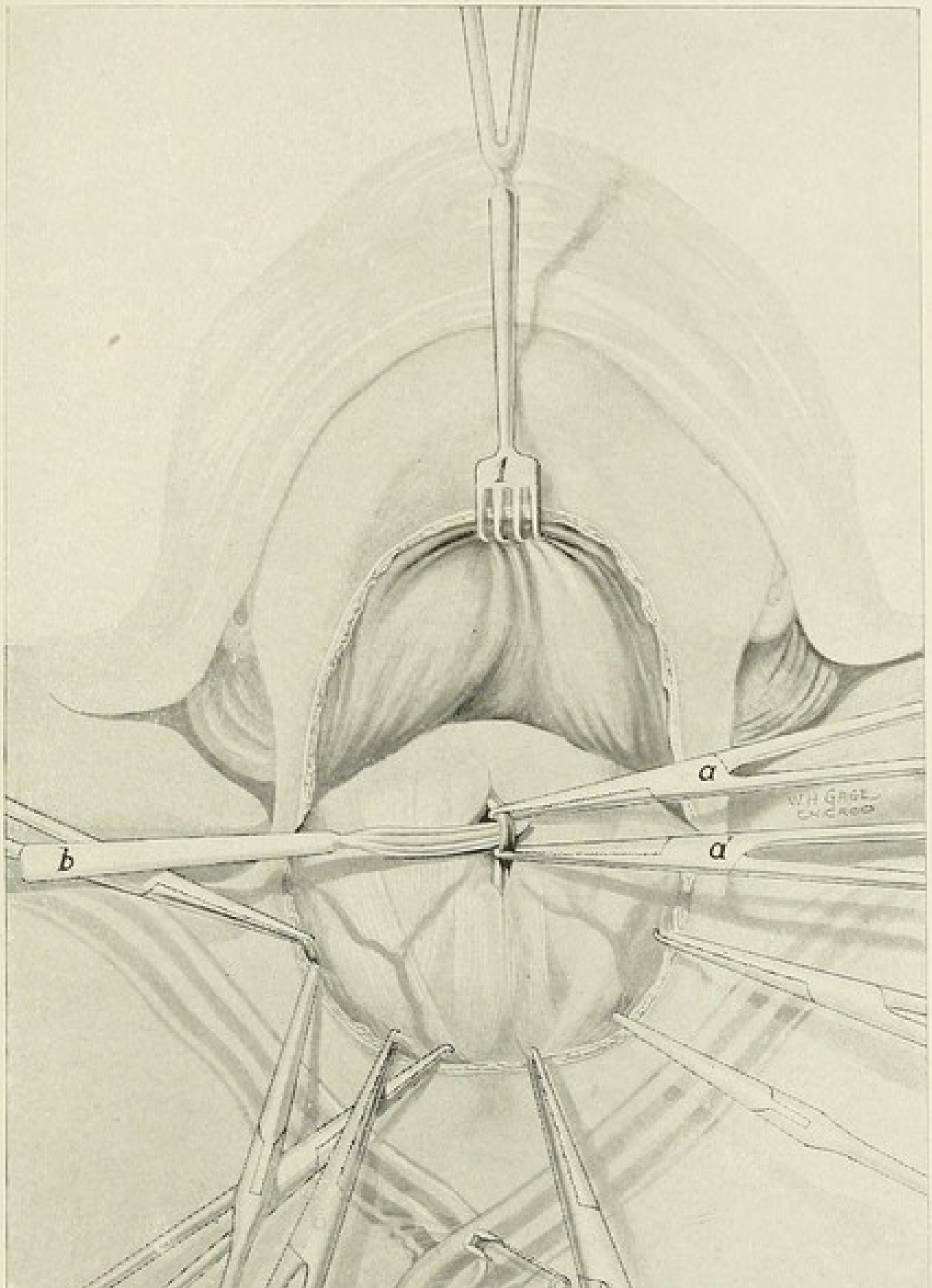
5, which will be referred to throughout the discussion of the various steps of surgical technic.

Plate 6 represents the flap of the skin together with the platysma myoides reflected upwards. A number of veins which are located immediately underneath the skin are so small in the normal conditions that they will not require any attention in operations upon the neck but are so large in patients suffering from goitre that they bleed very freely. These should be grasped at once with hæmostatic forceps which may be left in place as they do not interfere with the subsequent steps of the operation. Occasionally there is some bleeding from the under surface of the flap which should be controlled by hæmostatic forceps and ligatured at once. The edges of the sterno-cleido-mastoid muscles can be seen on either side, and over the surface underneath the fascia there are usually several large veins as indicated by the shaded lines in this figure. These may extend longitudinally over the surface of the gland parallel to each other or they may form a network. They are usually branches of the anterior jugular vein. It is also possible to see the sternohyoid and the sternothyroid and occasionally a portion of the edge of the omohyoid muscles through the fascia as shown in this figure.

The anterior horseshoe shaped flap is held out of the way throughout the operation by means of the retractor. It is well to fasten the towels to the skin by means of a safety pin as shown in this figure in order to prevent them from slipping up and down over the edge of the wound during the operation.

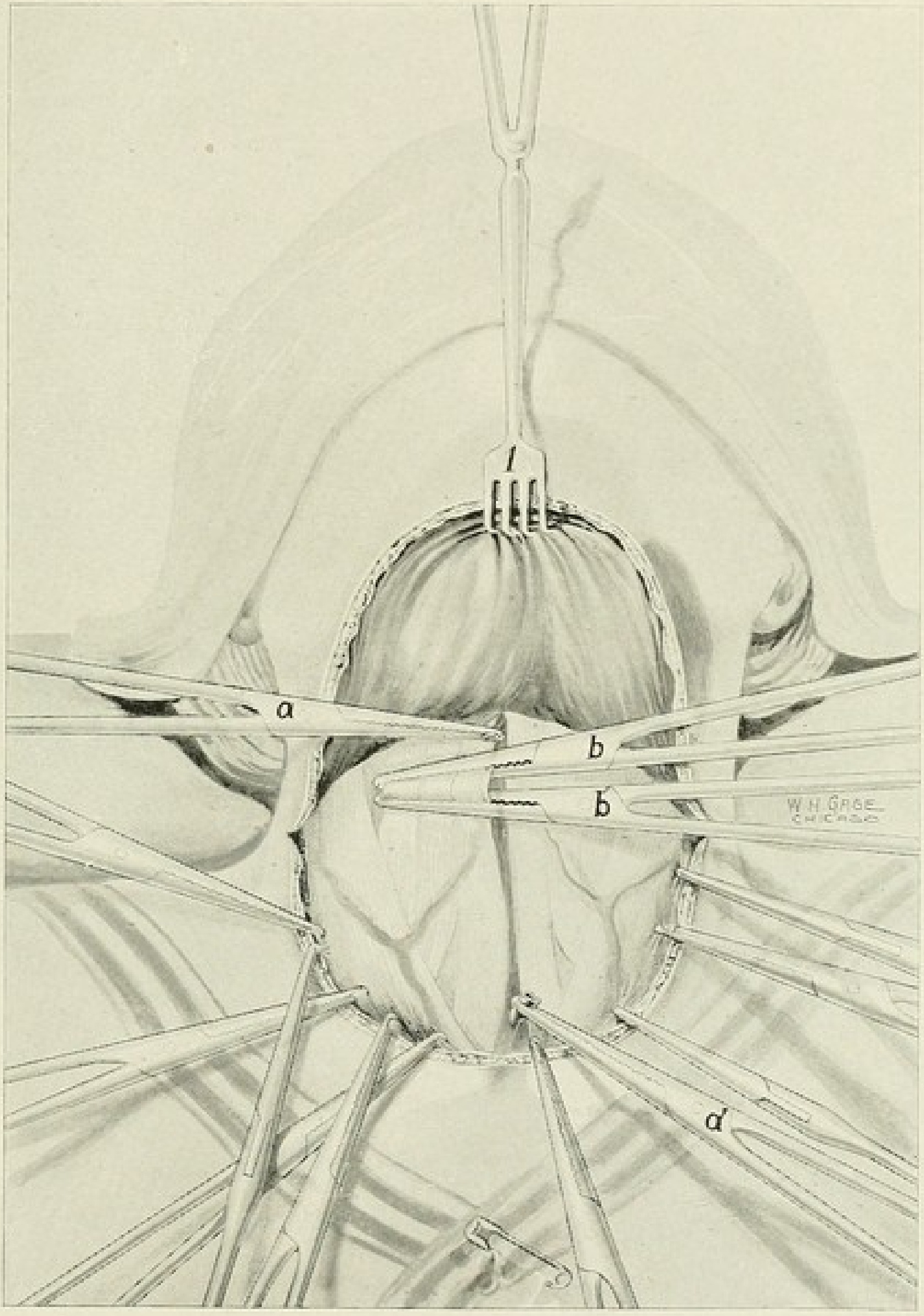
Plate 7 represents the same conditions as Plate 6 with the addition of illustrating an important step

PLATE VII



THE SAME AS PLATE VI, WITH KOCHER DIRECTOR (B) INSERTED UNDERNEATH ANTERIOR JUGULAR VEIN WITH TWO HAEMOSTATIC FORCEPS (A) AND (A′) APPLIED.

PLATE VIII



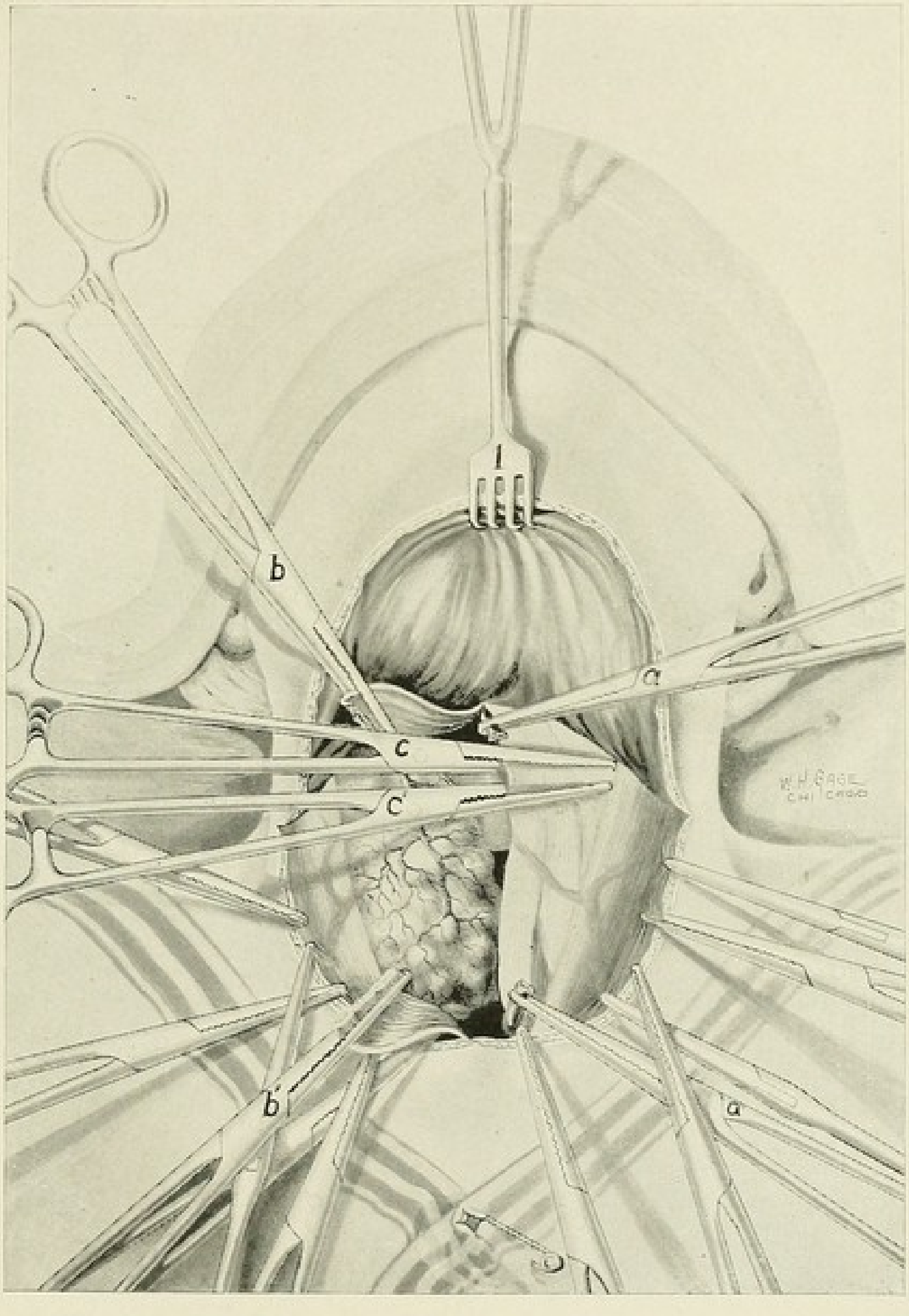
THE SAME AS PLATE VII, WITH LONG-JAWED KOCHER HAEMOSTATIC FORCEPS APPLIED TO STERNO-HYOID, STERNO-THYROID AND OMO-HYOID MUSCLES IN FRONT OF THE RIGHT LOBE OF THE THYROID GLAND.

in the operation. In order to keep the wound constantly free from blood Kocher has introduced a grooved director represented at (b) with its point inserted underneath the anterior jugular vein. In order to expose the vein the fascia overlying it is split longitudinally and then it is lifted up by means of the blunt pointed end of the Kocher director. Two hæmostatic forceps, preferably of the type introduced by Kocher and shown at (a) are applied to the vessel as indicated in this figure and then it is severed over the middle of the director. It is well to ligate both ends of the vessels at once in order to keep the surface free from instruments for the convenience of the subsequent steps of the operation. This leaves the sternohyoid, the sternothyroid, the omohyoid and the edge of the sterno-cleido muscles exposed. All hæmorrhage has been controlled either by the application of hæmostatic forceps which are still in place or by clamping and ligating. In most cases it will be necessary to apply two pair of forceps to the muscles covering the anterior surface of the gland as shown at (b) and (b′) Plate 8. These forceps should again be of the type shown in this illustration which were introduced by Kocher. They should be placed about 2 c. m. apart and parallel with each other and closed just tightly enough to stop all hæmorrhage but not sufficiently tightly to crush the muscle. It is usually best to ligate the veins caught in forceps (a) and (a″) before the present step of the operation is taken because slight traction upon these forceps sometimes causes a tear in the thin walls of these veins which gives rise to quite a severe hæmorrhage, and which may seriously obscure the subsequent steps of the operation.

The muscle is then cut transversely and the handles of the forceps are turned back as indicated at (b) and (b″) which results in the perfect exposure of the entire anterior surface of one lobe of the thyroid gland as shown in Plate 9. The same step will usually have to be repeated on the opposite side, although it is sometimes possible to obtain a sufficiently free exposure by simply retracting the muscles on the opposite side. Forceps (c) and (c″) are now applied precisely as (b) and (b″) were in Plate 8, so as not to interfere with the nerve supply of the muscles, and the muscles are severed transversely half way between these two forceps. When these are turned back to correspond with (b) and (b″) which are attached to the corresponding muscles on the opposite side the anterior surface of the entire thyroid gland is perfectly exposed as shown in Plate 10.

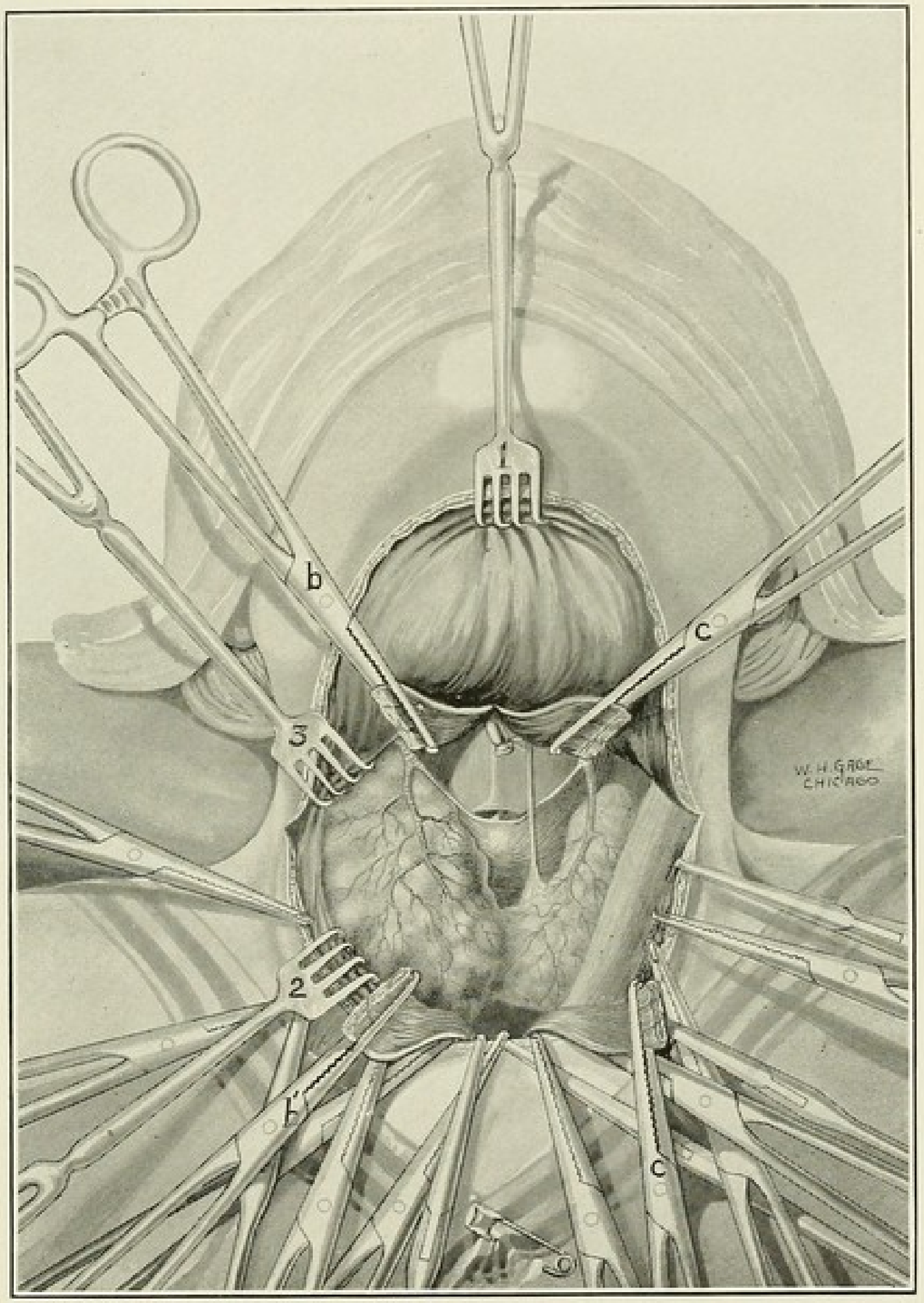
There are several advantages in turning both of these muscles back. It facilitates the operation because with so free an exposure the remaining steps of the operation can be accomplished so much more rapidly that in many cases it is really worth while. It requires only a moment to re-unite the muscles. Moreover, there is an advantage in treating both sides alike because of the resulting symmetry when the operation is completed. Again the amount of traumatism to the tissues will be reduced by having free access to the gland. In case the smaller lobe contains nodules of diseased tissues these will be discovered and can readily be removed. In many instances a more thorough operation will be performed if both

PLATE IX



THE SAME AS PLATE VIII, WITH THE MUSCLES CUT ACROSS BETWEEN FORCEPS (B) AND (B′) ON THE RIGHT SIDE AND SIMILAR FORCEPS (C) AND (C′) APPLIED TO THE MUSCLES OF THE LEFT SIDE.

PLATE X



THE SAME AS PLATE IX, WITH THE MUSCLES ALSO CUT TRANSVERSELY ON THE RIGHT SIDE BETWEEN FORCEPS (C) AND (C′), EXPOSING THE ANTERIOR SURFACE OF THE GLAND PERFECTLY.

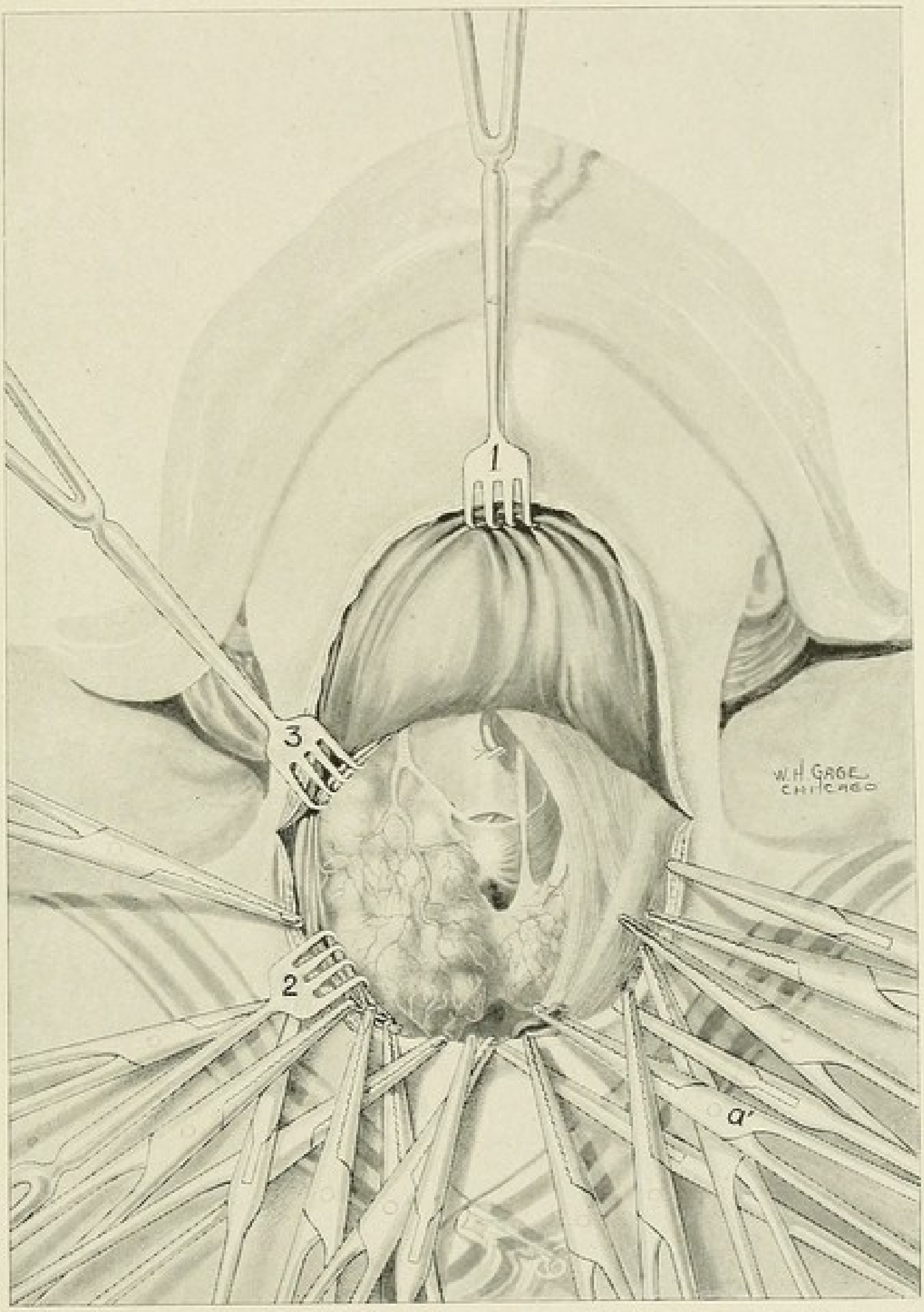
lobes are exposed because of the ease with which it is possible, under these conditions, to ligate the inferior thyroid artery and vein on the side on which the lobe is smaller. It may be well to advise this additional step to those who have not yet obtained a great amount of experience in this field of operation. With increased experience one acquires the ability to work with less perfect exposure.

Plate 10 shows a perfect exposure of both lobes of the thyroid gland with the right lobe somewhat enlarged. The form of retractor shown in Plates 2, 3 and 4 is very convenient for exposing the field of operation. Forceps (b), (b′) and (c) and (c′) serve the double purpose of preventing hæmorrhage from the cut ends of the muscles overlying the gland and that of very convenient retractors. Two precautions must be borne in mind. These forceps must not be closed too firmly but just sufficiently to prevent hæmorrhage in order not to injure the structure of the muscles, and assistants must not pull too heavily upon them during the operation. A portion of the muscle at least half a c. m. in width must be left projecting beyond the forceps in order to preserve perfectly smooth cut surfaces for suturing when the operation upon the gland itself has been completed.

The branches of the two superior thyroid arteries communicate very freely with each other which can be demonstrated easily on injected specimens but even in the living body it is apparent from the arrangement of these branches that this must be the case. At the upper end a narrow band extends upwards in front of the larynx, and is attached to the upper edge of the thyroid gland. This structure is usually present and represents the remnant of the duct which communicates between the gland and the œsophagus during foetal life. Occasionally the duct persists but this is very rare. Usually it is simply a small band of connective tissue which may be clamped between two pair of hemostatic forceps, cut and ligated.

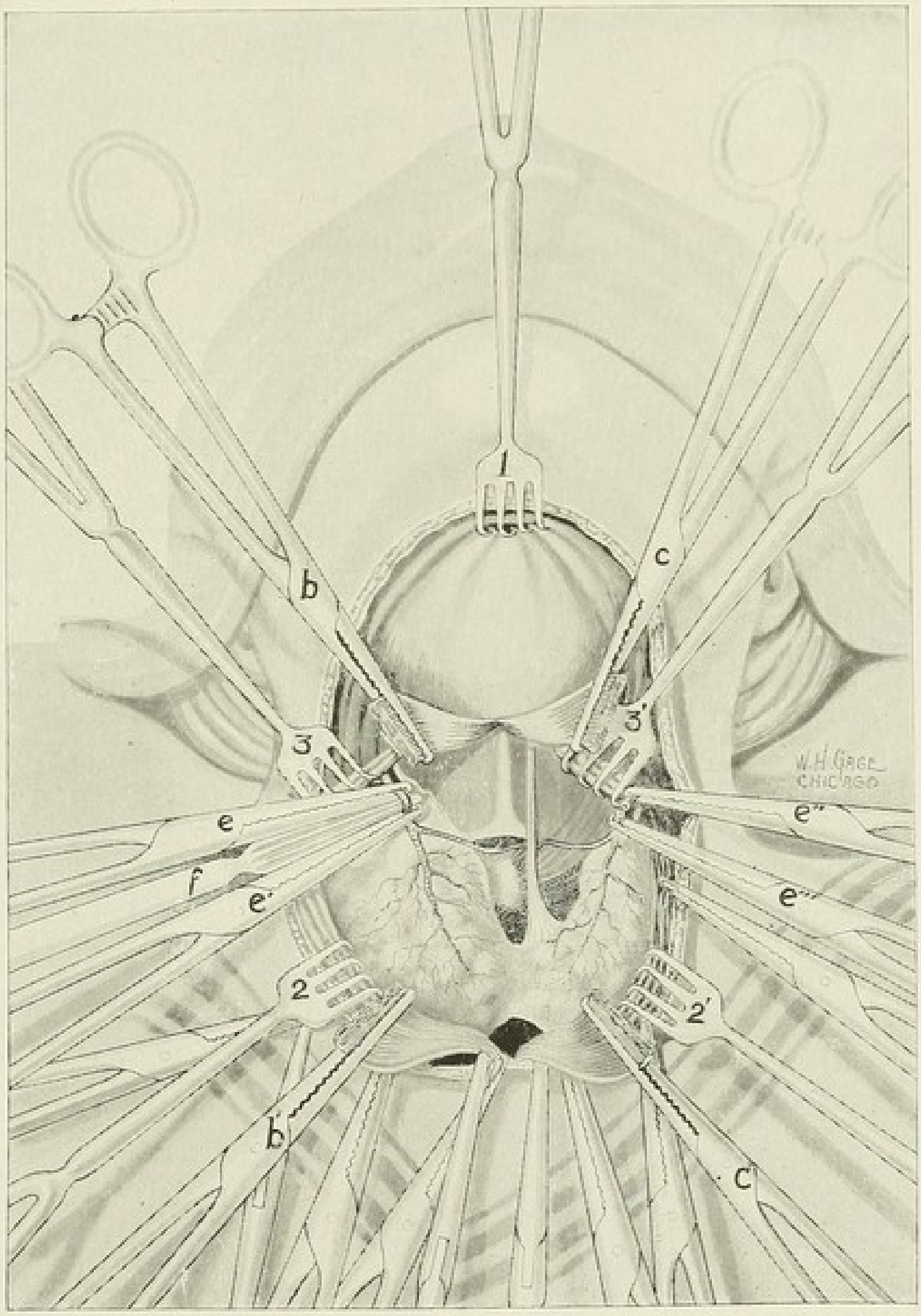
In many cases it is possible to retract the sterno-thyroid, sterno-hyoid and omo-hyoid muscles as shown in Plate 11, without clamping and cutting them. This may be done on both sides of the median line either simultaneously or successively. Some operators with great skill and much experience make this their typical operation and choose the method shown in Plates 8, 9 and 10, only in cases in which for any other reason it does not seem possible to complete the operation without taking this additional step. It is often especially difficult to dislocate the enlarged lobe forward if these muscles are left intact. One also may experience difficulty in controlling the bleeding from the small veins which may be torn in bringing forward the lobe. The ligation of the inferior thyroid vessels on the opposite side from the one on which the lobe has been removed is also very much more difficult if these muscles are left intact. There is a marked difference in the strength and elasticity of these muscles in different patients and consequently it is well to treat each case according to the conditions found after making a longitudinal separation of the muscles of both sides. This is usually best accomplished by means of dissecting forceps and scalpel. Separating the posterior surface

PLATE XI



THE SAME AS PLATE X, WITH THE MUSCLES COVERING THE THYROID GLAND RETRACTED BY RETRACTORS (2) AND (3) INSTEAD OF BEING SEVERED.

PLATE XII



SHOWS THE SUPERIOR THYROID ARTERY ON THE RIGHT SIDE RAISED ON THE POINT OF A GROOVED DIRECTOR (F) AND CLAMPED WITH HAEMOSTATIC FORCEPS (E) AND (E′), WHILE ON THE OTHER SIDE THE VESSEL HAS ALREADY BEEN SEVERED AND IS HELD BY FORCEPS (E″) AND (E‴).

of the muscle from its attachment to the thyroid gland is best accomplished by passing the index finger between the anterior surface of the gland and the posterior surface of the muscles on either side.

In doing this it is best to apply the greater amount of pressure anteriorly against the posterior surface of the muscles in order not to traumatize the substance of the thyroid gland. This step of the operation is only rarely accompanied with hæmorrhage which can be controlled at once with hæmostatic forceps. The anterior surface of the gland is always covered with a perfect network of large thin-walled veins which should not be injured because they bleed very freely and cover the field with so much blood that the remaining steps of the operation will be greatly retarded.

Plate 12 shows the same exposure as Plate 10. The hæmorrhage has been completely controlled by the application of hæmostatic forceps to all of the smaller bleeding points and by applying two hæmostatic forceps to each one of the larger vessels before cutting them and then ligating them at once. With the gland fully exposed the actual steps for the removal of the gland may be commenced. A Kocher director is passed underneath the superior thyroid artery and vein either separately as shown at Plate 12, or the two vessels may be taken together. After the end of the director has been passed through underneath one or both of these vessels two pair of hæmostatic forceps (e) and (e′) are clamped upon this vessel and then the latter is severed over the director between these forceps. The cut ends of these vessels are then turned up as shown at (e″) and (e″′) and ligated at once. Usually the superior thyroid vessels can be treated in this manner between their origin from the external carotid artery and their distribution to the gland but occasionally these vessels divide into various branches early and then it will become necessary to ligate two or more branches separately.

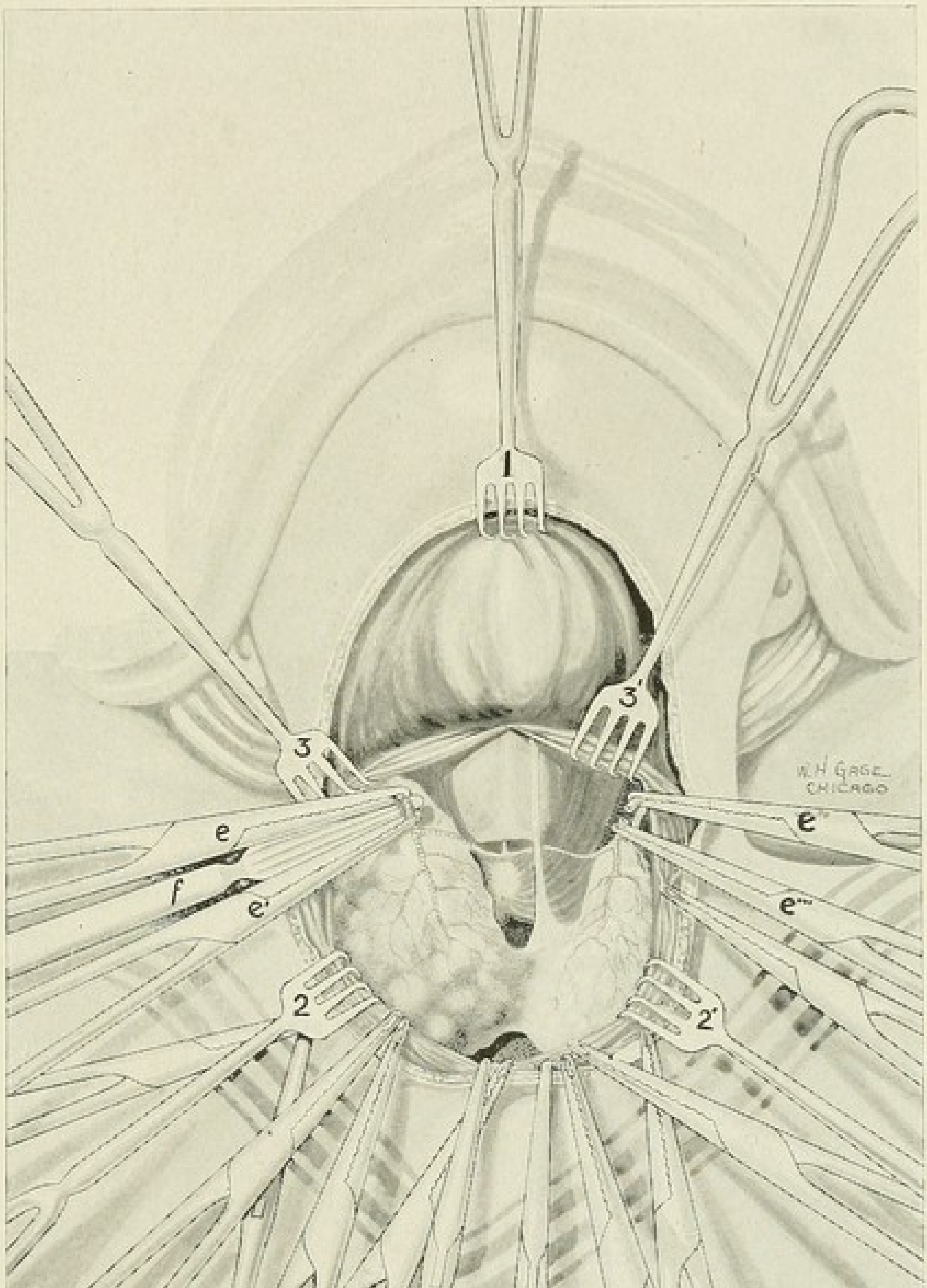
Only in rare cases do we find it necessary to ligate the superior thyroid vessels on both sides in the same patient. It is much more common to ligate one superior and both inferior thyroid vessels in the same case. In case it seems advisable to ligate the superior thyroid vessels on both sides it seems best to follow the method of Jacobson to be described fully later.

After the superior thyroid vessels have been clamped, cut and ligated on one side it is possible to dislocate the enlarged lobe of the thyroid gland forward, a method first introduced by Kocher and called "luxation of the thyroid gland."

The steps that have just been described and which have been illustrated in Plate 12, may be accomplished without cutting the muscles covering the anterior surface of the thyroid gland. This is shown in Plate 13. There is, however, much less space and if the operation is under local anæsthesia the patient suffers greatly from the necessary pulling upon the retractors (3) and (3′) and (2) and (2′) as shown in Plate 13. Unless the enlargement is confined to the middle lobe or is only moderately large in one of the lateral lobes it seems better when operating under local anæsthesia to secure the exposure of the gland indicated in Plate 12.

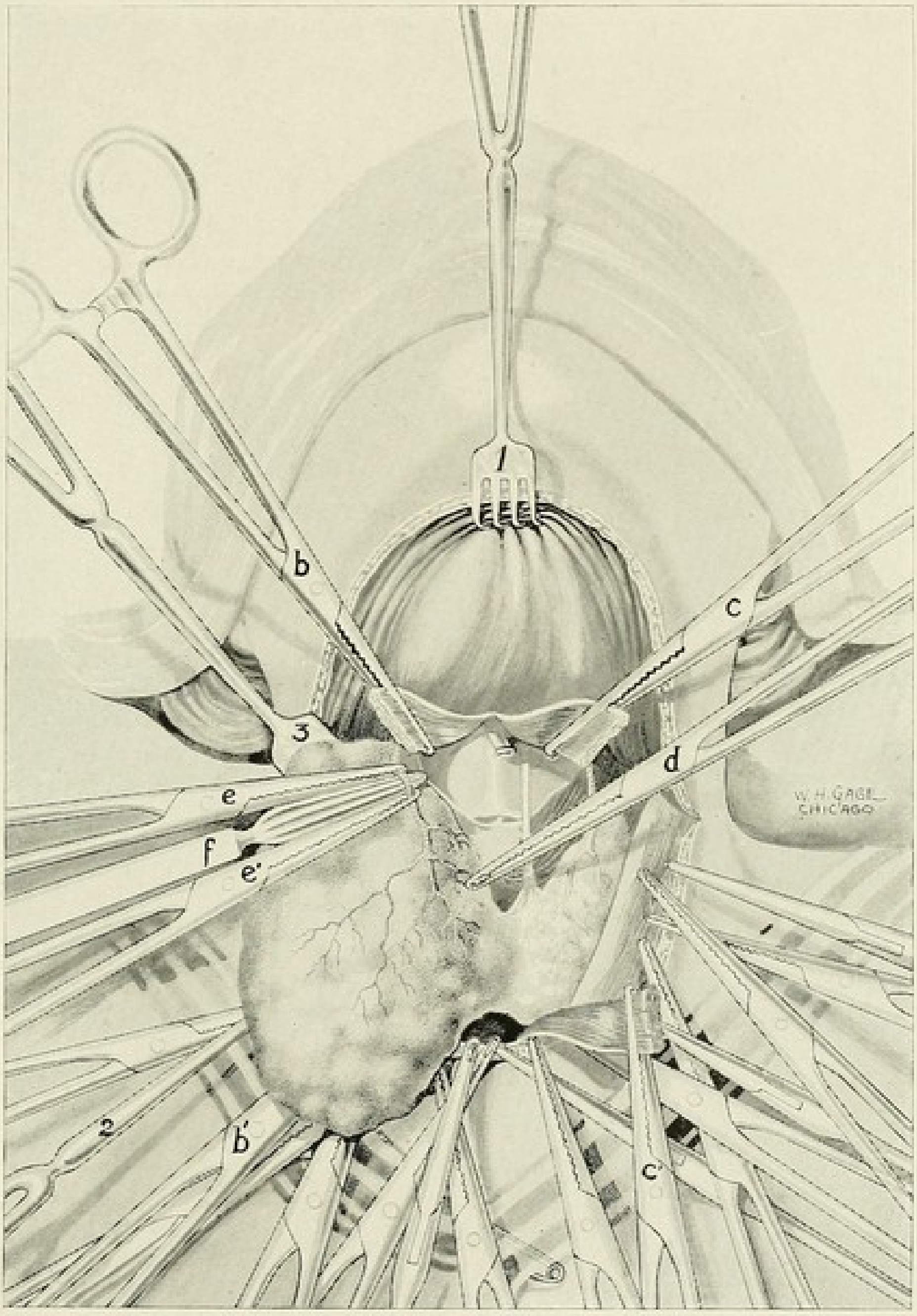
In Plate 14 the step which should have been completed in Plates 12 and 13 of severing the superior

PLATE XIII



REPRESENTS THE SAME STAGE OF THE OPERATION AS PLATE XII, WITH THE MUSCLES NOT SEVERED BUT RETRACTED BY INSTRUMENTS AT (2) AND (2′) AND (3) AND (3′).

PLATE XIV



THE RIGHT LOBE OF THE GLAND HAS BEEN LOOSENED FROM ITS ATTACHMENTS TO THE TISSUES EXTERNAL TO IT AND HAS BEEN DISLOCATED FORWARD.

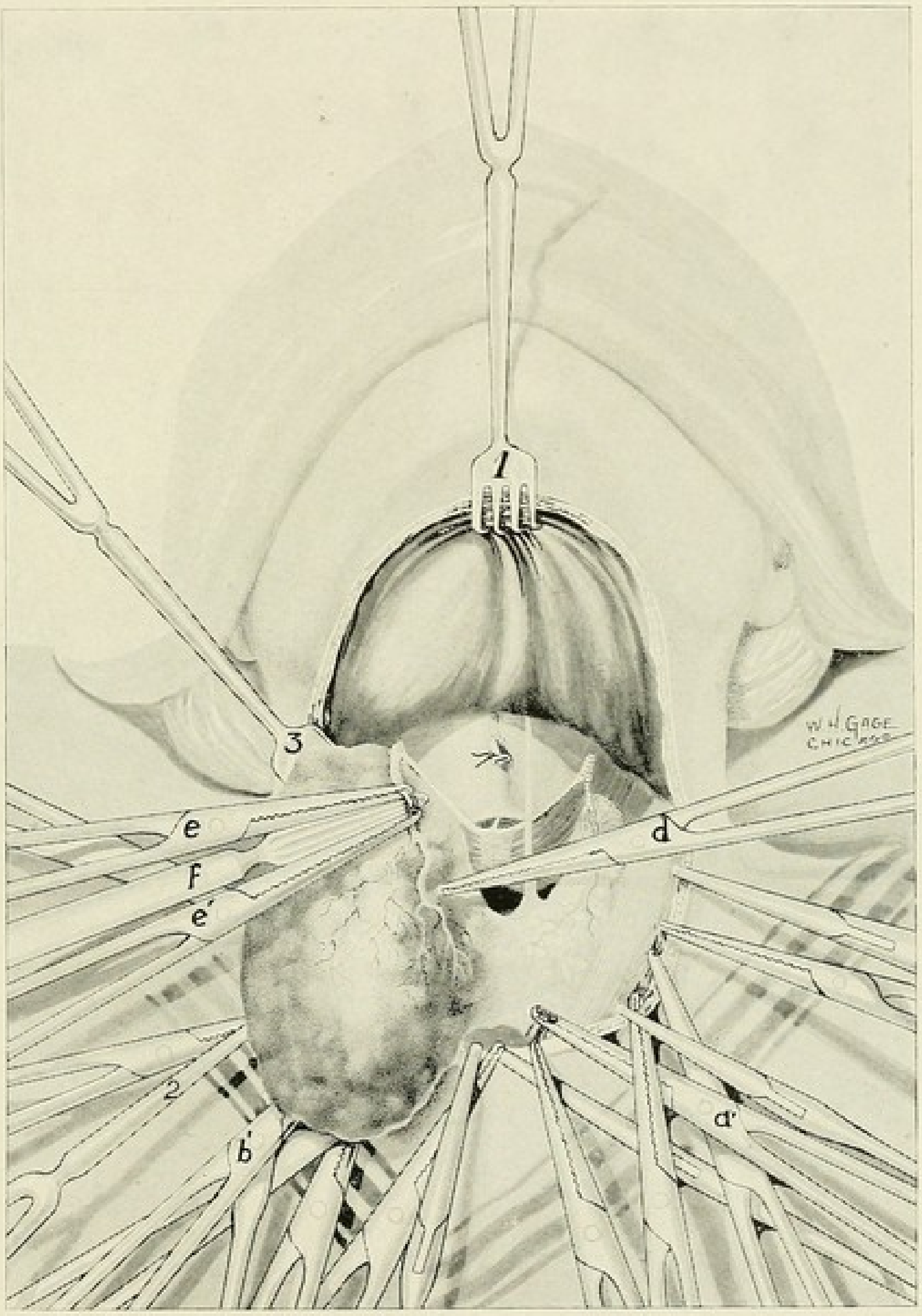
thyroid vessels is represented as being under way. The Kocher director (f) is represented as elevating the superior thyroid vein and the hæmostatic forceps (e) and (e′) have been clamped upon this vessel on either side of the director. The right lobe of the gland has been dislocated forward so that it now rests upon the hæmostatic forceps and retractors which appear in the previous figures on the surface.

It is possible in many cases to carry out this step of the operation before severing the superior thyroid vessels, but there is no advantage in doing this while there are several distinct advantages in first ligating and severing the superior thyroid vessels and then dislocating the gland forward. In this way the tension is removed from these vessels and the vein especially is protected against injury by traction. The manipulations may press some thyroid secretion into the circulation. The anterior jugular vein has also been severed early during the operation and this will be of advantage to the patient in the same direction. Occasionally there is some hæmorrhage from the small vessels which are torn when the gland is luxated, and if the superior thyroid vessels have already been disposed of it is much easier to control this bleeding either by pressure or by clamping with forceps than if they have not, because much space is gained in this manner. The luxation can usually be accomplished readily by passing the index finger between the gland and the connective tissue capsule and passing it from above downward at the same time lifting the gland forward.

In freeing the gland from the surrounding tissues it is again important to direct the pressure of the finger away from the gland instead of pressing toward the gland in order not to traumatize the gland for fear of pressing thyroid secretion into the circulation thus causing post-operative hyper-thyroidism.

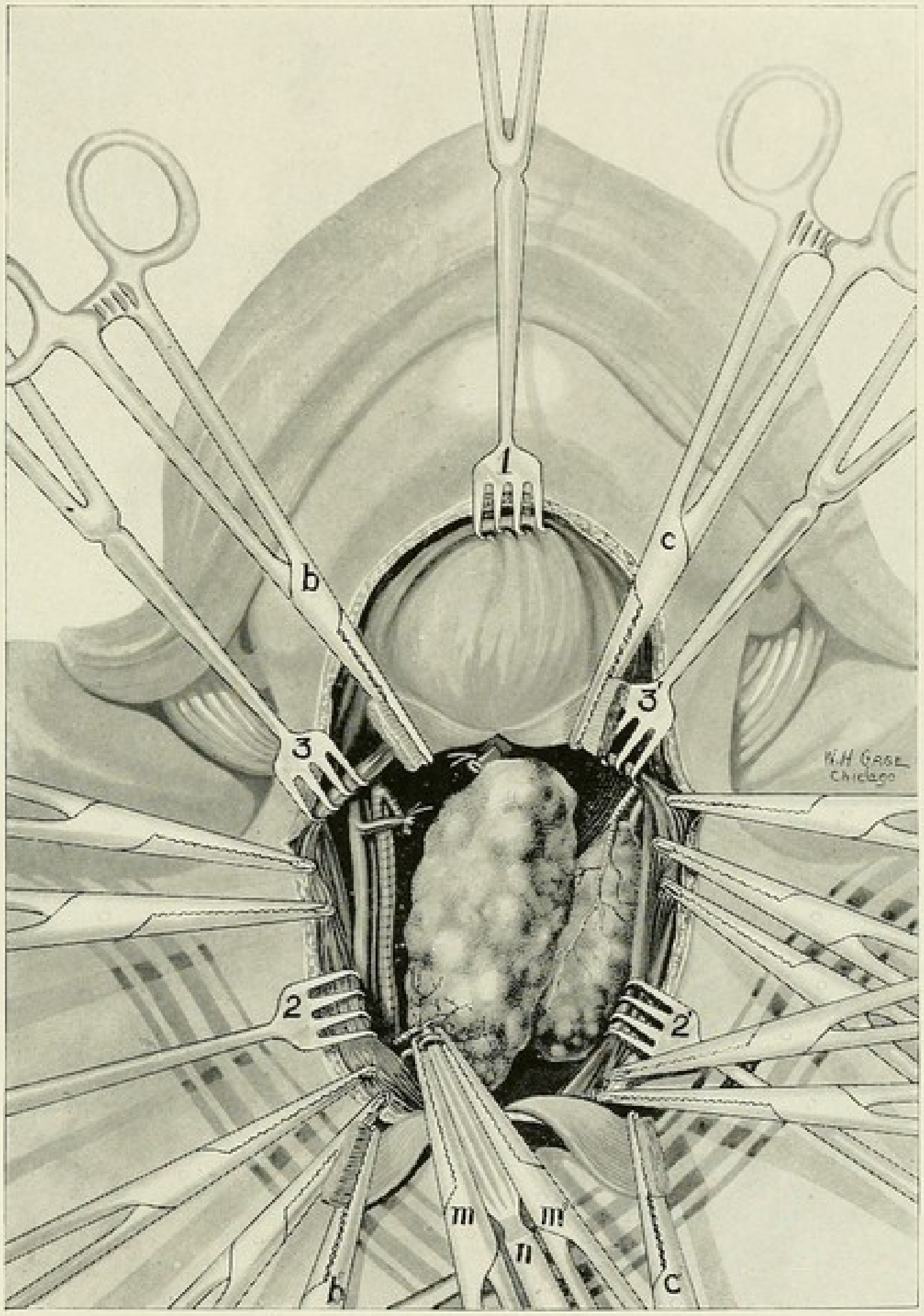
Many surgeons prefer not to luxate the gland in this manner, but to dissect the entire gland free from its attachment by sharp dissection with scalpel and dissecting forceps, laying bare all of the tissues, notably the inferior thyroid vessels and the recurrent laryngeal nerve. Landström goes no further than this with his concise dissection and prevents injury to the parathyroid glands by leaving the posterior capsule and a thin portion of thyroid gland tissue in place while a few authors go so far as to demand that the dissection must locate not only these structures but also the inferior parathyroid gland on the side from which the lobe is to be removed. It seems quite plain that it is quite unnecessary to expose the patient to the prolonged operation which is, however, of much greater harm if the patient is kept under general anæsthesia during this period of time than if local anæsthesia is employed. All of the steps which have just been described can be carried out in some patients through a field of operation as indicated in Plate 15 in which the muscles have been retraced but not severed. The luxation of the gland is especially difficult in cases in which there has existed an inflammation of the gland or a parathyroiditis or those in which the gland has been punctured by hypodermic needles for the injection of various substances. Cases that have been treated with x-ray or with electricity seem to be especially vascular and it is often difficult to stop the hæmorrhage after

PLATE XV



THE SAME AS PLATE XIV, WITH THE MUSCLES RETRACTED AND NOT SEVERED.

PLATE XVI



THE SUPERIOR THYROID VESSELS HAVE BEEN LIGATED DOUBLE AND CUT, THE RIGHT LOBE HAS BEEN ENTIRELY FREED AND DISPLACED FORWARD, THE INFERIOR THYROID VESSELS ARE ISOLATED AND HELD ON POINT OF KOCHER DIRECTOR (N) AND CAUGHT BY TWO PAIRS OF FORCEPS (M) AND (M').

luxating the gland. There may simply be diffuse general oozing without any hæmorrhage from vessels of considerable size. Usually tamponing with gauze into the cavity out of which the gland has been lifted will suffice to stop this bleeding. It is well to apply this gauze tampon immediately upon lifting forward the gland and to leave it in place during the time required for completing the remaining steps of the operation. Occasionally it may become necessary to pass a few catgut sutures over some of the oozing surfaces. In this case it is important to bear in mind the proximity of the anatomical structures shown in Plates 3, 4 and 5. It is possible to injure the internal jugular vein during these manipulations especially in cases in which there are strong adhesions due to parathyroid infection some time previous to operation.

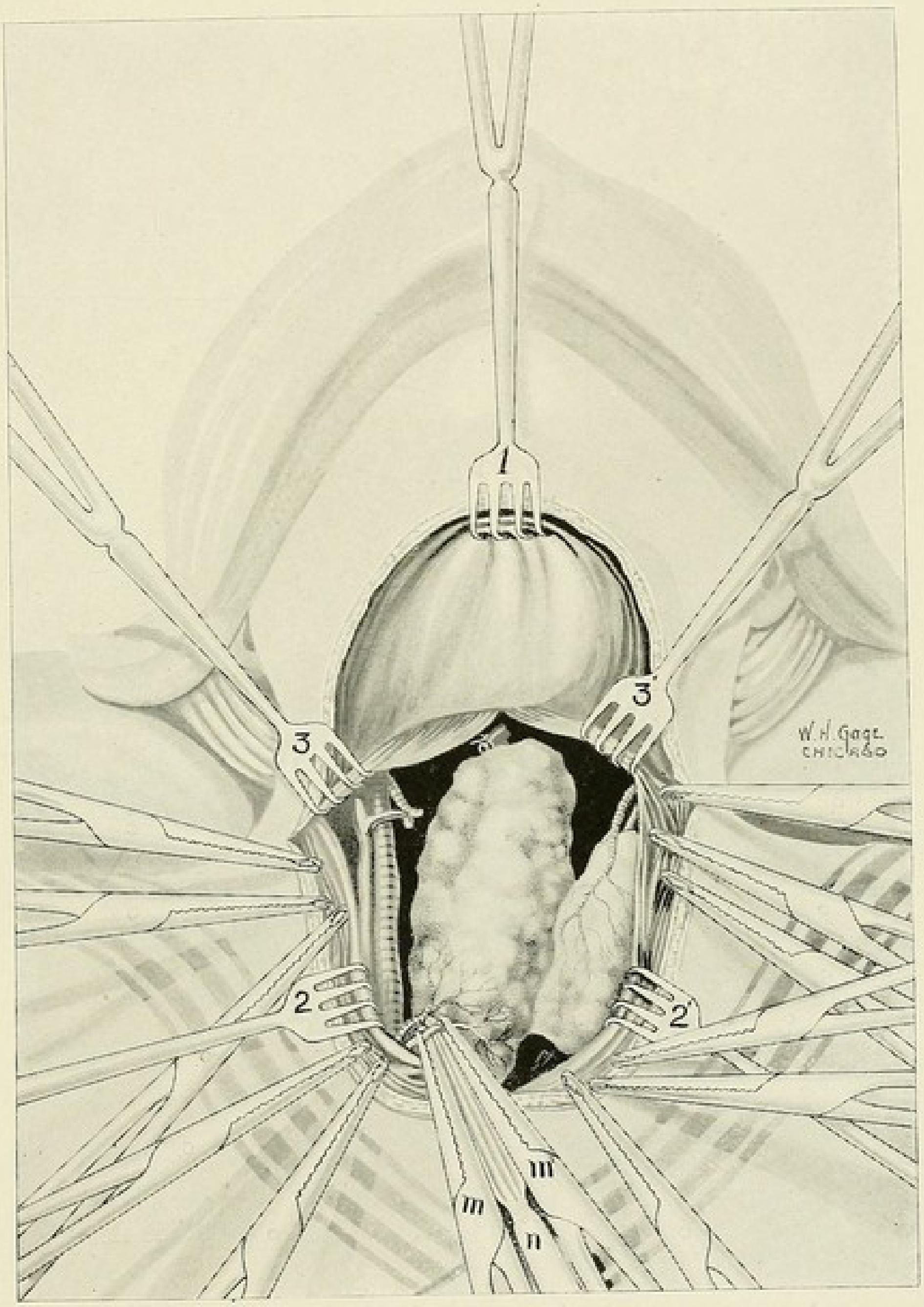
In order to make these dangers more apparent we have represented in Plates 16 and 17 the carotid artery, the jugular vein and the pneumogastric nerves as they would appear were a clear dissection made. In the operation upon the living patient, these structures never appear so clearly as here represented although they can be readily distinguished, the artery especially by its pulsation and the vein by its increase and decrease in size during inspiration and expiration.

Under the actual conditions a gauze tampon is packed between these vessels and the gland which has been lifted forward and pushed over to the opposite side but as this would cover up the portion it is desirable to show, it has been left out of the drawing. Upon lifting up the lobe of the gland and pushing it over to the opposite side it is possible to locate the inferior thyroid vessels as shown in Plate 16. A Kocher director is placed under one or both of these vessels, as in Plate 16, and hæmostatic forceps are applied to their side as shown at (m) and (m′). Usually the inferior thyroid artery and vein are farther apart than shown in Plate 16, and must be ligated separately, and most commonly bifurcation takes place at a point to the outside of the portion grasped by the hæmostatic forceps so that several forceps are required and several ligatures have to be employed.

Plate 17 shows the same steps of the operation illustrated in Plate 16 without section of muscles. It is often very difficult to expose the inferior thyroid vessels under these conditions because all of these muscles have their lower attachment to the sternum and their upper attachments are very much farther apart than the lower ones, consequently one encounters most difficulty during manipulations which must be made in the lower portion of the field of operation.

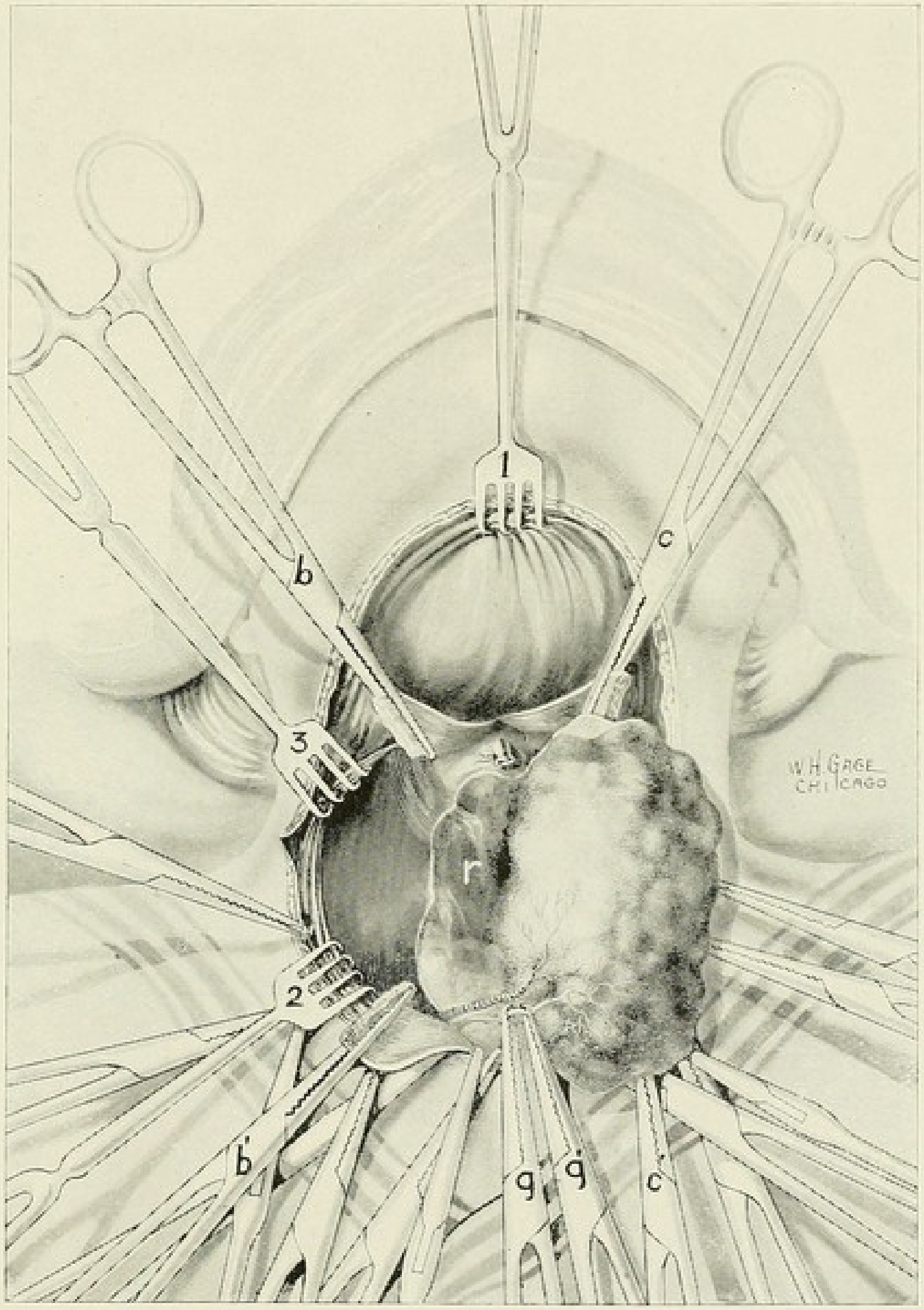
In comparing the relation of the inferior thyroid vessels in Plate 17 with those represented in Plate 5, it becomes apparent that the point of the forceps marked (m) is dangerously near the point where the recurrent laryngeal nerve crosses the inferior thyroid artery. As mentioned before in the discussion of Plates 3 and 5 it was pointed out that the recurrent laryngeal nerve is a very fine thread-like structure which can easily be located in a dissection whose object it is to expose this nerve either in the living body or in the cadaver, and many surgeons insist upon making this demonstration in every case dur-

PLATE XVII



THE SAME AS PLATE XVI, WITH THE MUSCLES NOT CUT BUT HELD OUT OF THE WAY BY RETRACTORS (2) AND (3).

PLATE XVIII



SHOWS THE RIGHT LOBE ENTIRELY FREE, WITH ITS POSTERIOR CAPSULE (R) AND A PORTION OF THE GLAND IN THE FORM OF A THIN LAYER OF THE POSTERIOR PORTION OF THE LOWER END OF THE LOBE LEFT IN PLACE.

ing the operation and before ligating the inferior thyroid artery or its branches in order that no harm may come to the recurrent laryngeal nerve during the operation. It is most important for every surgeon who performs thyroidectomy to expose this nerve repeatedly either in the cadaver or in the living body in order to be quite positive as to its location, but once having become familiar thus, it seems far better to plan the operation so that this tedious dissection may be avoided, provided the operation can be performed with the same safety to the patients. Fortunately this nerve is so located that it can always be avoided if the entire lower half of the posterior capsule of the thyroid gland is left undisturbed in its attachment to the anterior surface of the trachea. The same plan accomplishes the protection of the lower parathyroid gland which is still more intimately attached to the posterior surface of the thyroid gland than is the case with the recurrent laryngeal nerve.

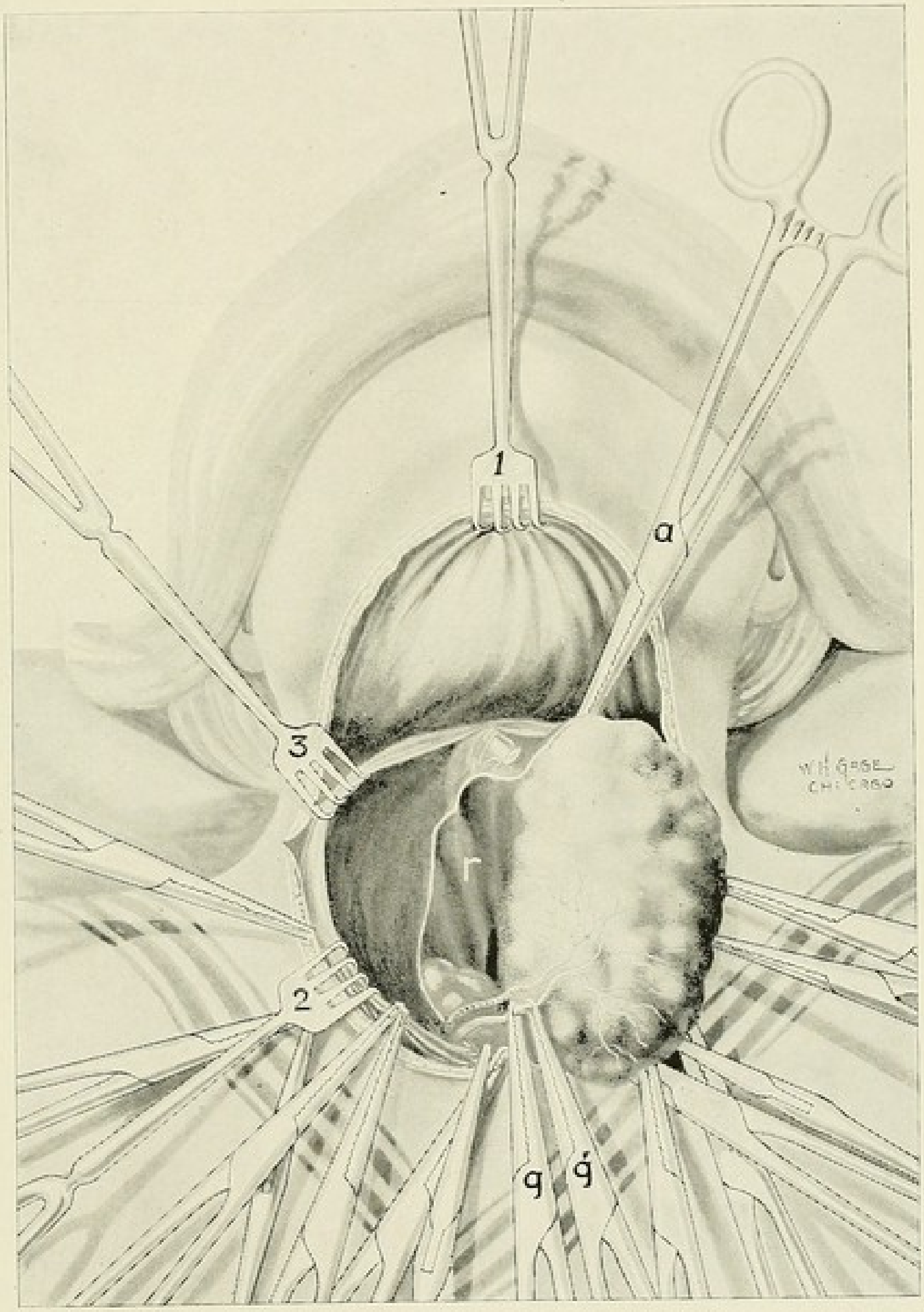
In Plate 18 this step of the operation has been illustrated. The letter (r) represents the posterior capsule together with a layer of the posterior portion of the thyroid gland which has also been left in place because the parathyroid gland some times is situated between some of the posterior lobules of the thyroid gland and by leaving this layer one is perfectly certain to leave the parathyroids undisturbed.

The forceps (g) and (g′) are attached to the inferior thyroid vein which enters the thyroid gland from its posterior surface, the gland being inverted by being folded forward over the opposite lobe, its attachment to the isthmus forming the hinge upon which the lobe is swung. The exposed portion of the inferior thyroid artery and vein is somewhat longer than is usually encountered, but it was difficult to represent it more nearly in its exact form. Frequently one encounters an artery of considerable size entering the gland at a point a little below the point in the posterior capsule marked (r). This is the middle thyroid artery which is usually not recognized until it has been severed. It must then be caught with hæmostatic forceps and ligated. It is well to apply these forceps very carefully because by grasping too much tissue in the bite of the forceps it is possible to include the recurrent laryngeal nerve causing a paralysis of the vocal cord. The bleeding from the cut surface of the gland usually is very slight. By picking up a few small vessels and then making light pressure with a gauze pad the bleeding ceases within a few minutes while the remaining steps of the operation are carried out. The dark space between the retractors (3) and (4) and the edge of the capsule (r) contains the carotid artery the internal jugular vein and the pneumogastric nerve, but these cannot be recognized separately except upon close inspection.

Plate 19 represents the conditions that have just been described in connection with Plate 18 with the exception that the muscles have been retracted instead of being severed.

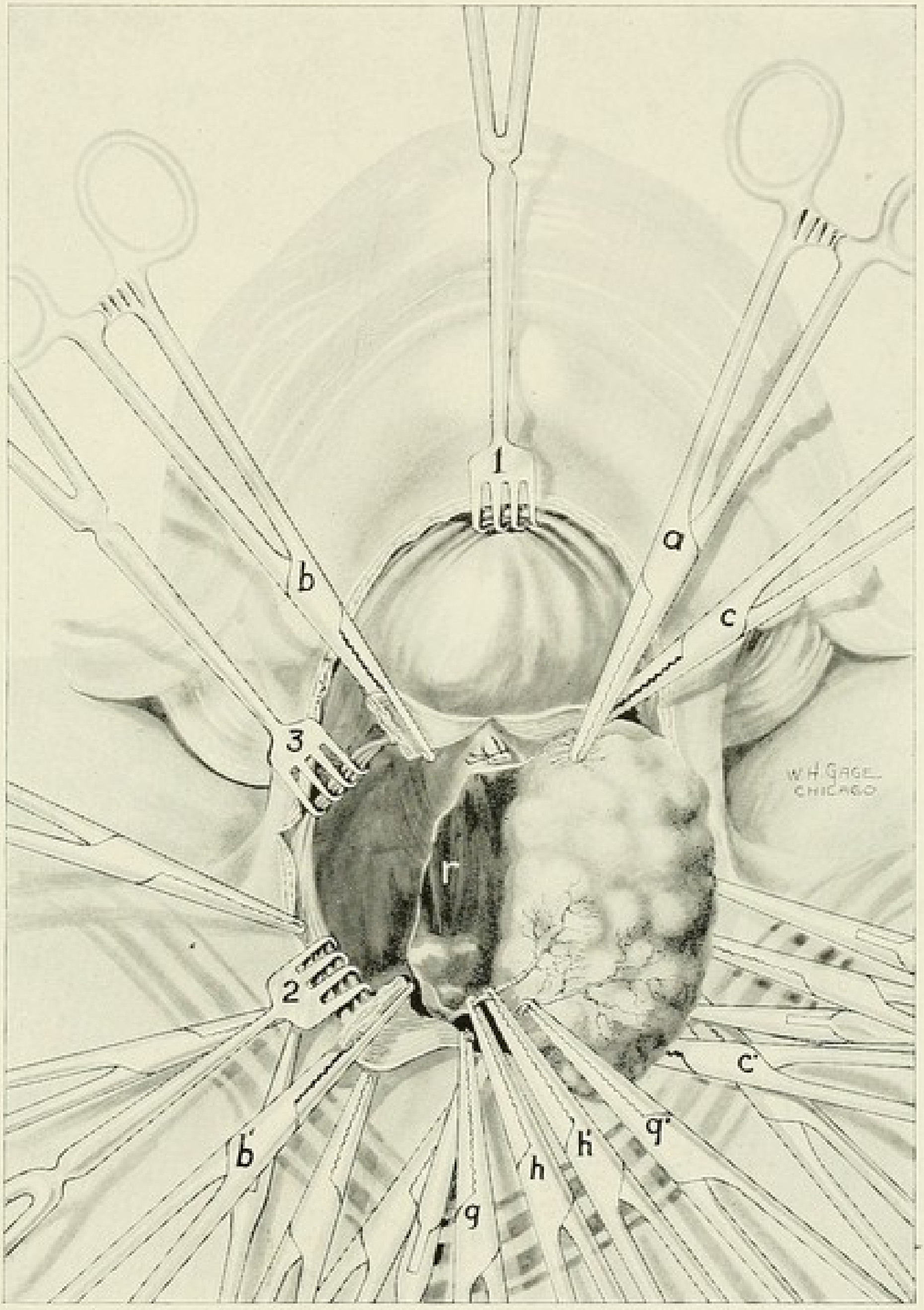
In Plate 20 the inferior thyroid vein has been severed and the inferior thyroid artery has been grasped between two haemostats (h) and (h″) and is ready to be severed. The distance between these two vessels, the former being held by forceps (h) and (h′) is more nearly as it is usually found

PLATE XIX



THE SAME AS PLATE XVIII, WITH THE MUSCLES RETRACTED BUT NOT SEVERED.

PLATE XX



THE SAME AS PLATE XVIII, WITH BOTH THE INFERIOR THYROID ARTERY AND VEIN CAUGHT IN SEPARATE HAEMOSTATIC FORCEPS.

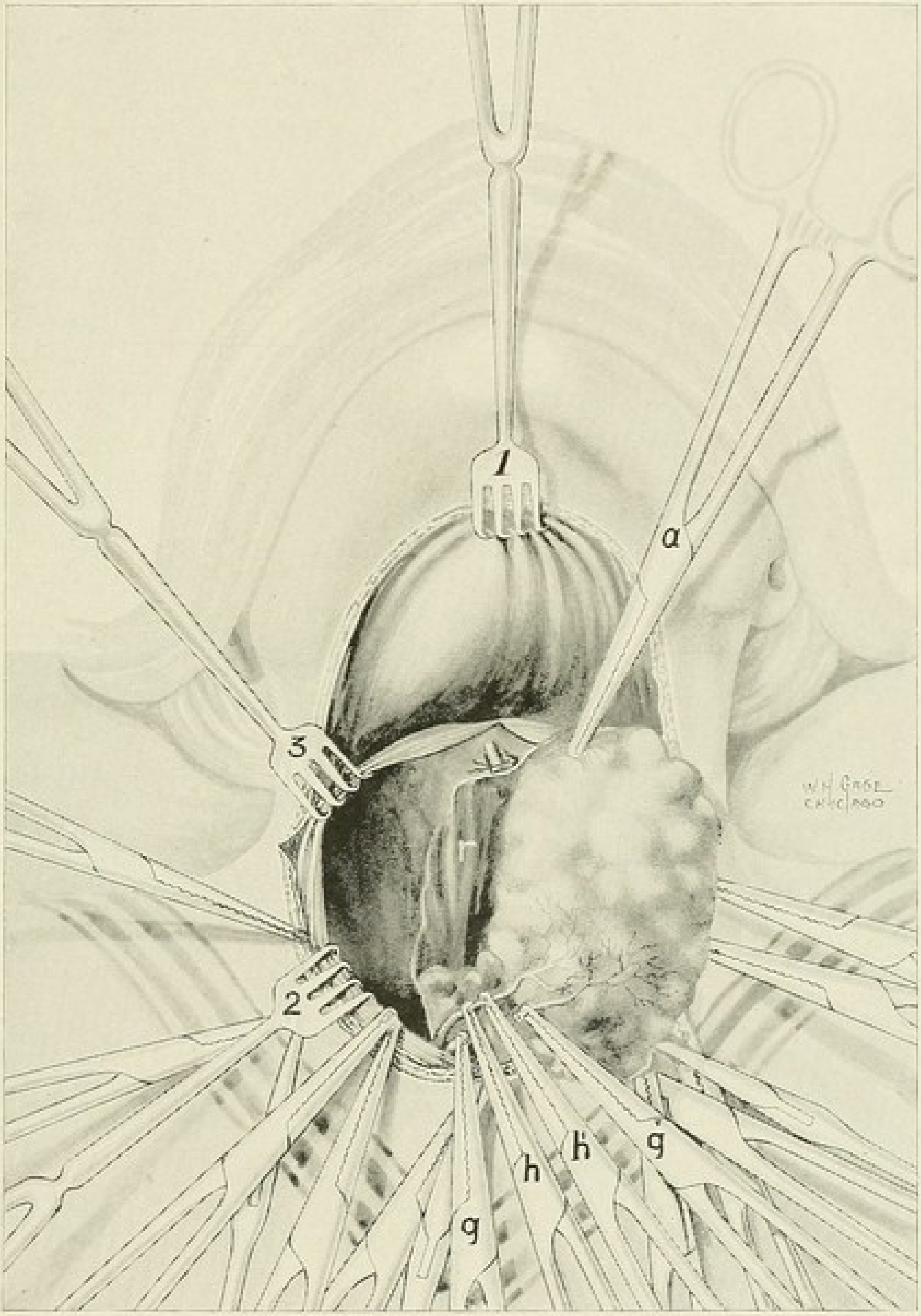
than that shown in Plates 18 and 19. In the other details this illustration will not require any further discussion, while Plate 20 is a simple repetition with the muscles retracted instead of severed. The inferior thyroid artery is then severed between the forceps (h) and (h″) and ligatures are applied to all of the vessels held by forceps (h) (h″) and (g) (g″). In this manner all of the vessels supplying the enlarged lobe of the thyroid gland have been disposed of with the least possible amount of trauma to the gland and with almost no loss of blood. The important structures behind the gland, the recurrent laryngeal nerve and the parathyroid gland have remained entirely undisturbed and the operation can be completed by simply removing this lobe at its junction with the isthmus. The point of section depends upon whether only one lobe is to be removed or whether a portion or the entire isthmus is to be removed or whether it seems advisable to add to this the removal of a portion of the other lateral lobe.

If the section is to be made through any portion of the isthmus a pair of forceps (k) Plate 22, is applied and the portion beyond these forceps is removed by cutting away this part and either ligating the remaining stump with catgut or suturing over this surface with a few fine catgut stitches. In exophthalmic goitre it is usually well to lift up the lower end of the gland by forceps (k) and then leaving the lower end of the posterior capsule together with a thin layer of gland tissue on the other side and ligating the inferior thyroid vessels or some of their branches as this was done on the other side as illustrated in Plate 21. In this manner only one upper thyroid vein and one upper thyroid artery possibly in connection with one middle thyroid artery remains.

In making a dissection of the isthmus it is important to exercise care not to injure the trachea which is exposed at this point. In one instance I had the misfortune of making a small incision into the trachea at this point of the operation. The opening was immediately closed with three fine catgut sutures and a small drain of gauze was placed against this surface. The patient recovered without any unfavorable symptoms but it is plain that the blunder should not occur. In advanced cases or in patients who have very hard nodules pressing upon the trachea one or more of the cartilages may have become softened as a result of pressure and when the isthmus is removed there is no support for the mucous lining of the trachea and the latter is drawn into the lumen of this tube by each act of inspiration giving rise to a valve-like obstruction. The patient will immediately become asphyxiated. If a general anæsthetic has been employed this may be blamed for the condition of asphyxia until it is too late. For this reason it is well to bear the possibility of this accident constantly in mind. The difficulty can be discovered at once upon inspecting the surface of the trachea because of the depression upon inspiration.

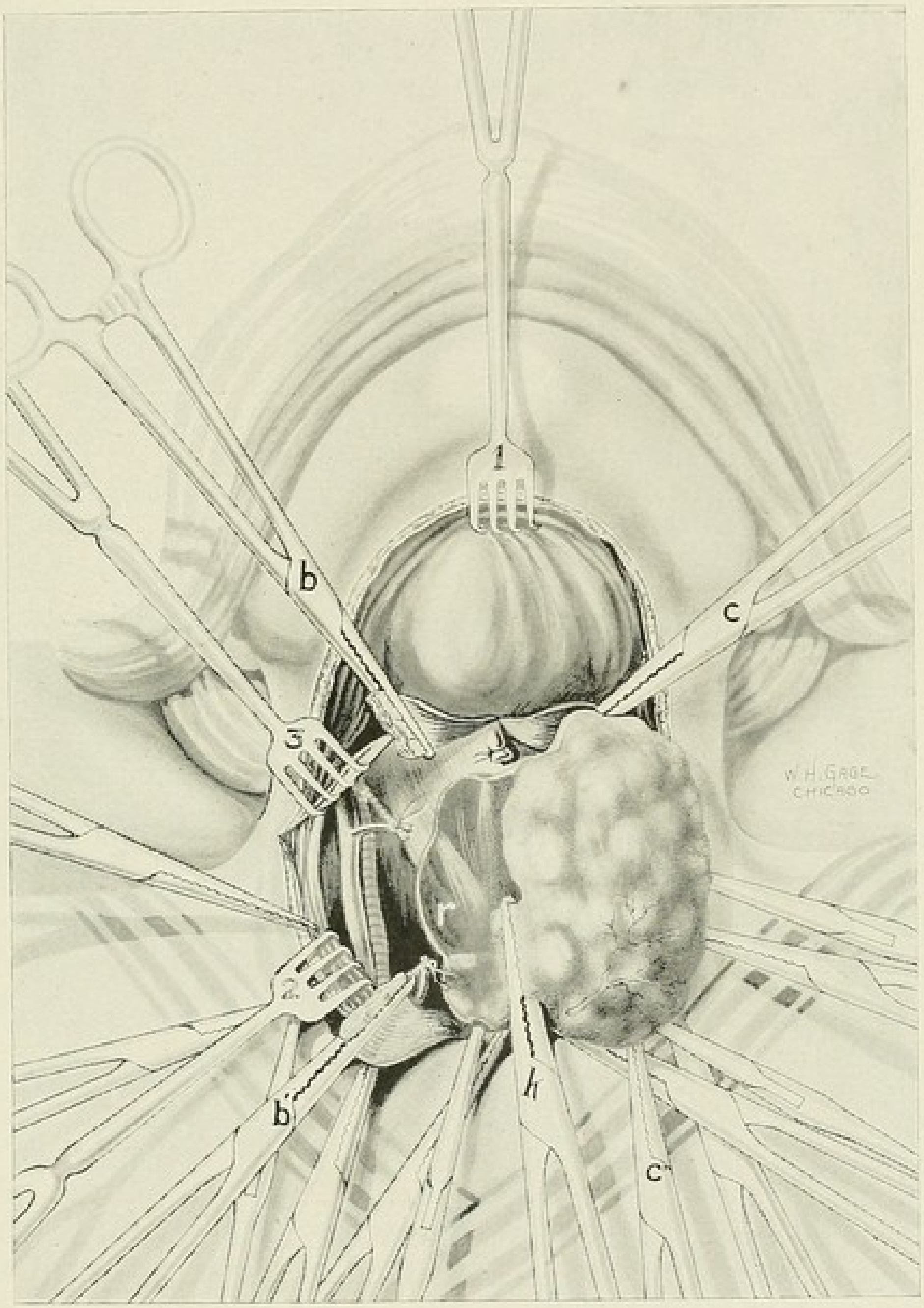
The remedy consists in the introduction of an intubation tube sufficiently long to reach to a point below the softened tracheal cartilage. For this reason a set of intubation tubes and a reliable gag should always be kept in readiness during goitre

PLATE XXI



THE SAME AS PLATE XX, WITH THE MUSCLES NOT SEVERED BUT RETRACTED.

PLATE XXII



THE RIGHT LOBE OF THE THYROID GLAND ENTIRELY DISSECTED OUT, BOTH SUPERIOR AND INFERIOR THYROID VESSELS HAVE BEEN SEVERED. THE POSTERIOR PORTION OF THE CAPSULE IS IN PLACE AND THE ISTHMUS IS BEING COMPRESSED WITH LONG-JAWED FORCEPS (K).

operations. If the obstructions cannot be relieved by intubation, tracheotomy should be performed. The depressed portion of the tracheal wall should be drawn forward and a longitudinal incision should be made and a tracheotomy tube should be inserted. If a tracheotomy tube is not available it is usually not difficult to improvise some plan to keep the wound in the trachea open. The patient should be protected against the inspiration of cold air by placing four thicknesses of aseptic gauze over a frame five c. m. or more above the wound. If the air in the room is very dry it is well to drop a few drops of water upon this screen sufficiently often to supply some moisture to the air inhaled. In these cases it is well to have the lower portion of the wound widely open in order to avoid serious infection which might otherwise give rise to septic mediastinitis.

Plate 23 represents the same stage of the operation as Plate 22 with the muscles not severed.

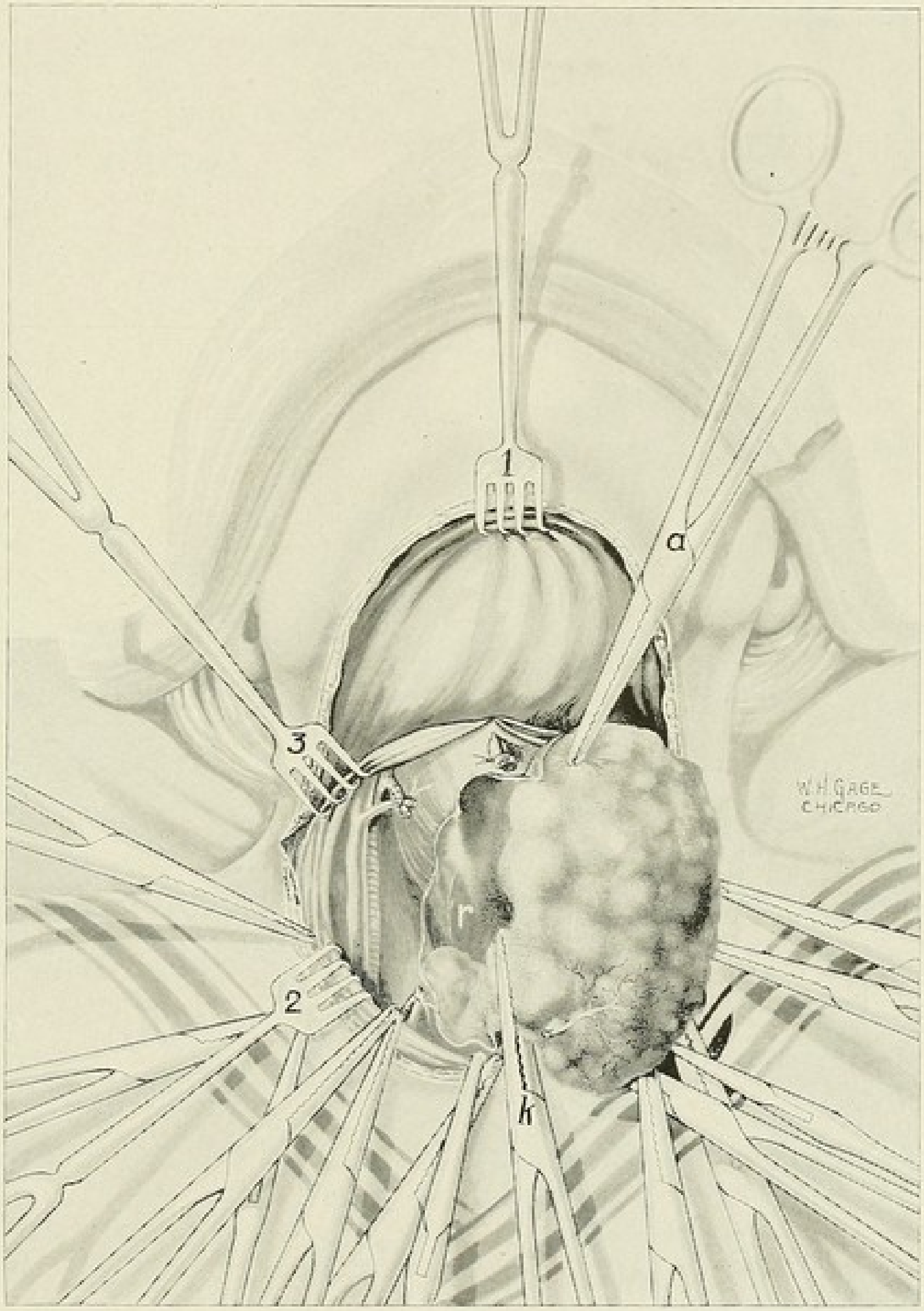
Plates 24 and 25 represent the completed operation with the exception of closing the wound. The entire right lobe together with the entire isthmus has been removed. Only the posterior capsule (r) together with a thin layer of the posterior portion of the right lobe remains, just enough to protect the recurrent laryngeal nerve and the parathyroid gland. The internal jugular vein and the common carotid artery together with the superior and inferior thyroid vessels are shown in a diagramatic manner. The stump of the thyroid gland has been sutured with a few fine catgut sutures as shown at the end of the forceps (o).

The left lobe of the gland remains in its normal condition and position. The superior thyroid artery and vein are represented as entering the upper end of this lobe, the muscles having been held back by the retractors (3) and (3″). In case it is desired to reduce the amount of blood supply for the remaining lobe this can readily be accomplished by ligating the superior thyroid vessels at this point.

In Plate 25, precisely the same conditions exist with the exception that the muscles covering the anterior surface of the thyroid gland have simply been drawn out of the way by sharp retractors (2) and (2″) below and (3) and (3″) above. Here also the superior and inferior thyroid vessels and the carotid artery and deep jugular vein are represented with the fascia entirely removed which is quite unnecessary. The capsule (r) which has been dissected off the posterior surface of the lobe which has been removed appears thicker and more substantial than in the actual operation, except in its lower half where quite a layer of thyroid tissue is left for the protection of the underlying structures.

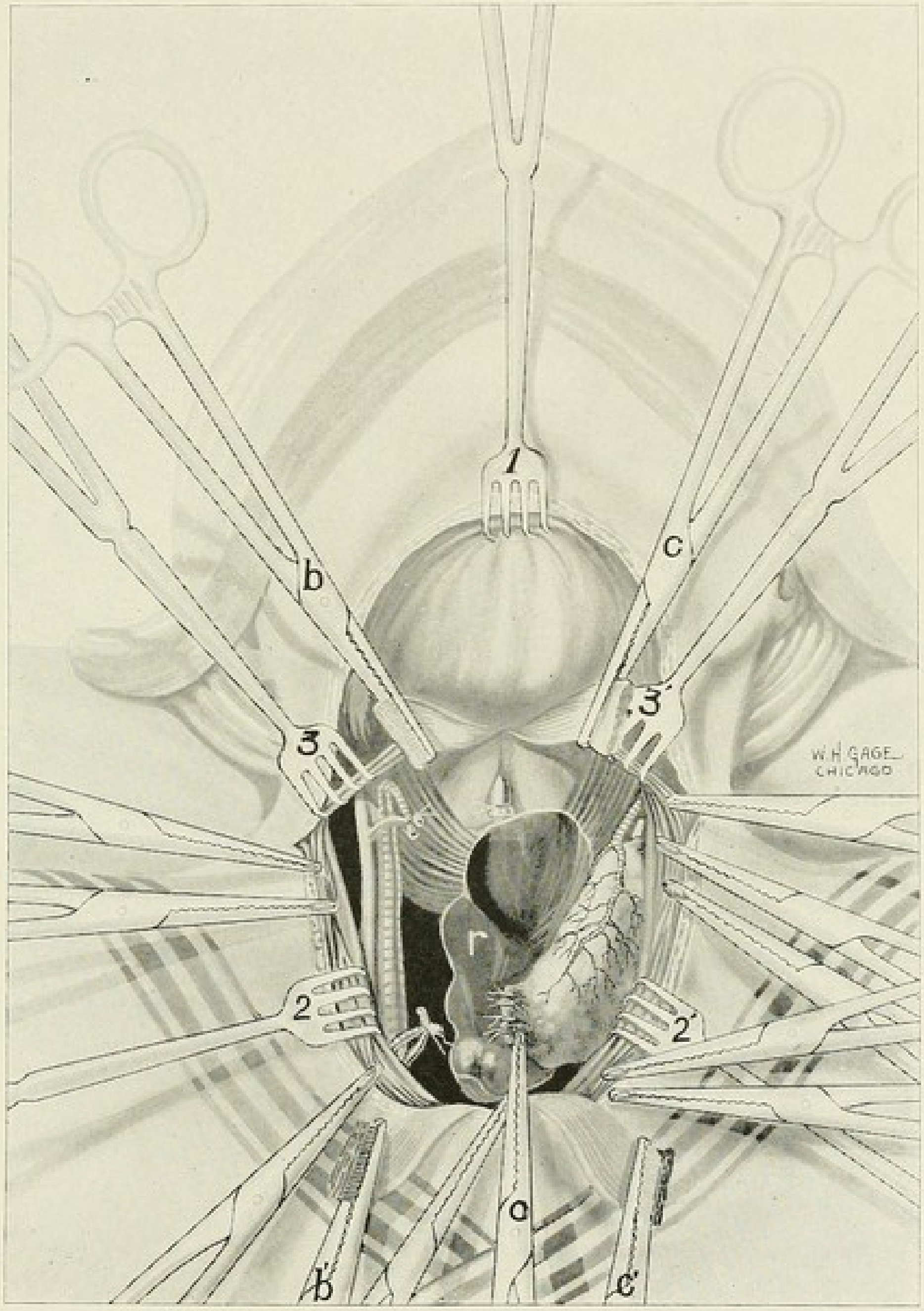
If the operation has been performed with sufficient care, the surface is usually quite free from blood. If any small surface remains from which there is general oozing, this can be controlled by the introduction of a few fine catgut stitches tied just tightly enough to stop the oozing but not with sufficient force to cause pressure necrosis. It is, of course, important not to injure the parathyroid glands or the recurrent laryngeal nerve in introducing these sutures but both can very readily be avoided with proper care.

PLATE XXIII



THE SAME AS PLATE XXII, WITH THE MUSCLES NOT SEVERED BUT RETRACTED.

PLATE XXIV



THE RIGHT LOBE OF THE THYROID GLAND HAS BEEN REMOVED AND THE PEDICLE SUTURED.

In order to prevent absorption of blood or thyroid secretion from the wound surfaces some provision must be made for drainage. It is best to drain through a separate opening as shown in Plate 26, in order that the line of suture may not be irritated by the introduction of drainage along any portion of its course. The drainage may be accomplished by a simple glass drainage tube or by a rubber tube or by the use of gauze surrounded with rubber tissue, the cigarette drain, or a simple gauze drain may be employed.

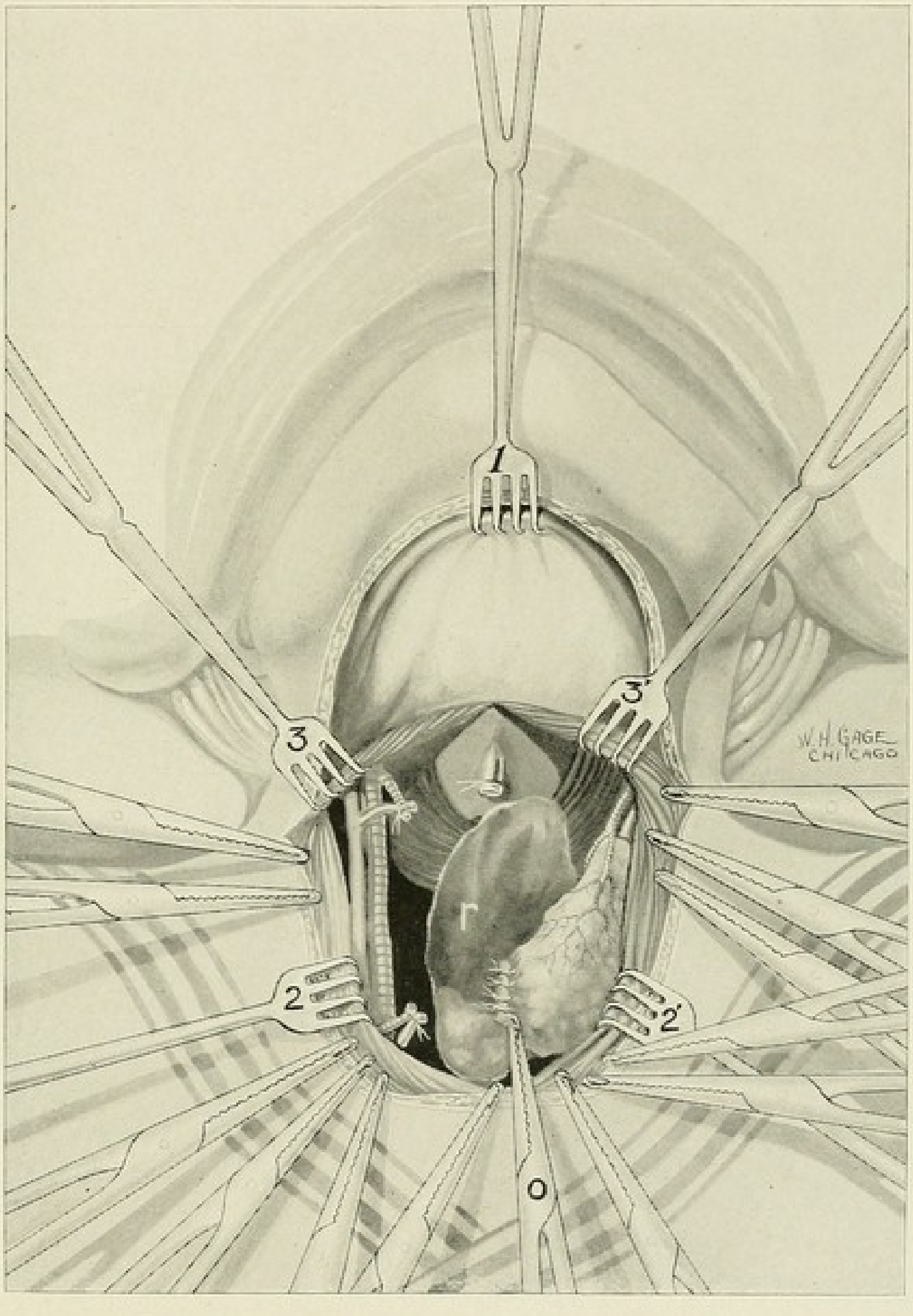
In our cases a combined drain composed of a layer of gauze loosely packed into the wound left after the removal of the lobe as shown at (s), Plate 26, with the additional introduction of a glass drain have been most satisfactory. Both the tube and the gauze, the latter surrounding the former, should be brought out at (p), Plate 28. It is best to place the gauze in such a manner that it can be withdrawn easily and without disturbing the tissues after first withdrawing the glass tube. The latter should be withdrawn on the second or third day after the operation, and the gauze a day or two later. It is important not to withdraw the gauze carelessly because this may give rise to quite troublesome hæmorrhage which may clot underneath the skin flap and which may ultimately cause quite a delay in wound healing.

Plate 27 represents all of the muscles on the anterior surface of the neck again in position. It is best to unite these muscles with a fine continuous catgut suture.

Plate 28 represents the muscles on the left side of the patient's neck already united, those on the right side are still held apart in the grasp of forceps (b) and (b'). The gauze drain (s) is in place and both this and the glass drain are represented as issuing through a small incision (p) about two c. m. below the transverse portion of the horseshoe incision. Plate 29 represents all of the muscles sutured, the symmetry of the neck having been quite as thoroughly restored as in Plate 28. It is important to give attention to these steps represented in Plates 27, 28 and 29, because this will prevent the very troublesome deformities which one is sure to encounter if this precaution is not taken.

The only step remaining in order to complete the operation is the closure of the principle incision as shown in Plate 30. If only the skin suture is employed there is usually a considerable amount of spreading of the scar because of the traction on part of the platysma myoides muscle. On the other hand if the wound is closed by the sub-cuticular suture alone, a rather unsightly thickening is likely to occur at the line of suture. In order to avoid both of these sources of annoyance it is advisable to place about six interrupted sub-cuticular sutures of fine catgut along the line of incision at regular intervals uniting the platysma myoides and the sub-cutaneous connective tissue. This will remove all tension from the skin proper and will leave an almost invisible line of suture provided silk or horsehair is used and the edges are carefully and evenly united and the sutures drawn just sufficiently tight to secure accurate coaption but not to cause any pressure necrosis.

PLATE XXV



THE SAME AS PLATE XXIV, WITH THE MUSCLES RETRACTED BUT NOT SEVERED.

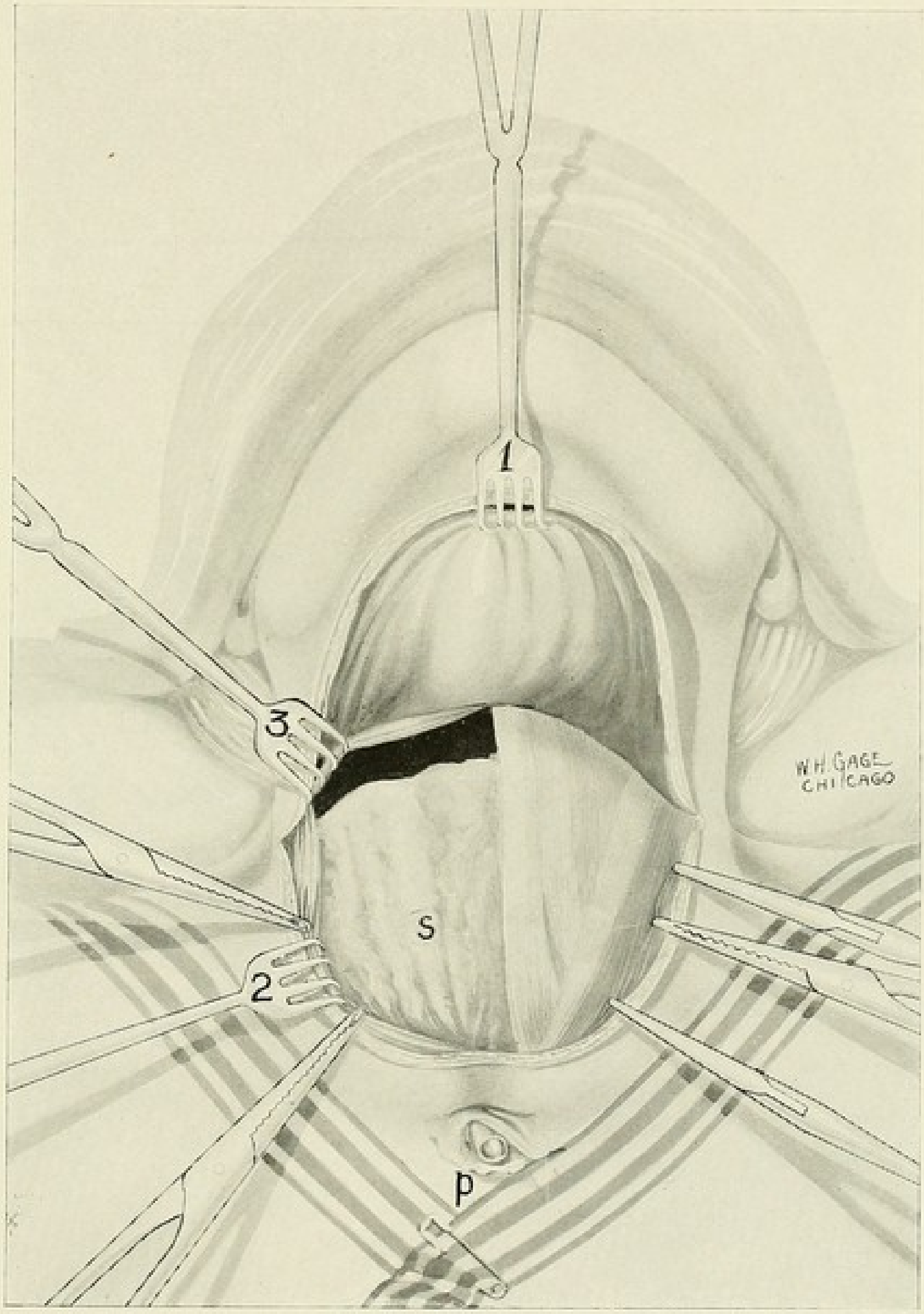
These sutures can be cut on the fourth or fifth day which will prevent the occurrence of even the slightest suture marks.

The operation which has just been described may be employed with equal satisfaction in the removal of portions of the thyroid gland for whatever condition may demand this procedure. The operation is, of course, more serious in proportion with the severity of the pathological condition present in the patient under consideration. Generally speaking, in patients suffering from exophthalmic goitre this condition makes the operation more serious than in simple goitre and it may be well at this point to insist upon the fact that although all of the steps of the operation are relatively simple, still the operation itself must be looked upon as one of the serious major surgical procedures which should not be undertaken by inexperienced surgeons, because in many, possibly in most of these patients, there is but a relatively narrow margin even with much experience and excellent skill and splendid surgical judgment. It seems proper to direct attention to this fact at this point because the low mortality of men with great skill and remarkable judgment might otherwise cause those not so well equipped to suffer severe disappointment and the loss of many patients.

Ligation of Thyroid Vessels. Kocher has pointed out the fact that in many cases the patient is too weak to bear the radical operation of thyroidectomy in cases of exophthalmic goitre. In all of these cases an attempt must be made to build up the patient's strength by rest, diet and the use of appropriate remedies, but there are some cases which seem to become worse constantly, notwithstanding this treatment. In some instances the patient's condition may be so bad that even the slightest operation would result fatally, but there is another class which will bear a very slight operation but cannot bear the shock of thyroidectomy. In this class of cases Kocher recommends the ligation of one or more vessels as a preliminary operation. This will reduce the production and absorption of thyroid poison to a sufficient extent that the patient's general condition may improve sufficiently to make it safe to perform a more serious operation after a few weeks of recuperation.

Not enough experience has been accumulated to determine positively whether this plan should be generally adopted. Kocher seems confident that it is indicated in certain cases and his enormous experience and wonderful surgical judgment must always carry more weight in this subject than that of any other surgeon with the single exception of Charles H. Mayo, consequently we must, for the present, accept this view, although its correctness has been questioned by many surgeons, no less an authority than Landströin among them. These surgeons have pointed out the fact that the mortality after simple ligation has been greater than after excision of one lobe, but as the former operation is employed only in cases that are in an almost hopeless condition while the latter operation is practiced in the less serious cases no comparison can, of course, be made· because the two operations are performed on patients whose prognosis would be entirely different were they operated for any other condition. Those upon

PLATE XXVI



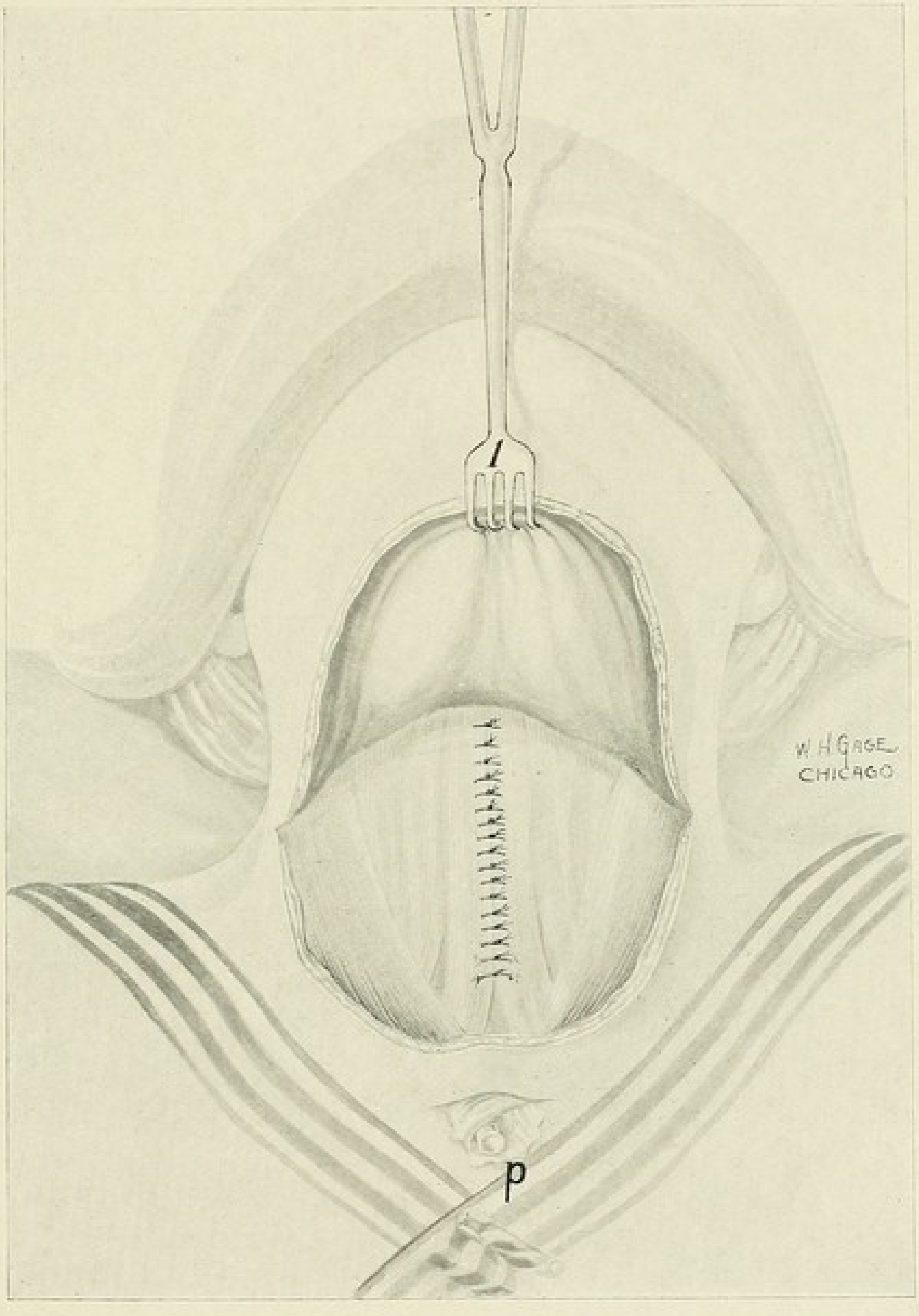
SHOWS THE OPERATION COMPLETED TO THE POINT OF CLOSING THE WOUND. (S) GAUZE TAMPON; (P) SEPARATE OPENING FOR GLASS DRAIN AND GAUZE.

whom the former operation is practiced would have but a very slight chance of recovery after almost any operation, while those subjected to the latter operation would be almost certain to recover from any operation which would not in itself be dangerous.

Having accepted the theory that ligation in itself is a less severe procedure than removal of one lobe, we must choose between the various operations which have been recommended, namely: The ligation of as many arteries and veins as it seems safe to ligate in any given case as recommended by Kocher; the ligation of as many veins as seems safe, as recommended by Tuholske; and the ligation of both upper poles of the thyroid gland including arteries, veins, and lymph channels by passing double ligatures around the entire upper pole on both sides, including the gland together with both superior arteries and veins and the capsule as recommended by Werelins and Jacobson.

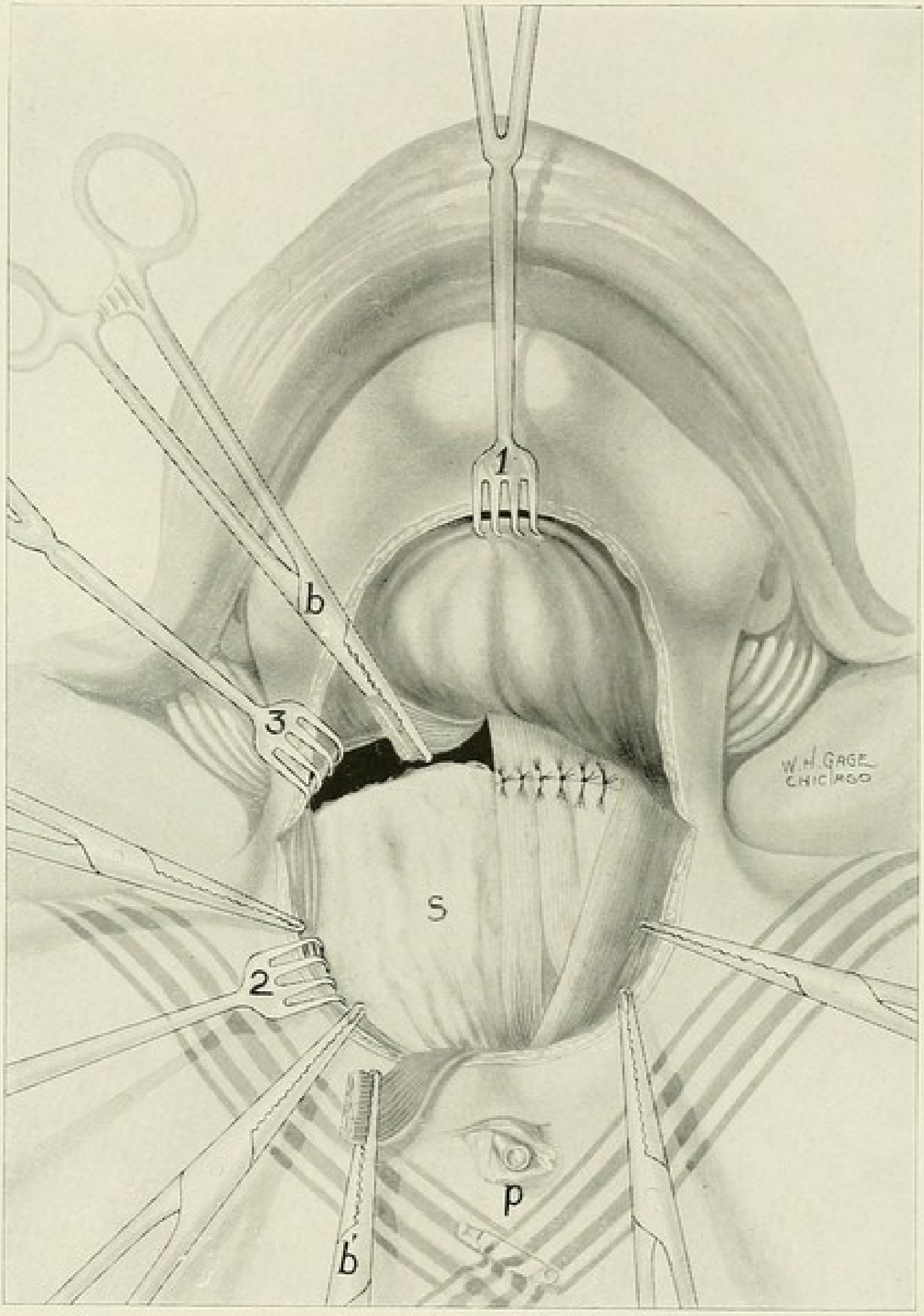
Of these methods the one recommended by Kocher has been employed most frequently. If it seems as though the ligation of the superior thyroid vessels on one side is as much as the patient can safely endure at the first sitting, then the skin is cocainized along the anterior border of the sterno-cleido-mastoid muscle from the point (a) or (b), Plates 2 and 30, downward for a distance of five c. m. A puncture is then made with a fine sharp scalpel through the skin at the point (a) or (b) according to the side on which there is the greatest amount of enlargement, then a blunt-pointed hypodermic needle with a lateral opening attached to a syringe containing the anæsthetizing solution is passed into the deep tissues along the anterior border of the sterno-mastoid muscle and a sufficient amount of fluid is injected to thoroughly anæsthetize the tissue to be manipulated later. After waiting for five minutes the skin is incised, the muscles covering the anterior surface of the lobe are retracted outward and the superior thyroid artery and vein are exposed, isolated and elevated with a Kocher director either singly as shown in Plate 22, or together. They are then caught with two pair of hæmostatic forceps and ligated as shown at (e) and (e′) and (e″) and (e″′), Plate 13. It is not necessary to expose the entire gland as shown in these figures to accomplish this which can easily be done through the incision described above. If the patient is in a satisfactory condition after this has been done on one side the same thing may be done on the opposite side immediately. This is usually the better plan because as has been shown all of the arteries and veins of the thyroid gland are so thoroughly anastomosed that the ligation of only one of the four principle arteries and veins has but little influence upon the production and absorption of thyroid toxins while the ligation of both superior thyroid arteries and veins seems to have a very marked effect. Were it possible at the same time to ligate also the inferior thyroid artery and vein on one side the results would be still better, but the amount of trauma inflicted by the ligation of one inferior artery and vein is much greater than that required in the ligation of both sides above, hence, most patients who are sufficiently strong to bear the ligation of three sets of vessels are quite strong

PLATE XXVII



THE MUSCLE IN FRONT OF THE THYROID GLAND HAS BEEN SUTURED.

PLATE XXVIII



THE SAME AS PLATE XXVI, WITH THE ADDITION OF SUTURING THE MUSCLES WHICH HAD BEEN SEVERED TRANSVERSELY.

enough to bear the excision of one thyroid lobe at the same time.

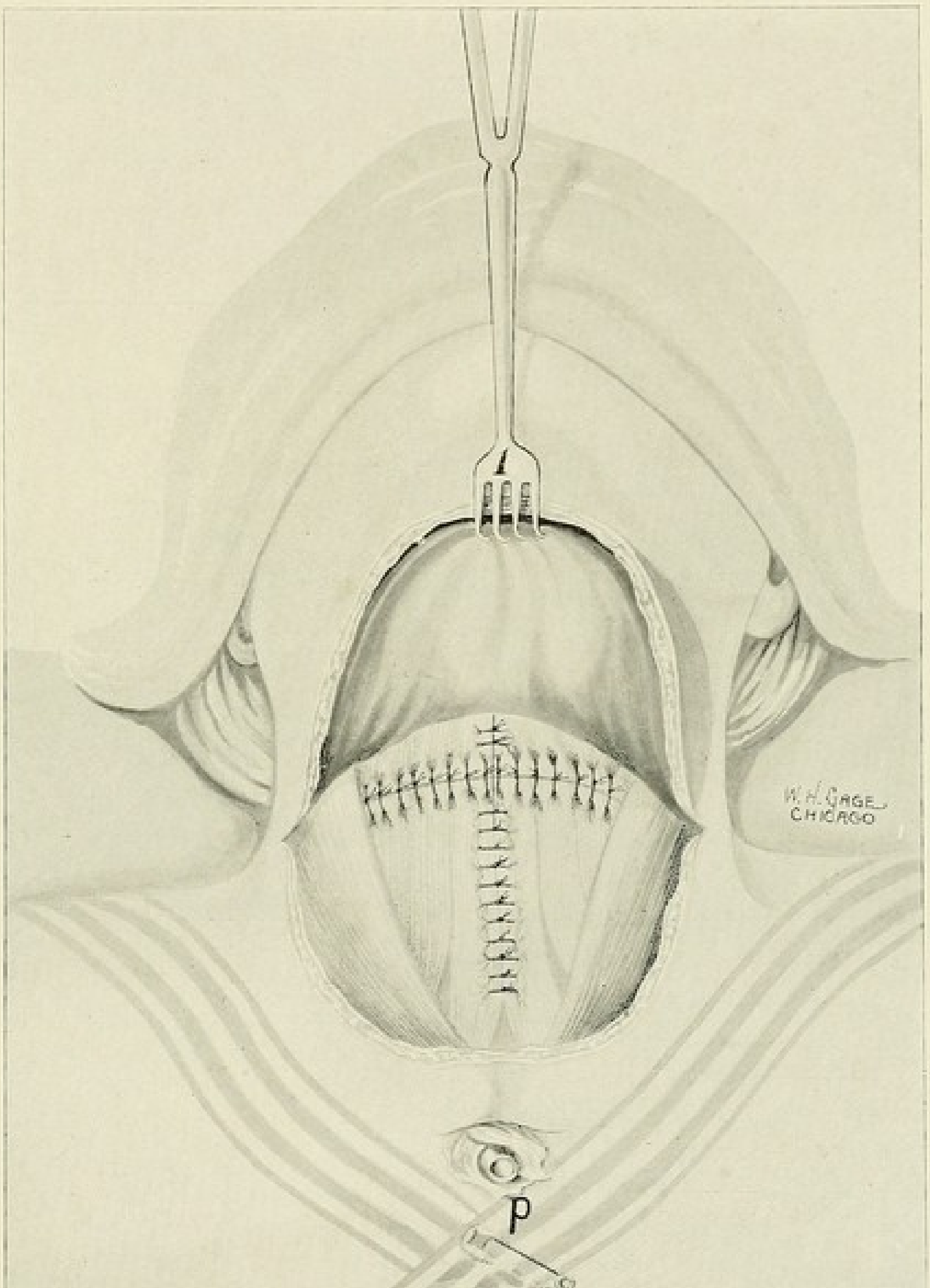
In case there is a sufficient amount of enlargement present to make it desirable to excise one lobe later, it is probably better to make the incision shown in Plates 22 and 30, and to turn up the flap as shown in Plate 31, because the incision can be made in a few moments entirely painless under local anæsthesia. The ligation of the anterior jugular vein as shown in Plates 31 and 32, will dispose of a greatly enlarged vessel. The muscles anterior to the thyroid gland can be separated easily and the ligation of the superior thyroid vessels can be secured in a shorter time than through two separate incisions. At the same time a double suture may be passed around a number of the superficial branches of the inferior thyroid vessels on the side on which the gland is enlarged. The flap can be brought down into place after all this has been accomplished and held in proper position by the insertion of from four to eight fine catgut sutures which grasp the platysma and the sub-cutaneous connective tissue.

This operation requires somewhat less skill than the one first described. In case the gland is not sufficiently enlarged on either side, however, to indicate its removal it is not necessary to make this long incision. On the other hand if it is desirable to remove an enlarged lobe, the patient will usually be in condition to have this secondary operation made in from one to two weeks, when the flap can be turned up again and the operation for excision of the thyroid gland which has already been fully described, may be performed.

Ligation of Thyroid Veins. It has been suggested by Tuholske that the ligation of the thyroid veins would reduce the introduction of thyroid poison into the general circulation to such an extent that the hyperthyroidism of exophthalmic goitre would be abolished while there would be no danger of myxœdema because the gland itself would not be removed. This theory seems to be borne out by the clinical observations as set forth in this most interesting article and it is possible that the operation suggested will receive a recognized position after it has been tested for a sufficient period of time. At this time it seems of sufficient importance to demand our consideration.

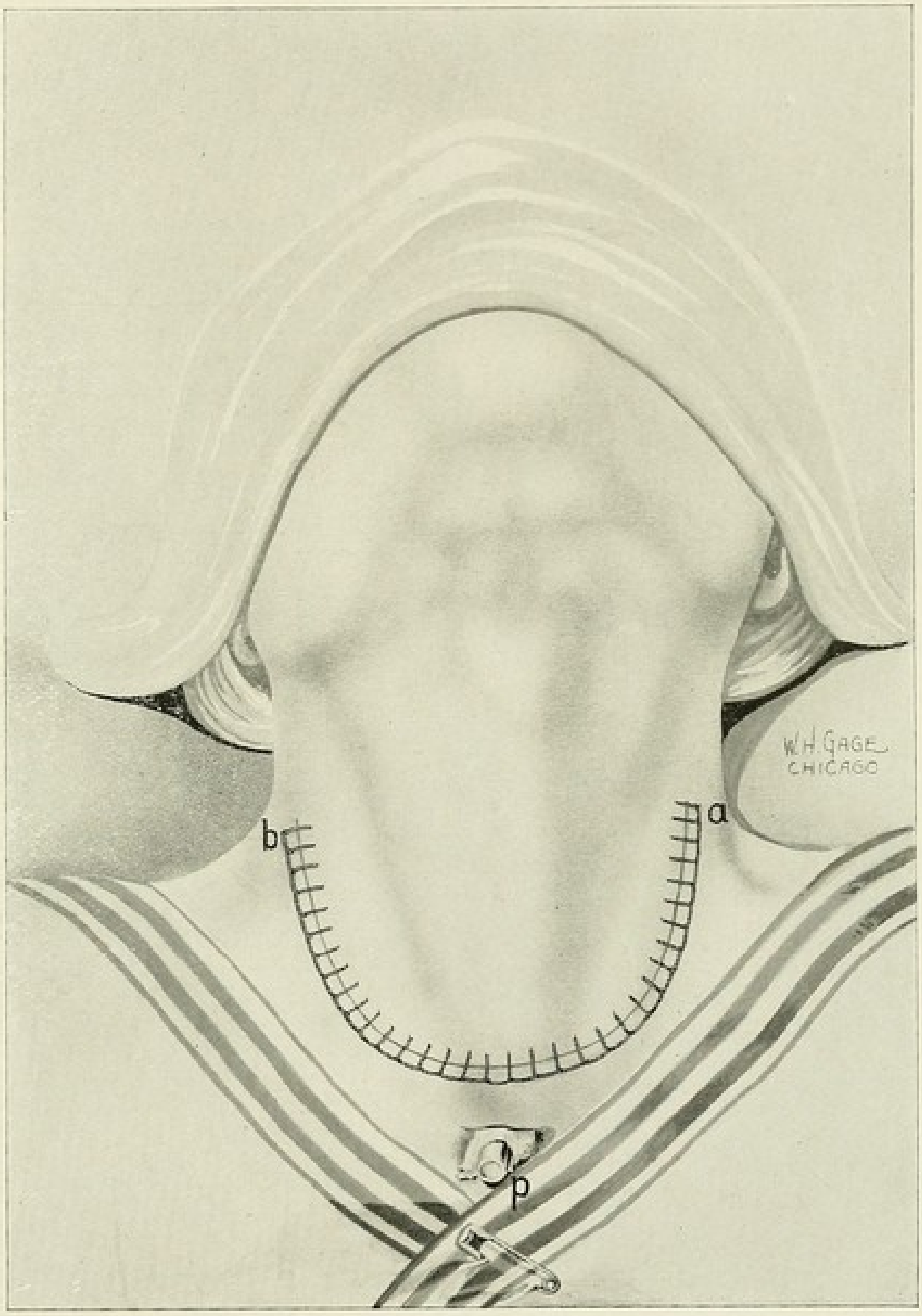
Operation. An incision is made as indicated in Plates 2 and 30, the flap of skin and platysma is reflected as shown in Plate 32, and the sternohyoid, sternothyroid and omohyoid muscles are retracted as shown in Plates 31 and 32. The anterior jugular vein and its branches are ligated, then the two superior thyroid veins are isolated, the Kocher director is inserted underneath each vein and two hæmostatic forceps are applied as shown in (e) and (e′), Plate 14, the veins are severed and ligated as shown in Plates 31 and 32. It is a relatively easy matter to ligate the superior thyroid veins because they are quite superficial and easily isolated. The inferior thyroid veins on the other hand cannot be isolated so easily because they enter the gland from behind and it is consequently necessary to lift the lower border of the gland forward in order to expose these veins. In discussing the excision of the lateral lobe of the thyroid gland it was shown that by first ligating the

PLATE XXIX



THE SAME AS PLATE XXVII, WITH THE ADDITION OF SUTURING ALL MUSCLES WHICH HAD BEEN SEVERED TRANSVERSELY.

PLATE XXX



SHOWS THE EXTERNAL WOUND COMPLETELY CLOSED, WITH DRAINAGE TUBE AND GAUZE ISSUING FROM THE SEPARATE INCISION BELOW AT (P).

superior thyroid vessels and dislocating the lobe forward it is not very difficult to ligate the inferior thyroid vessels, although there is great danger of injuring the recurrent laryngeal nerve and the parathyroid gland on the side involved.

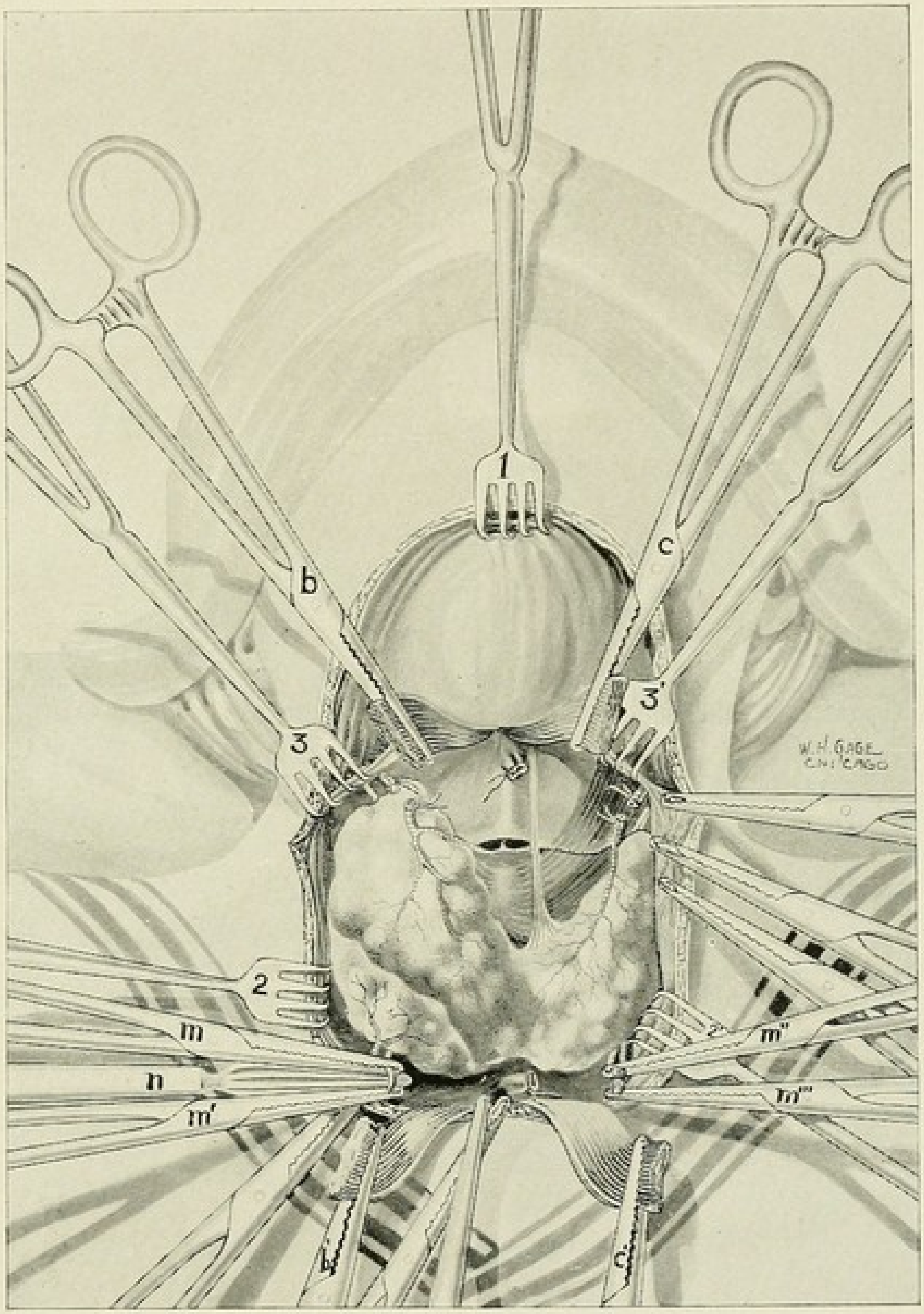
It is much more difficult to isolate the inferior thyroid vein when the superior thyroid artery has not been severed and this difficulty increases with the size of the lobe, but as this operation is indicated only in cases in which the excision of the lobe need not be considered because of its enlargement one will, of course, not be called upon to ligate the inferior thyroid veins in any case in which there is a considerable enlargement of either lobe, but only in cases in which the symptoms of exophthalmic goitre exist without much enlargement of the thyroid gland.

In this class of cases it is possible to draw forward the lower border of the gland sufficiently to isolate the inferior thyroid vein as shown in Plates 31 and 32, and to elevate it as shown at (n) with a Kocher director. Then two forceps are applied as shown at (m) and (m′), the vessel is cut and ligated as shown at (m″) and (m″′). The vein is located to the inner side of the artery and is not in as close relation to the recurrent laryngeal nerve as the latter, hence, the operation is easier and safer than the ligation of the inferior thyroid artery. In ligating the inferior thyroid artery it is always necessary to expose the recurrent laryngeal nerve because it is only by doing this that one can be certain that the latter is not injured during some part of the manipulation. In ligating the inferior thyroid vein, on the other hand, it is necessary only to expose the structure carefully on the Kocher director as shown in Plates 31 and 32, in order to avoid injuring either the recurrent laryngeal nerve or the parathyroid gland. In ligating the inferior thyroid artery it is also important to ligate near the entrance of this vessel into the gland in order not to ligate the branch which sometimes supplies the parathyroid gland. It is not necessary to take a corresponding precaution in ligating the inferior thyroid vein.

What has just been said would indicate that this operation requires much surgical skill and anatomic familiarity aside from that absolutely required in performing thyroidectomy, but if the results will justify the operation it will not be difficult to acquire these.

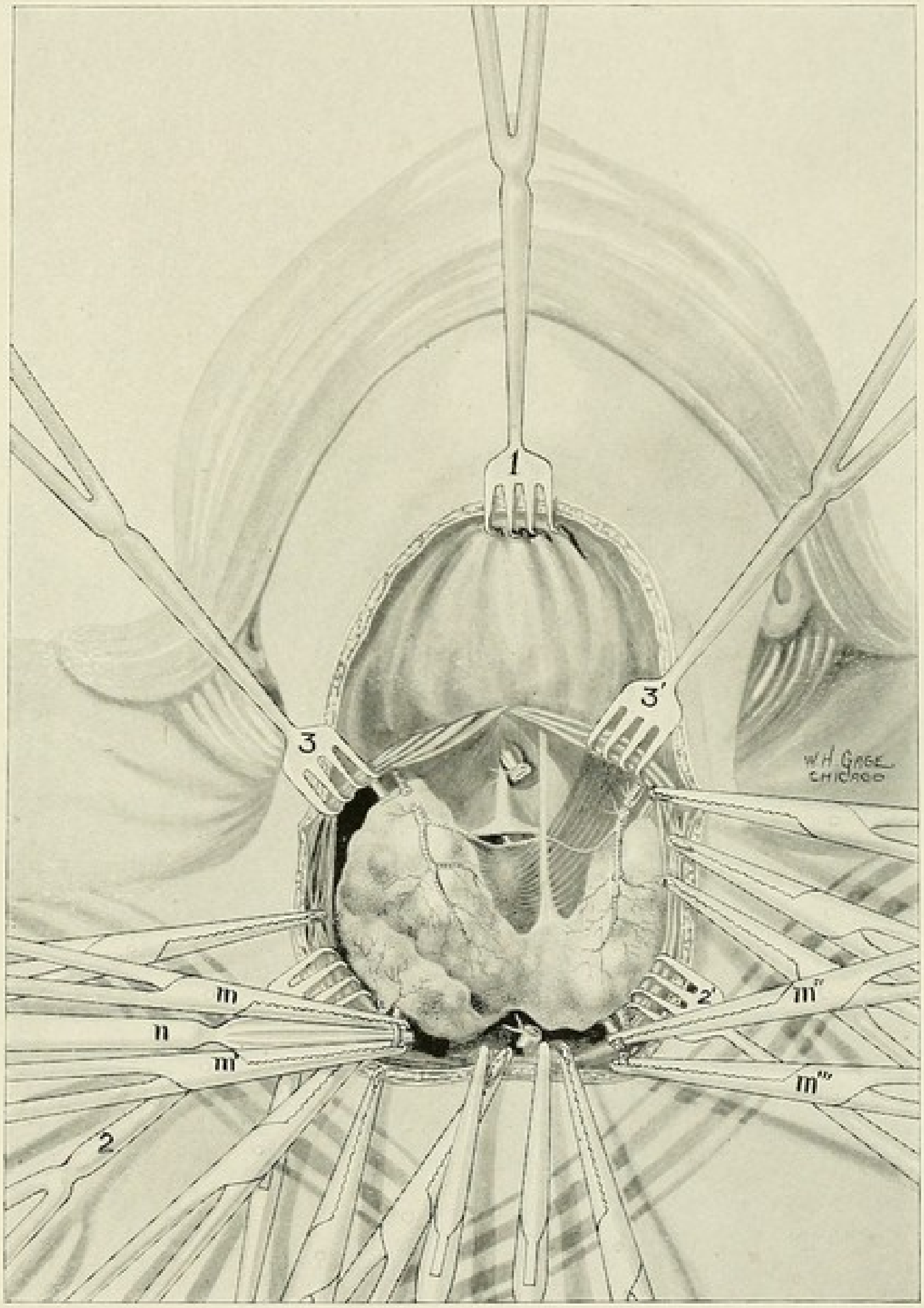
The closure of the wound should be the same as described in connection with Plate 30. It is not necessary, however, to make so extensive a flap in order to perform this operation. The superior thyroid veins can be ligated through two incisions parallel with the anterior border of the sterno-cleido-mastoid muscle five c. m. long, extending downwards from (a) and (b), Plates 2 and 20, and the inferior thyroid and the anterior jugular veins can be ligated through a transverse incision five c. m. long occupying the portion of the incision represented in Plates 2 and 20, passing across the middle of the neck. The deformity following the closure of these three incisions or the horseshoe incision is very slight in these cases if the platysma and sub-cutaneous connective tissue are sutured separately as described in connection with the previous operation.

PLATE XXXI



SHOWS THE ENTIRE ANTERIOR SURFACE OF THE THYROID GLAND EXPOSED, WITH THE SUPERIOR THYROID VEINS CUT AND LIGATED AND THE INFERIOR ONES CAUGHT IN HAEMOSTATIC FORCEPS AND CUT ON THE LEFT SIDE AND ISOLATED WITH KOCHER DIRECTOR ON THE RIGHT SIDE.

PLATE XXXII



THE SAME AS PLATE XXXI, WITH THE MUSCLES NOT CUT BUT SIMPLY RETRACTED.

CHAPTER IX.

OTHER OPERATIONS ON THE THYROID GLAND.

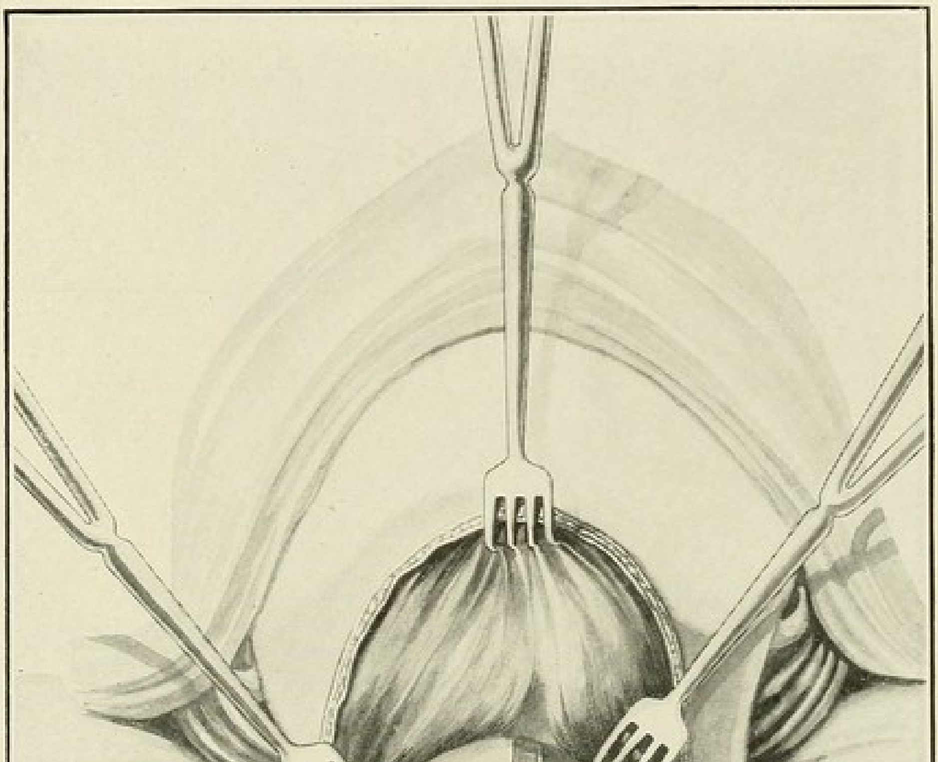
Ligation of the Superior Poles. Ligation of both superior poles of the thyroid gland has been developed and practiced by J. H. Jacobson of Toledo, Ohio, at the suggestion of M. Stamm, of Fremont, Ohio, for the cure of exophthalmic goitre. So far eight cases have been operated by this method. The underlying theory for this operation is based upon the fact that by ligating both upper poles of the thyroid gland in patients suffering from exophthalmic goitre, the gland is not only deprived of its most important blood supply, but the lymph channels through which the greatest portion of the thyroid secretion is supposed to reach the general circulation are included in the ligature and permanently interrupted. The results in all of the cases, with one exception, in which the operation was performed in a patient who was moribund at the time of operation have been most satisfactory. Of course, the number of patients is not sufficiently large, and the time expired since the operation is as yet too short to make a final judgment as to its value possible, but there seems to be enough in its favor to demand our careful consideration.

Stamm-Jacobson Operation. One upper pole of the gland is located by palpation and exposed by an incision from two to four c. m. in length through the skin, superficial fascia, and platysma exposing first the anterior border of the sterno-cleido-mastoid muscle directly overlying the pole. The authors make a transverse incision but as this leaves a more unsightly scar on the neck than an incision parallel with the anterior border of the sterno-mastoid muscle, the latter incision would be preferable in this as well as in the two operations just described.

The inner border of the sterno-mastoid is then loosened, raised and retracted exposing the fibres of the sternothyroid muscle which extend in the opposite direction. These fibres are retracted for about one inch exposing the deep fascia covering the thyroid gland. This fascia is next divided and the capsule of the gland brought into view. The muscles are well retracted by blunt hooks. A strong double ligature is then passed around the pole of the gland outside of the capsule by means of a ligature carrier, or a large pedicle or aneurism needle. The authors advise the use of heavy silk or linen ligatures because of the slowness with which these are absorbed. The two ligatures are separated one to one and one-half c. m. from each other and tied very firmly. Immediately after the ligation the tissues between and in the vicinity of these ligatures becomes very severely blanched and undoubtedly the tissue between the two ligatures will become absorbed, permanently disposing of the arteries, veins and lymph channels in both upper poles of the thyroid gland.

Plate 33 represents the appearance of each pole with the double ligature in place. In the actual oper-

PLATE XXXIII



SHOWS THE LIGATION OF BOTH SUPERIOR POLES OF THYROID GLAND.

ation the structures would, of course, not be exposed as thoroughly, as the operation is performed through a small incision, the extensive exposure shown in this figure not being necessary. If one does not injure the deep jugular vein or the carotid artery externally no harm is likely to be done by the passage of the ligature. In some instances it is difficult to pass the ligature because of the adhesions between the upper pole of the gland and the surrounding structures, especially on the outer side, but by a slight amount of blunt dissection this difficulty can readily be overcome.

This operation promises much but only careful observation of a large number of cases can determine its actual value.

Enucleation of Thyroid Tumors. Occasionally the surgeon encounters a circumscribed tumor in one of the lobes of the thyroid gland which may suggest its removal without excising the lobe in which this is found.

Usually the lobe contains a number of these enlarged lobules or cysts, and one can confidently expect that the removal of the large cyst will be followed by the development of others.

It is consequently wise to make an enucleation only in cases in which there is actually a solitary cyst or a solitary fibroma. The operation is usually safe and simple and readily carried out.

Operation. An incision is made over the most prominent portion of the gland directly over the cyst parallel with the natural lines of the neck. The muscles are separated and held apart with retractors. The vessels on the surface of the gland are caught with two pairs of forceps, cut and ligated doubly. Then the incision is carried down to the cyst through the substance of the gland. The cyst wall can be recognized by the abundance of connective tissue fibres it contains.

It is then enucleated either with the finger or by means of a blunt dissector. The cavity is tamponed with a hot gauze pad. If there are any vessels that continue to bleed these are caught with haemostatic forceps and ligated or a few fine catgut sutures are applied. Occasionally, though rarely, the hæmorrhage is so severe that the superior or inferior thyroid vessels have to be ligated and sometimes thyroidectomy must be made.

The cavity is then tamponed with gauze and a glass drain is inserted and the wound is closed. In this and in the previous operations the glass drain introduced by Kocher is most satisfactory.

Malignant Growths of the Thyroid Gland. Carcinoma of the thyroid is far more common than sarcoma, but as both conditions are hopeless so far as treatment is concerned, when advanced far enough to be diagnosed, it might be proper to consider these conditions together.

In a number of cases in which a thyroidectomy has been performed for the relief of simple goitre in which a postoperative microscopic examination has demonstrated the presence of carcinoma, the patient has remained free from recurrence because of the fact that the growth had not as yet advanced beyond the limits of the gland at the time it was removed.

In a structure with such complete anastomosis of arteries and veins and as vascular as this structure no other outcome could be expected. Unless some reliable plan for making a diagnosis is introduced which will demonstrate the presence of malignancy in the enlarged gland before it can be recognized by the unaided senses, we are not likely to be able to make a favorable prognosis in cases of carcinoma or sarcoma of the thyroid gland. At present it seems possible that some cytolitic method may be developed which will make it possible to recognize the presence of carcinoma during its earliest stages, but as yet this has not been perfected.

In carcinoma the gland is enlarged, somewhat nodulated, usually very sessile and there is a distinct tendency toward infiltration of surrounding tissues. Fig. 20 represents a patient suffering from carcinoma of the right breast and carcinoma of the thyroid gland. The picture shows how the nipple is retracted, and in the neck one can see how the skin is becoming involved by the invasion from below causing the latter to become adherent, indurated and retracted in places.

Later on there is usually marked obstruction to the venous circulation so that the veins stand out to a marked extent in the vicinity of the gland as shown in Figs. 21 and 22.

This condition can occasionally be mistaken for a sub-acute inflammation of the gland which is called strumitis when it occurs in a gland which had previously been enlarged, or thyroiditis if it occurs in a gland previously normal. In rare cases this condition may be due to tuberculosis of the gland.

This can be determined by the use of the tuberculin test. In four cases I have encountered an infection in a carcinomatous thyroid gland, consequently it is not safe to give a favorable prognosis because of the undoubted presence of an infection, because the proximity of the trachea and larynx makes an infection very possible in carcinoma. This complication is very likely to cause an obstruction of the

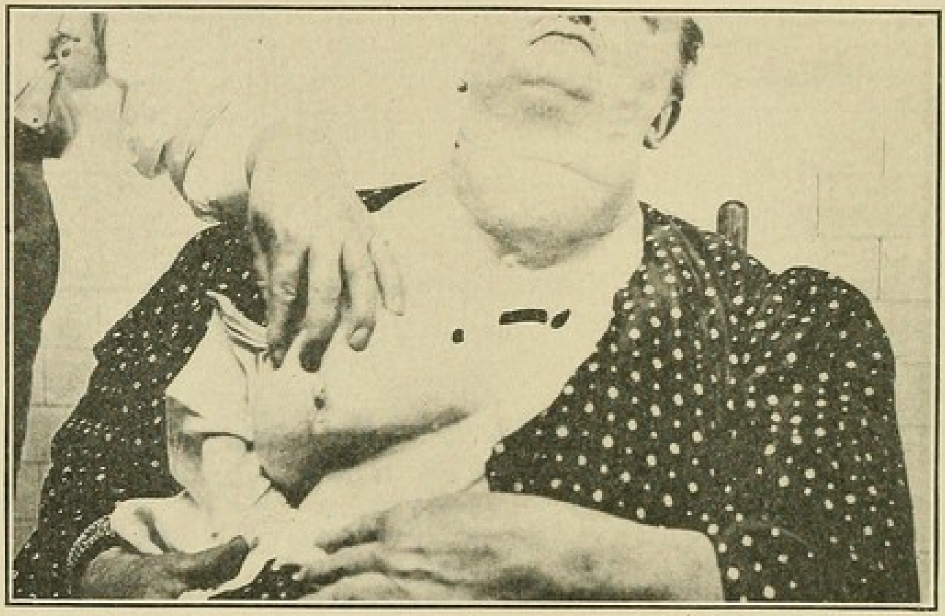


Fig. 20. Carcinoma of thyroid gland and of right breast.

larynx threatening the patient's life by suffocation. In this complication intubation or tracheotomy may be indicated but it is usually best simply to give a sufficient amount of anodynes to relieve the patient's suffering.

The growth may increase rapidly in size or it may remain almost stationary for weeks or months, or in rare instances even for years. When operated upon, however, there seems to be a rapid increase in size. It seems wise to remove the entire lobe and the isthmus of every goitre in patients forty years of age or older in whom one suspects the possibility of the occurrence of malignancy, because in this way it will undoubtedly be possible to remove a number of incipient carcinomata permanently. The operation is safe and the patient will be relieved of pressure and of a repulsive deformity, and may be saved the development of an incurable carcinoma.

It is not always possible to make a differential diagnosis between carcinoma and sarcoma of the thyroid gland but what has been said concerning the hopelessness of the former may properly be repeated concerning the latter. In my experience sarcoma has grown more rapidly than carcinoma. The skin has remained free from the underlying tumor and the surface of the growth has presented lobes rather than nodules. Figs. 23 and 24 represent a typical advanced case.

In one case of rapidly advancing carcinoma of the thyroid gland in a woman fifty-eight years of age, who came under my care two years ago, the patient's condition was so severe from pressure upon the trachea that she was placed in the hospital where an intubation or a tracheotomy could be made at any moment. In the meantime twenty-minute exposures were made with the x-ray daily with a moderately hard tube at a distance of twelve inches. Within a week the patient could breathe without gasping, in a month she could lie down and there was a slight reduction in the size of the growth and then it became stationary, and somewhat softer. It has remained in this condition for eighteen months without treatment. None of the other cases have responded in this manner. In sarcoma it may be advisable to employ the x-ray and possibly also Coley's serum, but all advanced cases must be looked upon as practically hopeless.

Transplantation of the Thyroid Gland. Experimentally it has been shown that the thyroid gland can be transplanted from its normal position

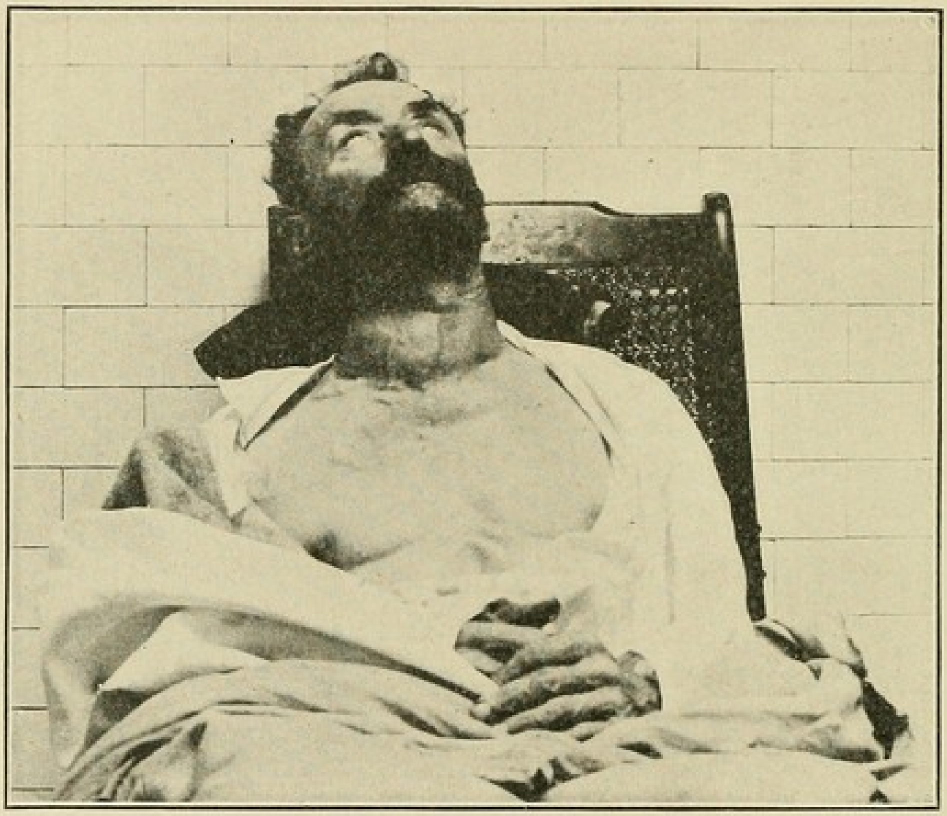


Fig. 21. Anterior view of carcinoma of thyroid gland showing greatly enlarged veins.

to other portions of the body of the same animal, or it may be transplanted from one animal to another of the same species. Many locations were chosen by various authors. Kocher transplanted a thyroid gland under the skin of the neck; Von Eiselberg into the peritoneal space; Payr into the spleen; Serman made a cavity in the tibia and transplanted the gland into this space. Schiff demonstrated in the year 1884 that it is possible to keep animals alive whose thyroid glands had been removed by transplanting the thyroid gland of the same species of animal into some portion of this animal, while other similar animals invariably died of myxœdema after complete thyroidectomy without transplantation. The histological examination of the transplanted gland has shown that a portion of the tissue is invariably absorbed. It has been found that rapid transplantation and aseptic healing decreases the amount of degeneration and that it is important not to injure the tissues of the gland by violent manipulations. Experiments have been made by injecting crushed thyroid substance sub-cutaneously or interstitially with the idea of supplying thyroid tissue to the patient without the necessity of subjecting her to an operation which in itself would subject the patient to a considerable strain.

Should we attempt to discuss the subject of transplantation of the thyroid gland in all of its phases too much space would have to be consumed and there would not be much practical advantage gained by this as these experimentations and clinical studies have not as yet reached a point where it would be proper to draw positive conclusions upon which one could reasonably base therapeutic practice. Salzer has recently reviewed this subject most carefully and has made a large number of most interesting animal experiments based chiefly upon the observations and experiments of von Eiselberg, Enderlen, Christens, Payr, Sultan and others, and it has seemed to me that for the present it will be wise to accept his view of this subject because he has reviewed the subject in a most logical manner and supports his views by definite postmortem findings in a sufficient number of animal experiments to make his theories plausible.

Salzer finds that in transplanting the thyroid gland into animals that have been completely deprived

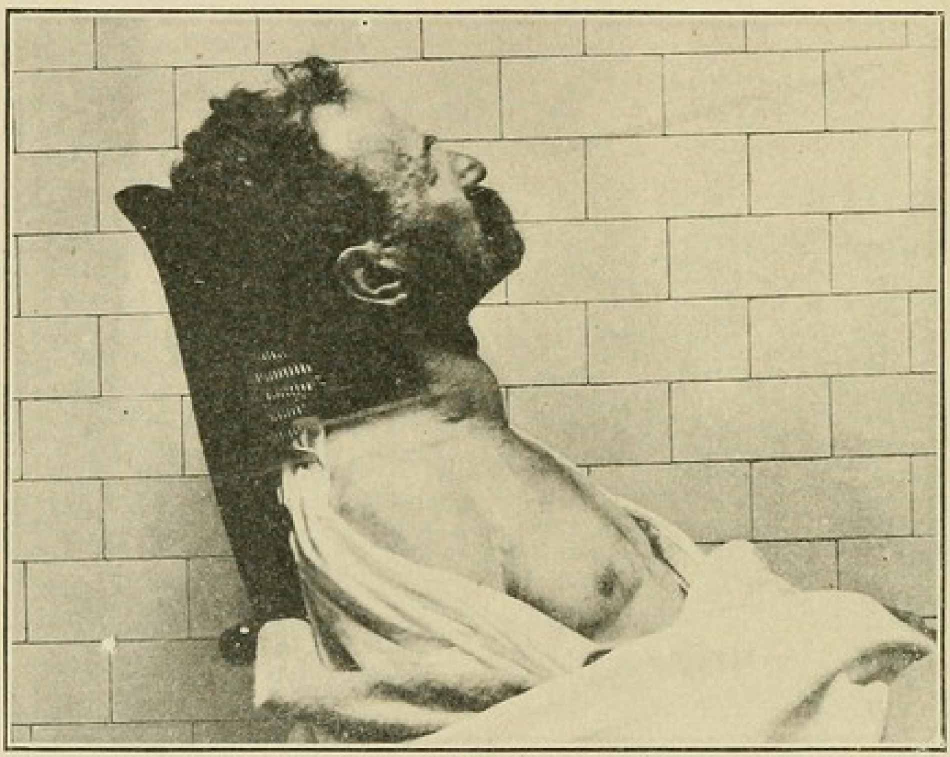


Fig. 22. Shows a lateral view of the same case. (Fig. 21.)

of this structure, the transplanted gland becomes an active part of its new host or of its old host in any location more quickly than it does if the animal has been deprived of only a portion of its thyroid gland or if its thyroid gland has not been disturbed. Moreover, the amount of degenerative changes under the former condition is much less than under the latter. In other words, the tissues of the animal seem to require the active thyroid gland as a part of the organism and when this has been removed from its normal location there seems to be an inherent tendency to provide for its participation in the physiological activity of the tissues of the body at the earliest possible moment. He also finds that under this condition the gland which has been transplanted to the abdominal wall actually takes up its physiological function, that the production of colloid substance is sufficient and that the vascularization of the gland equals that in its normal location. He favors the abdominal wall for the location because his experiments have demonstrated this to be satisfactory and because it is a simple surgical procedure which is perfectly safe and can, of course, be repeated in case it becomes apparent that the amount of thyroid tissue transplanted at first is not sufficient to supply the physiological needs of the patient which would become apparent by the recurrence of symptoms of myxœdema.

It seems likely that this method will be applicable in cases of myxœdema and especially in cretinism. The method employed in animal experimentation could be applied to these cases.

Technic of Transplantation of Thyroid Gland. The patient into whose body the gland is to be transplanted and the one from whom one lobe of the thyroid gland is to be removed are both anæsthetized simultaneously. An incision is then made splitting one of the recti muscles of the abdomen longitudinally through its middle for a distance of ten to twelve c. m. according to the size of the gland to be transplanted. All of the bleeding vessels are then caught in hæmostatic forceps. A space is formed by the separation of the rectus abdominis muscle from the transversalis fascia sufficiently large to conveniently hold the gland to be transplanted, care being taken not to injure the deep epigastric vein which lies between these structures and is especially liable to injury because of the thinness of its walls. A pad of gauze wrung out of warm normal salt solution is now packed into this space in order to control

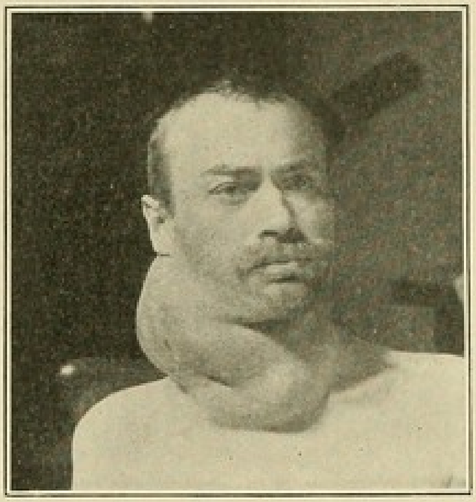


Fig. 23. Shows anterior view of sarcoma of thyroid gland. (By courtesy of Prof. Carl Beck.)

the oozing from the small vessels by its pressure. The salt solution should not be warmer than 105° F. in order not to impair these surfaces. Interrupted silkworm gut sutures are now applied but not tied, then the outer wound is covered with gauze and the wound is left until the gland has been removed. In removing the gland the technic described in the chapter on thyroidectomy should be followed, great care being taken to handle the organ with the greatest degree of gentleness. It is at once placed in its new cavity as soon as it has been removed without coming in contact with any fluid, antiseptic or otherwise. While an assistant completes the operation on the second patient, the surgeon adjusts the gland to the space between the rectus abdominis muscle and transversalis fascia of the new host and fastens it in this place at a few points with fine catgut sutures tied loosely in order to prevent pressure necrosis. Then the abdominal wall is closed with catgut sutures and the silkworm gut sutures are tied over all.

Selection of Material. Of course the same care must be taken in selecting material that one would employ in the transfusion of blood from one individual to another. It seems wise to choose a healthy individual and possibly to make serum tests for tuberculosis and syphilis and possibly for carcinoma. It seems that a simple hypertrophy would provide the best material and whether a cystic goitre or an exophthalmic goitre could properly be employed, future experimentation must determine.

That this operation can be performed successfully on human patients has been demonstrated by von Eiselberg and by Kocher. It has been suggested that this form of treatment should be employed in place of giving thyroid glands or thyroid extract in patients suffering from myxœdema from any cause and in cases of cretinism. The material for transplantation is no longer scarce since the operation of thyroidectomy has become so common. It is consequently to be expected that the next few years will demonstrate what can be expected from this method. At the present time the internal use of preparations made from thyroid glands has resulted in remarkable improvement in the growth and development of cretins, but these results have been satisfactory rather from an experimental point of view than from the standpoint of improving these patients as human beings, because in most instances they have simply been changed from small deformed repulsive but harmless creatures to larger, less deformed, less repulsive, troublesome imbeciles. It is to be hoped

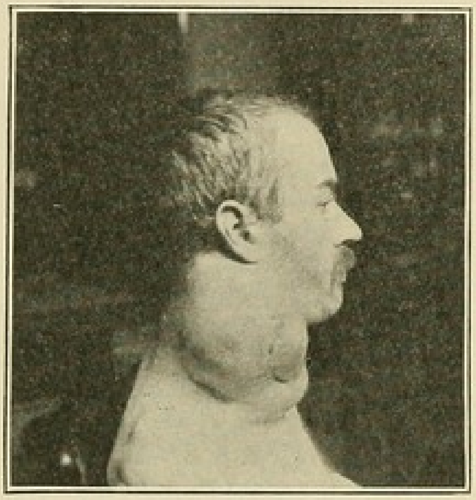


Fig. 24. Shows lateral view of sarcoma of thyroid gland.

that better results may be obtained by transplanting thyroid glands.

Mr. Lynn Thomas, of Cardiff, has transplanted tissue from an enlarged thyroid gland removed from otherwise normal patients into cavities formed in the tibiæ of four cretins. In all of these patients thyroid extract had previously been given with benefit but as soon as this was interrupted the patients became worse. Since the transplantation of thyroid gland substance these patients have not become worse notwithstanding the fact that the administration of thyroid extract was interrupted permanently.

It does not seem quite clear why one should undertake so tedious an operation as Thomas has described, when experiments in animals have given equally satisfactory results when the thyroid gland was transplanted between the posterior surface of the rectus abdominis muscle and the transversalis fascia.

CHAPTER X.

PROGNOSIS IN EXOPHTHALMIC GOITRE.

There can be no doubt but what the prognosis in Graves' disease has improved enormously during the past few years and that this improvement is due very largely to the recognition by Moebius of the fact that the disease is due to the circulation in the blood of toxic material secreted by the thyroid gland under certain conditions. Founded upon this theory the improvement in prognosis is due to recognition of the fact that the cause of this introduction of toxic material into the circulation can be stopped by the removal of the diseased gland. That this can be done safely in over 95 per cent. of all cases has been thoroughly demonstrated.

It seems likely that the prognosis in this disease will be still further improved in the future, primarily because the diagnosis will usually be made much earlier while it will still be possible to obtain a relative cure of the patient before great harm has been done, especially to the heart muscle. Moreover, it is to be expected that some neutralizing antitoxin will be introduced which will make the thyroid poison harmless even in advanced cases, a quality which is claimed at the present time for the serum of Beebe in early cases and also for the substance derived by Moebius from thyroidectomized goats to which has been given the name of antithyroidin.

In a recent report on the treatment of 426 cases by his serum, Beebe expresses his satisfaction with first introduction of his method. He is carefully observing these cases and if they remain permanently well for several years the method will undoubtedly receive general adoption. If, on the other hand, these cases ultimately come to operation, the latter form of treatment will surely be applied earlier in these cases.

There is undoubtedly a marked difference in the gravity of the prognosis between cases which begin slowly and progress in the same gradual manner and those which come on acutely and progress rapidly. The latter are far more grave. But even these cases are not so absolutely hopeless at present as they were some years ago since Kocher has pointed out a way of reducing the absorption by preliminary ligation of veins and by checking the secretion of more toxin by simultaneously ligating the accompanying arteries, and later removing one or more lobes of the gland if necessary. This is referred to at this point only because of its relation to prognosis and has been fully discussed in the chapters on operative treatment. Most clinicians seem to find that the prognosis is less hopeful in men than in women. Whether this depends upon the fact that men place greater strain upon the heart than do women before they come under observation, or upon the fact that in men the heart has so frequently suffered from the effects of alcohol or tobacco or both, or upon some other condition it seems difficult to determine.

My own experience bears out the general impression that the disease is more serious in men than in women. In a general way also the prognosis becomes more grave with the increase in the age of the patient although many patients quite advanced in years have recovered, some of these with and some others without surgical treatment.

Again it must be borne in mind that very chronic cases which have shown little or no change for months or years may flare up suddenly and take upon themselves quite as violent a character as other cases that started very acutely and developed into a violent condition very rapidly. On the other hand one may occasionally encounter one of these very acute violent cases which will later take upon itself a very mild chronic condition.

If there are a number of conditions which greatly depress the patient, such as severe diarrhœa, violent sweats, nausea, or extreme weakness, the condition should be looked upon as grave. When serious heart symptoms are accompanied by great emaciation one should always give a guarded prognosis. Severe intercurrent diseases and especially severe mental or emotional strain make the prognosis more grave.

In reviewing the actual statistics of various authors one is impressed most forcibly with two elements. First, that the immediate results with all authors have improved enormously with each individual observer's experience, and second that no one with the exception of Kocher has even a considerable number of cases that have been carefully observed for a number of years after recovery. This applies as well to cases that have been treated with hygiene, diet, and internal medication as it does to those cases which have been treated by surgical operation.

I have introduced a history blank for use in these cases which when carefully filled contains all important facts systematically arranged so that there is uniformity in all of these histories. It seems as though it would be well worth while to collect statistics for a period of ten years of all of these cases that are under treatment by careful clinical observers. This would then serve as a basis for reasonable conclusions. It is likely that some other clinicians can suggest a much more complete scheme for making such observations but in the meantime I will offer the following form:

HISTORY BLANK FOR EXOPHTHALMIC GOITRE No............

Date of admission.............................Date of operation.........................
Date of discharge.............................Age.......................Sex.......................
Nativity...Occupation...
Name...Address...
Name of friend...................................Address of friend...............................
Name of family Dr..............................Address of Family Dr........................
Diagnosis clinical...
Diagnosis pathological...
Family history...
Previous history...
Personal history...
Date of first symptoms of goitre..
Date of first symptom of exophthalmic goitre...
Exciting cause of exophthalmic goitre..
Influenced by adolescence?................Pregnancy?..
Puerperium?...Infection?...
Strain?..............................Nervous?.......................Mental?.........................
Emotional?.......................Onset Acute?................Sub-acute?....................
Gradual?..Continuous?...
Intercurrent diseases..
Symptoms and physical findings, goitre?..
Lobes involved....................................Degree?..
Exophthalmos?................Stellwag?.......................VonGraefe?....................
Moebius?...Pupils?...
Ophthalmoscopic findings..
Heart..
Tachycardia?.......................................Character of pulse?.........................
General strength?............Respiration?..................Nutrition?.....................
Tremor?...Muscle spasm?...................................
Chorea?...Mental symptoms?...........................
Sweating?.........................Pigmentation?..............Hyperæmia?..................
Anasarca?..Ascites?..
Blood Hæm.?..................R. B. C..........................W. B. C............................
Polymorph. Leuc. ....Lymph..
Trans..Eos...
Urine Sp. gr..Alb...
Sugar?..Casts?..
Larnyx. Before Oper.........................After Oper...
Course of disease...
Course after operation...
Condition when discharged...
Condition one year later..
Condition two years later...
Condition three years later..
Condition four years later..
Condition five years later...

GOITRE	Before Oper.	After Oper.	Remarks
How long present			
Exophthalmos			
Tachycardia			
Tremor			
Muscular weakness			
Nervous excitability			
Mental deficiency			
Vertigo			
Graefe's sign			
Stellwag's sign			
Moebius' sign			
Bryson's sign			
Intermittent Conditions			
Vomiting			
Diarrhoea			
Mental depression			
Exacerbation upon			
Psychic excitation			
Physical fatigue			
Mental fatigue			
Use of Thyroid extract			
Use of Iodine			
Emaciation			
Anaemia			
Myxoedema			
Oedema eyelids			
Oedema extremities			
Oedema circumscribed			
Visible pulsation goitre			
Pigmentation skin			
Erythema			
Blushing			
Urticaria.			
Enlarged lymph nodes			

From what has been said it is plain that it would not be profitable at this point to give much space to the actual statistics relating to the prognosis of exophthalmic goitre, because the older ones are in no way indicative of the results one may expect from treatment today and the newer statistics have no value as regards the most important question of what becomes of these patients a considerable number of years after the treatment has ceased in patients that have been treated by various methods.

For statistics regarding the prognosis of cases treated by internal methods I will quote Forchheimer who has personally treated 56 cases described in another chapter of this book, consisting in the administration of five grains of hydrobromate of quinine four times daily to which one grain of ergotine is added to each dose if the quinine alone does not give some relief in forty-eight hours. This method has also been employed by J. M. Jackson and L. M. Mead in the outpatient department of the Massachusetts General Hospital in eighty-five cases with the remarkable result of 76 per cent. cures, 13 per cent. benefited and 11 per cent. failures. There can be no doubt but that operative treatment of the 13 per cent. that were benefited but not cured and the 11 per cent. that were failures would result in a cure of at least 90 per cent. of these cases so that first treating all of these cases medicinally until it can be determined which will be cured by this method and then treating those that do not respond satisfactorily surgically, the entire mortality will probably sink below three per cent. in cases not complicated with other diseases. This would, of course, presuppose an early diagnosis in all cases and an early transfer to surgical treatment of all cases not benefited by internal treatment. Any intercurrent disease may, of course, bring about a recurrence in cases which have apparently been well for a shorter or longer period precisely as this can be brought about by severe fright, unusual physical exertion, or mental or emotional strain. Moreover, there can be no doubt but that patients who have suffered from this disease and have actually recovered have less resistance in case of any subsequent sickness than others who have not previously suffered in this way even though there may be no recurrence of exophthalmic goitre during the period the patient suffers from the later disease.

Before leaving the discussion of prognosis of exophthalmic goitre following internal treatment it may be well to point out the fact that the cases in which cures have been recorded have usually not been kept under observation for a sufficient number of years to make the statistics absolutely satisfactory, although in this result they are no more imperfect than are the statistics following surgical operations. In either case it seems of the greatest importance to assist these patients in planning their lives so that all strain, physical as well as mental and emotional be eliminated to the greatest possible extent. This element will undoubtedly do much to improve the prognosis in these cases. This is of greater importance in cases in which non-surgical treatment has been employed because in cases having undergone surgical treatment the amount of thyroid tissue has been reduced to so marked an extent that the flooding of the circulation with an abnormal amount of thyroid secretion from the remnant of the gland is less easily accomplished than from the entire gland in cases not operated.

The prognosis in cases treated with serum is still more uncertain than in cases in which either medical or surgical treatment has been employed. In 42 cases in which Beebe and Rogers used the cytolitic serum they reported 18 cases cured, 14 improved, 6 unimproved and 4 dead, which would represent 43 per cent. cured, 33.3 per cent. improved, 14 per cent. unimproved and 10 per cent. dead. Moreover, it seems to have been shown from the histories of these cases that the treatment promises success only in early cases in which the thyroid poison has not been carried through the circulation for a long period of time.

Regarding the prognosis of cases treated with Moebius serum, I have not been able to find definite statistics although many authors claim to have seen beneficial immediate results from the use of this remedy. In only one instance have I found harmful effects attributed to the use of this remedy, but on the other hand it has been impossible to utilize the reports either singly or collectively for statistics. This is the more to be regretted because it seems that we must expect ultimately to secure relief for patients suffering from exophthalmic goitre from this direction. It seems as though it must be possible to find some antibody that will neutralize the thyroid poison until the hyperactive gland portions have finished their abnormal activity. So far Beebe's serum seems to represent the nearest approach to this end, but not near enough to be depended upon. Many other conditions undoubtedly have a marked bearing upon the prognosis in patients suffering from exophthalmic goitre. A man who is able to earn a livelihood for himself and his family only by hard labor and who feels the responsibility of the support of those who are dependent upon him has a much less hopeful prognosis than a man who has no responsibilities and is not compelled to exert himself either physically or mentally.

In the same way women with great domestic or social responsibilities have a grave prognosis. Those who are active in the social world cannot obtain rest if they remain at home and if they seek rest at resorts or sanitoria their habits of life usually prevent them from obtaining the necessary rest and consequently they usually return home in a worse condition than was present when they left. Again, it seems that patients amenable to treatment with suggestion give a better prognosis in a general way than others not so constituted. Moebius suggests that this accounts for the fact that so many relatively inactive remedies have received so much praise in the treatment of this disease. So long as the remedy does no harm and the physician and patient believe in its usefulness the latter receives the benefit of mental and physical rest and his condition is improved as a result of this rest.

So far as the prognosis of cases of exophthalmic goitre treated surgically is concerned one can predict with certainty that none of the existing statistics will have any value even after a few decades because of a number of conditions already referred to. I will consequently give only the statistics of a few very widely separated authors who are at the same time the best authorities on the subject. I refer to C. H. Mayo, of America; Kocher, of Switzerland and Landström, of Sweden, although a score of others, like Halstead, Shephard, Curtis, Mikulicz, Rehn and others, have published lists of cases which are both interesting and instructive.

Kocher's statistics show a mortality of 3.5 per cent. in cases operated for the relief of exophthalmic goitre. This includes both early and late cases although if grouped separately the cases operated during the past few years would give a much smaller mortality. He states also that there is not a single case in which the patient has not been much benefited. In 83 per cent. of cases a cure is reported. 73 per cent. of cases with primary disease were cured and 92 per cent. of cases with the disease, combined with ordinary goitre were cured. 100 per cent. of cases with vascular goitres were cured.

The statistics of C. H. Mayo vary so little from those given above that it seems scarcely necessary to repeat them. Suffice it to say that the mortality is less than 3 per cent. in an experience based on more than 1,000 thyroidectomies for the relief of exophthalmic goitre. Landström's statistics based on 54 cases show very similar immediate results. He has subjected the histories of his cases to a most critical study from every point of view which makes his observations especially interesting and valuable, although the relatively small material makes his conclusions lacking somewhat in clinical support compared to the above authors.

Landström has shown from a most careful study of his cases that there is little postoperative improvement from actual injury to the heart as a result of the thyroid poisoning even in cases that seem to have recovered as a result of thyroidectomy. Although the tachycardia may subside there seems to be but little reduction in the size of the heart if dilatation has occurred as a result of the disease, so that we can speak only of a relative cure. Although a man may work after he has obtained such a relative cure as a result of thyroidectomy, still the prognosis cannot be good in such a case as compared with recovery from many other diseases in which the tissues have not been exposed to this toxic substance. No doubt a long period of rest following thyroidectomy will enable the tissues to recuperate to a marked extent although such defects as cardiac dilatation may not be overcome by the natural tendency of the tissues to recover under favorable conditions when the cause of their pathological changes has disappeared.

All symptoms which are due to the direct irritation of the thyroid toxin are certain to improve after thyroidectomy has eliminated the possibility of further production of this toxin, but it is quite different with the symptoms that depend upon actual degenerative processes like cardiac dilatation due to myocarditis. The same is true of marked exophthalmos. Although the muscles involved in the production of the exophthalmos may recover to a great extent in some cases, in others they will remain in a weakened condition and consequently the symptoms may remain although no fresh poison is introduced into the circulation.

It is an easy matter to determine the fact of a permanent impairment of the heart muscles and the cylinder-formed muscle of Landström which determines the exophthalmos, but it is much less easy to determine the permanent effect of exophthalmic goitre, which has persisted for a considerable period of time, upon the other tissues of the body. It is however, clear that the effect is not confined to any muscle or groups of muscles but that all tissues of the body suffer. The form of history proposed above will serve to give us data for reliable conclusions, provided a careful record is made in each case according to this form, and some provision is made for annual reports from patients after recovery.

In the meantime we know enough to be entitled to the opinion that the hyperthyroidism must be stopped early in order to prevent these permanent defects. If this can be accomplished with rest, hygiene, diet, and therapy, well and good, if not, then the case should be treated surgically. At this point it is well again to insist upon the fact that whatever form of treatment may be employed, all that can be expected primarily of this treatment is to stop the progress of the poisoning.

The repair of the harm that has already been done to the tissues must be accomplished by the after treatment which will have to consist of rest tonics, diet and general hygiene. This is quite as important after surgical as after internal treatment. In either case this after-treatment must be continued for many months and this will largely determine the ultimate prognosis.

CHAPTER XI.

HEREDITY IN GOITRE.

Heredity. The fact is well known that in innumerable cases one or both parents and a number of the children and again in turn their children have suffered from goitre. This has been observed as far back as the disease itself. Whether this indicates that the offspring have inherited the disease or a tendency for its development, or simply that the same conditions and habits have caused the same disease in the offspring that similar conditions brought about in the parent is much more difficult to determine. It is true that in communities in the United States in which large numbers of Swiss immigrants have established their homes, the number of goitres in the children born and reared in America is very small compared with the number in the parents. But this again is not a sufficient test because these children may have inherited a tendency to the development of goitre which under favorable conditions would have developed this disease quite to the extent it developed in the parents, but under the unfavorable conditions in which the child was placed in America for the development of this disease the simple tendency inherited from the parent did not suffice to produce the disease. It is rare to encounter a goitre in a patient in whom one cannot find the disease in some ancestor or near blood relative by carefully investigating the family history.

As regards heredity in exophthalmic goitre there seems to be more opposition than to the theory of heredity in simple goitre.

The most satisfactory case I have encountered in

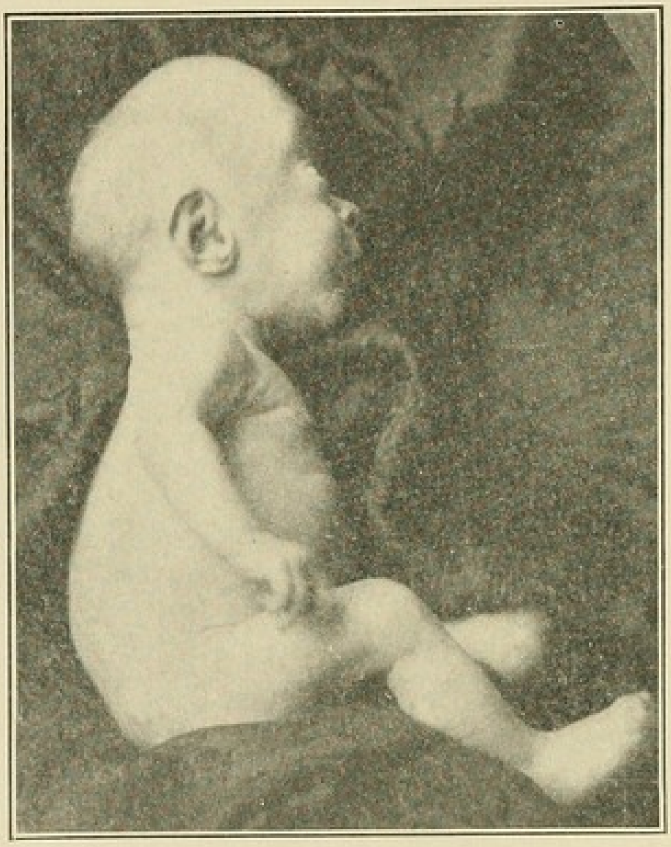


Fig. 25. Infant of 5 months shows distinct exophthalmos and turret head.

the literature is one described by Schmauch, in a woman thirty-five years of age, mother of four children, the last one born eight weeks prematurely.

At the time the different children were born the mother was twenty-six, twenty-eight, thirty and thirty-two years old. The goitre first appeared dur ing the second half of the first pregnancy and increased during each succeeding pregnancy. Distinct symptoms of exophthalmic goitre developed during her fourth pregnancy. She had marked exophthalmos, was cyanotic, had œdema over the entire body, was extremely weak, had a pulse of 145 beats per minute, and the neck measured 40 c. m. Three days after labor she was subjected to treatment with Moebius' anti-thyroidin, thirty drops twice daily, every second day. The dose was later increased to fifty drops twice daily, every second day, and then again reduced to twenty drops.

She improved steadily, increased in weight from 114 to 138 pounds. The pulse was reduced so that it varied from 90 to 110 beats per minute, while the average count had been about 35 beats higher during the severe attack, and her general condition was greatly improved.

The youngest child, a boy, born during the height of her attack, weighed scarcely four pounds at birth. Fig. 25 represents him at the age of five months. His head is irregular in shape, his abdomen is large, his eyes are protruding and there is distinct irregularity in the growth of the forehead. The occuput and forehead were bulging out, the parietal bones were sunken, giving the child's head the form of a saddle head and turret head at this age, a condition which has persisted to the present time to quite a marked extent as shown in Figs. 27 and 28. Five weeks after labor his eyes started to bulge out and the head as a whole seemed to grow rapidly, especially the forehead. A few days later the temporal bone began to protrude, then one side of the occiput, then the other side, then the left frontal bone in the region of the protuberance seemed to elevate.

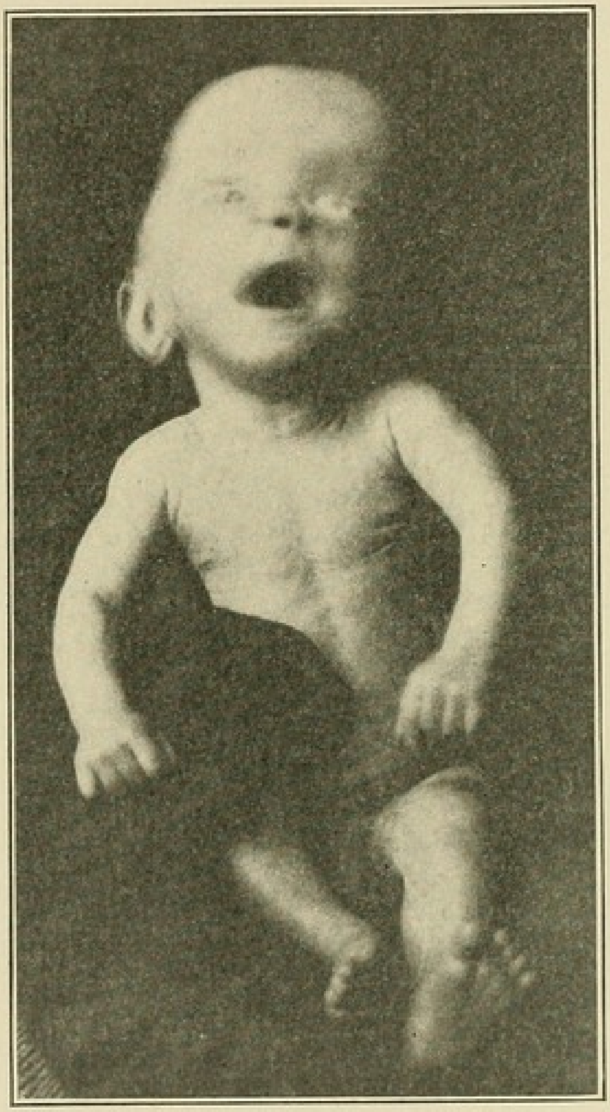


Fig. 26. Front view at age of 5 months of infant shown in Fig. 25.

These peculiarities are all shown in Figs. 25 and 26. At the age of 11 months the child weighed 19½ pounds, at the age of 27 months his height is 80 c. m., he weighs 35 pounds and his appearance is shown in Figs. 27 and 28, which still shows plainly the presence of exophthalmos. The conditions observed in this child seem to show that exophthalmic goitre is sometimes transmitted from mother to child. It would lead too far should we go into discussion more extensively at this point but for those who are

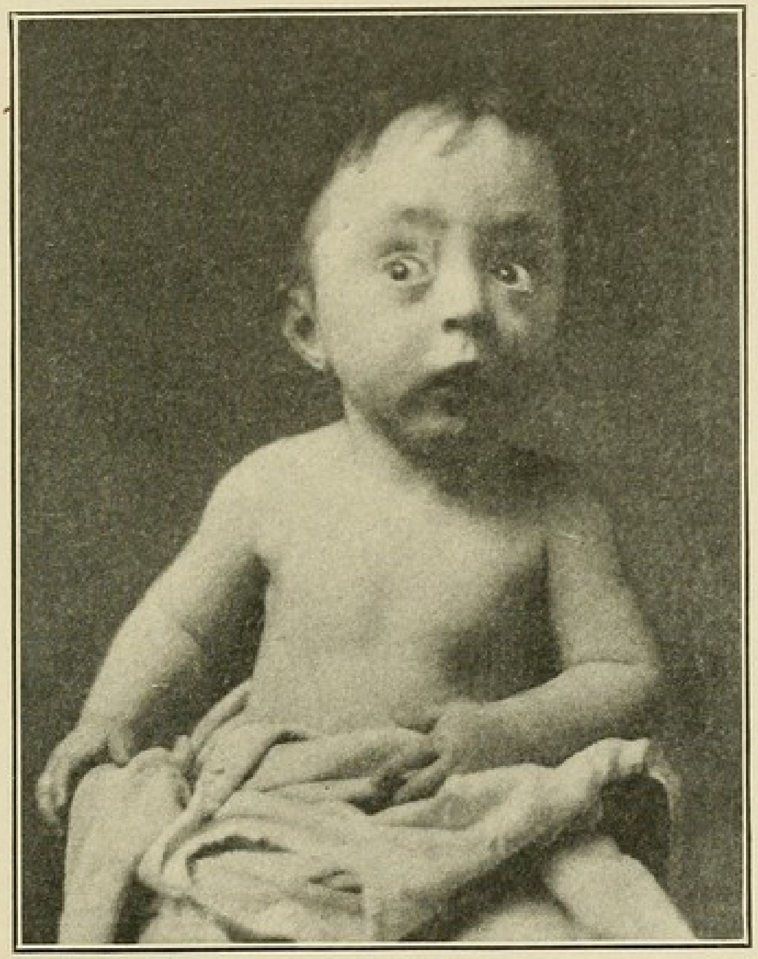


Fig 27. Front view at age of 27 months; the exophthalmos shows distinctly.

especially interested in this feature, a study of the essay by Schmauch, will furnish exceedingly interesting and profitable reading. In most instances in which authors mention the condition of children born of exophthalmic mothers there has been no transmission of this condition from the mother to the child.

Congenital Goitre. A large number of cases has been reported of infants born with goitres varying

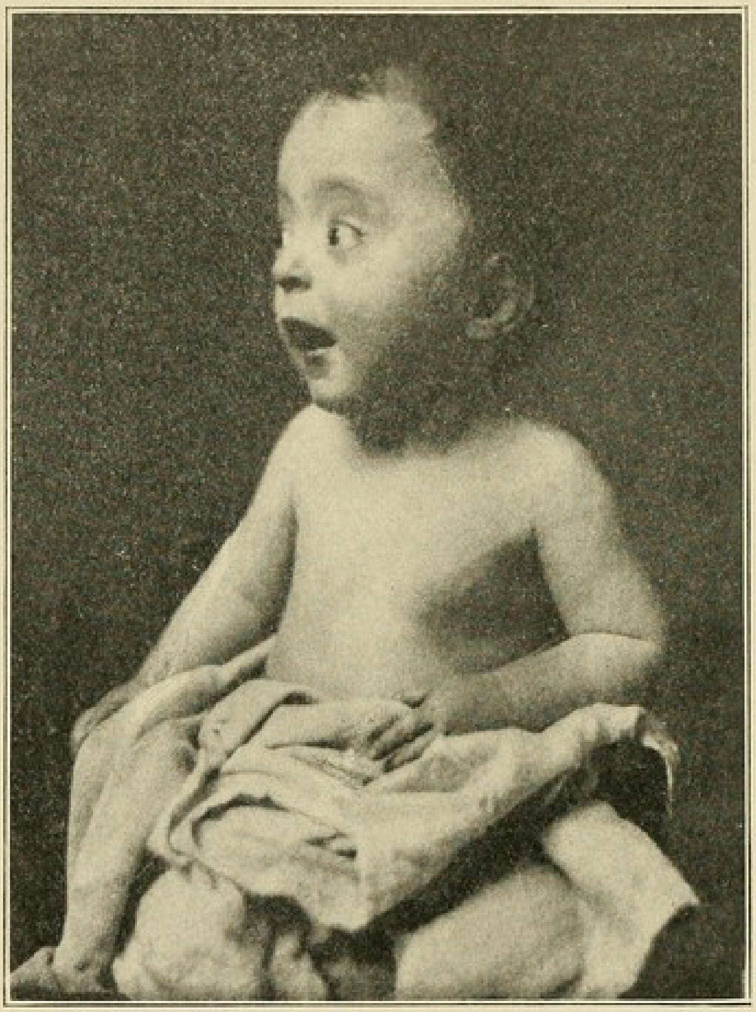


Fig. 28. At age of 27 months greatly improved in every respect but exophthalmos is still present.

in size. These usually decrease in size rapidly after birth or the infants die in convulsions or exhaustion.

Oswald has found that young calves have no iodin in their thyroids, but that after nursing and before taking other food iodin is found, hence, he reasons that the milk must contain iodin unless this comes from the blood of the young animal bringing this substance from other tissues in the body. It is possible that mother's milk supplies the iodin in infants with congenital goitre.

In an infant in which the neck had a circumference of 8 c. m. more than the head, due to congenital goitre, which became slightly worse during the first two weeks of life, I have seen the goitre decrease perceptibly from day to day by the administration of 5 grs. of thyroid extract three times daily to the mother and $\frac{1}{4}$ gr. twice daily to the infant. In four weeks the little patient was in excellent health and when two months old nothing of the former disease could be detected.

PART II.

THE PARATHYROID GLANDULES

CHAPTER XII.

INTRODUCTION—HISTORICAL—FUNCTION.

Tucked away behind the more prominent thyroid gland the parathyroid glandules for a long time escaped the eye of the anatomist, and even for a long time after they were finally discovered they were given no particular consideration. Finally a French investigator noted that a rabbit deprived of these tiny bodies died in tetany. Gradually the importance of this observation, through the extensive confirmation of animal investigation, dawned upon the surgeon and the practitioner of medicine.

The anatomist, the histologist, and the embryologist had proven these bodies to possess a structure different from that of any other tissue. The experimental investigator had shown their remarkable physiologic importance in a wide range of animals, and demonstrated that they were an independent vital organ. It remained for the clinician to take these results and apply them at the bed side and in the operating room. There was the whole range of tetanies to be considered, some of especial interest to the internist and others to the neurologist; some of importance to the gynæcologist and obstetrician. To the surgeon there was at once the question of the importance of these bodies in operations involving the thyroid gland. All diseases that manifested tetanic symptoms came at once into consideration in the light of this new discovery.

Many of these diseases for which a hypoparathyroid etiology was first suggested have lacked in post mortem morphologic findings, but a group of tetanies has remained that may, by their study from the standpoint of a parathyroid etiology, be brought into a closer relation.

To the surgeon the relation of tetany to parathyroid destruction has been so definitely proven that ultimately an exact acquaintance with these structures must be a part of all intimate surgical knowledge. Such knowledge has been delayed, save with the leaders of surgery, owing to the natural skepticism that would for a long time be maintained towards the striking phenomenon of the removal of such small bodies giving rise to so severe and often fatal tetany. But at the present time the truth is coming to be generally recognized, and the parathyroid glands are being given the place of real importance that they deserve.

The assembling of all that is known about the parathyroids is not an easy task, for it must be sought from many sources. So far there has been little regard paid to these glands by the writers of text books, but this disregard is not due to lack of work on these bodies. Considerably more than three hundred titles may be collected of important articles dealing with these glands from laboratory workers in Sweden, Germany, France, Italy and America.

HISTORICAL.

It was in the year 1880 that Ivar Sandström discovered the parathyroid glands. He found these bodies constant in fifty autopsies in man, and he further studied them in the dog, cat, rabbit, ox and horse. This work of Sandström's is so thorough and complete from both an anatomic and a histologic standpoint that he deserves all credit for the discovery. It will only add to the thoroughness of Sandstroem's work to cite a number of investigators before him who had noted these glandules but passed them by as being probably accessory thyroids or small lymph nodes.

Remak is cited by Sandström as having described these bodies. Virchow, in 1863, also noted them, as he described small rounded bodies, about the size of a pea, which he found in the loose connective tissue on the posterior surface of the lateral thyroid lobes, but he thought these bodies were lymph nodes or detached portions of thyroid tissue.

Baber, in 1876, described what we now know are the parathyroid glands of the dog, and the same author, independently of Sandström, published in 1881 a description of what he termed "undeveloped portions of the thyroid gland" which were undoubtedly parathyroids, but he failed to recognize their constant occurrence or significance.

Among other investigators who failed to recognize the significance of these bodies, although undoubtedly observing them, may be mentioned Kaydi, and Maselung, whose observations were published two years and one year respectively before Sandström's paper appeared. Immediately after Sandström, Woelfler described under the name "Glandulae Parathyreoideae" (the same term that had been used by Sandström), similar bodies which he considered as an embryonal developmental stage of thyroid tissue set free from the gland at an early time.

From this time on, the parathyroid glandules, as we will now term them, received more or less spasmodic attention. Rogowitz, in 1888, described what he called "restes embryonnaires" in the thyroid glands of animals. He considered them as parts of the thyroid in process of development. Christiani, in 1893, examined the parathyroids of rodents, finding only one glandule on each side. This author also considered these organs as portions of embryonic thyroid tissue. Liezenska, described these glands in the dog, and considered the tissue a sort of reserve material that could furnish fresh thyroid follicles when necessary.

Huerthle, at about this time, described, in a study of thyroid secretion, an "interfollikulaeres Epithel," which differed in its structure from thyroid and secreted no colloid substance. He considered this tissue as undeveloped thyroid.

It was not until 1895 that Kohn placed the anatomy and histology, as well as the genesis of these glandules, on a definite basis and established the fact that they were independent structures morphologically and functionally distinct from the thyroid gland. He also made clear the fact that in the rabbit there were two pairs of these glandules. The definite establishment of the number and situation of these glands in the dog, cat and rabbit by Kohn was of great importance to the development of the physiologic importance of these structures.

Next to the name of Sandström that of Gley is most intimately associated with the development of our knowledge of the parathyroid glands. In a series of fifteen papers appearing for the most part as short communications in the Comptes Rendus de la Société de Biologie from 1891 to 1897, Gley established for the first time by animal experimentation the important physiological function of the parathyroid glandules and showed that post operative tetany after thyroid operation was due wholly to removal of the parathyroids, and was in no way connected with the thyroid as had previously been supposed.

These organs, then, that for a long time had appeared so comparatively unimportant from an anatomic standpoint, and which presented so peculiar a histologic picture as to make the idea possible that they were rudimentary rather than functional organs, were, by the work of this investigator shown to possess, when regarded from an experimental side, an importance in the vital economy equal to that of any other functioning organ. And it is from the time of Gley that the question of this important function of these tiny glands has aroused the interest of the medical and surgical world, and the literature has multiplied in the effort to solve the complicated problems that the parathyroid glandules have presented to us.

Among the earlier investigators who took up and added to the work of Gley in establishing the fact that the loss of all the parathyroid glands results in death in tetany there are certain names of historical interest which may be mentioned here, though their work will be taken up in more detail in considering the physiology of these glands.

This list includes Verstraten and Vanderlinden in Belgium, Vassale and Generali in Italy, Edmunds and D. A. Welsh in England, Kohn, Pineles and Erdheim in Austria, Moussu and Alquier in France, and MacCallum in America.

The animals used for these experiments include the dog, cat, rabbit, rat and monkey, all of which animals respond to the complete removal of the parathyroids by severe tetanic symptoms ending usually in death. In the herbivora it seemed impossible to show at first this parathyroid tetany after operation, and it was thought the differences in these animals was due to their vegetable diet, but even in such animals as the sheep and goat, tetany, it was found, could be produced provided all parathyroid tissue was removed, the difficulty being to find the parathyroid tissue which apparently has a wide distribution in these animals.

The natural result of this experimental work in animals was a flow of ideas towards its application to certain conditions of importance from a clinical standpoint in the practice of surgery and internal medicine.

The pathologist, it might be mentioned in passing, found little to repay him for a morphologic study of these glands, although certain facts of interest and some observations of negative as well as positive importance have been brought out by the studies of

Peterson, Benjamins, MacCallum, Getzowa, Erdheim and others as will be duly chronicled.

To the internist the question of a hypoparathyroid etiology in the various tetanies became of interest; such as the so-called idiopathic tetany of workers in certain lines, children's tetany, the tetany of pregnancy and lactation, and gastric tetany. Epilepsy, exophthalmic goitre, paralysis agitans and other conditions attended with tremor have had their turn as diseases for which a hypoparathyroid etiology was tentatively advanced. Osteomalacia and rickets interest us as being possibly associated in some way with changes in the parathyroid secretion. Moreover there yet remains a variety of chronic nutritional disturbances, associated with marked diminished resistance to bacterial infection, to be carefully considered as bound up in some manner with lack of parathyroid substance.

It is to the surgeon, however, that these glands have appealed most strongly on account of the question of post-operative tetany in connection with thyroid surgery. Such tetany was not unknown to the earlier surgeons. Billroth, Reverdin and Mikulicz had a high per cent of tetanies following complete thyroidectomies in the early eighties and before. But based on the knowledge that it was the parathyroid and not the thyroid removal that was responsible for this tetany, the technic of modern thyroid operations, has practically obviated such untoward results.

Today perhaps the greatest interest centers around the question of parathyroid therapy, i. e., the matter of making good a loss of parathyroid tissue or controlling tetany after parathyroidectomy by the feeding of parathyroids or the use of gland extracts, or by the transplantation of parathyroid glands, or by the use of calcium salts as recommended by Parhon and Urechie in 1907, and, independently, by MacCallum and Voegtlin in 1908.

In detailing the main facts regarding the parathyroid glands in this brief outline it may be mentioned that they have not been brought forward without considerable conflicting opinion, both as to the function, the importance, and the independence of these bodies.

A critical examination of the literature, however, masses the weight of evidence not only physiologically and experimentally, but anatomically as well, in favor of the view that the parathyroid glandules are in no way associated with the thyroid save for the relationship of anatomical propinquity and that functional relationship (which may in certain instances be more intimate than we suppose) which must exist in normal man and animals between all important glands which have to do with internal secretion. In a careful survey of the literature we have failed to find any convincing proof that the parathyroids, either in structure or function, have even served vicariously for the thyroid gland or are in any way to be considered rudimentary thyroids. They are to be considered independent vital organs, as necessary to the existence of an individual as the liver, the suprarenal glands, or any other organ whose function is indispensable in the maintenance of life.

As to the part played by the parathyroids in the body, we can only say that their complete removal, as has been practiced so many times in a wide variety of animals, leads to death with severe symptoms of tetany which is in no way associated with or dependent on the thyroid gland as was once thought. We also know that by their gradual complete destruction, severe nutritional disturbances may be brought about ending in death in apathy, with no symptoms of tetany. When destruction is nearly, but not quite complete, transitory symptoms of tetany may appear for a time and then subside; the theory being that some small islet of parathyroid tissue left behind has undergone compensating hypertrophy sufficient to maintain the life of the animal. Thus it seems that we are wonderfully safeguarded by a rich abundance of over supply and that even though at a goitre operation three of the four glandules were accidentally removed there would be no untoward symptoms if the remaining glandule was fairly normal. In rabbits it is stated that seven-eighths of the parathyroid substance must be removed in order to produce the characteristic toxemia, and we know that fatal tetanic symptoms never develop in dogs that possess a single parathyroid gland.

While the exact mechanism by means of which the symptoms of tetany are brought about following the loss of the parathyroid glands is still open to investigation, it may be stated that there are two main hypotheses; first, the idea that a metabolic toxin (which under normal conditions is neutralized by the parathyroid secretion) gives rise to the symptoms; and second, that the symptoms are due to a diminution of calcium in the tissues (which has been shown to follow parathyroid removal), the withdrawal of which leaves the nerve cells in a state of hyperexcitability which expresses itself in tetany. While there is some question as to the fact that such a condition as exists in the second hypothesis is present following the removal of the parathyroid glands, nevertheless the administration of a soluble calcium salt will promptly check the symptoms of tetany. It is a mooted question at present as to whether this calcium deficiency is always present after parathyroidectomy.

That a poison is circulating in the blood, following parathyroid removal, seems to be shown by the fact that symptoms may be controlled for a time by bleeding and transfusing an animal with normal blood. Moreover, as Pfeiffer and Mayer have demonstrated, while the serum of a parathyroidectomized animal will not produce symptoms of tetany in a normal animal, it does bring on these symptoms in an animal that has suffered partial removal of the parathyroid glands.

In concluding this chapter it may be noted that there has been more or less lack of unity in the nomenclature of these organs. Sandstroem first designated the bodies "Glandulæ Parathyreoideæ," Gley used the term "Glandules Thyroidiennes;" Hofmeister, "Nebenschilddruesen;" Zielinska, "Accessorische Schilddruesen;" von Jacoby and Blumreich, "Nebendruesen;" von Tourneux and Verdun, "Glandules Thymiques." Kohn originated the term "Epithelkoerperchen," which is still used more or less extensively by German writers, and Verebely extends this to "Branchiale Epithelkoerperchen." By most writers these organs are today generally designated the "Parathyroid Glands," or "Glandules."

CHAPTER XIII.

ANATOMY.

Normally there are present in man four parathyroid glandules, situated on the posterior surface of the lateral lobes of the thyroid, two on either side, one above and behind the other, and separated from the thyroid by connective tissue. While the position of these glandules may vary, the variation is within certain definite limits, so that the position is fairly constant. The superior (external) glandules are more constant in position than the inferior (internal) glandules. They (the superior) are usually found, one on each side, on the posterior wall of the œsophagus, at the posterior edge of the lateral thyroid lobes, about opposite the cricoid cartilage midway between the upper and lower poles of the thyroid. The height may vary, the superior glandules have been found as high as the inferior cornu of the thyroid cartilage. They are usually wholly outside the thyroid, but they may be found within the capsule of this organ. The inferior thyroid artery and recurrent laryngeal pass up in front and internally to the glandules, and the superior bodies can usually be found at the entrance of the end branches of the inferior thyroid artery.

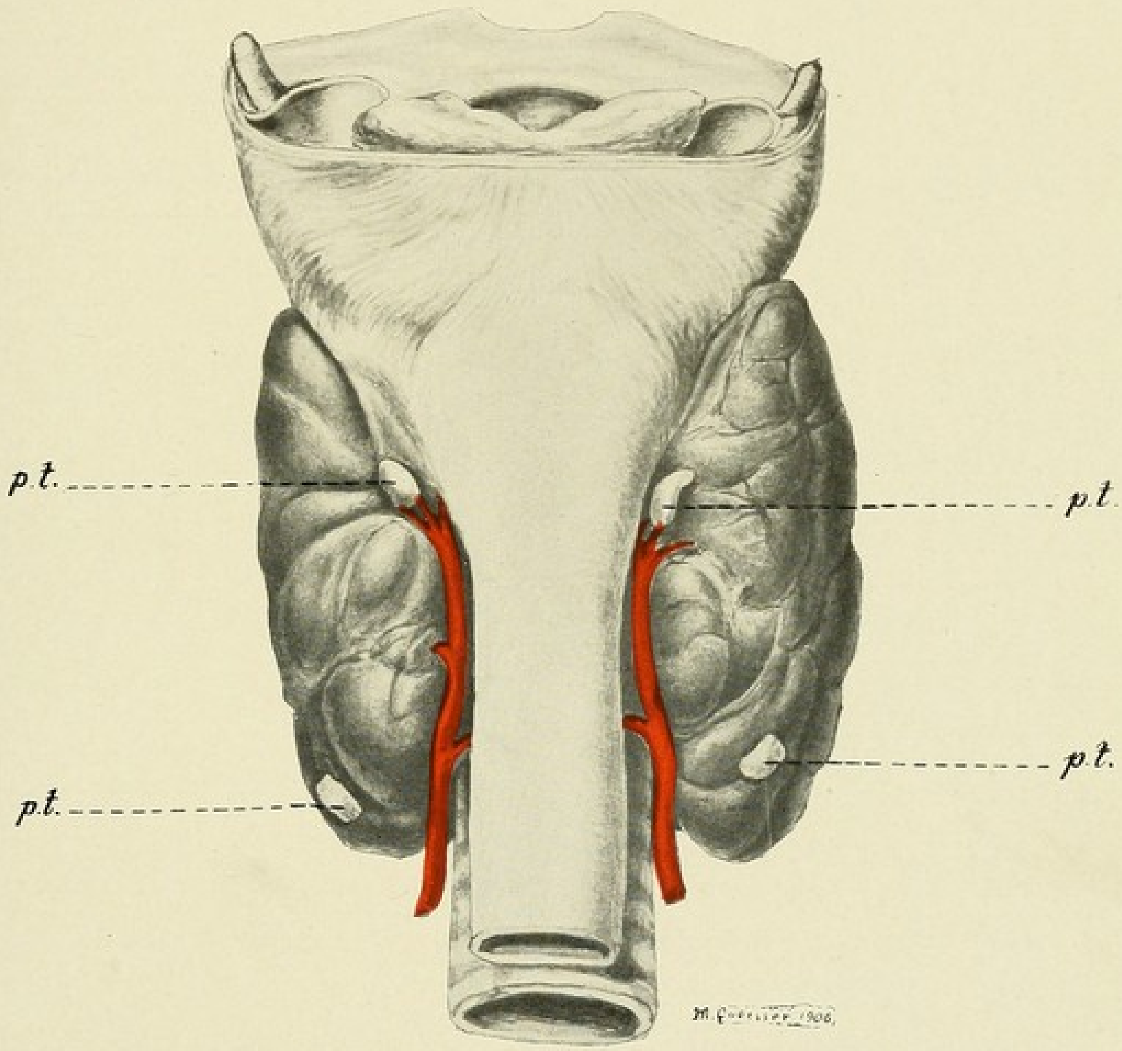
The inferior (internal) parathyroids are anterior to the upper bodies, lie always in front of the inferior thyroid artery, and are usually about opposite the lower pole of the thyroid, though they may be found as low as the fourteenth tracheal ring. They may be either postero-lateral or antero-lateral to the thyroid or may be at some distance from the thyroid (usually below it) imbedded in fat and areolar tissue. The fact that the inferior glandules are found less constantly than the superior is due to their inconstant position, and the difficulty in distinguishing them from small lymph nodules, pieces of thymus tissue, fat, and accessory thyroid nodules that may be found in this locality.

The parathyroids are rarely perfectly symmetrical in arrangement. The two on one side may be in normal position, while one or both of the glandules on the other side may be considerably above or below or laterally removed from their normal position.

When the neck organs are removed as at autopsy and observed from the posterior (œsophageal) side, the superior parathyroids are seen in the loose fatty tissue along the posterior edge of the thyroid lobes. By careful dissection the superior parathyroids can be exposed lying on the posterior wall of the thyroid near the œsophagus at the place where the artery divides. The inferior parathyroids lie near the posterior edge of the thyroid in the loose tissue that fills the space below the rounded lower pole of the thyroid, ventral to the inferior thyroid artery and the recurrent laryngeal nerve.

Size.—The average size of the parathyroid glands is six to seven millimeters long, by three to four

PLATE XXXIV



P. T. PARATHYROID GLANDULES IN NORMAL SITUATION ON POSTERIOR SURFACE OF THYROID GLAND.

millimeters wide, by one and a half to five millimeters thick. Their most constant dimension is their thickness. Sandstroem found one gland measuring fifteen millimeters in longest diameter. Berkeley gives the average measurement as 6x4x2 m. m. MacCallum's figures are about the same, six to eight millimeters long by three millimeters wide by one to two millimeters thick. Berkeley gives the maximum total weight of four glands out of 125 autopsies as .3763 grams.

Shape.—The parathyroid glandules usually appear as somewhat flattened, oval or spherical disk-like bodies. They may have a flattened pyriform outline. Sometimes they are bean or kidney shaped, resembling a small lymph node, but are usually more flattened. At times they may be nearly square or rectangular. The bodies have been compared with a hemp seed or a grain of maize.

Color.—In color the parathyroids vary from pale grayish white, to dark reddish brown. They practically always show a shade of yellow, due to their fat content which is apt to be more pronounced in older individuals. Their color is never exactly the same as the adjacent thyroid tissue or lymph nodules. They are less transparent than the lymph nodes, less elastic than thyroid tissue, and not so flabby as small fat tabs which may be found in this region. The surface of the glandules is smooth and shining, and a delicate venous tracery is to be seen under their capsule.

VARIATIONS IN THE NUMBER OF PARATHYROID GLANDS IN MAN.

While there are normally four parathyroid glands in man their small size, variation in situation, and their similarity to lymph nodules, accessory thyroids and other small bodies occurring in the neck region, make their identification difficult, and the average number found in any given series of examinations is less than four to each individual. The average number found, however, constantly increases with the experience of the searcher, so that while there may actually be less than four glands in certain cases, the difficulties attendant on their determination make the diminution in this number a matter of not finding all the glands in many instances rather than of the glands not being present.

Accessory parathyroids may at times be found. Erdheim found eight accessory glandules in one case and four in another; both were cases of thyroid aplasia. Schaper found six parathyroids in one case. Zuckerkandl reports a case in which there were eight glandules. Getzowa found displaced masses of parathyroid cells in seven cases, three of them in the thyroid. Thompson and Harris have found five glands in several instances; once the extra gland was imbedded deeply in the thyroid. Accessory parathyroids have been noted imbedded in remnants of the thymus, especially in children. Kursteiner

The author, in a number of instances, where the most careful search of fresh material yielded only three parathyroids, has found a fourth glandule by putting the neck organs in Pick's solution and subsequently developing the tissue in 80% alcohol. Often, however, even this method fails to disclose a missing glandule as a gland is easily lost in the material dissected away, or the neck organs are removed without taking tissue far enough below the thyroid, so that a glandule well below the thyroid, which is a not infrequent situation, is left behind. Hardening the neck organs in 10% formalin solution especially if there is much oedema and congestion of the tissue, also aids in finding glandules that might be overlooked in fresh material calls attention to the frequency with which remnants of the thymus are found in the loose tissue below the lower pole of the thyroid frequently enclosing a parathyroid fragment.

Sandstroem in fifty autopsies found never more than two parathyroids on each side; five times he was only able to find one on each side and twice he found only a single gland on both sides, but he himself says that his search was incomplete.

Von Verebély in 138 cases found four glandules 108 times. He states, however, that in the last 100 of these cases he found four glandules in ninety, which is significant of the increased number found with increased experience in their search.

Forsyth, who groups his findings unilaterally, observed in sixty cases one gland on a side in less than half his cases, two on a side in one-fourth, several times three, in two instances four and five, and once six parathyroids on a single side.

Welsh, who made a most exhaustive anatomical and histological study of these glands, found in nearly all cases in man two on a side, and he states that when fewer are found, either the glands have escaped observation or else there is a more or less intimate connection between two of the glands so that they appear as one mass.

Schreiber, in twenty-five cases, found usually two on a side, in four cases only one on a side was found, in two cases there was one on the right and three on the left side. He did not find more than four in any case.

Benjamins found the internal parathyroids so rarely that he questioned if their presence was not due to an abnormality of development.

Peterson, who studied 100 cases, does not give his exact findings, but says that his results confirmed the findings of earlier authors. He did not fail to find the parathyroids in any case. The external

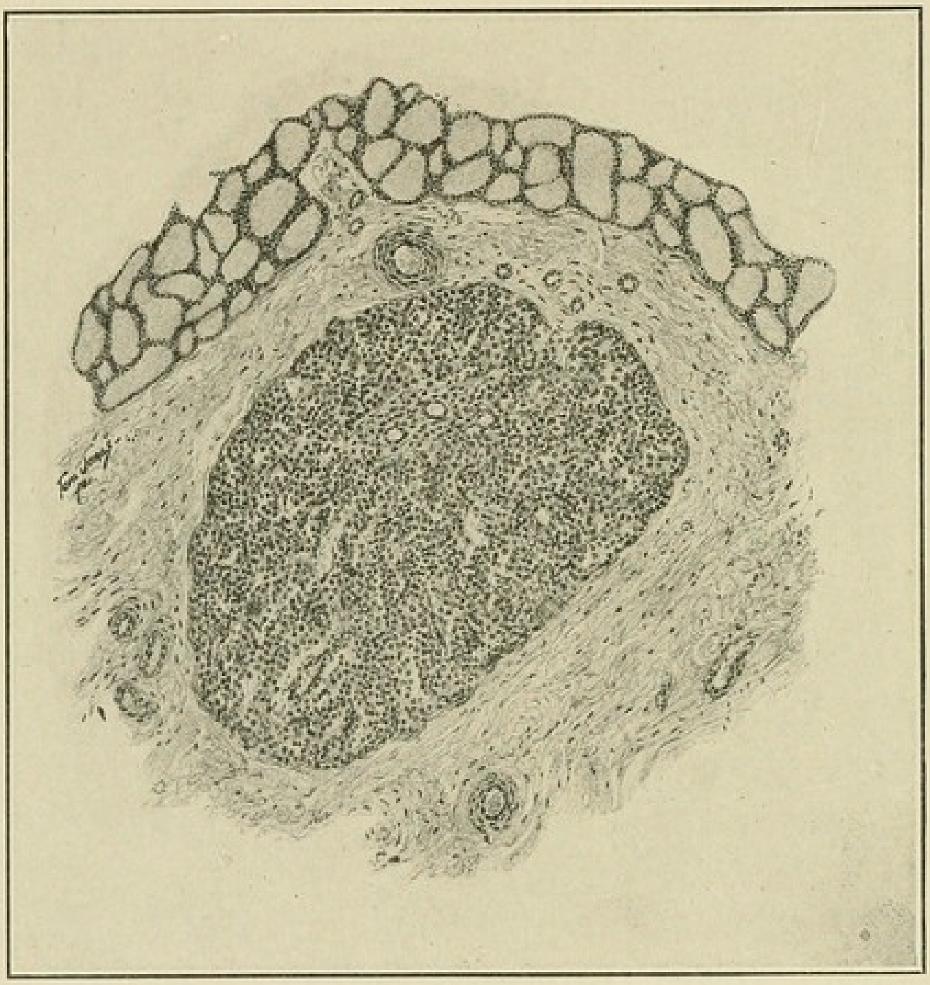


Fig. 62. Normal parathyroid glandule, low magnification. A portion of the thyroid gland is shown at the top of the section.

glandules he found most constantly present. In some cases he found three glandules on one side and one on the other.

MacCallum, in sixty-four cases, found four parathyroids thirty-six times, three ten times, two fifteen times, and three times only one glandule. MacCallum says: "The number found is directly proportional to the patience and persistence with which they are searched for." He calls attention, moreover, to the especial difficulty in recognizing these glands in the obese and in atrophic conditions.

Rogers and Ferguson examined forty-six adults and eight infants for parathyroid glandules. In twelve cases no parathyroids were found; in twenty, two were found; in four, three; in three, there were four glandules. The findings in these cases are much below the average although the investigation seemed to be attended with much care.

Berkeley tabulates the details of forty autopsies in which his average finding was about two and a half glands per case. In one instance he found six glandules. This author emphasizes the necessity of experience in searching for these glands. In his first twenty-five autopsies no glands at all could be found in about four cases. In his second twenty-five he failed only once or twice to find glandules. In the last fifty cases he never failed.

Thompson found four glandules in thirty-three out of forty cases. Three of these cases presented also accessory glandules (five instead of four in each instance.) In four of the forty cases only three glandules were found; in one instance one of the superior glandules was missing, in the other cases it was one of the inferior glandules that was not found. In two cases, only the two superior parathyroids were found; the inferior glandules were missing. In one case no parathyroids were found. In nearly all the cases where the author did not find four parathyroids there was some pathologic condition present that made the search difficult. Two cases were subsequent to carcinoma operations; one showed extensive tuberculous cervical lymphnoditis, and in others the neck organs were œdematous and congested.

Thompson and Harris found four parathyroids in ninety per cent of all cases, where careful search was made for the same.

THE PARATHYROID GLANDULES IN CHILDREN.

Thompson has found that the situation, general appearance, and microscopic structure of the parathyroid glandules of the infant does not differ essentially from that of the adult. The glandules are much smaller in the infant than in the adult. They average about two to five millimeters in diameter normally in the infant, while in the adult they average about eight millimeters in longest diameter. They are more difficult to find in the infant than in the adult, not only on account of their small size, but owing to their resemblance to certain lenticular bits of tissue which extend upward along the posterior border of the thyroid on both sides of the œsophagus. This tissue is continuous with the interscapular gland of Hatai, and at a later period of infant life is not to be distinguished microscopically from fat. In marantic infants, in whom there is no fat, this tissue persists, and the tiny nodules are extremely difficult to distinguish in size, color, and situation from the parathyroids. By preserving the neck organs entire in Pick's solution the author was able to get a color differentiation that distinguished this tissue from the glandules. Another source of difficulty is in distinguishing the parathyroids, especially the lower, from remnants of the thymus gland which are much more frequently found in the infant than in the adult. This in many instances can only be done microscopically. Several times Thompson found what microscopically appeared to be parathyroids, to be, microscopically, parathyroid incorporated in a remnant of thymus. This finding is explained by the close embryological relationship of the two structures, and Verebely has noted the same thing in the adult. The number of glandules found were, owing to these difficulties, less than in the adult. In twelve cases of marasmus the author found four glandules in six cases; three were found in five cases; in one case only two were found. In twelve routine cases in infants four glandules were found in eight; three were found in one case; two were found in two cases, and only one glandule in one instance.

BLOOD SUPPLY.

The parathyroid glands are supplied by the parathyroid artery which is a branch of the inferior thyroid artery. Vascular connections are also found between the capsule of the thyroid and the parathyroid glands. Evans states that complete injections have shown only a scant blood supply to the capsule, consisting only of a few minute capillaries. These capsular vessels have been brought out with considerable distinctness by Thompson and Leighton after ligation of the parathyroid artery in dogs.

While Welsh, Halsted and Evans, Ginsburg, and Geis, describe the parathyroid artery as a branch of the inferior thyroid, Pool has described the parathyroid artery as springing from the superior thyroid artery. It is possible that the superior thyroid artery may give off a parathyroid branch in the rare cases in which the bodies lie above and behind the upper pole of the thyroid gland. The parathyroid artery, according to Ginsburg, is about a centimeter long. Evans finds variations in length from four or five millimeters to two or three centimeters. Evans also describes a prominent anastomosing channel between the inferior and superior thyroid vessels running along the posterior margin of the lateral thyroid lobe in eight out of twenty cases. In these the superior parathyroid artery is a short branch from this channel. The parathyroid artery enters the gland at the hilum, and gives off branches which spread toward the periphery from which numerous capillaries arise.

Ginsburg calls attention to the existence of a secondary blood supply to the parathyroid glands by anastomotic channels from the opposite side, so that even though a ligature be applied to the superior and inferior thyroid arteries outside the capsule, the parathyroid glands may receive a blood supply from the opposite side.

The veins of the parathyroid glands are derived from the inferior thyroid vein either directly or by the intermediary of the veins which cover the surface of the thyroid glands.

Halsted has called attention to the danger of sacrificing the parathyroid glands in the control of hæmorrhage during goitre operations. He recommends therefore that the thyroid vessels be divided as far from the gland as possible so as not to cut off the blood supply to the parathyroids. This operation of "ultra ligation" is done by drawing forward the superior pole of the thyroid gland and putting

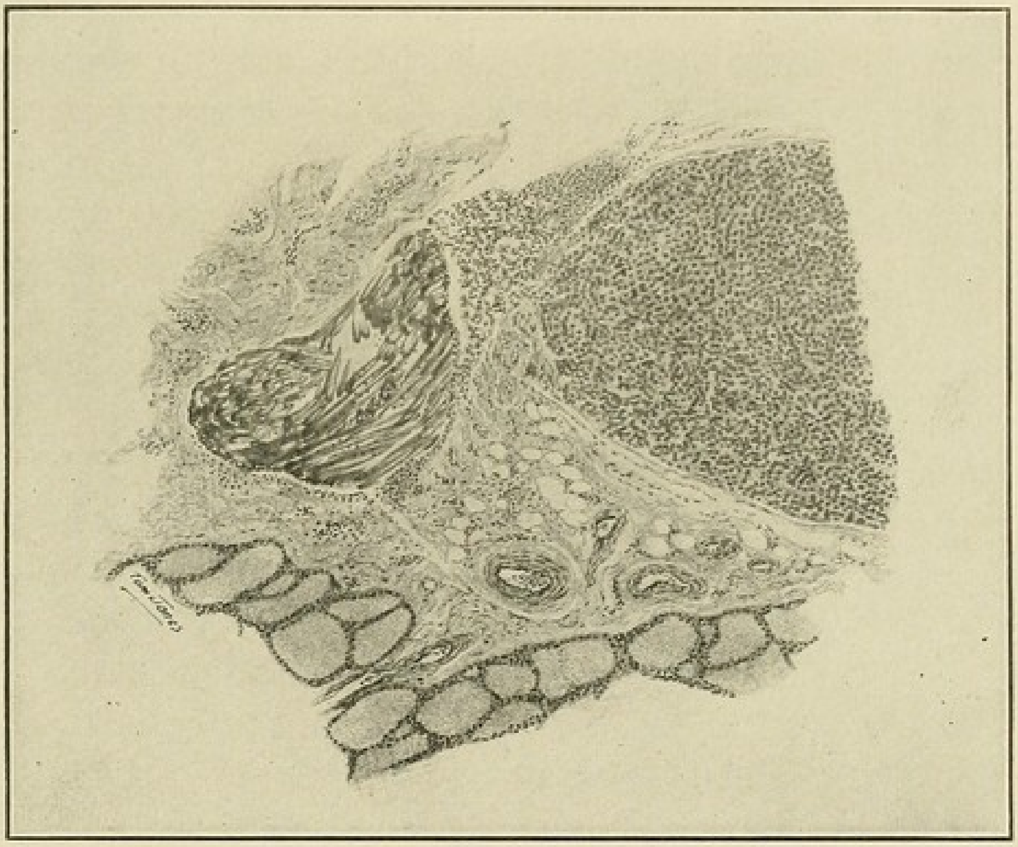


Fig. 63. Ligation of the parathyroid artery in the dog, showing that no change takes place in the glandule following such procedure. A moderate exudation of leucocytes is seen between the ligature and the parathyroid.

the superior thyroid vessels on the stretch. From above downwards and from before backwards the vessels are then divided at their point of entrance into the gland as far peripherally as possible.

Thompson, Leighton and Swarts have shown that in the dog the parathyroids possess sufficient collateral blood supply so that the ligation of their main vessel is of no importance. Dogs in which the parathyroid artery to one glandule was ligated and the other three glandules were excised showed no symptoms following the operation. If at a second operation, however, the ligated glandule was excised the dog died in tetany. This showed that the ligated glandule was functionally sufficient to maintain the life of the animal. Microscopic examination of ligated glandules at intervals of twenty-four hours to several months showed them to be morphologically intact.

PARATHYROID GLANDULES IN MAMMALS AND BIRDS.

On account of the experimental work that has been done on the parathyroid glands their anatomy has been worked out with much care in a wide variety of animals. While in general the situation and number of these glands is the same in animals as in man, there are certain variations that may be briefly reviewed.

Cat.—In the cat the thyroid consists of two separate lobes not connected by an isthmus. The parathyroids are four in number, two on each side, the external usually free but sometimes imbedded in the substance of the thyroid lobe near the internal surface. The internal gland is smaller than the external and is imbedded in the thyroid lobe. Kohn was the first to accurately describe these glandules in the cat. According to Harvier and Morel, accessory parathyroids are frequently found in the thymus of this animal.

Dog.—The glandules in the dog have a similar situation to those described in the cat, but are subject to more variation. The external glandule is situated superficially near the upper pole of the thyroid. It is usually in close connection with the capsule of the thyroid.

The internal parathyroid is ordinarily under the capsule of the thyroid, but superficially situated in the upper half of the internal aspect of the thyroid. It is identified with more difficulty than the external gland owing to its smaller size, greater variation in position and deeper situation than the former.

Gley noted fourteen variations in the situation of the glandules in thirty-three dogs, and Alquier found the classic situation of the bodies only nine times in fifteen dogs. MacCallum calls attention to the fact that accessory parathyroids may occur deeply imbedded in the thyroid. Thompson and Leighton noted the frequent appearance of accessory parathyroid glandules in this animal; eight glands were found in one animal. Moussu speaks of supplementary parathyroid tissue about the trachea and in connection with the branches of the thyroid artery. Pianca has noted these aberrant glandules in this animal. Alquier has also found accessory parathyroids in the dog, but these always in connection with the thyroid gland.

The size of the parathyroids also varies greatly in the dog. They may be so small as to be scarcely visible to the naked eye, or they may be found as large as five millimeters in diameter.

The irregularity of the glandules in this animal, and the frequent finding of accessory parathyroids should be borne in mind in considering the results of experimental work in the dog.

Monkey.—In the monkey the thyroid lobes may or may not be connected by an isthmus. The parathyroids are four in number, two on each side, an outer larger, and a smaller inner body. According to Vincent and Jolly both glandules are frequently imbedded in the substance of the thyroid so that simple parathyroidectomy is extremely difficult in these animals.

Guinea Pig.—Comparatively little attention has been paid to the parathyroids of the guinea pig. Vincent and Jolly state that the number and position of these bodies is extremely variable in this animal. As a general rule two of the glandules are more or less deeply imbedded in the thyroid, while the other two are distinct from the thyroid substance and separated from it by a variable interval. The above mentioned authors have found as many as six glandules in one animal.

Rabbit.—The superior parathyroids are imbedded in the thyroid lobes. The inferior parathyroids are distinct from the thyroid lobes, and sometimes considerably removed from them. The inferior bodies are considerably larger than the superior in this animal.

Rat.—This animal possesses only two parathyroid glands. They are situated within the thyroid lobes near the upper pole.

Horse.—Litty found in the horse a parathyroid gland on each side, embedded in the thyroid lobe, yellowish red, round or oval, measuring about one centimeter in diameter. Estes has described in the horse both an external and an internal parathyroid. The former is found easily and is from pea to hazel nut size. It has a peculiar lobulated appearance. It is most often found near the superior pole of the thyroid, usually in the peri-thyroid areolar tissue. Its position varies with the variations of the thyro-laryngeal artery. The internal parathyroid was found by Estes only by making histologic sections of the thyroid gland after hardening the same. Even by this method the internal gland was found in only about half the cases and its distribution was very irregular. It could be easily confused in gross with small adenomatous growths, which are not uncommon in the thyroid of the horse.

Sheep and Goat.— MacCallum, Thomson and Murphy have found a very irregular distribution of the parathyroid tissue in these animals. Four parathyroids were found quite regularly in the thymus and thyroid but this does not include all the parathyroid tissue in these animals. Two glands are to be found imbedded or partly imbedded in the thymus, one on each side, at the level of the thyroid cartilage and just in front of the carotid artery and vagus nerve, and may easily be distinguished with the naked eye. These glands measure from about three to five millimeters in diameter. The remaining parathyroids are imbedded in the thyroid lobes. They cannot be easily seen in the living animal. When the thyroid is removed and hardened, however, they stand out plainly from the surrounding thyroid tissue with which they come into very intimate relation through lack of capsule.

Ox.—In the ox the external parathyroids lie, one on each side, just under cover of the free dorsal borders of the lateral lobes of the thyroid opposite about the lower level of the isthmus. They occupy the stratum of fat which separates the thyroid lobe ventrally from the pharynx and œsophagus dorsally. They may be blended with islets of thymus tissue. The internal parathyroids are incorporated within the thyroid gland.

Forsyth has made a very complete study of the parathyroid glands in mammals and birds. He examined forty-two species of the former and thirty-five of the latter. This detailed search has led the author to conclude that the parathyroids vary widely in number in different species and even in different members of the same species. "An instance of this is afforded by three specimens of the Green Monkey in which the parathyroids numbered one, one, and eight respectively. Further, the existence of parathyroid tissue in the thyroid, not isolated by connective tissue, has been found to be of much commoner occurrence than was supposed. Even in the same species the parathyroids were found subject to considerable variations in number and in position. "Further, parathyroid tissue is commonly present in the thyroid, and intermediate types are readily found both in the thyroid and in accessory glands, with the result that the identity of some bodies has often presented difficulty."

"Isolated glands possessing a parathyroid structure were found in most, but not in all, the members of the series. When present their total number was two, three, or four; but these numbers were exceeded in certain specimens. A two-spotted paradoxure (*Naudinia binotata*) and a fossa (*Cryptoprocta ferox*) each had six; a Green Monkey (*Cercopithecus callitrichus*) eight, and a collared Fruit Bat (*Cynonycteris collaris*), ten."

"The parathyroids can scarcely be said to possess any definite anatomical relations in these animals, so widely do their positions vary. The commonest site of occurrence was on the convex lateral surface of the thyroid; but they were also found on the tracheal surface, or sunk in the thyroid either deeply or just beneath the capsule or in the immediate neighborhood of the thyroid, either dorsal anterior, posterior or external to it, or some distance remote, either isolated or in association with accessory thyroids or lymphatic glands. They present no naked-eye feature by which their identity can be established; and over and over again in this series they have been found unexpectedly on microscopical section. Frequently glands too small for macroscopic identification have been found attached to the capsule of the thyroid."

Birds.—The thyroid and parathyroids of birds, as examined by Forsyth, agree generally with those structures in mammals, but they also present certain points of contrast." As with mammals, so with birds, it has sometimes been difficult to decide whether a particular gland was to be regarded as a thyroid or parathyroid. Each of these in its typical appearance is of course readily identified, but the two structures are so often intermixed that it is not always easy to settle which name to give to the whole. A few examples will illustrate this difficulty. The anatomical thyroid of the Californian Quail was found to be wholly parathyroid in nature. In the Barn Owl only the cortex of the thyroid possessed thyroidal structure; the deeper parts were typically parathyroidal. In the Gray Parrot, the Oyster-Catcher, and other birds the anatomical parathyroid was directly continuous with the thyroid, no connective-tissue septum being interposed so that the whole formed a single gland."

In the majority of cases the number of parathyroids in birds was found to be limited to one on each side, lying in contact with the thyroid at or near the posterior pole. "In a few specimens the parathyroid is bilobed, while occasionally two separate parathyroids occur. When this last condition holds it is frequently found that the glands are some little distance remote from the thyroid. Most parathyroids are oval or spherical in shape, and their color is white or yellow without any translucency."

Among the papers that have appeared on the comparative anatomy of the parathyroids may be mentioned that of Pepere, who includes in his very complete anatomical study of the parathyroid glands, a description of these bodies in a number of animals as well as a study of variations in man from the fœtus to old age.

The nerve supply of the parathyroid glandules has been studied by Sacerdoti, who states that they are furnished by nerves of the thyroid. According to Anderson the nerves terminate within the interior of the epithelium of the glandule.

CHAPTER XIV.

EMBRYOLOGY AND HISTOLOGY.

When one studies the development of the parathyroids, and observes their changing relations to thyroid and thymus in its course, anomalies in the ultimate situation of these bodies are readily accounted for.

The thyroid gland arises from a median body at the root of the tongue, and two lateral bodies which begin as small buds from each side of the posterior wall of the fourth branchial cleft.

The thymus gland arises from two epithelial evaginations of the third branchial cleft which grow downward and meet to form the two lobes of this body.

The parathyroids arise as two separate pairs; one from the fourth branchial cleft, the other from the third branchial cleft. The former pair come to lie on the dorsal surface of the lateral portion of the thyroid and form the superior bodies. The other pair pass further backwards and come to rest behind the lower border of the thyroid, forming the inferior bodies. The name "inner" and "outer" bodies was given these glandules by Kohn because of the fact that in certain animals the parathyroids derived from the fourth branchial cleft were found within the thyroid lobe while those derived from the third groove were situated outside the thyroid.

Steida, as early as 1881, discovered in a pig embryo, in addition to the thymus, thyroid, and carotid gland, four other epithelial anlage, which Schreiber later described as the parathyroids. Among other earlier workers on the embryology of these bodies may be mentioned Prenant, who described an origin for these organs in the sheep from the fourth branchial cleft together with the lateral thyroid bodies. Tourneux and Verdun also described the parathyroids as arising from the dorsal part of the fourth branchial cleft in human embryos. Simon observed the bodies in rabbit embryos, and Groschuff in the mole. Soulie and Verdun differentiated in the rabbit the inner parathyroids (arising from the fourth branchial cleft) and the outer parathyroids (arising from the third branchial cleft). Benjamins, who included with his own work a discussion of previous articles, definitely stated that in man the bodies have independent anlage in both the third and fourth branchial clefts.

For a more complete abstract of the origin of these bodies in various species we are indebted to Maurer, who first described the parathyroids in amphibians:

Anura.—In tadpoles the parathyroids arise at the time when the outer gills form. They arise as compact epithelial buds on the ventral end of the third and fourth branchial clefts; the spaces also form a similar bud which, according to the observations of Maurer, goes to form the carotid gland. The last branchial cleft forms no parathyroid.

At first these glands are histologically composed of epithelial cell masses, which stand in relation with the epithelium of the gill cleft by means of an epithelial pedicle. This pedicle disappears and the small structure grows by increase of its cells to form an egg-shaped body which may be recognized by spiral, interwoven cell cords. A lumen is never found in these organs. Their construction is peculiar, differing from the thymus, the thyroid and the post-branchial body. These organs persist throughout life and are found even in very old animals, (frogs, toads, tree-toads).

Urodeles.—In triton the parathyroids are formed during the metamorphosis stage. They come from the epithelium of the closing third and fourth branchial clefts. At the same time the carotid gland arises in the neighborhood of the second cleft. The bodies lie here on the lateral convexity of the aortic arches, or are between these. Sometimes two such bodies are found between the third and fourth arches so that three are formed on one side. In other cases there is only one such structure on one side, so that individual variation is not uncommonly met with.

Reptilia.—In the lizard the parathyroids also arise from the third and fourth clefts. In serpents one body has been found in the second cleft. They arise at the same time as the thymus, during the closure of the branchial clefts. In the lizard the bodies arise from the third cleft on the ventral end of the thymus and are in connection with this through an epithelial cord. The ventral pocket of this cleft suffers a complete atrophy. The parathyroid of the fourth cleft is formed from the wall of this cleft which throws out a lateral projection from the œsophagus. The middle portion of this projection thickens and forms the anlage of the parathyroid. The body is loosened from the œsophagus and for a time is in connection with the post-branchial body.

At first this organ consists of epithelial cells which form the boundary of a lumen, but with increase of epithelial cells this lumen disappears, and at the same time connective tissue elements enter, so that the body possesses a complex of epithelial cells which are separated from one another by delicate interstitial connective tissue. In this condition the parathyroid of the lizard remains throughout life. It never contains a lumen and colloid substance is never secreted, so that the structure cannot be confounded with that of the thyroid.

Aves.—In birds the parathyroid glands are present in varying number. They are formed by the third and fourth gill cleft and lie ventrally to the thymus. According to Verdun, in the chick and the duck, a third body is formed in connection with the post-branchial body which is possibly a derivative of the fifth branchial cleft. Verdun further concludes that the first two are often in connection with the thyroid and that the derivative of the fourth cleft is frequently attached to the post-branchial body.

In mammalia, as we have already noted, these structures arise from the third and fourth branchial clefts and differ in their relation to thymus and thyroid from the parathyroids of the lower vertebrates.

At first the parathyroids of the third cleft are in direct relationship with the thymus; the two being separated from the œsophagus at the same time. It is only later that the parathyroid of the third cleft separates itself from the thymus, and indeed, we see that at times a parathyroid becomes imbedded in the thymus lobe.

The relations of the parathyroids of the fourth cleft are even more complicated. The primary connection here is thymus, parathyroid and post-branchial bodies, and through this latter connection the parathyroids acquire a connection with the thyroid lobe.

HISTOLOGY.

Kohn was the first to establish the independence of the parathyroid glands by his ground breaking histologic and genetic study of these organs. He clearly made evident the distinct independence of parathyroid from thyroid. Previous authors although they had carefully recorded the histologic structure of these glands regarded them as embryonic thyroid.

The histology of the parathyroid glandules has been described in detail by various authors, including Sandstroem, Kohn, Welsh, Erdheim, Peterson, Verebely and Getzowa, and save for minor differences, the descriptions are fairly uniform. All authors describe two main types of cells which may be grouped as follows:

Type 1.—Comparatively small cells (somewhat larger than those of the thyroid) with relatively large nuclei which stain deeply. The cell cytoplasm is colored with difficulty, but the cell border is distinct. These cells constitute the greater part of the gland tissue and are always present in every glandule, but may vary in size, shape, and intensity of cytoplasmic stain, and in size and shape of the nucleus. These cells will be referred to as the "principal" cells.

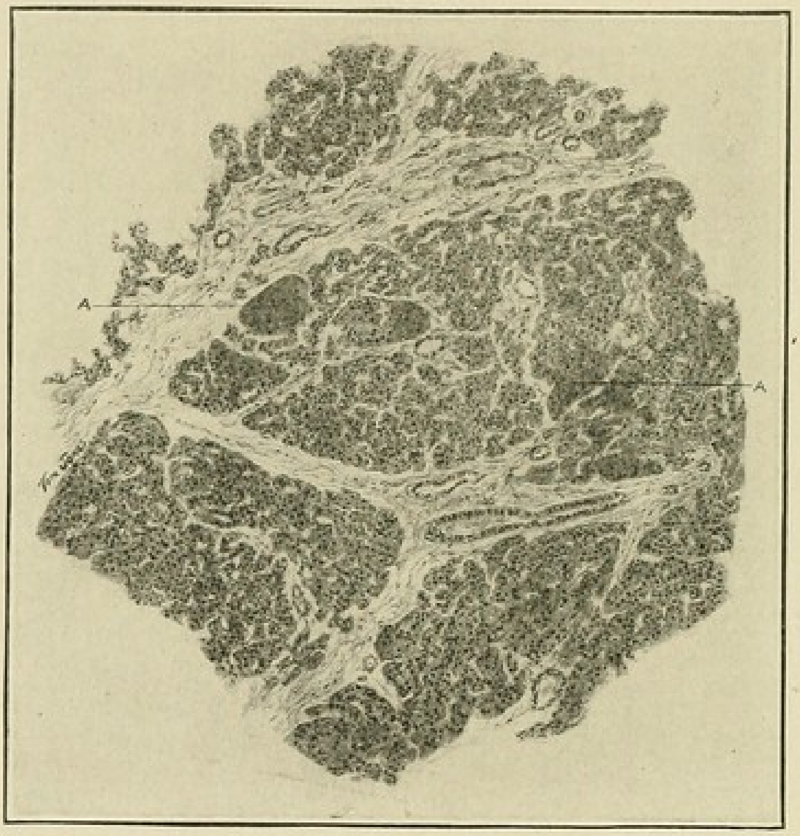


Fig. 64. Normal parathyroid glandule, ordinary type of cell arrangement. A—Groups of "functional" cells.

Type 2.—Comparatively large cells with small deeply staining nucleus and considerable deeply staining, eosinophilic, granular cytoplasm. These cells have a distinct cell boundary. They are not found in every glandule, though they are present in almost all cases. They are never so numerous as the "principal" cells. These cells will be referred to as the "functional" cells.

The number and arrangement of these cells is subject to wide variation. They may occur in masses forming small islets scattered throughout the gland tissue, or may occur irregularly scattered among the principal cells, either singly or in groups of three or four, without any definite arrangement. Sometimes they form definite acini or occur in continuous anastomosing columns.

The principal cells are also subject to a great variety of arrangement, giving different pictures in different glandules. The cells may form a uniform mass continuous in every direction, being broken only at infrequent intervals by delicate strands of connective tissue carrying small blood vessels. The cells in this instance appear irregularly polyhedral, and the cell walls are everywhere in direct contact with each other.

The glandules may show connective tissue, with blood vessels, between the masses, thus breaking them into anastomosing columns, or cell trabeculæ. Here the cell cytoplasm stains more deeply and the cells are apparently rounder than in the former arrangement. There may be seen further subdivision of the cell masses by fibrillar stroma or capillary reticulum, or denser fibrous stroma with blood vessels, so that small islets of epithelial cells appear within the stroma somewhat akin to the arrangement in carcinoma.

In parts of the glandules the principal cells may form definite acini, so that the structure resembles secreting gland, the center of which usually contains colloid.

The glandules present, then, in general, a together-hanging cell mass composed for the most part of small cells with indistinct cytoplasm and deeply staining nucleus, interrupted irregularly by small islets, or groups of two or three, larger eosinophilic cells, which may or may not have a characteristic arrangement. These cell masses are divided irregularly by blood vessels into lobular or reticular cell strings, or may be separated into distinct lobules by connective tissue septa. Both the cells and the connective tissue may contain considerable fat, which is believed by most authors to arise in the organ itself without outside influence.

Sandstroem, who described the glands with considerable accuracy, grouped them histologically into three main types: 1. A continuous mass of epithelial cells penetrated by a considerable capillary network. 2. A continuous cellular reticulum, the meshes of which are occupied by blood vessels and connective tissue. 3. An arrangement of cells into numerous small follicles, in some of which are drops of a colloid-like substance.

Welsh confirmed and added to the work of Sandstroem. He described four types: "1. The cells form a uniform mass, their protoplasm taking little if any stain, and there being but slight degree of vascularity. 2. The cell masses show a tendency to break up into anastomosing columns, between which are capillaries borne in a fine connective tissue stroma; the protoplasm stains somewhat more deeply than before. 3. The cells form branching columns between which lies a fine or dense stroma, bearing blood vessels. These cells are large and faintly staining. 4. The cells are arranged in a single layer around a central lumen to form definite acini. These cells are large, with cytoplasm staining variously and the lumen is usually occupied by a small globular mass of colloidal substance." Welsh specially notes that commonly several "types" coexist in one gland.

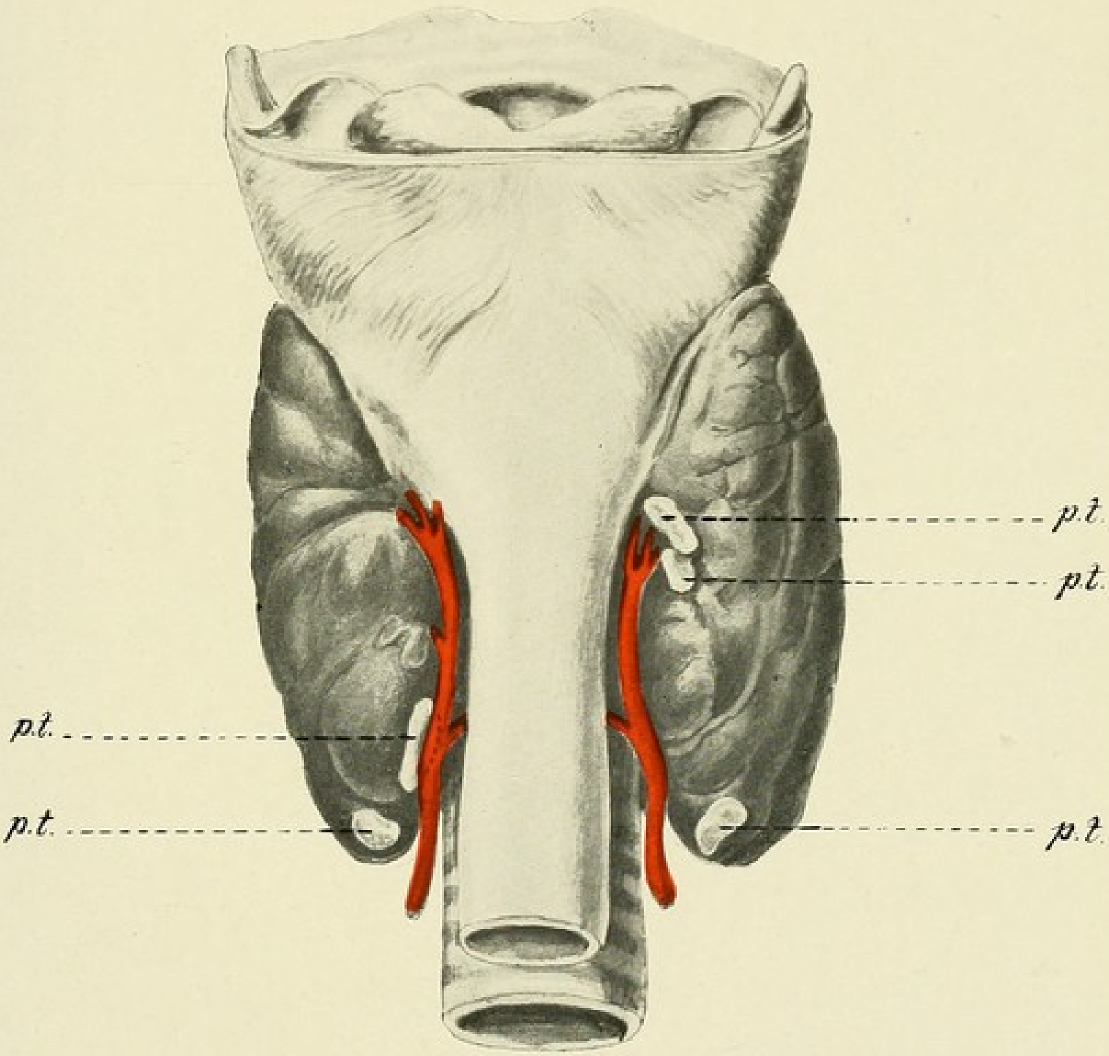
Welsh also added a description of what he terms "oxyphile" cells. These he mentions as occurring in a very large proportion of cases, though not in all, and never attaining the same abundance as the above mentioned cells, ("principal" cells). They have a relatively large amount of cytoplasm, which is usually full of fine oxyphile granules, and he recognized what he considered differences between the nuclei of the two varieties of cells; those of the oxyphile being smaller, more nearly circular, and with their chromatin more dense. According to their grouping he makes four types of these cells also. They occur as: 1.—Uniform masses forming islets scattered irregularly through the gland; 2.—Anastomosing columns; 3.—Cells either singly or in groups of twos and threes; 4.—Cells forming definite acini, the lumina of which are occupied by colloid material—a very exceptional type.

Ebner, Chantemesse and Marie, Benjamins, Kohn and Kollman were among the earlier contributors to the histology of these glands. Their findings in general agree with what has been related.

Peterson, who carefully studied the glands in one hundred autopsies, noted that the structure of the parathyroids varied from a compact cell mass, to a gland composed of independent islets of cells separated by connective tissue in considerable amount. He separates the cells of the parathyroid distinctly into two main types. The first type is distinguished by its strong affinity for the eosin, and when a considerable number of these cells are massed together the picture is similar to that of the adrenal gland. The cells of the second cell type are less characteristic than the first. The cell bodies may run into one another without sharp differentiation and are much smaller than those of the first type. The cytoplasm may be so diminished that one sees only a complex of strongly colored nuclei. Between these extreme forms are all possible variations. Peterson also notices that rarely there may be observed cylindric cells with basal nuclei which group themselves in tubular gland-like form. The appearance of a third cell type, noted by this author (large voluminous cells) may represent a degenerative change rather than normal histology.

Peterson's work shows that the parathyroid gland is a secreting organ which presents certain (functioning) cells which set free a secretion product. The parathyroids possess no duct; the carrying away of the secretion is by the blood stream, with which the cells are directly continuous by means of capillaries as in the adrenal. A proof of the entrance of this secretion into the blood is offered by Peterson in the regularity with which the red blood corpuscles show an increased affinity for eosin (similar to the cytoplasm of the functioning cells) in congested organs where secretion is increased.

PLATE XXXV



P. T. PARATHYROID GLANDULES. THE RIGHT SUPERIOR GLANDULE IS DOUBLE. THE LEFT SUPERIOR GLANDULE IS SITUATED ABNORMALLY LOW.

Koenigstein, who studied in serial section 200 glands, described a passing over in successive series of the different types of parathyroid cells. The large, polygonal, eosinophilic, sharply bounded type may be transformed into another distinct type, smaller, shrunken and having but little affinity for the eosin. He considers the difference in picture due to different stages in the function of cells of the same original type, which after filling with their secretion present different forms.

Von Verebély in reviewing these various cell types suggests that it is best to consider that the parathyroid is made up of a single cell type which changes its form and appearance under different conditions of secretion and rest. This is in line with the views previously expressed by Koenigstein and later emphasized by Forsyth and by Thompson.

Getzowa describes four types of cells which are designated: 1.—*Wasserhelle* cells; 2.—*Rosarote* cells; 3.—Oxyphile cells; 4.—Syncytium-like cells.

Forsyth lays special emphasis on the histologic variations of activity and rest. The so-called oxyphile cells are those distended with granular secretion, and the so-called principal cells represent the exhausted stage; intermediate forms are common. This author states that the granular secretion of the cells is extruded into the surrounding lymphatic spaces.

So far we have called attention to the parenchyma rather than to the framework of the parathyroid, although we have spoken of the considerable variation in the amount and distribution of the latter. A most careful study of the framework of the parathyroid glands by digestion methods has been made by Flint. In the dog and monkey this author states: "In thin digested sections the framework appears as irregular septa which do not form a continuous network throughout the organ, but are broken up into smaller processes which support the irregular coiled columns of cells of which the organ is composed. These septa carry the arteries, capillaries, veins, and nerves. They are in some places built up of fasciculi

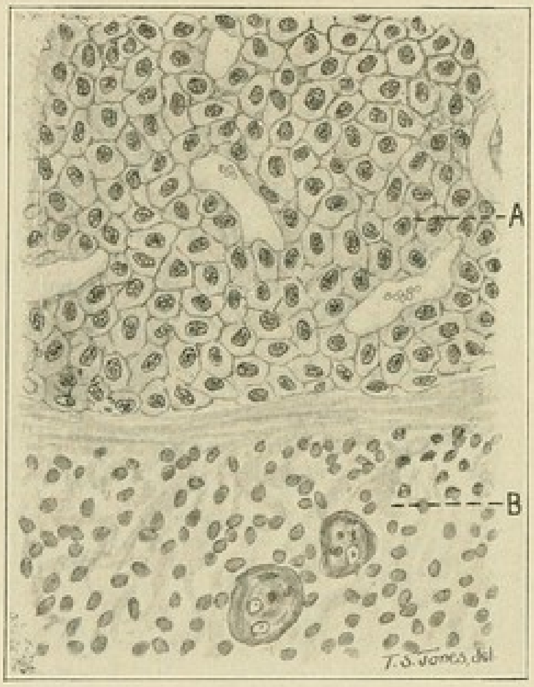


Fig. 65. Normal infant parathyroid (*a*) in connection with (*b*) remnant of thymus gland. (Magnified 575 times).

of reticulum fibrils, in others, of a thinner, looser formation of anastomosing and branching fibrils. When thick stained, digested sections from fifty microns up are studied, these broken septa are obviously continuous in the third dimension with other processes that turn off and occupy various planes according to the branching of the anastomosing cell columns. In sections stained by the ordinary methods, and thin sections varying from three to six microns in thickness, stained by Mallory's connective tissue stain, numerous cells with oval nuclei are found imbedded in the fibrils. These are the connective tissue corpuscles, and do not differ in this position from those found in other parts of the body."

HISTOLOGY OF THE INFANT PARATHYROID.

Microscopically, certain differences between infant and adult parathyroid may be noted. The most noticeable difference seems to be that there is only a single type of cell in the infant glandule. The differentiation into "principal" and "functional" cells, as described for adult parathyroids, cannot be made.

In the infant Thompson has found that, microscopically, the parathyroid glandules present a fairly uniform picture. They consist of closely set cell masses arranged in groups or in strands, which are separated by a rather delicate connective tissue stroma bearing blood vessels. The relation between parenchyma and stroma is more uniform, and there is less tendency to form varying types of arrangement than in the adult. The cell masses consist of cells a little larger than those of the thyroid, which vary in size and shape and intensity of nuclear and cytoplasmic staining, but which conform to a single type, the so-called principal cells of the adult glandule. The cytoplasm of these cells may be indistinct or lacking, but the cell membrane is usually distinct. Along the capsule and septa these cells frequently assume a radial arrangement, the so-called "palisade" formation. As previously noted, the functional cells of the adult do not appear in the infant gland.

Erdheim notes that the structure of the parathyroids in infants is more solid than in adults, but after the twentieth year the parenchyma undergoes a breaking up by the penetration of connective tissue trabeculæ. He finds the functional cells first at the tenth year of life. After the fifth year fat cells appear in the connective tissue of the gland. This fat increases with age till it includes quite generally the whole gland.

Forsyth says that during the first few months of life the parathyroid glands show no activity, and that this inactivity may persist for some years, although in one case colloid secretion was found as early as the third month.

HISTOLOGY IN ANIMALS.

In general the histology of the parathyroid glands in animals bears a close resemblance to the picture seen in man. Forsyth, to whose extensive work we have already referred, finds that these glandules are usually made up of solid masses of polygonal cells whose cytoplasm may be pale and clear or filled with oxyphile granules, or intermediate between these extremes. Often the cells may arrange themselves around a lumen which is filled with a drop of colloid. In birds this author found that the glands possessed a similar structure, with less attempt at follicular formation. The cytoplasm of the cells showed the same variations in activity and rest as has been described in mammalian parathyroids. On the whole, the parathyroids in birds are more often inactive than those in mammals.

Alquier has carefully described the structure of these glands in the dog, and divides them into three types. The first type (*Type ordinaire*): the cells are large and possess a clear finely granular protoplasm with a large nucleus. These cells are arranged in anastamosing cords within a mesh-like network in varying dimensions. The second type (*Type compact*): consists of polyhedral cells disposed without order. The cells are voluminous and clear. The third type (*Type reticulé*): the cells are smaller and the intercellular spaces are not clearly defined.

In the sheep and goat the parathyroids are practically not to be distinguished from one another histologically, according to MacCallum. The glands are very compact and very vascular. The cells are apparently all of one type and are closely arranged in anastomosing strands and cords so that the intervening capillaries come into direct contact with all the cells. The cell nuclei are large and round and the cytoplasm very abundant with a somewhat granular structure. The perfectly clear cells and the eosinophile cells seen in the human parathyroid are not to be found here.

SECRETION OF THE PARATHYROID GLAND.

Various substances have been noted in the parathyroid gland appearing either as degeneration products or as gland secretion. Among these may be mentioned colloid, fat droplets and granules, glycogen, hyaline, and pigment. These substances will be specifically dealt with in the chapter on pathologic histology.

It was stated by Gley that the parathyroids (of the dog and rabbit) contained considerably more iodine than did the thyroid. Chenu and Morel, on the contrary, found only a very small amount of iodine in these glandules. The work of these latter authors is sustained by Estes and Cecil who state that if iodine is present at all in the parathyroid it is in such minute quantities as to be of no functional significance. Nagel and Ross found that ablation of a parathyroid did not modify the iodine content of the remaining glandules.

Fiori, who has removed portions of the parathyroid glands in animals, found that no regeneration of parathyroid tissue whatever took place following injury. The removed epithelial tissue was replaced by connective tissue and a cicatrix resulted as is the case with all highly specialized tissues.

CHAPTER XV.

THE PATHOLOGIC HISTOLOGY OF THE PARATHYROID GLANDS.

While the greater part of the work on the parathyroids has been along experimental lines, nevertheless morphological observations relating to alterations from the described normal histology have been made by a number of investigators, although perhaps it might be truthfully stated that the negative observations on these bodies have been of more value in clearing our mind in regard to certain diseases than any described pathological alteration.

Sandstroem mentioned that cystic degeneration, and amyloid infiltration of the vessel walls and capsule occurs in certain cases. Müller called especial attention to fatty change. Königstein studied especially the secretion of the glandules from a histological standpoint, but stated he could not bring anatomical changes into correlation with clinical conditions. Harnett, in a series of routine autopsies, found no changes in the parathyroid glands that could be differentiated from normal glands at the corresponding period of life. Verebely in one hundred and thirty-eight cases described various lesions of the glandules, including two instances of tuberculosis, three cases of cyst, three of hemorrhage, and one tumor. Getzowa called especial attention to the colloid content, which was found present in nearly all cases over ten years of age. Pepere noted a number of progressive and retrogressive changes, including suppuration. Guizzetti described dense mononuclear cell infiltration of the parathyroid in two cases of tetanus. Yanase found hemorrhage thirty-three times in eighty-nine children showing tetanoid conditions. Kohn described hemorrhagic cysts. Peterson, who examined one hundred cases, noted the frequency with which degenerative changes are found in the glandules from cases over twenty years old. Among these changes he found atrophy of the parenchymatous cells brought about by fatty changes, cloudy swelling, and cystic degeneration very frequently. In twenty-five of his cases he found cloudy swelling; in fifteen, colloid; in six, cyst formation; in twenty-one, fatty infiltration. This author was unable to correlate changes in the gland with clinical conditions. Garnier described slight changes in severe infectious disease.

Benjamins, in twenty cases of goitre, found no progressive changes in the glandules but a variety of retrogressive changes. In a general study of the parathyroids he found hydropic degeneration twenty-five times, pigment, atrophy, connective tissue increase, and frequent colloid. He described a tumor of the parathyroid the size of a child's head.

Erdheim found glycogen and colloid frequently and observed mast cells in the connective tissue of certain of the glandules. He also noted the frequency of cysts. He found hemorrhage in eight cases.

Thompson has called attention to the condensation of the cytoplasm at the edge of the cell in these glands, due to various degeneration products such as fat, glycogen, and colloid. This produces the optical appearance of an intercellular framework

Fig. 66. Sclerotic type of parathyroid glandule showing epithelial islets separated by considerable connective tissue.

which characterizes many of these glands. In a later paper by the same author, degenerative and especially progressive changes were described in these glandules in cases of primary infantile atrophy.

Forsyth, who regards the cells of the parathyroids as all of a single type representing different stages of activity and rest, has described excess of colloid, connective tissue proliferation, both general and perivascular, and also speaks of instances (in animals) where there is a similarity between thyroid and parathyroid structures. This author also notes that the cortex of the gland stains more deeply than the medullary tissue, and that drops of colloid and regular vesicles are met with more frequently near the surface than elsewhere. The nearer the surface, the more abundant the secretion.

MacCallum, who has worked extensively on these glandules, found in certain of the glandules examined following thyroid removal for exophthalmic goitre, some increase in fibrous stroma and moderate atrophy of the cells. In general, however, the parathyroid tissue was abundant and normal in these cases. A tumor of a parathyroid, and hyperplasia of the glandules in gastric tetany has also been noted by this author.

Tuberculosis of the parathyroid glands, occurring as a part of general miliary tuberculosis, has been described by Carnot and Delion, Benjamins, Verebely, Eggers and Winternitz.

Amyloid infiltration of the parathyroids has been especially well described by Schilder who found these glandules involved in three cases of amyloidosis.

The attempt to establish a symptom complex for diseases of the parathyroids has been due to the results of physiological experimentation rather than to histological findings, and a great range of diseases, in which tetanic symptoms are present, has been advanced as due primarily to deficiency in parathyroid secretion. In many of these diseases, however, examination of the parathyroids has failed to reveal constant morphological change when symptoms were such as to suggest severe or complete loss of their functioning power.

The various tetanies for which a parathyroid etiology seems most probable will be discussed in a later chapter. At present we will only concern ourselves with such morphologic work as concerns these conditions, as well as the results of a study of these bodies in those diseases in which a parathyroid etiology has been suggested but found lacking.

Exophthalmic Goitre.—The suggestion that exophthalmic goitre might be due to lesions of the parathyroid glands suggested itself very soon after tetanic symptoms were noted following the removal of these bodies. Moussu was probably the first to formulate this theory. At about the same time papers appeared by Gley and by Edmunds, the former suggesting alterations in the thyroid apparatus involving in the first place the parathyroids, and the latter partial aparathyroidia as an explanation of this disease.

Edmunds has also stated that when the parathyroids are removed in the dog the thyroid gland undergoes compensating hypertrophy with changes similar to those found in exophthalmic goitre, namely "enlargement of the vesicles with alteration in shape from round to oblong or branched; intracellular growth takes place, the secretory cells become columnar instead of cuboidal and the colloid contents of the vesicle tend to disappear."

Humphry, on the basis of this assertion, describes two cases of exophthalmic goitre in which the parathyroids (only two of which were found in each case) exhibited extensive infiltration of fat. In another case there was some fat, and in a fourth case (age, twenty-two years), there was no fatty infiltration. For comparison the author examined microscopically the parathyroids in eighteen cases, not goitre, and came to the conclusion that it would be premature to consider this fatty change as a pathological feature of Graves' disease without further observation.

Haskovec, on the ground of his experimental investigation of exophthalmic goitre, concludes that, while this disease has its origin in the thyroid gland, the parathyroids should be considered as participating in the condition.

In general it may be stated that no characteristic histological changes are found in the parathyroid glands in connection with this disease. Erdheim examined a case, in which exophthalmic goitre and epilepsy were combined, and found no changes save for the usually fatty infiltration that might be expected in a fifty-three-year old man. Benjamins also failed to find changes in the parathyroid glands in this condition. This author examined the parathyroids from twenty cases of goitre of various kinds including three cases of exophthalmic goitre.

MacCallum, who has examined the parathyroids from a number of cases of exophthalmic goitre, states that there are no constant lesions in these organs in this disease.

On the negative histological findings, then, as well as on the fact that the symptoms in parathyroidectomized animals are very different from those of exophthalmic goitre, and considering that parathyroid therapy is of no benefit in the disease, we can conclude that the parathyroids have little or nothing to do with this condition.

Myxoedema.—It is to be questioned if the parathyroid glands play any role whatever in the causation of myxœdema, which is definitely known to be due to loss of the thyroid gland. Occasionally, however, certain disturbances in the muscles have been observed in the course of this disease, as reported by Lundborg, Schlesinger, Rosenberg, and others, which might suggest that the parathyroids were also involved.

Maresch and Peucker found the parathyroids present in cases of congenital absence of the thyroid. Erdheim found in several cases where there was absolute aplasia of the thyroid, not only the four normal parathyroids but a number of accessory glandules, none of which presented any pathological alteration.

Forsyth has reported a case of myxœdema of four years standing in a woman aged fifty-eight, which showed in addition to the typical sclerotic changes in the thyroid, certain departures from the normal structures of the parathyroid glands. The bodies showed a marked tendency to form vesicles lined by a cubical epithelium, with a profuse secretion of colloid which filled the follicles and lay among the masses of cells and distended the lymphatic channels. There was also observed an abnormal increase in the connective tissue and a thickening of the arterial walls of these glandules. Such a change as this is too commonly observed, however, in parathyroid glands from ordinary cases of people of this age to make Forsyth's observation of any importance. Both fibrosis and colloid are frequently found in the parathyroids.

Brissaud considers the parathyroids to be involved in myxœdematous idiots, and not involved in myxœdema frustes.

Epilepsy.—Owing to certain of the symptoms that have been observed in animals following incomplete operation on the parathyroids it was early

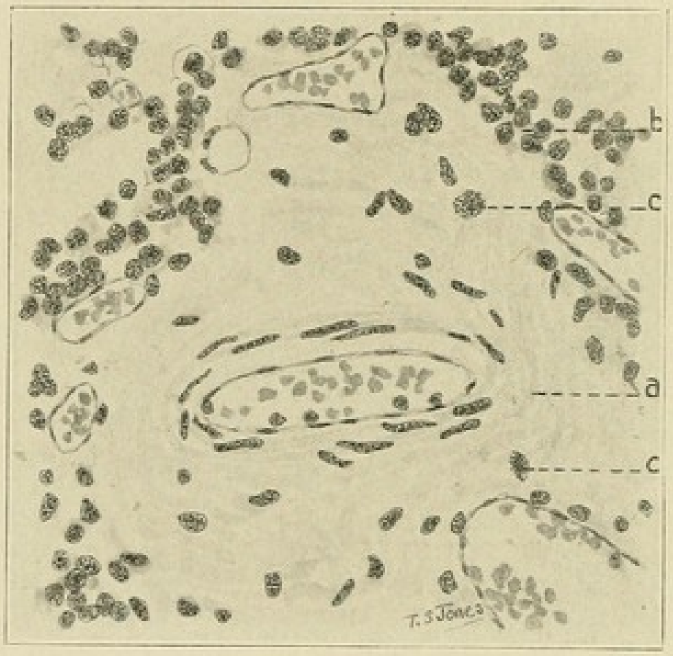


Fig. 67. Parathyroid glandule of the sclerotic type, from a case of primary infantile atrophy, high power, showing (*a*) perivascular increase of connective tissue, (*b*) crowding together of epithelial cells, and (*c*) mast cells in connective tissue. (Magnified 575 times.)

suggested (Jeandelize, Vassale, MacCallum), that epilepsy might in certain instances have a relationship to changes in the parathyroid gland. Erdheim, indeed found considerable increase of connective tissue of all four parathyroids in a case of epilepsy in a twenty-three-year old male, but in another case he found the glands perfectly normal. Schmorl found hemorrhage in the parathyroids in two cases of epilepsy.

Claude and Schmiergeld examined the parathyroids, as well as the thyroid glands, in seventeen cases of epilepsy, and found no changes in the former that they were able to construe as pathologic for this condition.

Paralysis Agitans.—As early as 1885, Horsley from observations on thyroidectomized apes, described certain muscular tremors and stated that the causation of the constant tremor such as that in paralysis agitans might find an explanation in the loss of the thyroid apparatus. He did not consider the parathyroids at that time, as up to then little or no attention had been paid to these organs, but of course, a considerable amount of parathyroid tissue had been removed in his animals. Despite Horsley's observation no attention was paid to these organs as far as paralysis agitans was concerned until 1904, when Lundborg's well known paper on the relation of the parathyroids to paralysis agitans appeared. The same hypothesis was advanced by Berkeley independently although his paper did not appear until later.

Both these papers were wholly hypothetical, Lundborg having no autopsy material on which he could prove his assumptions, and Berkeley being able to secure but one autopsy in this condition. In this case he found two parathyroid glands, which are described as less than average size, and as presenting sclerosis and thickening of the blood vessels in part, with other parts of the gland appearing normal.

The hypothetical part of both these articles is not without interest. Lundborg cited Luzzato, Dana, Mobius, Frenkel, Burzio, Casteloi and Schiefferdecker, all as expressing the idea that the disease is an endogenous toxemia. He emphasized the tetanic symptoms that arise in animals after parathyroidectomy; and after a considerable discussion which it is impossible to abstract completely, gives a diagram wherein the system of thyroid and parathyroid hypo and hyper function is delineated in terms of myxœdema, morbus Basedowii, paralysis agitans, and paralysis myasthenia respectively. Lundborg's paper must be read in its entirety to appreciate the full force of his argument. He concludes with the statement, however, "*das es aber noch für ausserst hypotetisch gehalten werden muss, ob die glandulae parathyroidae eine bestimmte Rolle in deren Pathologenese spielen.*"

Berkeley cites in support of his theory: tetanic symptoms observed in slowly dying parathyroidectomized rabbits; the endogenous toxemia concept of the disease, which seems to be borne out in a measure by the fact that the author considered that the administration of parathyroid gland extract was of therapeutic value in a majority of his cases; and the possibility that, in cases of concurrent myxœdema and paralysis agitans the parathyroids may have been diseased or atrophied through contiguity with the diseased thyroid.

Alquier in a general review of this subject adds the weight of his opinion to this hypothesis on the ground, especially, that it seems more probable than any of the previously advanced theories.

Thompson, however, failed to find any constant changes in the parathyroid glands of nine cases dying of this disease, which were controlled by the examination of the glandules from forty autopsies not paralysis agitans. In summing up these nine cases of paralysis agitans it was found that the parathyroid glandules, in individuals dying with this disease, presented no changes either in number, size, position, or histologic structure that would serve to distinguish them from the parathyroid glandules in individuals dying from other diseases.

In two of the nine cases, only three glandules were found (in one other case where only three glandules were found the technic was faulty). Many writers find three glandules more often than they find four, in routine examination. In three cases five glandules were found. The finding of the minute accessory parathyroids in these cases more frequently than in the routine cases was undoubtedly due to the extra care that was used in searching for them in the paralysis agitans material.

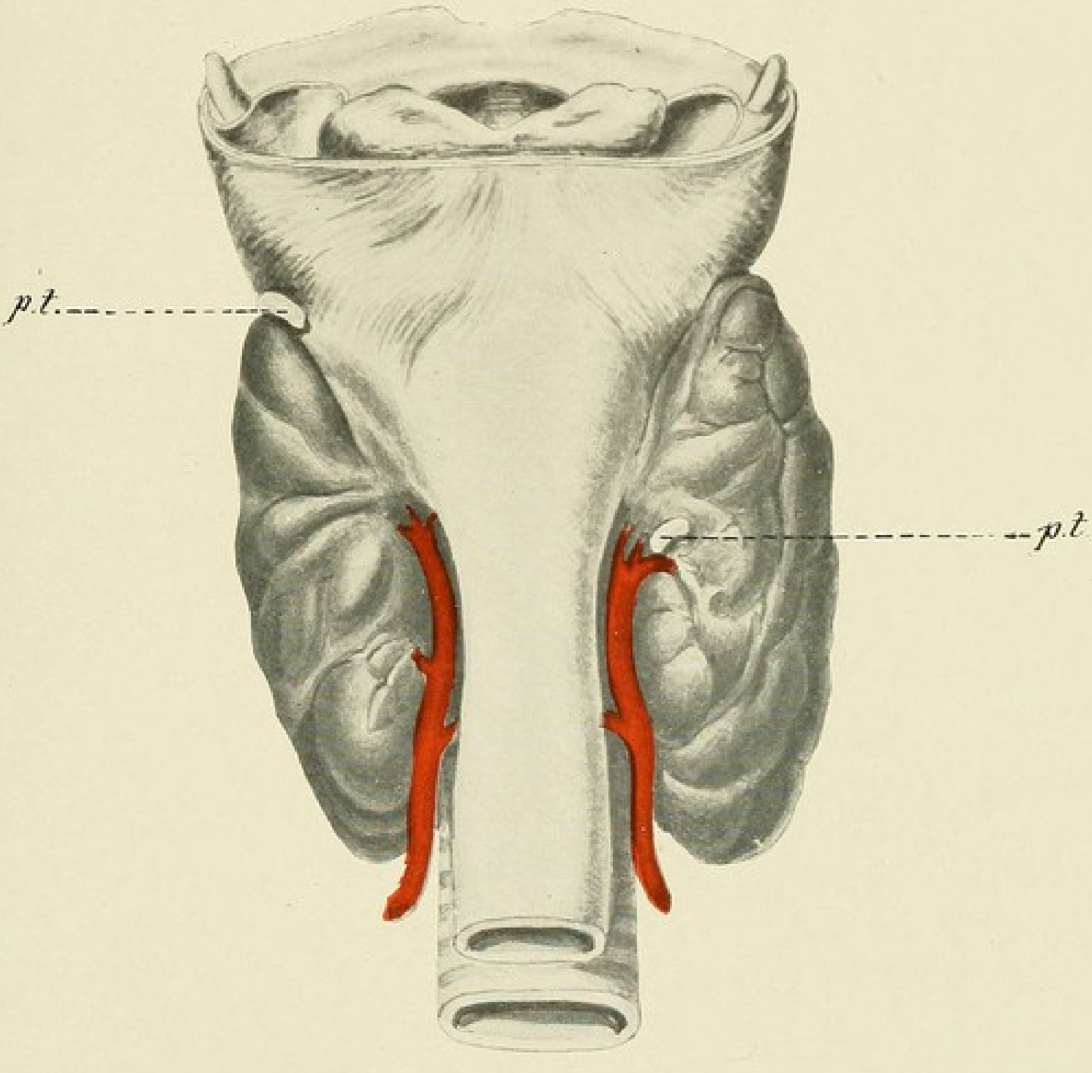
The average size of the glandules was a little smaller in the cases of paralysis agitans than the general average of the routine cases. This could be accounted for by the fact that all the paralysis agitans cases were over seventy years of age. Routine cases over seventy years of age show in general smaller glandules than young individuals.

There was nothing to be found microscopically in the parathyroids in the paralysis agitans cases that could differentiate them from other parathyroids. Five of the cases can be passed over without remark; they were in every way identical with the type picture presented by the majority of the glandules in routine parathyroid examination. Two of the cases presented a moderate increase of connective tissue stroma. The percentage of glandules showing a considerable connective tissue stroma was higher in the routine cases than in paralysis agitans. Eight of the routine cases were of this type. One of the paralysis agitans cases showed a great amount of interlobular fatty connective tissue, so that only small islets of glandular tissue were seen. Three of the routine cases, however, gave even greater connective tissue stroma, with corresponding atrophy of the parenchyma. Fat was found in every glandule examined, both in the paralysis agitans and the routine cases. Some of the paralysis agitans cases showed a great amount of fat. Many of the routine cases showed an equal amount, and some even more. The glandule that showed the most fat was from a case of diabetes.

All the cases of paralysis agitans showed both types of cells (principal and functional), although the ratio between the two varied greatly in different cases and in different glandules from the same case, as they did also in the routine cases. In one case, one of the inferior glandules exhibited apparent increased activity of the functional cells. No mitotic figures were seen in the principal cells, in either the paralysis agitans or the routine cases.

Erdheim also examined the parathyroids in three cases of paralysis agitans and found no evidence of hypoplasia. In two of the cases the glandules were perfectly normal. In the third case one glandule was greatly enlarged and showed marked increase

PLATE XXXVI



P. T. SUPERIOR PARATHYROIDS. THE LEFT IS ABNORMALLY HIGH. THE INFERIOR GLANDULES (NOT SHOWN) ARE ON THE ANTERIOR SURFACE OF THE THYROID LOBES.

in the functional cells while the other three glandules were normal.

In conclusion, then, it must be stated that there is no morphologic ground for the assumption that the parathyroid glandules are insufficient in paralysis agitans. Whether or not there is faulty secretion of these organs; whether they are unable to cope with a poison circulating in the blood that their cells or their secretion is not able to neutralize; or whether the specific relation between these glandules and some other organ is upset, must be determined by experimentation other than morphologic, and offers a promising field for investigation. On morphologic grounds there is every reason to oppose the hypothesis that paralysis agitans is a chronic, progressive hypoparathyroidismus.

Tetany.—Microscopic lesions have been described in the parathyroids in various forms of tetany, which will be dealt with in more detail in a later chapter. MacCallum found hyperfunction of the glandules in gastric tetany, and Königstein also reported a case in which similar changes were found.

Tetanus.—In tetanus Guizzetti found infiltration of mononuclear cells in two cases in which the disease had lasted for four and seven days, respectively. Two other cases were negative. Babonneix and Harvier have described changes in the parathyroids in three cases of tetanus, consisting especially in hypersecretion of colloid. Thompson found no changes in the parathyroids in five cases dying from tetanus infection that could be considered specific. Erdheim found the glandules normal in one case.

In a case of experimental tetanus the glandules were found normal by Garnier.

Tetany of Children.—Erdheim (three cases) and Königstein have found hemorrhage in the parathyroids in children exhibiting tetanic symptoms. Verebely, and also Thiemich, have found hemorrhages in cases where there was no tetany. The most convincing work in this line has perhaps been done by Yanasse who examined the parathyroids in eighty-nine children showing tetanoid conditions and found hemorrhage in thirty-five cases. Degeneration of the parathyroids in a case of tetany in course of a case of tuberculous meningitis has been described by Escherich.

Eclampsia.—The greater amount of work on this condition has been experimental and is given in more detail in a later chapter, but several authors have examined the parathyroids histologically in this condition. Pepere found changes in the glandules in four cases. Zanfrognini found only two glandules in a case, but these were both normal. Erdheim in four cases found hyperemia, circumscribed injury once, hemorrhage once. Schmorl in five cases of eclampsia found hemorrhage four times. He considers that the hemorrhage was the result of the convulsions.

Rachitis.—Escherich, under whom the work of Yanasse previously cited was done, has suggested congenital parathyroid hypoplasia as the etiological factor in rachitis. This assumption is based on the frequent coincidence of tetany and beginning rachitis as well as on Erdheim's findings in the teeth of parathyroidectomized rats. At present this hypothesis lacks morphological confirmation. Schmorl found no changes in the parathyroids in four cases of rachitis.

Osteomalacia.—In two autopsies in this disease Erdheim found hyperplasia of the parathyroids in one case and normal glandules in the other case. Schmorl in four cases found the glandules normal three times and hyperplasia in one case of one of the upper glandules.

Primary Infantile Atrophy.—In this disease Thompson found constant changes in the parathyroids, practically all of a progressive nature, which the author considered the result of this condition rather than an etiological factor in the same.

In the cases of infantile atrophy the changes that are found in the parathyroids can be quite sharply differentiated into two types, which may be designated as (a) degenerative, and (b) sclerotic. In the first type the glandules may be diminished in size or may be of normal size, and are pale in color, or, as in one case that showed intense congestion, the glandules were cherry red. Microscopically, no increase of connective tissue is found, but the epithelial cells show everywhere a marked degeneration. They are larger and more irregular than normal, the nuclei are swollen and the cell boundaries are usually thickened, appearing as though the protoplasm had condensed in part at the cell periphery, as happens in certain forms of reticular degeneration. In places there was complete loss of cell structure with crowding together of the cytoplasm into a fused mass, in which the nuclei were irregularly arranged. The blood vessels may be greatly distended, but are usually moderately injected.

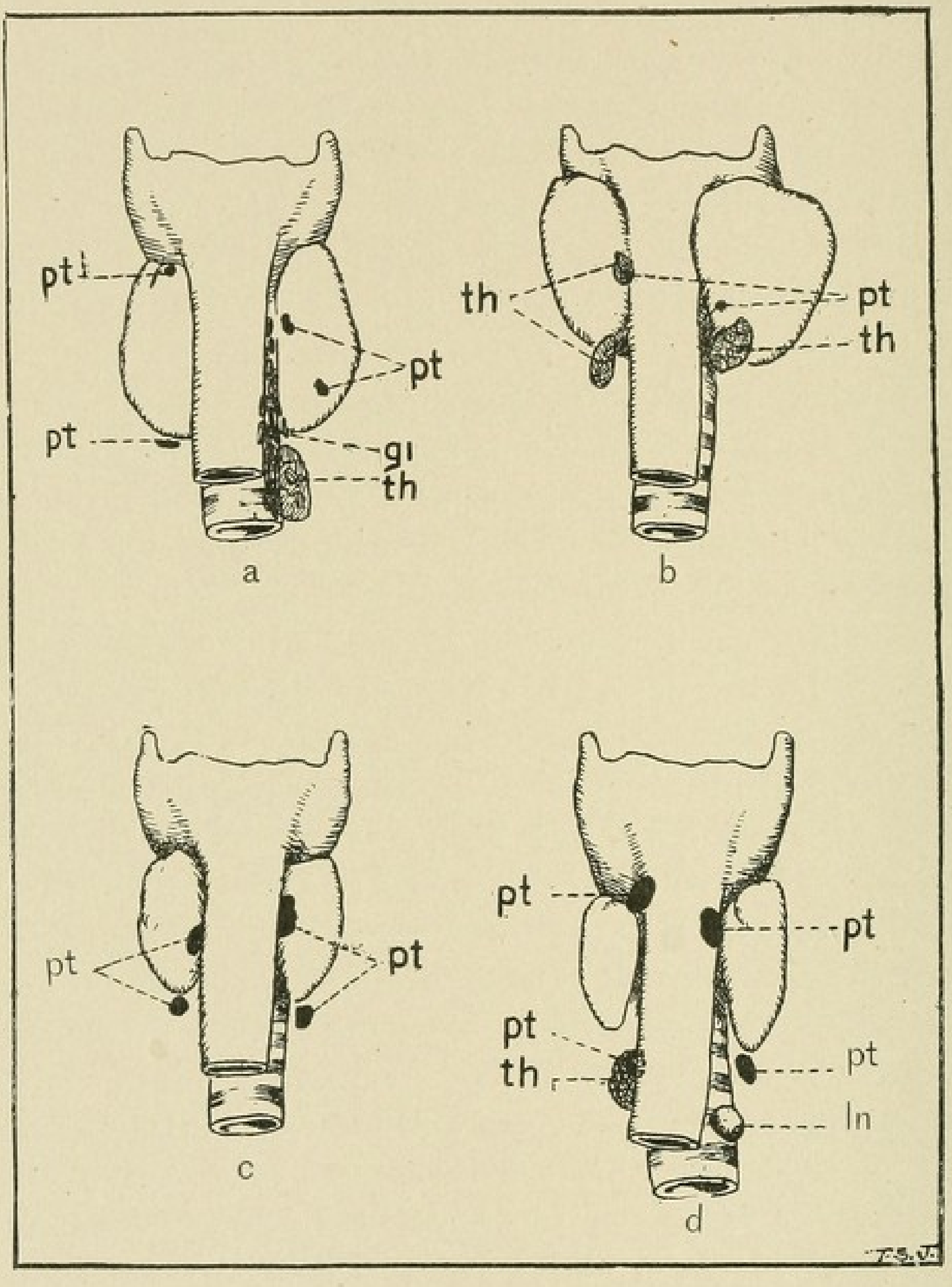


Fig. 68. *A* and *B*. Sketch of the neck organs from cases of primary infantile atrophy, showing the small size of the parathyroid glandules; compare with *C* and *D*, which are control cases of infants of the same age. (*pt*) parathyroids, (*th*) remnants of thymus gland (in *B* replacing the two lower parathyroids and surrounding the left upper); (*gl*) represents tissue continuous with the interscapular gland. (*ln*) lymph node.

The most common finding, however, in these cases of marasmus is a marked increase in the connective tissue stroma of the glandules, which corresponds closely to the sclerosis (chronic fibrous parathyroiditis), described in the adult. These cases are called, therefore, the sclerotic type. In these cases the glandules are smaller than normal, dark brownish-red in color, and firm. Microscopically the connective tissue stroma separating the cell masses is found increased in amount in varying degree. The epithelial cells appear as irregular strands between the thickened bands of connective tissue. This connective tissue increase is frequently noted about the blood vessels. The connective tissue is loose, vascular, and rich in nuclei, which have a spindle shape. Mast cells are frequently seen in the connective tissue. In the epithelial islets between the connective tissue strands the principal cells are crowded together so that the typical sharp-lined epithelial structure is lost. The cell membrane is usually not seen, but masses consisting of closely set, irregularly arranged nuclei, without definite cell boundaries, are apparent. Groups of five or six cells occasionally in the centres of these islets preserve their original structure. As tetany was never observed in these cases the findings are interesting as tending to show that extensive changes may take place in the parathyroids without exhibition of any tetanic symptoms, a finding that might serve as a check, perhaps, upon a too liberal interpretation of morphological change in cases that do exhibit tetany.

Pellagra.—Marinesco has recently described atrophy and marked fatty change in the external parathyroids in two cases of this disease.

General Pathology.—Thompson and Harris, in a study of these glandules from a morphologic standpoint in two hundred and fifty routine autopsies, state that they have been unable to correlate to any extent clinical symptoms and morphological parathyroid alteration. They nevertheless add the following report of certain histological findings in these glandules that are of interest:

Fat.—The fat content of these glandules is so constant in the adult that it gives a distinct yellow color to the gland and serves as a macroscopic aid in differentiating parathyroids from lymph nodes, accessory thyroids, or thymus, sympathetic nerve ganglia, or other bits of tissue which make the search for these organs more or less difficult, especially to one who has not had considerable experience in their isolation. Microscopically one should differentiate perhaps between the fatty content of the connective tissue of the gland and the fatty content of the cells of the parenchyma, although as a matter of fact it is doubtful if one occurs to any marked extent without the other being present. In a great number of the glandules there was a replacement of considerably more than half the parathyroids with fatty tissue and in addition, the principal cells of the gland contained fat; but such cases showed nothing clinically that would serve to call attention to a lack of parathyroid function.

While it may be stated that in general more fat is to be found in elderly individuals than in those of middle age, still one would hesitate to accept the view that a regular and constant increase of fat is an accompaniment of increasing age. A number of glandules in individuals over sixty years of age were found that were only moderately fatty, and on the other hand, there were found glandules in patients from twenty to thirty years of age in which there was marked fatty change both in parenchyma and stroma. One would not, therefore, limit the diagnosis of fatty degeneration to the earlier years of life, although admitting the increased difficulty of making such a diagnosis in the later years.

The fat content is, as previously stated, so physiologically variable that one hesitates to attempt any classification for fatty degeneration of the glandules. The most marked changes in these cases, the factor of age being kept in mind, have been found in the following conditions: cirrhosis of the liver; chronic nephritis, especially chronic parenchymatous nephritis; chronic heart affections with the usual associated lesions; chronic tuberculosis; diabetes. Especially are the glandules apt to be fatty when an acute infection is superimposed on a chronic condition. The most constant and marked fatty change in any one series of cases was in five instances of ascending infection of the genito-urinary tract with pyelonephrosis. In all these cases, which were of various ages, marked fatty change in the parathyroids was found. These cases are representative only of a type of rather long continued acute infection where considerable chronic disease of the lungs, heart, and liver was present.

The association of marked fatty change in the parathyroids with cases of infection of the gall-bladder and ducts, with extreme jaundice in four cases of this condition, might be noted in passing. In malignant diseases, carcinoma especially, of either comparatively long or comparatively short duration, there was no fixed condition of fatty content in the parathyroids. At times these organs showed marked fatty change; at times there was no apparent increase of fat. The same was true in regard to the parathyroids in cases dying from uncomplicated acute infectious diseases of short duration such as lobar pneumonia. A case of tertiary syphilis (the only one in this series), showed marked fatty degeneration of the glandules.

Colloid.—It would be unfair to exclude the presence of colloid unless serial sections are made of all glandules, although if colloid is present at all it is usually more or less widely distributed in a given glandule. Colloid was found in about fourteen per cent of all cases. This agrees with the statement that the presence of a certain amount of colloid in individuals over twenty years of age is not to be considered abnormal. The interesting point in regard to colloid is the fact that its secretion not infrequently leads to appearances in the parathyroid that makes circumscribed areas within them exceedingly suggestive of thyroid structure. These areas begin by a dozen cells, more or less, assuming an alveolar arrangement. In the center so formed a droplet of colloid appears. Continued secretion of colloid pushes back and flattens the cells so that finally a follicle, similar to those seen in the thyroid gland, appears.

If enough of these are formed in juxtaposition, thyroid-like structure results. Usually, however, these colloid follicles are discrete, or the amount of colloid is not sufficient to alter the general topography of the glandule.

Even though a picture somewhat like thyroid structure may be produced, one should remember that on embryological, anatomical; and physiological grounds there is no relationship between human thyroid and parathyroid, save that of propinquity. They are independent of each other, and there is no reason for assuming that one acts for the other, although it is probable that there is some interaction between the two. There is no reason to believe, as stated by Forsyth, that histologically intermediate stages between thyroid and parathyroid are common, in the human being at least, or that the difference in the glands is merely a difference in the amount of secretion; neither have we reason to suppose that the parathyroids exhibit a partial change to thyroid structure with advancing age as claimed by Rogowitz.

Vincent and Jolly find that parathyroid tissue left behind after thyroid extirpation "approximates in appearance to ordinary thyroid tissue," and believe that the parathyroid functionally replaces thyroid. Their view is directly opposed by Hagenbach, however, who obtained a typical cachexia thyropriva when two parathyroids were left behind.

Thompson and Harris did, however, find in this region appearances which they chose to consider accidents of propinquity and in which there was an apparent transformation of one organ into the other, but which they considered should be interpreted on more rational grounds than transformation of parathyroid into thyroid.

In this case (which showed at autopsy caseous tuberculous pneumonia, chronic pleuritis, localized peritonitis, and peri-hepatitis) there were fairly firm adhesions in places between the capsule of the thyroid and surrounding tissue. The upper parathyroids were normal; left lower not found; left right lower pole showed a circumscribed thickening of the surrounding structures and was excised. Microscopically, section of this showed, on the outer edge, fairly typical parathyroid structure penetrated by a dense connective tissue stroma. The inner part of the section showed typical thyroid structure with a similar increase of stroma. There was no line of demarcation between the two, but one seemed to run into the other so as to suggest the transformation of parathyroid into thyroid tissue. It seems more rational to assume, however, that a perithyroiditis leading to proliferative changes in both glands joined the two organs together in this peculiar manner, the connective tissue ingrowth being so distributed that both appear to be one and the same organ.

Degenerations.—Acute degenerative changes occur in the parenchymatous cells of the parathyroid glandules, but a diagnosis of "cloudy swelling" or "acute degeneration" is to be made only when one can exclude post-mortem changes and other adventitious factors that might arise wholly apart from intrinsic parathyroid changes. In many cases the glandules are microscopically enlarged, are soft and pale, or firm and tense. These changes are usually due to increased fluid content (œdema) and are practically always a part of a general œdema of the neck organs. Microscopically the cells in such glandules are larger than normal, the cytoplasmic granules are more distinct than usual and the nuclei large and pale. Frequently the usual structure of the gland is lost and no good cell pictures obtained. The authors have been unable to fix such appearances as being of significance.

Hemorrhage.—Hemorrhage was found in these cases of Thompson and Harris only three times. The rarity of hemorrhage in adults has been noted by Erdheim, who found it seven times in children but only in one instance in an adult. Getzowa found it only once in the adult. Yanase also speaks of the infrequency of hemorrhage in these glandules in adults although he has been able to demonstrate it frequently in the first year of life, as previously noted. Verebely found hemorrhage only once in the adult (twice in children), in his one hundred and twenty-five cases. Benjamins and Peterson only report single cases, the latter in one hundred autopsies. Our cases of hemorrhage were found in connection with toxic glomerulo-nephritis, marked general anemia secondary to syphilis, and acute parenchymatous nephritis, respectively. In none of these cases was there any clinical manifestation of tetany.

Fibrosis.—The amount of connective tissue found in the parathyroids is, in general, subject to wide variation. The gland may consist of a continuous mass of epithelial cells penetrated by a considerable capillary network, unaccompanied by connective tissue, or there may be a continuous reticulum running throughout the gland. When the gland is broken up into distinct islets by a decided connective tissue stroma there is in the gland more connective tissue than should be considered normal for the structure. Some authors, however, choose to classify this as a particular "type" of gland. In any event the widening of such a stroma and the decreased size of the islets leads to the different degrees of what may be termed "chronic interstitial parathyroiditis;" or, as Verebely, who found the condition well marked in two cases, terms it, "parathyroiditis chronica fibrosa." The best examples of this condition have already been described under primary infantile atrophy.

In the series of cases described by Thompson and Harris every possible variation in connective tissue content of these glandules was met with.

The cases exhibiting connective tissue increase in the parathyroids are, in this series, almost without exception in poorly nourished individuals showing at autopsy chronic heart lesions with general chronic passive congestion, cirrhosis of the liver, and chronic tuberculosis. However, the greater number of cases exhibiting the above lesions show no changes in the parathyroids, so that chronic fibrous parathyroiditis is not necessarily an accompaniment of these conditions, although it may be most frequently found in connection with such.

That specific infectious agents may bring about this condition is suggested by the extreme sclerosis found in a lower parathyroid in a case of acute miliary tuberculosis. The reaction in this case can be compared with the appearance sometimes seen in very chronic, tubercle bacilli poor, tuberculosis of lymph nodes, where there is little or no caseation or tubercle formation but marked connective tissue hyperplasia.

In the opinion of these authors the fact that even in extreme age and in a great variety of severe diseases the parathyroids are so comparatively free from lesion is more noteworthy, and a better proof of their importance than would be the frequent finding of lesions that would seriously impair their function. In none of the cases that showed fibrosis was there any clinical manifestation of tetany.

CHAPTER XVI.

CYSTS AND TUMORS.

Cysts occurring in connection with the parathyroid glands may be broadly classified as (1) retention cysts; (2) polycystic degeneration; (3) cysts arising either without, or in the neighborhood of, the parathyroids (branchial cysts). The production of cysts of the former class has already been discussed under colloid. These small cysts are quite common. Thompson and Harris found them in about five per cent of their cases. Peterson found cysts six times in his one hundred cases. Cysts have also been noted by Benjamins, by Pepere and by Kohn. The latter author was the first to describe retention cysts. They may be single, or three or four may be found in a single glandule; rarely do these cysts exceed the diameter of a low power field.

Polycystic degeneration has been found by several authors—Schaper in the parathyroid of a sheep; Erdheim in an eighty-three year old woman. Verebely also describes a similar picture in the parathyroid, but on account of the variation in the lining epithelium of the cysts prefers to class his case as a branchial polycystoma.

It would seem that colloid filled spaces are in general so frequent that there is no necessity for considering these "retention cysts" in detail unless they assume a number or size that brings them into relation with the condition described elsewhere, namely: true cysts and thyroid-like structure.

The cysts included in class (3) are to be considered as developmental anomalies. Verdun has contributed extensively to their embryological development, and more recently Erdheim has sought a classification for these branchial cysts. The latter author finds two different types of cysts in relation with the upper parathyroids which arise from the fourth gill pouch. The more common and better known cysts are, however, in relation with the lower parathyroids which arise from the third gill pouch. Verebely describes in detail two cysts in connection with the upper glandules, one of which he terms a post branchial cyst, the other a branchial cyst.

Thompson and Harris found only two cysts of the parathyroid of any considerable size. The first in a woman seventy-two years old with atrophic thyroid (lateral lobes measured only 3x2.5 centimeters), upper parathyroids in normal position but quite small (5x1.5x.5 millimeters). Left lower parathyroid not found. At the base of the right lower lateral pole of the thyroid is a parathyroid gland forming a flattened cap to a cyst which measures two by two by two and one half centimeters in diameter. The cyst wall is lined with a single layer of flattened epithelium. The second cyst was also in connection with a lower glandule and practically its equivalent in size (7x4x3 millimeters). This was a simple cyst.

TUMORS OF THE PARATHYROID GLANDS.

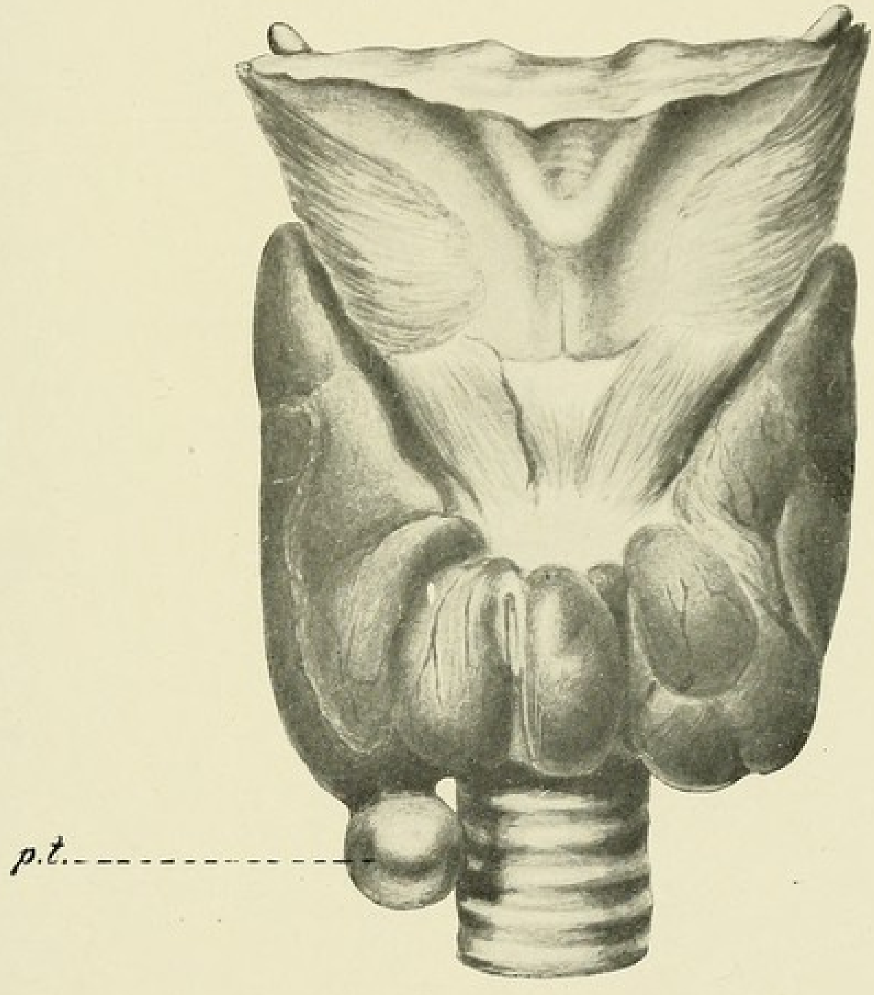
Tumors of the parathyroid glands have been reported by a number of writers, and we can now find in the literature a number of these growths which are described in considerable detail.

The first of these was a tumor described by de Santi (1900) as a rather large vascular growth, the structure of which corresponded to parathyroid tissue. The tumor grew with considerable rapidity, but was classified as not malignant.

Most of these tumors represent reproduction of parathyroid tissue, and should be designated, perhaps, as examples of hypertrophy and hyperplasia rather than classified as true tumors. Weichselbaum and others lean toward the designation of adenoma for these growths, although, as this author states, a distinct boundary line between adenoma and hyperplasia cannot be sharply drawn. Most of these growths have been of small size. In certain of these tumors, as those of Benjamins, of Hulst, and of Thompson and Harris, the proof of parathyroid origin is lacking, save for the resemblance of the tissue to parathyroid structure, and the latter authors refer to their growth simply as a "parathyroid-like" tumor.

Verebely has noted the fact that there is a great similarity between the cells of the parathyroid and rapidly-growing parenchymatous thyroid nodules, so that one must keep in mind the question of congenital fetal anomalies in the origin of these growths; such, for instance, as the failure of closure of the central canal of Prenant. The work of Getzowa and

PLATE XXXVII



P. T CYSTIC PARATHYROID GLANDULE.

of Langhans has thrown much new light upon these epithelial forms of malignant struma and brought up the question of the origin, of certain types, at least, from the post-branchial bodies.

Tumors of the parathyroid glands may be grouped primarily as (1) Extrathyroideal (2) Intrathyroideal. To the first group belong the cases reported by Erdheim, MacCallum, Weichselbaum, and Verebely.

Erdheim's case occurred in an eighteen year old individual in one of the inferior parathyroids. It was situated below the lower pole of the thyroid and entirely separated from the same; it measured two and a half, by one and a half centimeters in diameter. The tumor consisted of a fine, faintly vascularized stroma in which were imbedded strands and irregular masses of epithelial cells. The cells corresponded to those of the normal parathyroid and between them, here and there, colloid droplets were to be seen; there was no definite follicular structure. In one part of the tumor a small cyst lined with a single layer of epithelium and having a fatty content was noted.

MacCallum reported a tumor found at autopsy in a male, aged twenty-six years, who died of uremia. This tumor was just below the lower pole of the thyroid, on the right side and separated from it. It consisted of a long, smooth mass about two centimeters in diameter, enclosed in a delicate capsule and richly supplied with blood vessels. The thyroid gland in this case was normal, and two normal parathyroids were found. On microscopic examination the tissue comprising the tumor was found to closely resemble parathyroid. The mass was made up of strands and large groups of cells separated by a delicate vascular stroma. No colloid was found in either the cells or the alveolar spaces and the blood supply was less than was normally present in the parathyroid. MacCallum classified the tumor as an adenoma.

Goris found a tumor in a twenty-two year old male consisting of three closely connected cysts which contained colloid and degenerated parathyroid tissue. This case should perhaps be classified under cystic degeneration of the parathyroid rather than in this place.

Von Verebely has described a tumor of the parathyroid, belonging to the first group. This tumor was found in a forty-two year old woman in whom three parathyroids were found, normal in size and position. The tumor appeared as an oval, flabby, concave body under the lower pole of the right thyroid, measuring two and a half, by one and three-quarters, by one and a half centimeters in diameter. It possessed a thin, stretched out capsule. On section it was found to be made up of a soft homogeneous, vascular tissue. Microscopically the capsule gave off delicate septa ramifying within the tumor and connecting with the perivascular tissue, so that a delicate framework was formed, carrying capillaries, and possessing spaces filled with epithelial cells. The epithelial cells formed rows and strands, and were sometimes arranged in round or irregular islets. Three extreme types of cells, which shaded into each other by various gradations, were described in this growth. These cells corresponded to the type of principal cells of the parathyroid for the most part. The cells of the second type were vacuolated, and appeared singly or in small groups. The third type corresponded to the functioning cells, and varied considerably in size. No mitoses were to be seen in any of the described cells.

Weichselbaum described a tumor of the parathyroid found at autopsy in a woman who died of pneumonia. In this case both of the lower parathyroids and the right upper parathyroid were normal in size and position. In the left upper glandule was a flattened tumor measuring four and three-tenths by three and six-tenths, by one half to one centimeter in diameter. It covered a part of the posterior surface of the left thyroid as well as the posterior surface of the right thyroid. It was very soft, and gray-red in color. Histologically the tumor consisted essentially of normal parathyroid structure, with no suggestion of malignant tendency. The tumor possessed a delicate connective tissue capsule, strands of which penetrated the mass, separating the cells into groups of different size. These cells could be divided into four different types—the first corresponding to the principal cells of the normal parathyroid; the second corresponding to the functional cells of the normal parathyroid; the third characterized by the grouping of the cells around a central lumen; and, finally, cell groups not definitely separated by a stroma in which cells and nuclei were quite small.

Intrathyroideal tumors have been described by Benjamins and by Hulst and, as previously stated, their origin is open to question, as are the other tumors whose description follows. The tumor described by

Benjamins was in a fifty-seven year old male; situated in the right thyroid lobe. This tumor developed within three years to the size of a child's head, and recurred after extirpation. This tumor showed a connective tissue framework in which cells similar to those of the parathyroid were found arranged in groups; they possessed a pale nucleus with clear protoplasm and showed a tendency toward palisade arrangement; they were a little larger than the normal parathyroid cells. Mitoses were rarely seen in the cells. Here and there small masses of colloid were found. A normal parathyroid was found in the capsule of the tumor.

The tumor described by Hulst was found in a very old woman, in the right lobe of the thyroid, posteromedial, about the height of the isthmus of the gland. It measured two and a half, by two and a half, by two centimeters, and was inclosed in a calcified capsule. Microscopically this tumor consisted of a stroma rich in blood vessels and made up of cells of two types; the larger were polygonal and stained deeply with eosin, and their nuclei showed signs of degenerative change; the smaller which appeared in groups among the other cells possessed little protoplasm, and showed an eccentric nucleus which stained intensively. There were various gradations between these two types of cells. Mitoses were not found. The author characterized the tumor as an adenoma arising from parathyroid; he makes no mention, however, of other parathyroid glands in this case.

Askanazy has called attention to a tumor apparently derived from parathyroid tissue which he found in a case of ostitis deformans.

Thompson and Harris have described a tumor possessing a parathyroid-like structure which was removed at operation so that no careful dissection of the neck could be made. These authors state: "The extreme similarity of the greater part of the structure to parathyroid tissue justifies its discussion in this place although certain parts of it suggest the possibility of its origin from the post branchial body.

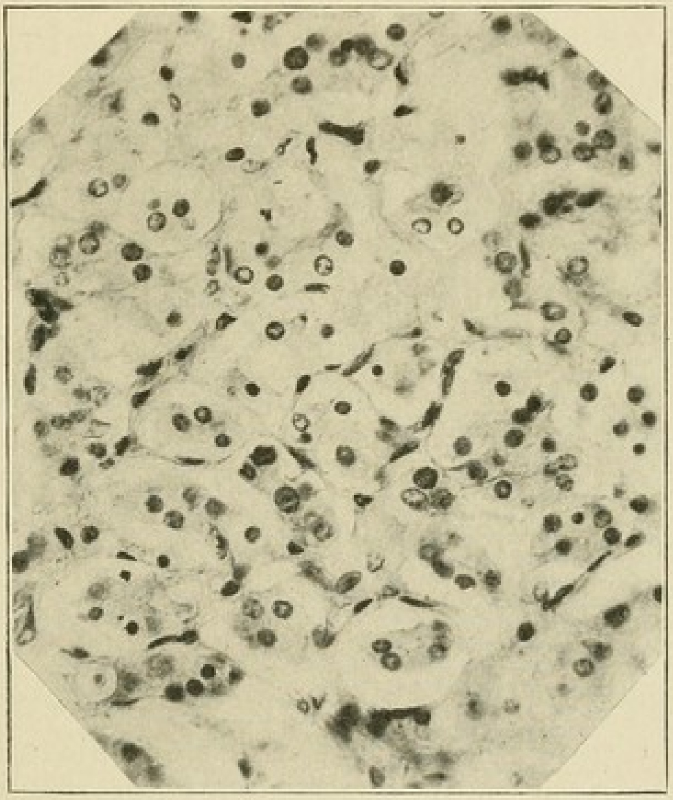


Fig. 69. Section of parathyroid tumor, magnified 400 times. (Thompson and Harris.)

We have chosen to call the growth simply a parathyroid-like tumor and regret that circumstances were such that neither a careful topographical study of the neck region could be made in the case, nor even, owing to the way the tumor was received, could the differential histological study, especially in regard to glycogen content, be done that was desired.

"The specimen is a nodular encapsulated mass (15x10x6 centimeters), weighing two hundred and fifty grams. Some of the nodules push sharply above the level; others are low, broad, and seemed fused together. The larger reach a diameter of four centimeters; the smaller measure one-half to one centimeter. The tumor is firm throughout. The capsule is thick, fibrous, and tense, and entirely covers the mass with the exception of an area, four by five centimeters, which represents the severed point of attachment. This capsule dips between the nodules and marks their outlines. The color is brownish yellow, mottled by scattered hemorrhagic areas in and upon the nodules. There are no large or congested vessels to be seen.

"On section the mass is found to consist of many discrete and confluent light brownish yellow areas separated more or less by fibrous trabeculæ. These areas correspond to the superficial nodules. They are firm, homogeneous, and friable; their cut surface presents a milky exudate, rich in cells. Variations in the appearance of these areas depend, in the main, upon the blood content. Some are pale and bloodless, some show congested capillaries; others contain bright red or dark brown areas of hemorrhage. In one nodule the cut surface is marked by translucent, silver-gray anastomosing bands of connective tissue which arise from the capsule. There are a few small cysts filled with a gelatinous semi-solid material.

"The capsule, which on the surface is distinct both in color and structure, loses its fibrous character as it passes into the mass and fades into a broad brownish yellow band. Numerous small blood vessels course along the connective tissue trabeculæ.

"For microscopical study a segment about five millimeters in thickness, cut from the median zone, was carefully plotted so that in the end it was possible to reconstruct the entire cut surface of the gross specimen. Histologically, the specimen is an epithelial tumor in which the cells are arranged as tubules or in nests and cords resembling the structure of parathyroid glandule. The connective tissue in places is prominent and forms anastamosing septa between the epithelial islands. In other parts it is present only as a delicate basement membrane, or very fine interlacing reticulum between the cords and clusters of loosely lying epithelial cells. Different lobules show wide variations in this proportionate distribution of epithelial cells and stroma. In an individual lobule this relationship is constant. The epithelial cells vary in diameter from twenty to twenty-five microns. The nuclei measure from four to eight microns and stain deeply. The protoplasm is vacuolated and stains lightly. As a rule, the cell boundary is not sharply defined. For the most part the cells are cuboidal or columnar and rest upon a distinct but delicate basement membrane.

"The structural formation follows the type of a simple gland with a small lumen, or the cells are grouped into small solid nests of six or more cells. From this original gland-like type, two variations arise. In the one the lumen becomes dilated, with the formation of numerous small cysts, the epithelium becomes flattened, and papilliferous outgrowths arise from the walls. In the other variation the cells are freed from their attachment to the basal membrane and appear as compact or loose clusters, cords and nests; the lumen disappears and all structural regularity is lost.

"For the most part the tumor is rich in capillaries upon whose delicate walls the cells are attached directly. In a few nodules the blood supply is surprisingly scant, entire fields being apparently free from determinable vessels. The hemorrhagic areas are numerous in certain lobules, the blood lying in large lakes and tubules and nests. The absence of large blood vessels with well developed walls is striking."

DaCosta found in a female aged thirty-two years, on the right side of the neck, a tumor about as large as an orange. His tumor is described as follows: "It passes to some extent back of the level of the upper border of the thyroid cartilage above. It also passed to one centimeter to the left of the median line. It was smooth, regular in outline, except for a bulb-like projection at its lower anterior portion; and of firm consistency throughout. The growth was in extremely close relation with the recurrent laryngeal nerve of the right side, and great difficulty was experienced in effecting a separation between the nerve and the tumor mass. No parathyroids were identified. The tumor was brownish yellow and irregular, and presented, in front of the lower portion, a bulb-like projection the size of a walnut, which was somewhat softer and decidedly darker than the remainder of the mass, but apparently a portion of it."

The growth is described histologically as consisting of parathyroid gland (tissue), surrounded by a fibrous capsule. The epithelial-like cells were arranged in fairly distinct columns, or masses separated by thin walls of vessels, or vascular intercellular tissue. In some areas, the tissue was arranged in the form of acini, lined with cuboidal or polygonal cells; although even in these instances, there was no sharp demarcation between neighboring cells. The protoplasm of most of the cells was granular or vesicular, and showed weak affinity for acid stains. The nuclei of these cells were small masses of material that gave the staining reaction of chromatin. In a number of the acini were small masses of colloid. Bands of fibrous tissue, enclosing numerous areas of weakly acidophile substance, or distinct masses of cells, were distributed through portions of the section. Many areas of hemorrhage appeared at various points in the section. Most of these were recent; but at a few points there were degenerative changes in the bordering gland tissue. Separated from the parathyroid structure by a broad, distinct band of fibrous tissue, containing many large blood vessels, was a portion of attached thyroid.

De Paoli has reported two tumors of the parathyroids occurring in males aged twenty-one and forty-one years, respectively. These tumors are described as being composed equally of thyroid and parathyroid tissue.

Pepere has reported two cases of angioma of the parathyroid as well as two cases of myoma and a lymphoma of these glandules. The same author also described a parathyroid adenoma the size of a large apple. A similar tumor, but smaller in size (1.5 cm. x 7 min. x 5 min.), has been described by Claude and Schmiergeld. Tumors have also been described by Makai, by Walther and, quite recently, by Bérard and Alamartine, who also give a considerable review of the literature.

Metastatic involvement of the parathyroids from malignant growths arising elsewhere has been reported by Königstein, from a bronchial carcinoma which involved thyroid and three parathyroids; by Pepere, two cases, from a breast carcinoma and a thyroid carcinoma; and by Thompson from a breast carcinoma in which there was involvement of all four glandules. In none of these cases was tetany observed.

CHAPTER XVII.

RELATION OF THE PARATHYROID GLANDS TO POSTOPERATIVE TETANY.

It is rather a peculiar coincidence that the discovery of the parathyroid glands by Sandstroem in Upsala and the first description of tetany following goitre extirpation by Weiss in Vienna, should have occurred in the same year. Ten years elapsed, however, before the relationship of these observations was disclosed. It was just about this time that operations for goitre, which had previously been uncommon, were, thanks to the work of Billroth and Kocher, becoming more frequent. Following such operations it was noted that either cachexia or tetany might manifest itself.

Also for many years it had been noted that certain animals after thyroidectomy showed convulsive or tetanic symptoms which quickly led to death, but no one had considered these symptoms, either in animals or man, due to anything other than removal of the thyroid gland. Schiff (1883), performed a complete thyroidectomy (which of necessity included the parathyroids) on sixty dogs, fifty-nine of which died in tetany and convulsions as a result of the operation. Horsley in 1892, in ignorance of the work of Gley on the parathyroids which was then just appearing, made the following statement in connection with thyroidectomized apes: "In the monkey I have found that, as a rule, the animal, after complete thyroidectomy, appears perfectly well for about five days. Then there is noticed a slight fibrillation of the intrinsic muscles of the hands, feet, and jaws following this order in successive invasion. As a rule the fibrillation soon becomes a constant tremor. The constant tremor is soon added to by a series of powerful clonic spasms. This paroxysmal stage usually appears about the second or third day after the tremors are first noted, and persists about twenty days. They gradually fall in force, reassume the type seen at their onset and disappear sometimes as much as ten days before death."

Another suggestive picture of a thyroidectomized ape is given by Langhans, who thus described the animal: "*Ich habe die Tiere vielfach gesehen, wo sie hülflos auf dem Boden sassen, zum Theil mit Zwangsbewegungen, namentlich des Kopfes und selbst des ganzen Körpers nach links, ein rechtes mitleid erregendes Bild.*"

In herbivora, after the removal of the thyroid no such accidents occurred. We now know that a considerable amount of parathyroid tissue must be present in sheep and goats outside the thyroid gland, and in the rabbit two of the parathyroids are situated at some distance from the thyroid, so that they were always left behind in removal of this latter gland. Therefore it was the lack of removal of all parathyroid tissue in these animals that was the reason for the lack of tetany, and not the fact that animals feeding on vegetable diet were immune to these symptoms, while animals feeding on a meat diet succumbed to them.

At this point begins our second important epoch in the history of the parathyroid glands, which was inaugurated by the discovery of Gley, in 1891, that the tetanic symptoms which appeared after removal of the thyroid were not due to the loss of the thyroid but were due to the loss of the parathyroid glands which were removed with the thyroid.

Gley demonstrated that in the rabbit there were two parathyroids separate from the thyroid and if these were removed together with the thyroid, which contained the other two parathyroids, the same tetanic symptoms arose in the rabbit as had been obtained in the dog.

Gley removed in his first experiments both the thyroids and the parathyroids from sixteen rabbits. Fourteen of these animals following such treatment showed rapidly fatal symptoms, which began within twenty-four hours after operation and led to death in a few hours. Gley continued these experiments and, in all, removed the parathyroids in more than fifty rabbits. When the external parathyroids alone or the thyroid lobes alone were removed there was no tetany, but when these external bodies plus thyroid (which contained the remaining parathyroids) were removed tetany and death resulted. It is to be noted that the islets of parathyroid tissue that are sometimes found in the thymus, were then unknown, and therefore in the rabbits that survived all the parathyroid tissue was probably not removed.

Gley also showed that in the dog if the thyroid was removed and the parathyroids were left intact, the animal did not show acute symptoms, while if the parathyroids were subsequently removed the usual fatal tetany resulted. Similar results were obtained in the rabbit. When the parathyroids were removed a month subsequent to the thyroid removal, the animal died with acute symptoms.

In all this work, however, Gley failed to recognize the internal parathyroids which are within the thyroid lobes, and therefore, he concluded that the negative effect of removing the thyroid alone was due to the vicarious action of the external parathyroids.

These researches of Gley were begun in 1891, and covered a number of years. Soon after his first articles appeared, a number of other investigators took up this fascinating problem.

Hofmeister confirmed the work of Gley in so far as to find that severe symptoms and death followed the extirpation of the parathyroid glands; he did not observe the compensatory hypertrophy of the organ after extirpation of the thyroid that Gley had described.

Moussu in a number of experiments on the rabbit and cat brought forward proof that thyroid and parathyroid each possessed a distinct function; the loss of the thyroid was followed by chronic trophic disturbances, such as myxœdema and marked cachexia, while extirpation of all the parathyroids led to acute tetanic symptoms and death. This teaching, which involved a strong separation between the symptom complex of thyropriva and of parathyropriva was for a time a much vexed question. Moussu's experiments, which comprised fifty-five complete parathyroidectomies, principally on dogs, were followed by tetanic death in thirty-three cases. In the animals which survived, the author considered that the operations were incomplete, as at autopsy one or more parathyroids that had escaped ablation were found in a number of instances.

Moussu gives the following description of parathyroid insufficiency in a dog where ablation was not quite complete: "*Appétit capricieux, élévation légère et permanente de la température, augmentation du nombre des battements cardiaques, tachycardie, dyspnée, polypnée dès que les sujets sont soumis à un exercice un peu actif: secousses fibrillaires ou crampes musculaires momentanées, albuminurie légère et inconstante, etc.*"

Christiani extirpated the parathyroids of the rat, together with the thyroid, and observed with great regularity death in tetany after the operation.

Kohn, in 1895, published a most important work on the parathyroid glands in which he gave us a more perfect knowledge of the anatomy of these bodies than we had previously possessed, and definitely established the independence of these organs which up to this time even Gley himself despite his experimental work had continued to regard as embryonic thyroid. After the publication of Kohn's paper establishing the identity of the "internal" as well as the "external" parathyroids, a more sure basis for experimental work was offered.

As a result of this work of Kohn, Vassale and Generali for the first time removed all four parathyroid glands without removing the thyroid. These experiments were done on ten cats and nine dogs with the following results. Of the ten cats only one survived (and this one developed chronic cachexia); the other nine died as a result of the operation with convulsive symptoms (fibrillary tremors, muscular twitchings, depression, rigid and staggering gait, anorexia, tachycardia, loss of weight and death). The maximum time of death was ten days. The nine dogs all died in less than eight days; usually on the

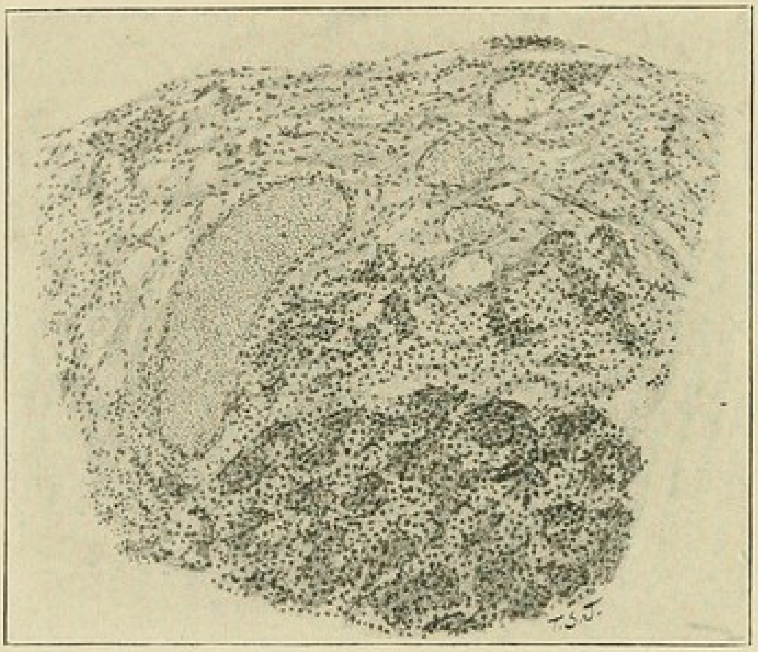


Fig. 70. Persistent islet of parathyroid tissue with granulation tissue twenty-eight days after mass ligation of glandule.

third or fourth day with the respiratory and convulsive symptoms that are now so well known.

Vassale and Generali supplemented their first experiments by a series of two-stage operations on a number of animals. They found the results were the same following total parathyroidectomy if the glands were removed in this way as were obtained in the first experiments, save that the dog survived a little longer after the final complete parathyroid removal.

Out of three dogs, two survived for twelve days after the second operation, the third died on the fifth day. Out of four dogs in which two parathyroids were left there were no symptoms save in one instance where a little transitory rigidity occurred which soon cleared up. Out of two dogs in which a single parathyroid was left one presented transient symptoms, the other no symptoms whatever.

Rouxeau removed the parathyroids in twenty-one rabbits leaving the thyroid intact and only three of these animals escaped death. The symptoms were the same in general as when complete thyro-parathyroidectomy was performed. The author concluded from this that in the rabbit parathyroidectomy is a grave offense, while removal of the thyroid is inoffensive.

Since that time these experiments have been frequently repeated and always with analogous results. Among these early workers may be mentioned DeQuervain, Verstraeten and Vanderlinden, Paladino, Cadeac, Guinard, Capobianco, Edmunds and Van-Ecke. The details of the early work may be found in the very complete monograph of Jeandelize which includes as well experiments of his own. Jeandelize was the first to make a sharp distinction between the chronic symptoms that follow thyroid removal and the acute symptoms that follow parathyroid removal and to establish the independence of these latter organs.

Although, with the earlier workers, the rabbit was the favorite animal for experimentation, the dog, owing to its larger size and its more direct connection of thyroid and parathyroid has been the animal most generally employed by later investigators. Gley himself has used the dog in a number of his experiments. It is well to remember, however, that in many cases in this animal the glandules may be so situated as to make a total parathyroidectomy impossible.* Not only may there be accessory parathyroids buried in thyroid gland but aberrant parathyroids have been found at times quite a distance removed from the thyroid.

Lusena was able to produce tetany in nineteen dogs by parathyroidectomy, which was always rapidly fatal, (three days on the average after operation). Walter Edmunds on the contrary had of nine dogs similarly operated on, four which survived. Such apparent discrepancies can only be accounted for by the lack of complete parathyroid removal which is to be accomplished only by the most careful operative procedure.

D. A. Welsh removed the four parathyroids in the cat and obtained severe and fatal symptoms; even with one parathyroid left in situ the experiment was fatal for some of these animals. If two parathyroids were left no serious acute symptoms resulted.

Pineles operated on the ape, cat and rabbit. He noted in the ape that the symptoms were of more chronic character than in the other animals. His operations were done for the most part in two or three stages; tetanic death was obtained only after

*Gley noted 14 variations in the situation of the glandules in 33 dogs, and Alquier found the classic situation of the bodies only 9 times in 15 dogs. Accessory glandules are at any time liable to complicate the work. Vassale found one on the right side of the cricoid at the first tracheal ring, five in the mediastinum, three on the posterior surface of the aorta. Pianca found parathyroids on the aortic trunk. MacCallum, and Thompson and Leighton have repeatedly called attention to extra parathyroids.

removal of all parathyroid tissue, the loss of three parathyroids gave rise to practically no symptoms. In two apes in which all parathyroids were removed, a progressive tetany developed with flaccid paralysis and contraction with final apathy, spasm and death. Apes, from which the whole thyroid and nearly all the parathyroid tissue was removed, showed trophic disturbances, such as falling of the hair, anemia, skin ulcer, and œdema of the upper eyelids. Cats, from which all the parathyroids were removed, died on an average in five and a half days in acute tetany. If, in the cat, the entire thyroid and only a part of the parathyroid was removed, apathy and trophic disturbance appeared, but no muscle spasm. As result of these experiments, Pineles concluded that fatal tetany resulted from extirpation of the parathyroid glands, while trophic disturbances arose from the loss of the thyroid substance.

Walbaum obtained results similar to those of the authors previously cited. His results will be dealt with more fully in the chapter on parathyroid transplantation, as will also the results of Biedl whose work on apes, as well as on the dog and fox, is in line with that previously cited.

We may mention in passing that fatal results have been obtained following parathyroidectomy in birds by Doyon and Jouty, and in the turtle by Doyon and Kareff.

MacCallum performed either complete or partial parathyroidectomy on twenty dogs. His classic description of the symptoms in the parathyroidectomized animals is as follows: "Beginning with symptoms of unrest and anxiety with slight twitchings of the muscles here and there and fibrillary tremors of the tongue, the animal rapidly passes into a state in which the most violent tetanic spasms of all the muscles occur. The dog is able to walk at first but rather stiffly, the hind legs being especially awkward and beyond his control, frequently with a sudden twitch, they slip from under him and bring him down upon the floor. Sometimes in walking about or climbing stairs the dog suddenly falls to the floor in an epileptiform convulsion, the legs are stretched out rigid, the head stretched forward, all the muscles of the neck being thrown into a tetanic contraction—breathing stops for a few moments and is then gradually resumed, the legs finally relax and the dog recovers and walks about again. Usually however, the onset of tetany is more gradual and continuously progressive and from the condition in which spastic walking is possible the dog goes on to that stage in which, with all the muscles rigid and twitching violently, he is unable to stand at all. The most violent trismus with snapping of the jaws appears and the tongue is often bitten; saliva pours from the mouth; all the facial muscles twitch and the eyes project from the fact that the upper lid is much retracted. Respiration is profoundly affected and the dogs appear to stretch out their heads, panting for breath. The rate of respiration is greatly increased, even up to 200 or 250 a minute. With this there is no sign of cyanosis and the blood is readily arterialized by shaking up in the air. Exhaustion soon supervenes and the convulsions become less violent and the respiration less rapid, so that if the animal does not die in the height of the attack he lies relatively quiet for a time before death."

Vassale and Donaggio found in the spinal cord of six parathyroidectomized dogs a microscopic alteration (after Mueller's fixation) which they considered a degeneration in the crossed pyramidal tracts identical in situation with that following ablation of the motor cortex, and also a similar change in the posterior tracts. This apparent degeneration, however, could not be demonstrated microscopically with either the Marchi or the Weigert-Pal method. With a nigrosin stain the axis cylinders showed swelling and a granular appearance, and the myeline sheath showed atrophy and did not stain well.

Russell examined the brain and cord of seven dogs which died of tetany after parathyroid removal and found rather extensive chromatolysis, shrinkage and distortion of the pyramidal cells and increase in the number of neuroglia cells. He concluded that the anatomical alterations were sufficiently well marked to afford a basis for the functional changes which led to tetany.

Edmunds also found changes in the brain and cord of parathyroidectomized dogs. The Nissl bodies were no longer defined; chromatolysis was striking. Sometimes the substance took the stain deeply; in some cells the chromatophilous substance was absent. Swelling of the nucleus and various stages of destruction was observed. The changes are similar to those observed after acute poisoning.

Alquier and Theunveny found that in dogs after partial parathyroidectomy the menstruation periods were less frequent and duration brief, and conception more difficult to obtain. Study of the ovaries failed to show any changes after these operations.

Manca reports the observation of changes in the kidney in various animals after complete thyro-parathyroidectomy. These changes are not specific and appear sometimes in parenchymatous, sometimes in interstitial, form.

Christens may also be cited as contributing to the etiology of the parathyroid glands in the production of tetany by experiments on the cat and goat.

Berkeley has removed the parathyroid glands in over seventy-five rabbits, seven dogs and fourteen cats. While he usually obtained lethal results, he sometimes noted recovery in the animals even after they had exhibited severe symptoms. He concluded that in these instances a remnant of gland left behind had time to hypertrophy.

Erdheim has contributed one of the most interesting, important and complete articles that have appeared on the subject of postoperative tetany in parathyroidectomized animals. His experiments include partial and total operations in fifty rats. The parathyroid glands were destroyed in these animals by a fine cautery.

Erdheim made careful serial microscopic sections of the neck organs in all these cases exhibiting tetany and demonstrated conclusively the presence of thyroid and the absence of parathyroid; thus establishing beyond a doubt the parathyroprivic nature of the tetany.

Different grades of tetanic symptoms appeared following his operations. Usually symptoms were noted in the first twenty-four to thirty-six hours, consisting of tremor and spasm, continual movement of the whole body musculature, shaking, tonic spasm, and status epilepticus. In twenty-nine rats both parathyroids were destroyed (this animal possesses only two parathyroids), and, in all but two cases, tetany appeared in between three and seven days. In some of these animals where a third (accessory) parathyroid was found in the apex of the thymus, this glandule seemed to have no influence on the course of the tetany.

In twelve of these cases where total parathyroidectomy was performed the death of the animal was delayed, occurring in fifty-four to one hundred and sixty-two days. In these cases the tetany showed an outspoken chronic character. In addition, in these twelve animals, there occurred notable trophic disturbances, especially in the incisor teeth. Enamel defects showed themselves as white flakes on the normally yellow colored tooth. In addition the teeth became brittle, and gave rise to considerable pain if broken off within the alveolar process. Gangrenous stomatitis was noted in the lower jaw about the broken off roots while the teeth of the upper jaw increased in length. Erdheim considered these trophic disturbances an absolute constant symptom of tetany, due to a lack of calcium deposit in the growing tissue. In addition cataract formation was observed in the rat.

If in Erdheim's animals one-half a parathyroid was left behind, no tetany at all, or only very mild tetany, appeared. In eight cases only one parathyroid was removed, and in a third of these cases there were seen only slight indications of tetany. In eight rats a part of the thyroid was removed without injury to the parathyroids and in these cases no sign of tetany or of cachexia appeared. This work of Erdheim's, in addition to proving conclusively the tetany parathyropriva, is especially significant in calling attention to the trophic disturbance that may occur as the result of a partial loss of parathyroid tissue.

Alquier has observed the classic results following parathyroidectomy in a considerable number of dogs, the symptoms appearing from three to five days after complete ablation of the parathyroid glands. This author calls attention to the care that must be used in speaking of hypertrophy of the parathyroids, as he finds great variation in size under normal conditions (some authors have stated that if two or three of the glands are removed the ones left behind undergo hypertrophy). Alquier states that he attempted to produce hypertrophy, and has studied histologically glands left behind from several days up to six months, after a part of the glands have been removed, and he is unable to state with certainty that any hypertrophy takes place.

Hagenbach found that in the cat it was possible to extirpate the thyroid plus the inner parathyroids and leave the outer. When this was done the parathyroids left behind protected the animal from tetany. Later removal of the remaining parathyroids was followed by pronounced tetany. This author found that the parathyroids did not act vicariously for the thyroid, as a typical cachexia thyropriva developed after the first operation. Hagenbach insists that functionally, as well as anatomically and embryologically, the thyroid and parathyroid are separate organs.

Frommer's experiments have confirmed the work of other investigators. These will be referred to in more detail later on. Segale has also published the results of much experimental research on these bodies and discusses these results from a metabolic standpoint. This author states that tetany, although of frequent development after parathyroidectomy, is not a fundamental symptom. After parathyroidectomy such profound disturbance of metabolism occurs that all efforts on the part of the organism to repair it are absolutely ineffectual. He emphasizes the importance of a cachexia strumipriva due to the removal of the parathyroid glands.

Pfeiffer and Mayer have also studied extensively post operative tetany in a number of animals. In twenty-nine dogs it was found that the full-grown animal developed tetany on the average in forty-three hours after removal of the parathyroid glands. The longest latent period in the adult dog was sixty-three hours, the shortest twenty-eight hours. In four "goitre" dogs the latent period was somewhat shorter, symptoms appearing as early as sixteen hours after the operation. In puppies the latent period was prolonged to an average of sixty-nine hours, and the animal died on the average in a hundred and ten hours after the operation. These authors also operated on twenty-four rats, removing the parathyroid on one side in six cases, and on both sides in eighteen cases and observed chronic and acute forms of tetany similar to those described by

Erdheim. In addition, the parathyroid glands were removed from sixty-eight mice, on both sides in sixty-three, on one side in five. The latter showed no notable symptoms, but thirteen of the former developed the typical tetanic symptom complex and death.

Iselin has extirpated the parathyroid glands in young rats (five to twelve weeks old). Seven of these animals after excision of the parathyroids developed acute tetany and death within two days, showing that the young rats are much more susceptible to this injury than the full grown animals. Still more susceptible are young rats born from parathyroidectomized parents. These animals survived operation usually only four hours, and died in epileptiform fulminating tetany. This work is significant in regard to its bearing on children's tetany.

A second article of this same author has to do with the body development of the young rats which have survived partial parathyroidectomy. In some of these animals a chronic form of tetany developed which showed itself through apathy, trembling and continued moderate paralysis. Later nutritional disturbances, fracture of the teeth, the result of alveolar periostitis, and fistula formation appeared. Moreover, these animals acquired a roughing of the fur and suffered loss in the whole body development.

Berkeley and Beebe have obtained the following results, which are too positive to need discussion "The entire thyroidparathyroid apparatus has been removed, a complete thyroparathyroidectomy, with the result that the animals have almost invariably developed symptoms of tetany in twelve to forty-eight hours. In two cases, after what was supposed to be the complete operation, there was no development of symptoms and the animals were kept in one instance for six weeks, and in the other for some months without symptoms. Probably an accessory parathyroid not removed was responsible for the nondevelopment of symptoms in these cases, although no such gland was found at the autopsy. Thirty-four dogs were operated upon in this group."

Fig. 71. Parathyroid glandule sixteen days after mass ligation showing fusion of masses of degenerated parathyroid epithelium. (Thompson and Leighton.)

A second group of sixteen animals having a complete thyroparathyroidectomy were fed or inoculated with thyroid proteids, in order to determine whether provision of thyroid function would modify the development of symptoms. Even the hypodermic injection daily of the extract of two normal dog's thyroids had no effect in retarding the development of symptoms.

A third group of eighteen animals was submitted to operation by resection of a portion of the glands (thyroid and parathyroid combined); in one set the anterior one-half, in the other set the posterior one-half. In resecting the anterior one-half of the gland, careful search was always made for the parathyroid on the external surface of the thyroid, and care was exercised to make the dividing line posterior to this glandule, so that in a successful removal of the anterior one-half all the parathyroid tissue would be removed and yet an amount of thyroid tissue sufficient to provide for the physiological need of the animal would remain in a normal functional condition. In six out of eight cases in which four parathyroids were seen at the operation and removed with the anterior half, the characteristic symptoms of tetany developed in the usual time. Subsequent removal and section of the thyroid tissue remaining showed it to be in a physiological condition. In those cases in which the posterior half was removed, the dividing line being posterior to the external parathyroid, no symptoms were observed.

In a fourth group of nine animals an attempt was made to destroy the parathyroids with the actual cautery, with a minimal amount of injury to the thyroid. In four of these animals four parathyroids were found and cauterized and in these the operation was followed by the characteristic symptoms of tetany. The cautery caused only a small amount of injury to the thyroid. Microscopic section showed no pathological condition of the latter gland and its blood supply was not impaired, so that there can be no doubt that it was capable of functioning in these cases, but the symptoms of tetany came on promptly and were quite as characteristic in this group as in the others having a more complete operation.

Thompson, Leighton and Swarts, in connection with their work on ligation of the parathyroid artery referred to in the first chapter, have shown that a single parathyroid glandule is sufficient to maintain life in a dog, but when this is removed the animal quickly dies in tetany.

These authors selected dogs in which four normally situated parathyroids could be found and at their first operation three parathyroids were excised and one glandule (with its artery ligated), left in place. Following such operation no symptoms, save in a few instances slight transient tetany, occurred, When the sustaining glandule was excised, however, the dog died in tetany. In three dogs removal of the fourth glandule did not result in tetany and autopsy showed extra parathyroids in these latter instances; so that not infrequently it may happen that four superficial parathyroids may be excised in this animal and extra glandules (usually intrathyroidal) protect the animal from death. As long as a single glandule remains the animal does not exhibit tetany. When this last glandule is removed the animal dies in tetany.

EXPERIMENTS OPPOSED TO TETANY.

In consideration of the vast amount of proof that has been brought forward by so many skilled investigators in favor of postoperative tetany as a result of the removal of the parathyroid glands, it seems hardly necessary to quote the few articles that have appeared from time to time in opposition to this theory. That doubt should arise, however, is quite natural from the small size of the parathyroids and the seeming inconsistency that such little organs could be of such vital importance. As Erdheim says: "Between the small size of the parathyroid glands and the severe, often fatal result of their removal there is such a striking contrast, that the function of these bodies strikes us as something marvelous, and we are apt to maintain a skeptical attitude thereto."

Blumenreich and Jacoby have denied the influence of the parathyroids in the production of the tetanic symptoms described by other authors. A careful examination of their work fails to show that they removed all the parathyroid tissue in their experiments, and we know that a single parathyroid left intact is sufficient to prevent the development of tetany. In twelve rabbits these authors removed the thyroid and two parathyroids, in five animals the thyroid and one parathyroid, and in four only the thyroid. They found no difference between removal of the thyroid alone and the thyroid with one or two parathyroids.

Blum has declared that in his opinion the parathyroids are nothing more than embryonic thyroid possessing no particular function in the body. He rests this assumption, however, on the work of Kishi which has been severely attacked by Erdheim as showing sovereign ignorance of the work of previous investigators on the embryology and anatomy of these glands Kishi seems to be absolutely unaware of the presence of the internal parathyroids in cats and dogs and his work, therefore, is practically without value.

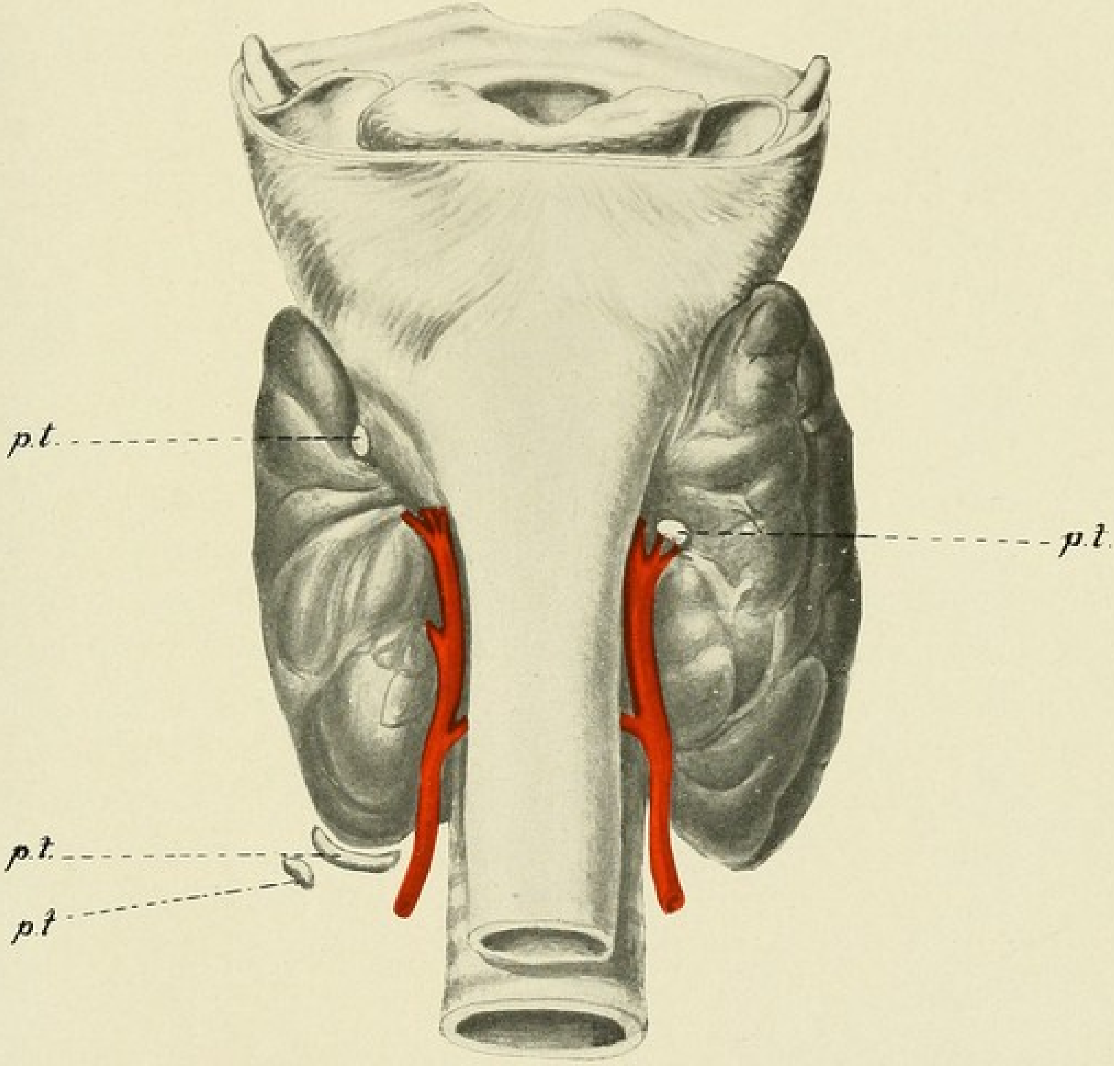
As a further proof of his assumption Blum offers the results of his experiments on a number of dogs from which the greater part of the thyroid and (presumably) the parathyroids were removed without obtaining tetany. However, in several of these dogs on which a second operation was performed for the extirpation of the tissue left behind death in tetany was obtained. Blum describes changes in the thyroid that have been left behind consisting in an extraordinary cell increase which caused them to appear similar to parathyroid in their structure and he thinks that the small thyroid rests were able to perform the duty of both thyroid and parathyroid. In this conclusion he has few supporters and his technic may be criticised as not definitely proving the removal of all parathyroid tissue.

Bayon has, incidentally in the course of other work, made the observation that thyro-parathyroidectomy is not fatal for the rabbit. Apparently this author has not taken into consideration the extrathyroidal parathyroids in the rabbit and in his experiments failed to remove two parathyroid glands.

Caro thinks that the accidents observed by previous authors cannot be separated into those due to loss of thyroid and those due to loss of parathyroid. His experiments on dogs led him to conclude that a very small amount of thyroid protected the animal from tetany, but when these remnants were removed death of the animal in tetany resulted. These thyroid remnants he describes as being entirely free from parathyroid tissue. This author attacks especially the work of Erdheim, but as Schirmer, who has critically reviewed both the results, states: "If one compares the large amount of material of Erdheim worked out with such rare industry, and such minute exactness in its technical and histological detail, with the work of Caro's which lacks weight in many essential points and leaves important details to incomplete footnotes, one will be convinced that the attack of Caro will have little effect in weakening the results of Erdheim's extensively compiled evidence."

Vincent and Jolly have also reached results that differ considerably from those of previous investigators and are not so easy of criticism since the work appears to have been carried out with much care and exact knowledge of anatomy on a large number of animals of many different species. These investigators did obtain tetany and death in a number of instances after parathyroid removal, but not with the same uniformity as did the other investigators that we have previously quoted. These authors conclude that neither the thyroid nor parathyroids are essential to life since it is frequently possible to remove either or both without causing death. Out of fifteen cats on which the complete operation was performed ten died with the usual "nervous symptoms." Of the five surviving animals three showed grave "nervous symptoms." One cat showed no symptoms, and a young cat ceased for a time to grow but otherwise remained normal. These authors used the term "nervous symptoms" rather than "tetany." These symptoms are described as a curi-

PLATE XXXVIII



P. T. PARATHYROID GLANDULES. TWO INFERIOR GLANDULES FOUND ON THE LEFT; THE INFERIOR ON THE RIGHT SIDE NOT FOUND.

ous "paw-shaking" and some malaise. This is followed in rapid succession by "tremors," stiffness of gait and convulsions. "Even in a quiescent state, the forelegs tend to be flexed, while the hind legs are extended, a position exaggerated during the convulsions."

Out of five dogs operated on by these authors typical tetanic symptoms were produced in all save one Although these authors state that in this case there cannot be the slightest doubt that thyroids and parathyroids were completely removed, the not infrequent finding of accessory parathyroids, at times considerably removed from their normal situation, as we have previoulsy chronicled, makes it impossible for us to accept such a statement as absolute. In four foxes from which thyroids and parathyroids were removed all died in severe tetany, the symptoms appearing with remarkable rapidity. In seven monkeys on which the same experiment was performed none died and in only two were tetanic symptoms observed. Their experiments on rats while negative were too few to admit comparison with the extensive work of Erdheim on this animal. Finally, following the complete operation upon four guinea pigs, no symptoms of any kind were observed. As the authors themselves state the extreme variability in the anatomy of the parathyroids in this latter animal has rendered their experiments rather unsatisfactory.

In a later article these authors continued their experiments with results similar to those just recorded. One monkey died in convulsions on the day following the operation, but the authors state that in this case the recurrent laryngeal nerve on one side was included in a ligature. Of two prairie wolves one developed a convulsive attack with typical rapid respiration which lasted for two days but subsided and death did not occur until thirty-eight days after the operation. The other animal showed no symptoms. Two badgers exhibited no symptoms after "complete" operation.

A careful analysis of this work fails to show wherein the authors are justified in their somewhat sweeping assertion that neither thyroids nor parathyroids are essential to life. While their results have not been so striking as those of some of the previous investigators, still it will be noted that a great many of their experiments show the same fatal outcome that we have been led to expect following the removal of the parathyroid glands. Where such outcome was not forthcoming it was usually in animals in which the distribution of the parathyroid tissue has not been carefully worked out and we can only assume in such instances that the parathyroid glands were not removed with absolute completeness. In fact, since the publication of this work Harvier and Morel have shown that in the cat accessory parathyroids are to be found in the thymus in fifty per cent. of cases.

While it is impossible to note the opinions of all authors who have thrown their argument to either one side or the other of this question, we may note that Munk has laid considerable stress on the cases of survival after the removal of the thyroid and parathyroid glands and he states that in his opinion the tetany observed in such cases is the result of nerve injury; a statement that is disproven by the numerous experiments in which a single parathyroid left behind will protect the animal from tetany despite extensive trauma.

CHRONIC DISTURBANCES DUE TO PARTIAL LOSS OF THE PARATHYROID GLANDULES.

In the emphasis that has been put upon the tetany following the complete loss of the parathyroid glands, nutritional disturbance following parathyroid operations has been given scant attention, although trophic disturbance following interference with, but not complete loss of, these glandules has been casuistically noted since the time of Gley, who stated that in both dogs and rabbits he had sometimes observed only nutritive disturbances after parathyroidectomy.

Vassale and Generali noted that one of their parathyroidectomized cats survived for two months with symptoms of chronic cachexia. Pineles described trophic disturbances in the ape consisting of falling of the hair, anemia, skin ulcers and œdema of the upper eyelids (in these cases thyroid as well as parathyroids was removed). Also in cats following similar operation apathy and trophic disturbances were observed by this author. Walbaum recounted cachexia appearing in rabbits with nutritional disturbances, especially roughening of their coats, in the course of his experiments. Segale insisted that we must regard cachexia as depending especially on the removal of the parathyroid glands. MacCallum has observed cachexia as a result of parathyroid removal in certain of his dogs, and in three sheep he reported that a marked emaciation and apathy followed parathyroid removal. Vincent and Jolly noted cachectic symptoms in a number of their animals operated on.

Pinto found that while a total ischemia of the thyro-parathyroid apparatus was followed by tetany in from sixteen to thirty-one hours, if it was longer continued, symptoms of tetany and cachexia or only pure symptoms of cachexia were observed.

The work of Erdheim, who obtained chronic nutritional disturbances, especially enamel defects leading to fracture of the teeth, in parathyroidectomized rats, is especially significant along this line. We have already quoted his results at length.

That disturbances of a trophic nature may occur in connection with partial loss of parathyroid tissue, then, is a well established fact, and its occurrence, apart from tetany, has been especially studied by Thompson and Leighton, in twenty dogs. In these animals the parathyroids were gradually destroyed by mass ligation instead of excising them as had been done by previous experimenters. These authors state: "Following the ligation of the parathyroid glandules in the dog one of two things may happen: (a) Functioning islets of gland tissue may persist, keeping the dog alive for a considerable length of time; (b) The glandules may eventually be replaced by dense fibrous tissue and the dog die. In either event a train of symptoms of a trophic nature arises, entirely different in character from the severe acute tetanic manifestations that follow complete parathyroid excision in these animals." This brings two facts into prominence that are worthy of note.

First, which is important for practical surgery, that ligation of the parathyroids, whereby they are left in situ with their usual blood supply destroyed, does not always destroy the glandules and is not the same thing as excision. Second, that by this ligation of the parathyroids, disturbances of nutrition, which may ultimately end in death, can be brought about without producing any tetanic symptoms whatso-

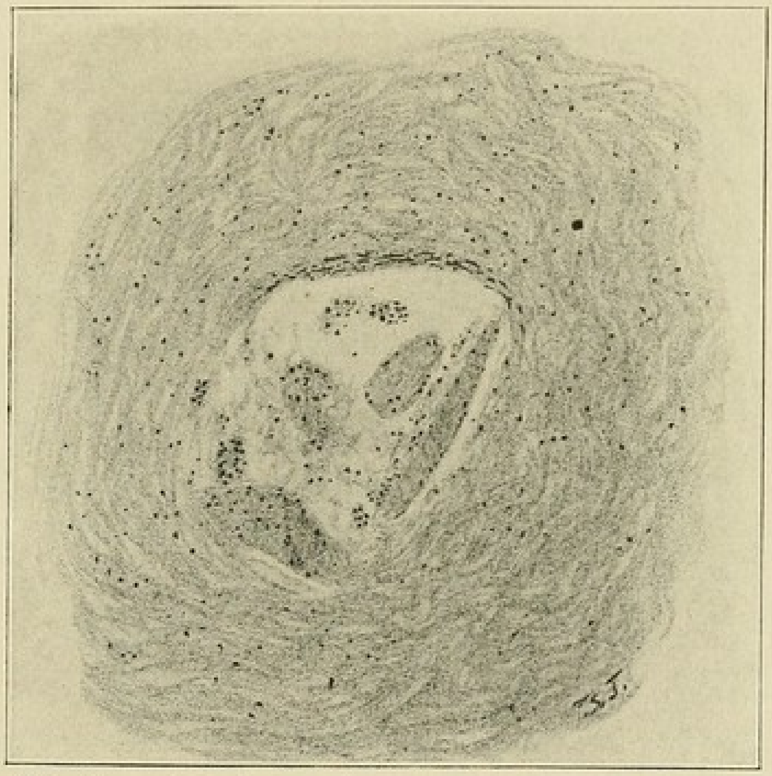


Fig. 72. Complete destruction of parathyroid by mass ligation, forty-eight days. Death in cachexia with no tetany followed this gradual complete destruction of parathyroid tissue.

ever, although the death can be definitely proven to be due to loss of the parathyroid glands.

In these experiments the glandules, after partial separation from thyroid or capsule and identification of the parathyroid artery, were lifted up by wide rat-tooth forceps, which were crushed into the underlying thyroid tissue, and a strong linen ligature passed around the whole mass. This procedure seemed to approximate the conditions of accidental injury that might occur in connection with thyroid operations whereby granulation tissue could form from injured tissue about the parathyroids.

The following is a brief summary of the results obtained in these dogs where chronic death with nutritional disturbances replaced the tetany that usually occurs subsequent to loss of the parathyroids.

Operation: ligation of two parathyroids on right side. Removal of thyroid (with parathyroids) on left side. Dog recovered from operation and showed no symptoms for several days. On fifth day animal slept a good deal and took food sparingly. On the sixth day dog appeared weak and refused food. Died on the seventh day very quietly, but with the development of a slight tremor just before death. Microscopic examination of the ligated parathyroids showed them to be replaced by fibrous tissue.

Operation: ligation of two parathyroids on right. Removal of thyroid (with parathyroids) on left. Dog recovered perfectly from the operation and lived thirty-three days. During this time it progressively lost in weight and strength. The animal lay curled up in his cage in an apathetic condition, refused food, and was finally found dead. At autopsy the ligated glandules were found completely replaced by fibrous tissue.

Operation: five parathyroids found (the left external double) and all ligated. Despite the apparently complete operation the dog showed no acute symptoms. The animal lost rapidly in weight, however, and a slight conjunctivitis developed. Forty-four days after first operation neck was again opened and a large (hypertrophic?) parathyroid found on the right (evidently analogous to the double glandule of the left side) that had escaped at the first operation. This was ligated. Ligatures of the previous operation in place and only connective tissue thickening to be seen macroscopically about them. Neck closed up. Dog soon began to show marked weakness, could scarcely stand on his feet a few days after the operation, and took food sparingly. Despite this great emaciation and weakness the dog remained in this condition for eighteen days, getting toward the end so weak it was difficult to tell whether it was living or dead. The animal lay curled up and sleeping for days without change of position and without taking food. Finally found dead in this position.

The conclusions reached as a result of this work, are: "Following the gradual destruction of the parathyroid glandules in the dog a train of symptoms arises different from those obtained by parathyroid excision. After ligation of all parathyroid tissue the dog passes the time limits of tetanic death that occurs after excision of the glandules, practically without symptoms. Gradually, however, chronic symptoms, trophic in nature, arise. These consist in gradual but progressive loss of weight and strength, greatly diminished resistance to infection, and a final stuporous condition ending in death without tetany.

These nutritional disturbances are as marked when the thyroid is not injured as they are when the thyroid is removed on one side.

These observations should lead to a modified consideration of diseases that are supposed to be hypoparathyroid in origin, and suggest a revision of the epitomized statement of Jeandelize, "that insufficiency of the thyroids causes nutritional disturbances, while insufficiency of the parathyroids causes acute convulsive troubles." The preferable statement regarding the parathyroids as the result of this work is, that while sudden loss of the parathyroids results in acute convulsive troubles, slow destruction of the same gives rise to chronic nutritional disturbances, which eventually end in death without tetanic manifestation.

The recent observations of Iselin on the disturbances of nutrition, and even the prevention of development, in young rats following partial parathyroidectomy make necessary the consideration of these bodies as having an influence on retarded body development.

CHAPTER XVIII.

SURGICAL ACCIDENTS IN MAN DUE TO REMOVAL OF THE PARATHYROID GLANDULES.

Let us now return to the more practical side of this question, namely: what role do the parathyroid glands play in the tetany sometimes observed after operations on the thyroid gland in man? Accidents following such operations, to which we have already casually referred, have fortunately been reduced to a minimum, but formerly they were not so rare.

Weiss, in 1883, was able to collect thirteen cases of postoperative tetany from the literature. He maintained that the symptoms were the result of injury to the blood vessels and their accompanying sympathetics. Because of the injury to these an irritation was set up in the anterior horn of the spinal cord which expressed itself in the tetanic symptoms. This theory, with certain modifications, had some supporters until the work of Reverdin and of Kocher appeared.

Reverdin and Kocher demonstrated that the symptoms were a result of the goitre removal and that one was able to escape tetany and cachexia strumipriva by leaving in place a part of the thyroid gland The part naturally left behind was the posterior border and therefore by this method the parathyroid glands were not sacrificed. The importance of this observation may be emphasized by the fact that before that time such observations as the ten cases of tetany in thirty-eight thyroidectomies by Billroth, three cases out of seventeen operations by Reverdin, and four cases out of seven by Mikulicz were reported.

It was no longer ago than the early eighties that such reports as the preceding, and such graphic descriptions as follows, might be read as the result of thyroid operations: "Some days after thyroidectomy, ordinarily on the third or sixth day, sometimes a little earlier or later" (at the end of four months in a case of Kocher's), "the patient was seized with convulsions of the extremities, more often the superior, which were sometimes preceded by tingling in the fingers or twitching of the muscles. Usually chronic contractions appeared, the hands closed with such violence that the nails often penetrated the skin. The limbs were sometimes contracted so that it seemed they were going to break; even the diaphragm was at times involved."

Kocher has noted epileptiform crises of short duration, followed by loss of consciousness. Crises renewed themselves as often as fifteen times a day. Sometimes the tetany ceased rapidly after a duration of eight to fifteen days, or at times it was prolonged for months and years with remissions. Death in these cases seemed to result from a dyspnœa which was not allayed by tracheotomy.

It was sometime before the fact was brought to light that these postoperative tetanies in man were due not to the loss of the thyroid gland, but to the loss of the parathyroid glands. And the acceptance of the functional significance of the parathyroids has been brought about only by a great amount of work; to the finishing touches of which we are especially indebted to the Vienna School. Biedl, Eiselsberg, Erdheim, and Pineles may be mentioned among those who have given special attention to this question.

Among the first to study the relation of the parathyroids to goitre was Benjamins, who examined the parathyroids in twenty cases of goitre which had been dealt with surgically. While he found no histologic changes in the parathyroids, as we have previously noted, nevertheless he brought forward certain clinical observations relating to the removal of these glands. Out of nine cases in which clinical histories were obtained, parathyroids were found in five that had been removed with the thyroid; in the other four cases the parathyroids had not been removed. Of the former five cases only one failed to develop tetany; of the latter there was no tetany in any of the cases.

This was in 1902, and it was about this time that Jeandelize made his significant statement that insufficiency of the thyroid causes chronic nutritional disturbances, while insufficiency of the parathyroids causes acute convulsive disturbances. This statement was at once upheld by Biedl, Pineles and Kocher.

Pineles collected from the literature sixteen cases of tetany following partial parathyroidectomy and with a clear idea of the relationship of the parathyroid glands to postoperative tetany in mind, this author has given us a very complete discussion of this question. He discusses separately the total and the partial thyroidectomies, and has collected fifteen cases in which partial removal of the thyroid gland was followed by more or less severe symptoms of tetany. These cases are tabulated as follows:

Observer	Operation	Tetany appeared after Operation	Tetany—Continued
Szuman....	Lateral thyroid lobes....	Fourth day...	Four months.
Hoffman...	Both thyroid lobes......	Third day.....	Fifteen days.
Turetta....	Both thyroid lobes......	Fifth day......	Died on eighth day.
Czyhlarz...	Both thyroid lobes	Third day......	
Eiselsberg..	Both thyroid lobes	Third day......	Death on sixteenth day.
Westphal..	Sparing of isthmus and upper pole............	Second day...	Six months.
Eiselsberg.	Sparing of isthmus and one upper pole.........	Second day...	Seven days.
Eiselsberg.	Sparing one upper pole...	Fourth day...	Ten days.
Eiselsberg.	Sparing one upper pole...	Fourth day...	One year.
Meinert....	Right lateral lobe.......	Fourth day...	Fourteen days and recurrence with pregnancy.
Kummer....	Right lateral lobe.......	....	One year.
Eiselsberg..	Right lateral lobe.......	Third day......	Nine days.
Schilling...	L. lateral and middle lobes.................	Four months..	Eight days.
Bruns.....	Nodules and cysts extirpated..................	Fourteen days.	Death on 18th day.
Eiselsberg.	Tumor	Second day...	Mild facialis tetany.

It is to be noted that in the first six cases only the isthmus of the thyroid was left behind. The lateral lobes of the gland on both sides were removed whereby a good opportunity for removal of parathyroids was offered. Likewise in the second group where the isthmus and the uppermost part of a thyroid lobe were spared parts were unfortunately selected that were not in relation with the parathyroid glands and no protection was offered these bodies by leaving such portions of the thyroid behind. Why tetany should arise in the last three cases where a lateral thyroid lobe was spared in one side is not easily accounted for, but an examination of the detailed reports of these cases shows that in the first the operation was undertaken during the course of pregnancy; in the second the thyroid lobe left behind is described as very small; and in the third only a mild tetany was present which cleared up completely in nine days.

From these observations Pineles concluded that it is the same in man as in animals, that when the parathyroids are spared no tetanic symptoms follow a thyroid operation. The cases developing tetany are those in which such parts of the thyroid only were spared as did not protect from removal of the parathyroid glands. This view was supported by Escherich who clinically confirmed the rarity of tetany following operations, in which loss of these glandules was more carefully guarded against.

Kocher has strongly differentiated between the symptoms arising from thyroid insufficiency, and those the result of parathyroid insufficiency. The latter symptoms he classifies as an intoxication, making its appearance as a tetania parathyropriva.

Perhaps the most practical contribution to this important question is the work of Erdheim, who examined histologically in serial sections the neck organs in three cases from patients dying of tetany after partial double thyroidectomy. In all three cases, although some of the thyroid had been left behind, all four parathyroids had been removed (in one case two very tiny accessory parathyroids were present). From this unequivocal result Erdheim concludes that it is the plain duty for the surgeon of the future to assure himself that the parathyroid glands are spared in thyroid operations.

The rarity of tetany today following such operations is due to the technical methods by which the thyroid is now removed. Especially to be commended is the subcapsular procedure of Dr. C. H. Mayo, which was suggested primarily to avoid injury to the recurrent laryngeal nerve, and the ultra ligation of the thyroid arteries as is recommended by Halsted. So it has come about, as we have noted in detail in the first chapter, that tetany following thyroid removal has been reduced to less than one-half of one per cent for all cases.

In discussing the paper of Erdheim, Eiselsberg reports that up to 1890 there were in his clinic twelve cases of tetany as a result of complete thyroid extirpation. In four of these cases the patients died with violent symptoms; three had chronic tetany which kept recurring, and one recovered. In eighty partial extirpations there were only two cases of tetany and those were not severe. Since 1890 he had observed only one case of deadly tetany but there had been sixteen light tetanies following goitre operation.

In this country postoperative tetany is less frequently encountered. Frazier reports the result of personal inquiry from fifty-four surgeons representing from 1,500 to 2,000 goitre operations. Only eight cases of tetany were reported, three of which were fatal. Of the remaining five, one was transitory, and one was described as a slight case. C. H. Mayo had had but one slight tetany in connection with his numerous goitre operations.

Kocher reports that in his last 1,000 goitre operations tetany has been observed only five times. Moreover, these five cases were all secondary operations where firm connective tissue adhesions complicated the operative technic.

Even when tetany has occurred following goitre operation a means is now offered for its control by the administration of parathyroid gland extracts, calcium salts and transplantation; the details of which will be considered in a later chapter.

CHAPTER XIX.

THE RELATION OF THE PARATHYROID GLANDS TO MEDICAL TETANY.

A loss of parathyroid function was first suggested by Jeandelize as the cause of tetany in adults and later emphasized by Pineles, who grouped together thyroid tetany, occupation tetany, tetany of childbirth, children's tetany, and gastric tetany. This identity of different forms of tetany was accepted by Chvostek, who stated that for all, only one cause could be considered, namely, functional diseases of the parathyroid glands.

It is well to have a definite subdivision of these various tetanies in mind for purposes of discussion, and the following grouping of Frankl-Hochwart is perhaps the best. This author divides the tetanies as follows: Tetany following or accompanying certain infectious diseases. Tetany in cases of gastric dilatation with stagnation of the stomach contents. Tetany in infants and children. Tetany occurring in connection with certain trades (*Arbeiterstetanie*). Tetany associated with osteomalacia, and rickets. Tetany occurring in the course of pregnancy and lactation.

In all these tetanies there is an increased excitability of the central nervous system which is shown by quantitative tests with faradic and galvanic currents, hypersusceptibility of the facial nerve being usually easily demonstrable. There may bé spasmodic rigidity of the muscles, sometimes with such violent twitchings as to constitute an epileptiform convulsion.

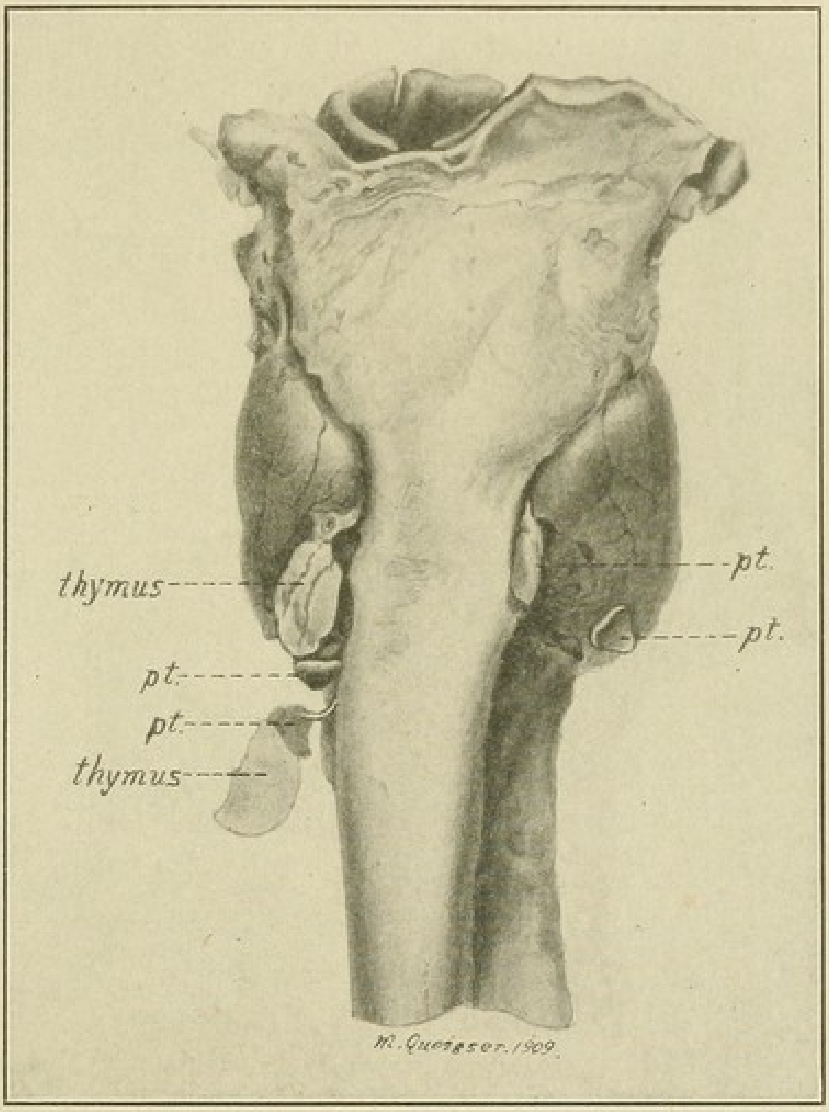


Fig. 73. On the left, masses of thymus tissue are seen in connection with the parathyroid glandules. These aberrant thymus fragments are not uncommon in infants and may be mistaken for the parathyroids themselves.

Fibrillary tremors of the tongue and rigidity of the jaws may be present. Quickening of the pulse and elevation of the temperature are sometimes observed.

Pineles was one of the first to call attention to the uniformity of symptoms in postoperative tetany in man and animals on the one side, and in the different forms of idiopathic tetany on the other side. This uniformity, according to Pineles, points towards a specific intoxication common alike to all these various tetanic forms, and he brings forward as the causal factor in these conditions insufficiency of the parathyroid glands.

Chvostek has accepted the view of Pineles concerning the general identity of all forms of tetany, the cause of which may be found in the functional disturbances of the parathyroid glands brought about usually by disturbances of circulation in these organs. The typical symptoms can arise through a special poison which so acts that a specific tetanic reaction may be brought about in a susceptible individual by an injury, which in another person would not give rise to tetany. This susceptibility to tetany may be congenital or acquired.

Chvostek also believes that tetany, just like goitre, is epidemic in certain localities and preponderates especially at certain definite seasons. Tetany is frequent, for instance, in Vienna and Heidelberg, while it is rare in Paris, although some years ago it was common in that place. In Vienna tetany is most frequently observed in the months of March and April, occurring most frequently in shoemakers and tailors. Chvostek states that there is a definite antagonism between goitre and tetany; tetany being rare in regions where goitre is endemic. In the Tyrol, where goitre is endemic, tetany is extremely rare. In a later article Chvostek states that he regards mechanical hypersusceptibility of nerves, first the facial, as an easily demonstrable and essential symptoms of disease of the parathyroids, a fine test which shows functional disturbance of these bodies. The appearance of the facial phenomenon in cases of pulmonary tuberculosis can be explained by the view that tuberculous lesions are in the apex and thus affect the parathyroids. Chvostek's view is supported by the case of Stumme in which a distinct facialis phenomenon was benefited by the removal of a tuberculous parathyroid during thyroidectomy on account of goitre.

In this connection a case that can be included in the tetany accompanying infection is reported by Carnot and Delion, who observed during the terminal period of a pulmonary phthisis various convulsive movements, with loss of consciousness, which lasted several days. The autopsy showed absence of meningitis, the kidneys were practically normal, the thyroid was sclerosed, but especially interesting was the condition of the parathyroids. The inferior glandules showed sclerosis and infiltration, the right superior was not found, the left superior showed extensive caseation.

Frankl-Hochwart has called attention to the fact that persons who have had tetany usually continue to show some symptoms during the rest of their lives.

Gastric Tetany.—In gastric tetany MacCallum has found what appears to be evidence of hyperfunction of the parathyroids. In this case five glandules were found, rather large in size, which showed especially large groups of functioning cells, as well as a considerable development of mitotic figures in the principal cells. The author suggested that in this case the enormously dilated stomach elaborated more material than the parathyroids were normally called upon to neutralize, and that this failure of neutralization of the toxin gave rise to the severe tetany from which the patient died.

Koenigstein also reported a case of gastric tetany in which similar changes in the parathyroids were found, as well as characteristic tinctorial reactions to iodine and Best's glycogen stain that could not be observed in normal glands.

In opposition to this concept Erdheim found the parathyroid glands perfectly normal in two cases of gastric tetany. The first patient was a thirty-eight year old woman, the second a fifty-four year old woman. Autopsy showed marked stomach dilatation in both cases and in both cases the functioning cells of the parathyroids (in contradistinction to the previous cases), were relatively few.

Kinnicutt has reported a case of gastric tetany in which the parathyroid glandules (examined by Opie), exhibited no abnormality. In this case the tetanic symptoms were promptly relieved by calcium salts, but parathyroid nucleoproteid given by the mouth had practically no effect on the nervous system.

Pfeiffer and Mayer have tried to produce gastric tetany in the dog but without success.

Children's Tetany.—We have already noted certain lesions (hemorrhage) of the parathyroid glands that have been found in children exhibiting tetany. It appears that the parathyroids of the infant are disposed toward hemorrhage, which may especially be brought about by intrauterine asphyxia. Erdheim has observed hemorrhage in three cases of infant's tetany, and suggests that while the lesion does not necessarily bring on this condition it predisposes to it. In one of this author's cases, dying in typical tetany, hemorrhage was found in all four parathyroid glands.

Koenigstein has also observed changes in the parathyroid glands in two cases of children's tetany consisting in relative increase in size, hemorrhage and tinctorial differences in the iodine and glycogen reactions.

Thiemisch found the parathyroids normal in three cases of children's tetany. These cases have been criticised, however, as not being representative cases of this condition.

Verebely describes two cases of hemorrhage in the parathyroids of children in which there was no tetany. Escherich describes a case of tetany in a seven year old boy, occurring in the course of a tuberculous meningitis, in which the parathyroids showed marked degenerative changes which might well have led to impairment of function. This author believes that the parathyroid theory of tetany explains in a very positive manner the enormous frequency of tetany in the earliest period of life, and he calls attention to the fact that it is not necessary to demonstrate anatomic changes in the parathyroids in all instances, for a functional deficiency may easily occur without histologic changes being demonstrable.

One of the most valuable studies, and one of the most convincing as regards the parathyroid origin of tetany, is that contributed by Yanasse. He examined the parathyroids in eighty-nine children showing tetanoid conditions, particularly galvanic changes in the peripheral nerves. Hemorrhages in parathyroids were found in thirty-three cases, (37 per cent). Yanasse asserts that the hemorrhages are acquired mainly in postfetal life, perhaps as with

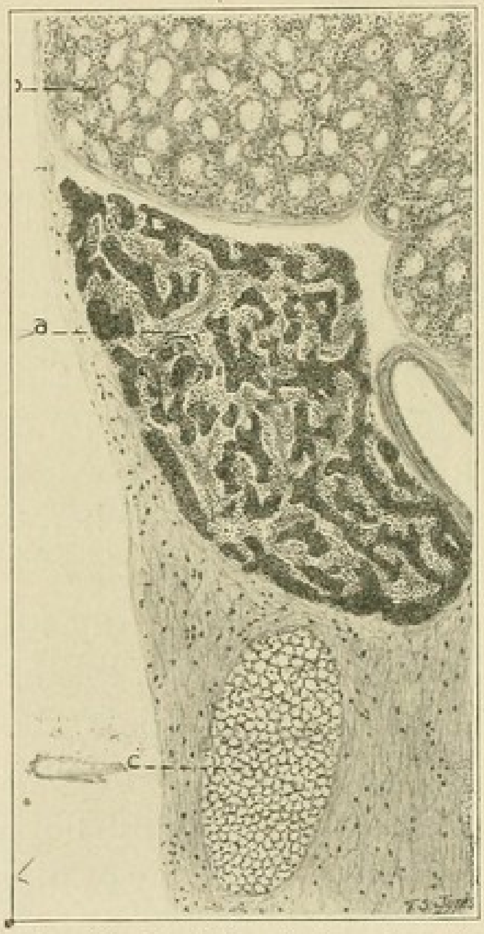


Fig. 74. A parathyroid glandule of the sclerotic type, from a case of infantile atrophy. The dark masses represent the parenchyma; the light areas the increased connective tissue. Above (*b*) is thyroid gland. Below (*c*) is a remnant of the tissue continuous with the interscapular gland. (Magnified 105.)

pleural and pericardial ecchymoses, at the time of birth. Hemorrhages in these glands can be demonstrated with certainty only during the first year of life; after this the possibility progressively becomes smaller and after the fifth year one cannot say from histologic study that hemorrhage had ever occurred. Late hemorrhage, in older children or adults, seldom occurs. Yanasse divides the fifty cases in which the electrical reaction was determined into four groups: Normal galvanic reaction, thirteen cases. In twelve there were four each, in one three parathyroids. Hemorrhage was found in none. Group 2. Anodal irregularity, twenty-two cases; hemorrhage in twelve or 54 per cent. In the ten other cases the age must be considered. Of the twenty-two, nine were in the first year of life and all showed hemorrhages. Thirteen were above one year and hemorrhage was found sparely in three and was absent in ten. Therefore, all ten of the negative cases were of such age that signs of hemorrhage could have disappeared. Hemorrhage was found in eight, or 61 per cent. The other five were all over one year. Group 4. Two cases, one of tetany with meningitis in a child of two and a half years, and one of muscle cramp in a child of three months. Hemorrhage was found in both. Eleven (ten under one year), of thirty-nine cases in which the electrical reaction was not taken showed hemorrhage. Certainly it was not accidental that all cases with normal reactions had normal parathyroids and that all cases with hemorrhage, that were tested electrically, showed abnormal reactions, or clinically forms of spasm. Yanasse concludes that between parathyroid hemorrhage and tetany there is doubtless a connection. The question is, what is this connection? His explanation is as follows: It has been proved experimentally that the parathyroids are poison-destroying organs whose principal function most probably is to neutralize metabolic poisons which are detrimental to the nervous system. Therefore we must recognize in metabolism the origin of the so-called tetany poison, in the nerves the principal tissue attacked by it, and in the parathyroids the organ that neutralizes this poison. The total loss of parathyroids causes in man and animals tetany of which the clinical picture is essentially like that of other forms of tetany. Hemorrhage in the parathyroids does not totally destroy, but only partly damages the glands, hence it is not the actual cause or alone the cause of tetany but it can so act as finally to produce that affection. The poison increases because the parathyroids damaged by hemorrhage no longer exert their usual function. Only in this way can be explained how parathyroid hemorrhage early in postfetal life leads in many cases to tetany much later in the life of the affected individual.

Rickets and Osteomalacia.—It is quite recently that the suggestion has been made that there may be some relationship between the parathyroid gland and these diseases. In the course of both diseases, as is well-known, tetany may occur. The most important fact that has been developed in this line is the observation of Erdheim, who noted the changes in the teeth of rats which we have previously chronicled. Moreover, in these diseases there is obviously some profound disturbance of calcium metabolism, and MacCallum has shown the intimate relation that exists between the parathyroid glands and calcium metabolism. It is from this latter observation that we may hope to solve this question rather than from any distinct changes that have been observed in the glands, although such have been noted. Erdheim found in an autopsy on a case of osteomalacia a noticeable hypoplasia of the parathyroids, but in a second case these glandules were entirely normal. Hecker, who has discussed this relationship, thinks that there is probably some disturbance of the parathyroids in both osteomalacia and rickets and calls attention to the fact that lack of calcium in the organism leads to tetany and that calcium metabolism is doubtless influenced by the parathyroid glands.

Kassowitz has suggested that rickets might be the underlying basis of the tetany of children and Escherich has suggested congenital parathyroid hypoplasia as an etiological factor in rachitis.

Weichselbaum states that he has found noticeable enlargement of the parathyroid glandules in rachitis.

The chronic nutritional disturbances on which we have laid so much emphasis that have been proven in animals to be a result of the impairment of the function of the parathyroid glands must also be borne in mind in considering the parathyroid etiology for these diseases. From a morphological standpoint, however, we have little ground for such assumption. Schmorl who has examined the parathyroids in six cases of rickets found no changes. In three out of four cases of osteomalacia the parathyroids were also normal, but in the fourth case one hypoplastic glandule was found.

Eclampsia, Tetany of Pregnancy and Lactation.—The role of the parathyroids in the tetany of pregnancy was one of the first suggestions pointing towards the function of these bodies. Vassale and Generali, in 1896, noted that partially parathyroidectomized animals, which usually showed only light and transitory tetanic symptoms, were apt to develop severe tetany during pregnancy and the puerperium. Vassale removed from a dog three of the four parathyroids. Eighteen months after the operation the dog gave birth to eight puppies. On the fifth day of lactation it was taken with severe convulsions which seemed to be relieved by taking away several of the puppies and feeding with thyroid extract. The convulsions were renewed, however, and combated anew with the thyroid extract, which was continued to the end of lactation and the dog recovered.

Verstraeten and Vanderlinden had previously noted in a thyroidectomized cat, (partial parathyroidectomy), the appearance of eclampsia at the time of parturition, three months after the operation. The symptoms were severe but were ameliorated by subcutaneous injections of fresh sheeps' thyroid, and, following accouchement, the animal recovered.

Lanz has also observed, without any apparent thought of the parathyroids, that pregnant cats can not withstand so great a loss of thyroid as the non-pregnant animals. He noted that after a considerable amount of the thyroid gland had been resected (which probably included several of the parathyroids), the pregnant cats frequently developed severe tetany. Halsted found that a pregnant dog from which the thyroid had been removed (thyroparathyroidectomy), was taken near the end of pregnancy with tetany and died.

Lange, also operating on cats, who removed four-fifths of the thyroid (including of course a considerable amount of parathyroid tissue), noted that out of ten pregnant animals five died in coma, three after having shown convulsions. The author described renal and hepatic lesions in these animals.

Moussu criticised the preceding experiments on the ground that the thyroidectomy probably provoked renal lesions which were responsible for the eclampsia. He performed the same experiments on four goats (thyroidectomy), three of which came to accouchement without accident save for a transient albuminuria in one; the fourth suffered from severe convulsions during the third month of the pregnancy (twenty-five days after the operation). These experiments of Moussu are in favor rather than against the parathyroid theory of eclampsia for in the goat one can remove very frequently the entire thyroid without notable interference with the parathyroid function. His experiments are more to be criticised, as well as those of Pineles, Gross and Zanfrognini, on the ground that they were undertaken on already pregnant animals.

Perhaps the most important contribution to this question is the extensive work of Thaler and Adler, who operated on forty female rats, which they observed carefully for two hundred days. The animals in gestation suffered always a severe tetany following even a relatively small loss of parathyroid tissue, while the non-gravid animals suffered little or no tetany from a similar operation. In another series of experiments non-gravid rats were parathyroidectomized and watched for the appearance of gravidity. Out of four of the animals from which one parathyroid was removed, three later became gravid and two of them died from tetany. Of twenty animals with only half a thyroid fourteen became gravid and died without exception in typical tetany. The tetany usually began in the last third of the pregnancy and the non-fatal cases ended with parturition.

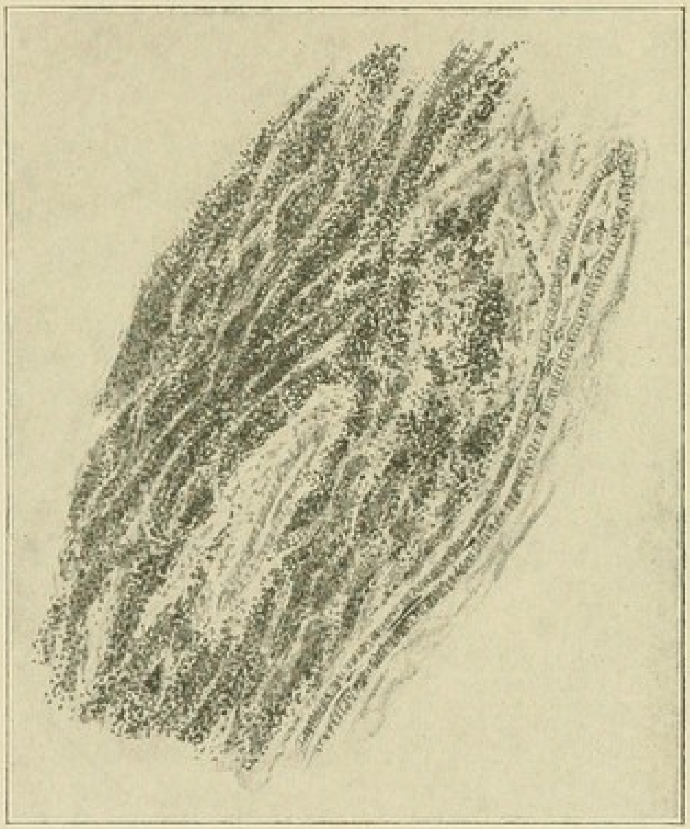


Fig. 75. Chronic parathyroiditis. The epithelial cells are crowded together with loss of original structure and connective tissue greatly increased.

This significant work of Thaler and Adler was suggested by the work of Erdheim on rats which we have previously quoted. In that work Erdheim observed one animal, having a large accessory parathyroid (both parathyroids had been removed), which remained free from tetany until it became pregnant, when it suffered typical tetany and premature delivery. In a following gravidity the tetany recurred and stopped with parturition.

Frommer, after partial removal of the parathyroids in rabbits has injected normal human placental tissue into the abdominal cavity, with the result that severe disturbances followed. In a gravid dog three parathyroids were removed and some tetanic symptoms occurred; five days after the operation, twelve grams of human placenta was introduced into the peritoneal cavity; four days later during parturition severe tetanic symptoms appeared but the animal later recovered. The three offsprings died although apparently healthy at birth. He assumes from this that the parathyroids have an antitoxic function and that the placental tissue was toxic in this experiment because the antitoxic function that should have been supplied by these glands was removed.

In a later article Vassale states it has been shown that in death from eclampsia either changes in, or congenital absence of, one or two parathyroids is found. Also clinical observations show that parathyroid therapy gives relief against the convulsions in eclampsia. Moreover, work on cats and mice shows that latent parathyroid insufficiency in the last third of pregnancy produces experimental eclampsia. In two out of three dogs in which the parathyroids were removed the author was able to prevent the eclampsia of pregnancy by means of administration of strong doses of parathyroids by mouth. The author believes the effects on the parathyroids in childbirth to be mechanical and not autotoxic and that the longer the duration of the birth the more danger there is of eclampsia.

Gross adds to a rather lengthy discussion of the relation of functional disturbances of the parathyroid glands to tetany the following two experiments: In two pregnant cats he removed three of the parathyroids and left one behind. In the first cat muscular twitchings in the facial region were observed twenty-five days after the operation. Twelve days later the animal gave birth to healthy young, and the twitching ceased. The second animal showed no symptoms.

We have already referred to rather slight anatomical changes found in the parathyroids in cases of eclampsia by Pepere, Zanfrognini and Erdheim. These are too minute, however, to be given any marked consideration.

Mossaglia, on the ground of experimental work, believes that the eclampsia is secondary to kidney changes. He states that parathyroid deficiency leads to diminished kidney function and albuminuria, and that it is the influence of the parathyroid, not directly, but on the kidney that is responsible for this condition. Quadri holds a similar view.

The recent work of MacCallum offers the most plausible theory for these forms of tetany. This author states that in the tetany that accompanies pregnancy and lactation the drain of calcium in the production of the fetus or on the secretion of milk may be so great as to cause tetany without lesion of the parathyroid glands. If, however, the functioning power of these organs is impaired just so much is the calcium content of the tissues diminished and tetany thus the more liable to express itself.

As to the general relationship between tetany and the parathyroid glandules, Rudinger has given the opinion, based on his own work as well as a study of the literature of the subject, that all forms of tetany rest upon a parathyroid insufficiency. To substantiate this theory the author removed the outer parathyroids of cats after injecting them with such poisons as calomel, morphine, atropine, tuberculin and ether. Although the injection of the substances mentioned gave rise to no "nervous" symptoms, such as increased electrical excitability or other indications of tetany, the injection plus the partial parathyroidectomy, did give distinct tetany in some animals and increased susceptibility to tetany in others.

CHAPTER XX.

PARATHYROID THERAPY.

The evolution of our knowledge of the parathyroid glands has come along in logical sequence. At first we were concerned with the anatomy of these bodies; then came the experimental work in animals revealing the results of their loss. This work was followed by a consideration of the application of this experimental knowledge to symptoms, post-operative and other, in the human, and finally we arrive at the stage when effort centers itself in an attempt to combat or modify these symptoms. Naturally with our present knowledge of organotherapy at hand the use of the parathyroid glands themselves was first offered for such combat.

Diet.—It was found after the first parathyroidectomies were performed that the severe metabolic disturbances arising from parathyroid excision could be modified by diet, to a slight extent at least. Fasting animals, it was found, failed to develop tetany as soon or with such severity as well fed animals. Feeding on a diet of bread, or of bread and milk seemed to be more favorable to the animal than a meat diet. Berkeley and Beebe state that they have observed symptoms in an operated animal from one to five hours after a heavy meal of meat, and that they have occasionally made use of this method to bring on tetany at a favorable time for experimental work. These authors use this point to emphasize the toxin hypothesis of parathyroid tetany, bringing in as collateral evidence the fact that a meat diet predisposes to convulsions in those cases of pregnancy which have disturbances of metabolism characteristic of the preeclamptic state. These authors state: "The nitrogen partitions in the urine in such patients are in most cases abnormal, with relatively high ammonia, high rest nitrogen, notable quantities of kreatinin, but with diminished urea and kreatinin excretion. Such findings indicate severe nutritional disturbance, and the possibility of metabolic toxins being responsible for the symptoms in such cases is commonly accepted. The means of relief in acute conditions by the very active stimulation of excretion through skin, bowel, and kidney, through the use of the hot pack, diaphoretics, purgation, the high saline irrigation, vigorous diuresis, and occasionally by bleeding and saline infusion are all based on the belief that the symptoms are caused by an active toxic substance in the circulating blood. A similar method of treatment is of clinical value in the treatment of parathyroid tetany. The fact that under disturbed conditions of nitrogenous metabolism a meat diet gives rise to metabolic products which may provoke convulsions suggests that the meat diet has more than a passive role in producing the symptoms of parathyroid tetany."

Parhon and Goldstein have found that maternal milk feeding prolongs life after thyroparathyroidectomy. Suckling kittens did not die so soon after this operation as kittens fed on a partial meat diet.

MacCallum supports the calcium deficiency hypothesis by the suggestion that the high content of calcium in milk is the factor that makes it a more favorable diet than meat for parathyroidectomized animals.

We have already referred to the fact that in the early study of the function of the thyroid the error was made that carnivora could not withstand the loss of that gland while herbivora bore its loss frequently without acute symptoms. This observation, however, had nothing to do with diet but rested on a lack of knowledge of the anatomy of the parathyroids. In the dog (carnivora) removal of the thyroid included removal of all the parathyroids, while in the rabbit (herbivora) such removal did not include the two external parathyroids which are quite separate from the thyroid and therefore protected the animal from tetany.

Transfusion has also been tried in animals exhibiting tetany, on the ground that some poisonous material was circulating in the blood of the operated animal. MacCallum and Davidson introduced the blood of a normal dog into a dog with tetany with the result that the symptoms rapidly and completely disappeared. The tetany recurred the next day and the dog was bled and a considerable quantity of salt solution allowed to run into its veins. This again stopped the tetany, but again it returned on the following day. The infusion was repeated with success, but the dog passed gradually into a state of cachexia and died after several days.

Colzi, Fano and Zanda and Cannezzaro have also noted the favorable influence of bleeding and transfusion of blood from a normal animal on the symptoms of tetany produced by thyroidectomy (thyroparathyroidectomy). Fano and Zanda have also observed the same effects from infusion of salt solution. These experiments were made before the relationship of tetany to the parathyroid glandules had been suggested.

Pfeiffer and Mayer injected a parathyroidectomized dog with ox serum, beginning the day after the operation, during the latent period and again on the second, fifth and eighth day. Following the second and third injection, done while the animal was apparently at the point of death, was combined bleeding and the subcutaneous injection of warm salt solution. This gave almost immediate relief which was, however, only temporary and the dog died.

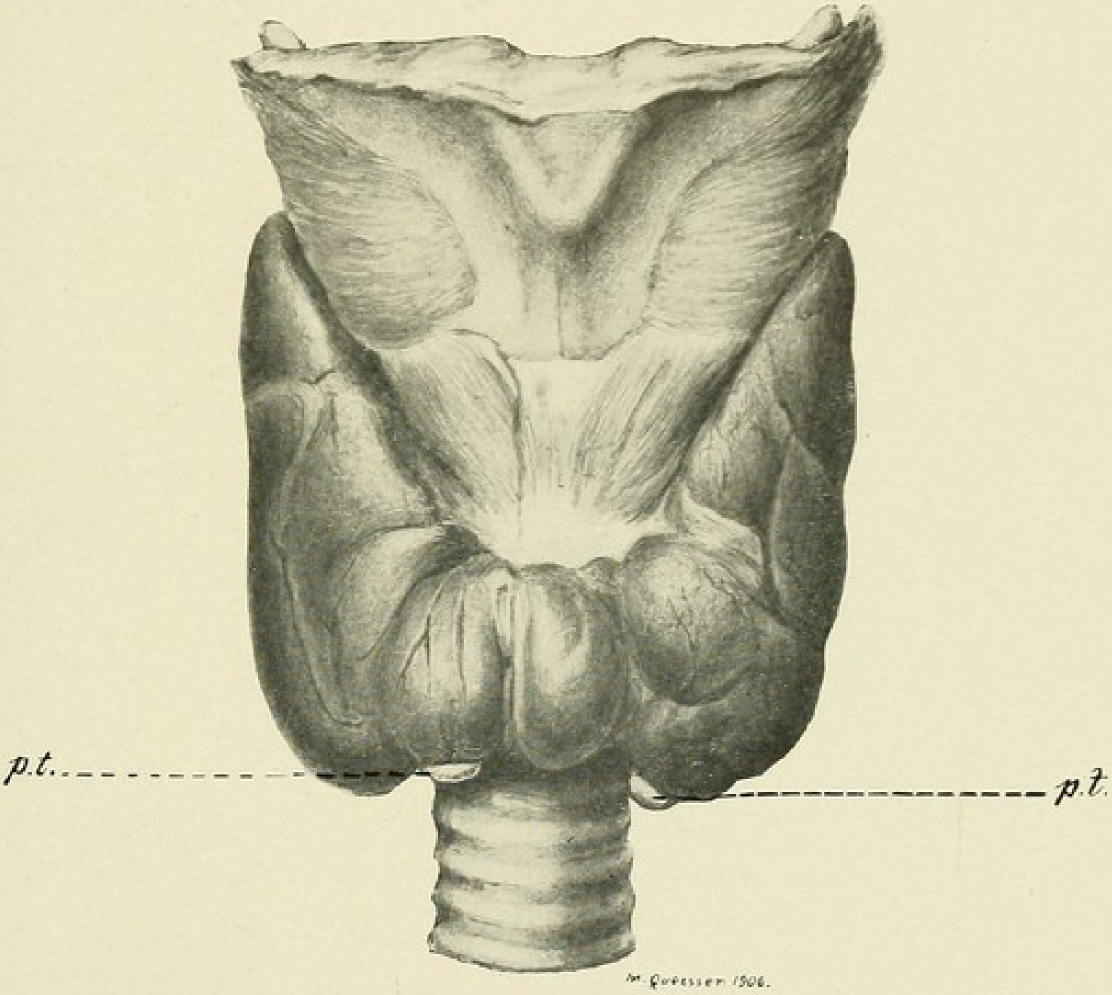
Parathyroid Therapy.—The therapeutic use of the glands themselves has been practiced extensively from the time the symptoms resulting from parathyroidectomy were first established. Vassale obtained results from the use of thyroids in which parathyroids were included in 1890, and his work was confirmed by Gley in 1891.

One of the most striking results, and one that later investigators have not been able to repeat, was that obtained by Lusena. This author kept a dog alive for four months after removal of the parathyroids by subcutaneous injections of parathyroid emulsions for eight days followed by transplantation of one parathyroid subcutaneously every fifteen days. It is to be questioned in this case whether the parathyroids were completely removed.

Edmunds reports feeding a large quantity of parathyroids to an animal in tetany practically without result, and Vincent and Jolly state that they were unable to prevent the onset of symptoms in the complete operation by the use of thyroid or parathyroid tissues. In general, however, the results of parathyroid feeding and injection show that the symptoms of tetany may be temporarily stopped by this measure, and even repeatedly, but that eventually the animal succumbs.

MacCallum and Davidson report the following results on four dogs. In the first, three parathyroids from the cow were introduced intraperitoneally after tetany had begun; symptoms continued followed by emaciation, apathy and death in five days. In the second, beef parathyroid and morphine were injected subcutaneously; next day there was no tetany but the following day tetany recurred and the animal died. In the third, one intravenous injection of parathyroid emulsion stopped the symptoms of tetany but five days later the dog died from an infection. The history of the fourth animal is interesting. After the development of tetany the parathyroids of twenty dogs were injected into the jugular vein. This stopped the tetany but it recurred and the parathyroids of thirty-seven dogs were injected. The symptoms did not return for three days and then the parathyroids of twenty-two dogs were injected into the peritoneum. Again symptoms ceased only to recur four days later when the parathyroids of eighteen dogs were injected with the usual cessation of symptoms. Three days later the symptoms again recurred and no further supply of parathyroids be-

PLATE XXXIX



P. T. INFERIOR PARATHYROIDS ON ANTERIOR INFERIOR SURFACE OF THE THYROID (A RARE SITUATION).

ing available the animal died of tetany. This experiment seems to show very conclusively that the life of a dog can be maintained temporarily after complete parathyroidectomy by the use of a great amount of material, but that when therapy stops the symptoms recur and the animal dies. Cases that are reported as recovering permanently from symptoms of tetany after the injection of one or two parathyroid glands are undoubtedly cases in which the parathyroids were not entirely removed.

Moussu was able to arrest postoperative tetany in dogs by the subcutaneous and intravenous injection of extracts of the horse parathyroid. His results were only temporary as nearly all the dogs died later in a cachectic condition. Alquier and Theunveny report similar results in dogs.

Esterbrook was probably the first to administer parathyroid glandules to the human subject. He employed ox parathyroids in insane patients with no particular reference to symptoms of tetany, but merely to compare the results of parathyroid feeding with those obtained from the use of the thyroid gland. Esterbrook first gave one dried ox parathyroid by the mouth every day for a week; two glands a day were given the next two days, and three on the next three days. Then hypodermatic injections were administered. These were followed by glycerine extracts of the glands. In one case as many as nine parathyroids were given daily. From this treatment practically no effects were obtained; temperature, pulse and respiration remained normal, urinary nitrogen and phosphoric acid showed no change. Only a slight increase in pulse tension was observed.

These results were so different from the striking symptoms following the use of thyroid extract that the author assumed that the symptoms arising from parathyroidectomy were due to injury to the thyroid or its nerve connections rather than to removal of the parathyroids.

In 1901 Moussu and D'Ausset at the Congress of Gynecology in Nantes, reported cases of tetany benefited by thyroid therapy (the internal parathyroids being included in the thyroid extract.)

Scanning the literature since this time we find many favorable reports on the use of these glands in a wide range of diseases showing symptoms of tetany. And while in many instances it does appear that their employment has been of real value, nevertheless the suggestive effect of such treatment must be borne in mind.

Vassale by the use of a parathyroid extract prepared in a special manner, the details of which he fails to disclose, reports beneficial results when used either by mouth or subcutaneously on cases of eclampsia, infantile tetany and epilepsy, and thinks it would be equally efficacious in all varieties of tetany.

Berkeley has employed parathyroid therapy on eleven cases of paralysis agitans in various stages of the disease. He reports that nine of these patients showed improvement, the earlier cases especially, and one very early case considered himself nearly relieved while under the influence of the treatment. "All the patients remarked upon a curious increase in courage, comfort and mental energy, while taking the remedy." Castelvi has reported equally good results in this disease by the use of thyroid extracts.

Zanfrognini has employed parathyroid therapy in five cases of eclampsia with general improvement of symptoms. Michelazzi also reports favorable results in eclampsia from the use of parathyroids.

Rensburg and Rey obtained completely negative results with parathyroid therapy in infant's tetany; and Spieler likewise had no result following the use of parathyroid tablets in this disease.

Loewenthal and Wiebrecht have reported good results in many instances following parathyroid feeding in tetany. Marinesco has reported favorable results following the use of ox parathyroid in a seventeen-year-old girl, suffering from exophthalmic goitre combined with intermittent tetany.

Murraron reports having suspended epileptiform attacks in two goitrous cretins by the use of parathyroid extract, and Mant and Shaw apparently cured by the same means a young girl of nine years suffering from tetany in connection with grave gastro-intestinal symptoms.

Brandan reports a case where, after the removal of a colloid goitre from a girl aged fourteen years, tetany developed forty-eight hours after the operation. By the use of subcutaneous injections of parathyroid emulsion the symptoms disappeared, and the patient has remained free from the same for one year. This phenomenon is explained by the fact that the parathyroids were probably not all removed at operation, but were so damaged that their function was suspended temporarily, and that the parathyroid emulsion sustained the patient until the glandules resumed their normal work, possibly by compensatory hypertrophy.

Berkeley has relieved symptoms of gastric tetany in a thirty-nine year old man by oral administration of fresh ox parathyroid. Putnam has reported effective relief in a case of surgical tetany by the use of a similar preparation.

Beebe was the first to prepare and administer a nucleoproteid principle of the parathyroid gland, which has been quite active in dispelling the symptoms of tetany. In a later paper Berkeley and Beebe give in detail the methods for preparing this extract from beef parathyroids obtained by roughly trimming out the small mass of tissue containing the two superior glands. "The carefully cleaned glands were cut into small pieces with scissors, and the comminuted tissue was then ground to a fine pulp in a large mortar with the help of enough sand to give the whole mass a moist, pasty consistency. The crushed glands were next shaken for two hours at room temperature with six to eight volumes of physiological salt solution to which had been added two drops of ten per cent sodium hydroxide solution. The jar was now transferred to the refrigerator and the extraction allowed to continue for eighteen to thirty-six hours. Filtration first through gauze, to remove the fat and coarser particles of tissue, and then through moderately thick paper gave a clear extract which was preserved by the addition of chloroform and kept at low temperature until biologically tested."

It was shown that an extract so prepared relieved the symptoms of tetany in a parathyroidectomized dog in ten to fifteen minutes after injection. As this extract contained nucleoproteids, globulins, and albumins it was decided to separate it still further, and it was divided into three portions. The first portion was precipitated by acetic acid, the second by half saturating the filtrate with ammonium sulphate, and the third by complete saturation with ammonium sulphate. The precipitate from the first portion (nucleoproteid) was most abundant; the second (globulin) was about one-fifth the first; while the third (albumin) was so small that it was abandoned. The activity of these proteids is summarized by Beebe as follows:

"1. The nucleoproteid of the parathyroid when freshly prepared is equal to the whole gland in relieving the symptoms of acute tetany in dogs.

2. The globulin is of no value in relieving tetany.

3. Boiling the nucleoproteid solution or heating it to 80 degrees C. for one-half hour completely destroys the activity of the nucleoproteid.

4. The nucleoproteid is most active when freshly prepared and rapidly deteriorates when kept in solution or in suspension at refrigerator temperature. Freezing also destroys its activity, although not so rapidly as room temperatures.

5. Tryptic digestion or the action of pepsin and hydrochloric acid for forty-eight hours severely injures, but does not completely destroy, the activity of the nucleoproteid.

6. The nucleoproteid will relieve tetany if given by mouth, but is much more quickly and certainly effective when given subcutaneously or intraperitoneally."

The results following the use of this parathyroid nucleoproteid are strikingly illustrated by its efficacy in relieving tetany in thirty-two animals as detailed by Berkeley and Beebe, who report positive results

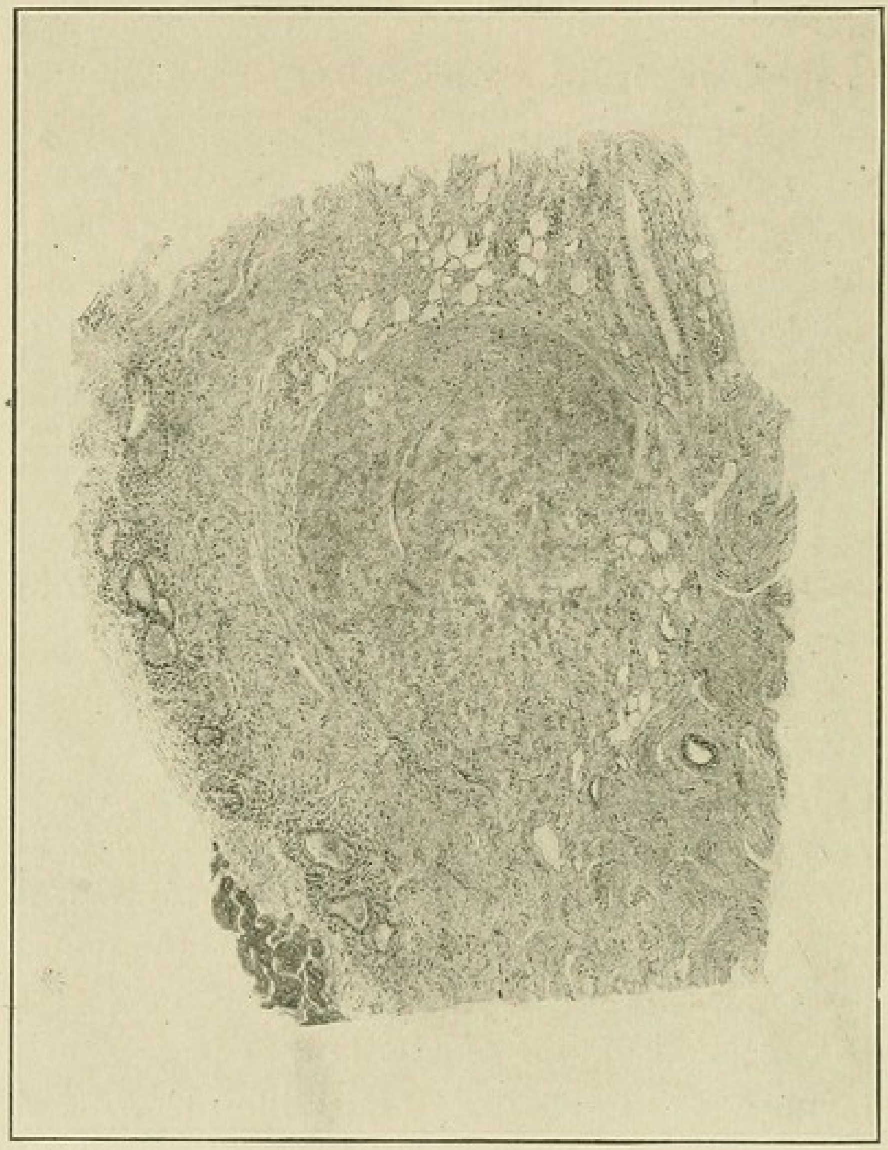


Fig. 76. Transplantation of thyroid and parathyroid into the tibia of a dog. Some thyroid persists (at the edge of the section), but the parathyroid has undergone necrosis. The animal died of cachexia, with no tetany, although all other parathyroid tissue had been removed.

in ninety-five per cent of the trials in which a comparatively fresh preparation was used. The boiled proteid, and the globulin, however, always gave a negative result. The digested proteids gave relief only when used in large doses.

The clinical value of the nucleoproteid has also been proved in cases of post operative tetany in the human subject. Halsted reports that in a patient suffering greatly from subtetanic hypoparathyroidism as the result of two operations upon a large colloid goitre, tetany has for two years been averted and the condition made endurable by the use of hypodermic injections of the nucleoproteid of the parathyroid gland (Beebe) and by parathyroid feeding.

Pool reports a case of a young woman who had had two thyroid operations. Despite the use of Vassale's serum and implantation of the parathyroid glands a typical tetany, which developed four days after the second operation, continued for thirteen months. Improvement was finally secured by repeated administration hypodermatically of large doses of Beebe's nucleoproteid.

Calcium Salts.—While the development of our knowledge of the parathyroid glands has been fraught with dramatic incidents throughout, a fitting climax was lacking until the discovery that the severe tetanic symptoms arising from their removal could be instantly stopped by the administration of soluble calcium salts. And thus a new field of investigation was opened which promises to lead to practical therapeutical results and to the throwing of new light on certain interesting features of metabolism in the human body.

In the summer of 1907, Parhon and Urechie in the Revista Stiintelor Medicale published an article on the influence of the injection of sodium chloride and calcium chloride into animals that have experimental tetany. While they found that sodium salts increased the tetany of parathyroidectomized dogs, they made the important observation that one gram of calcium chloride dissolved in one-hundred cc. of water and injected into the peritoneum held in check all acute symptoms.

Independently, in March, 1908, MacCallum and Voegtlin published a communication on the relation of the parathyroid glands to calcium metabolism and the nature of tetany, which they have followed (1909), by a more lengthy and detailed account of their investigations in this line.

These observations rest on the clinical studies of such conditions as rickets and osteomalacia which have suggested that tetany might stand in relation to disturbances in calcium metabolism; and further on the observations of J. Loeb and J. R. MacCallum that the effects of various salts which cause muscular twitching may be counteracted by calcium. Moreover, the observation of Erdheim on the changes in the teeth of parathyroidectomized rats seems to have a bearing on this question.

The use of calcium salts in tetany had previously been recommended, but without regard to the parathyroid glands. Quest, as well as Silvestri and others, has called attention to the low calcium content in the convulsive stage of tetany, and Sabbatini noted that trisodic citrate solutions would cause convulsions and muscular twitching because they combine with the soluble calcium salts in the body fluids.

Whether we accept this calcium deficiency hypothesis, or consider it only as a secondary factor in the cause of parathyroid tetany we must admit that such a deficiency exists and that the restoration of calcium to the tissue will prevent the tetany due to parathyroid deficiency.

The same effects can be obtained up to a certain extent by the use of soluble salts belonging to the same natural group as calcium, such as magnesium, barium, and strontium.

MacCallum and Voegtlin were able to relieve the tetany of parathyroidectomized animals by injections of magnesium salts, but found it was too dangerous a salt to use on account of its depressant action. Berkeley and Beebe have found that the symptoms of tetany are relieved with nearly the same degree of promptness and completeness by strontium salts as by calcium salts. They use ten c. c. of a ten per cent solution of strontium chloride to a ten kilogram dog. On ten animals they found the effect of strontium salts differed practically not at all from the effects obtained by the use of calcium salts. These authors also found that barium salts will relieve tetany, but that they should never be given as a therapeutic measure because an efficient therapeutic dose is too near the border line of a fatal dose.

Berkeley and Beebe, following the suggestion of MacCallum and Voegtlin's first article, have tried the effects of calcium salts on a number of dogs, and while they agree with those authors that calcium quickly stops the symptoms of tetany, they consider that the symptoms are due to a metabolic poison, the abnormal excretion of calcium being an accompanying phenomenon. They cite in favor of this hypothesis the fact that the symptoms have a central origin; that symptoms are shown best in young animals, and are more severe if the animal has been kept on a meat diet; that the symptoms have a close relation to certain clinical conditions which are accompanied by severe nutritional disturbances. Moreover, that gastric tetany is accompanied by severe metabolic disturbance, it has similar symptoms and is promptly relieved by intravenous calcium injections and by parathyroid nucleoproteid; that bleeding, followed by intravenous infusion, relieves tetany as well as does the injection of fresh parathyroid nucleoproteid. In addition injection of poisons such as ammonia and xanthin produce symptoms which can be promptly relieved by injection of calcium or strontium salts, and it is known that increased excretion of ammonia follows complete thyroidectomy.

The work of MacCallum and Voegtlin, which marks so important an epoch in our knowledge of the parathyroid glands, is exhaustive and includes a considerable study of metabolism in parathyroidectomized animals, as well as the negative effects of injection of sodium and potassium salts. An idea of the effects obtained by these authors by the use of calcium salts in dogs can best be obtained by quoting in detail several of their experiments.

"Thyroparathyroidectomy; four days later violent twitching of muscles, pulse 160, respiration labored. Given ten c. c. of a five per cent solution of calcium acetate into jugular vein. Respiration became rapid two hundred to minute, twitching rare but sharp. Twenty-five minutes after the injection, pulse was eighty, very irregular and slow. Dog thought to be dying, occasional slight twitches. Next day dog was found walking about and fairly well but was found dead the day after. In this experiment the animal was apparently restored to life from a moribund state, but the amount of calcium salt had not been large enough to remove tetany instantly."

"January 9, two parathyroids and one lobe of thyroid extirpated, no results. January 18, second lobe of thyroid removed. January 19, violent tetany; at 11:30 given ten c. c. of five per cent calcium lactate subcutaneously. 11:35, respiration 240 marked twitching, pulse 180, breathing very rapid and labored. 12:10, still tachypnœa and twitching. 1:10, respiration slowed, 40 to minute, muscular twitching still marked. 1:30, respiration quiet; 1:32, twitching has almost disappeared, slight muscular tremor, walks about but looks dejected. 3:00 p. m., respiration 24, pulse 124, dog is quite normal in appearance, no tremor nor twitching. Respiration perfectly quiet and animal has perfect control of himself and eats hungrily on being taken to cage."

The effects of the administration of these salts are of course not permanent. The dog last cited, for instance, developed tetany again the next day. This temporary relief may be of permanent value, as for instance in a case of one of Halsted's dogs in which tetany was tided over by the administration of calcium until a transplanted parathyroid became able to function actively enough to prevent tetany.

MacCallum and Voegtlin also cite cases in which an opportunity to observe the effect of calcium upon cases of tetany in human beings has been offered. In a case of Musser's in which violent tetany had developed, following the removal of a malignant growth of the thyroid, calcium lactate was administered in large and frequent doses. This caused the disappearance of the tetany in the course of one day, but with the cessation of calcium medication for two or three days the symptoms of tetany reappeared. Again they disappeared with the renewal of the calcium treatment. A second case occurring in the practice of a New York physician, responded to the administration of calcium salts in the same way. And a third case, of a little girl suffering from gastric tetany was completely relieved by the administration of calcium.

In the case previously cited of Halsted's, in which tetany had been averted for two years by the use of parathyroid gland extracts, the latter reports the same effect for the third year by the use of calcium salts.

MacCallum and Voegtlin summarize the role of the calcium salts in connection with tetany as follows: "These salts have a moderating influence upon the nerve cells. The parathyroid secretion in some way controls the calcium exchange in the body. It may possibly be that in the absence of the parathyroid secretion, substances arise which can combine with calcium, abstract it from the tissues and cause its excretion and that the parathyroid secretion prevents the appearance of such bodies. The mechanism of the parathyroid action is not determined, but the result, the impoverishment of the tissues with respect to calcium and the consequent development of hyperexcitability of the nerve cells, and tetany is proven. Only the restoration of calcium to the tissues can prevent this. This explanation is readily applicable to spontaneous forms of tetany in which there is a drain of calcium for physiological purposes, or in which some other condition causes a drain of calcium. In such cases the parathyroid glands may be relatively insufficient."

Leopold and Reuss found a slight increase rather than a decrease of calcium in adult rats exhibiting cachexia parathyropriva, including enamel defects of the teeth, after parathyroidectomy. In young rats after the same operation, a lowering of calcium was observed as well as lack of growth and lack of weight increase.

Parhon, Dumitresco and Nissipesco found in cats and dogs after thyroparathyroidectomy, an increase of calcium in the nerve centers.

In the tetany of infants Oddo and Sarles have found an increased amount of calcium in the urine. In a case of post-operative tetany Musser and Goodman found a diminution of calcium in the urine.

TRANSPLANTATION OF THE PARATHYROID GLANDS.

The limitations to tissue transplantation in warm blooded animals are, of course, well known. When portions of various glands have been implanted into regions well supplied with blood they soon lose their original structure, become absorbed, and only a bit of cicatrical tissue eventually marks the site of transplantation. Certain glands have responded to transplantation much better than others, especially the thyroid. It has been found in the cat and the dog that while the central parts of transplanted thyroid lobes undergo necrosis, the other portions may persist, and blood vessels from surrounding granulation tissue enter and give life to an apparent new growth of the gland, including even lumina filled with colloid.

It is of extreme interest then to know if such important organs as the parathyroid glands may be transplanted with any possibility of permanent success in saving a patient from tetany or death following the unfortunate removal of these bodies as has occurred in operations involving the thyroid gland.

The first experiments in which parathyroids were successfully transplanted have to be gathered from the earlier literature on thyroid transplantation where, as in the dog, the parathyroids are included in the thyroid lobes and transplantation of the latter glands included the former. Proof of this is to be drawn from the functional results that followed the removal of the transplants, where, in many instances death with more or less severe manifestations of tetany followed the removal of the transplanted tissue. As some of this work was done before we knew about the relation of the parathyroid glands to tetany there was no proper interpretation of the results until after the work of Gley on the parathyroid glands appeared.

Kocher (1883) recommended thyroid transplantation to prevent postoperative tetany as well as cachexia strumipriva, myxœdema and cretinism.

Eiselsberg (1892) transplanted one thyroid lobe between the peritoneum and fascia in four cats and later (five days to one month), extirpated the remaining thyroid lobe. The animal showed no symptoms following such procedure, and in from one to three months after the operation the implanted thyroid was removed. As a result of the removal of the transplant the animals quickly died with severe tetanic symptoms. Histologic sections of the removed tissue showed it to have the appearance of normal thyroid. While there is no mention of parathyroid tissue, we must assume from the results of the experiment that sufficient parathyroid to preserve the animal from tetany was transplanted with the thyroid and persisted up to the time of its removal.

Enderlen (1898) in his transplantation experiments in dogs and cats took into account the parathyroids and stated that they persist after transplantation even better than thyroid tissue.

Payr extirpated the thyroid lobes of cats and dogs and transplanted the same into the spleen. In some instances one lobe was transplanted and the remaining lobe removed ten or twelve days later. In other cases the whole gland was removed from the neck and placed in the spleen at the first sitting, and twenty or thirty days later the other lobe was transplanted into the spleen in a different place. As far as the functional results of these experiments went, the animals in general exhibited no symptoms even after many months. After extirpation of the spleen, however, the animals quickly died, usually with symptoms of tetany.

Examination of the transplant showed the implanted thyroid to be reduced to one-fourth or one-third its normal size. The central necrosis was less marked than in other reported transplants and regeneration processes were prominent, so that a picture of normal colloid-forming thyroid tissue was present. Payr concluded that a gland with an inner secretion was better adapted to transplantation than other functional tissue.

Christiani reported the persistence of parathyroids transplanted into a cat. After five years they were found practically unchanged. This author, together with Ferrari, was one of the first to transplant thyroid and parathyroid and consider each separately.

Camus seems to be the first to attempt the transplantation of parathyroid glands only. The site chosen by this author was the rabbit's ear. His results were not satisfactory and he stated that the transplanted glandules showed an early atrophy.

Walbaum attempted to transplant the parathyroids into the serosa of the stomach of a cat, but without success. After transplantation of the superior glandules, he destroyed the remaining glandules and the animals promptly died from tetany or went gradually into a state of chronic cachexia from which they died.

Biedl reported two cases of successful auto-transplantation of parathyroids into the dog's spleen. In the first animal, thirteen days after the transplantation, the thyroid and remaining parathyroids were removed without the dog exhibiting any symptoms of tetany. The second dog, however, developed tetany four days after the thyroid and remaining parathyroid removal. The symptoms were controlled by parathyroid feeding and the dog recovered. In two other animals, foreign parathyroids were planted in the spleen with removal of the normal glands sometime after the transplantation and a year later the author reported survival of one animal with no signs of tetany for seven months, but death from cachexia thyropriva. The two intact parathyroids were found in the spleen. The second dog was still alive, the transplanted parathyroids being apparently sufficient. Halsted has criticised this work of Biedl's as he had been unable to get similar results by "foreign" transplants or without creating a parathyroid deficiency before transplanting. Moreover, functional proof is lacking in these experiments, as transplants were not excised during life to see if their removal would cause death from tetany.

Pool, following the technic of Payr, has tried transplantation without success. In eight dogs, sixteen rabbit parathyroids were grafted into the spleen. In four dogs, ten dog parathyroids were transplanted in the same manner. These transplants were made from eight to twenty-eight days before removing the normal parathyroids. In none of these cases did the transplants influence at all the usual development of tetany following parathyroid removal and all the dogs died with acute tetanic symptoms.

Pepere states that after removal of the external parathyroids in the rabbit (which brought on symptoms of parathyroid insufficiency), he was able to control symptoms by implantation of one or several parathyroid glandules. However, the graft was soon absorbed. Its effect was sufficient, however, to tide over a parathyroid deficiency until certain accessory parathyroid tissue (which this author describes), had had time to hypertrophy and keep the animal in normal condition.

Capebelle removed transplanted thyroid from a dog two hundred and forty-five days after operation, and found it in good condition. The animal, however, died of tetany following its removal, showing that parathyroid must have been transplanted with the thyroid and preserved its function.

Pfeiffer and Mayer have successfully transplanted the parathyroids in two six weeks' old puppies. They state that they prefer dogs to rats for this work because the outer parathyroids are well separated from the thyroid in the former and because dogs manifest tetany much more acutely than rats. These authors transplanted one outer parathyroid gland into the abdominal wall between the muscle and peritoneum and extirpated the thyroid lobe and inner parathyroid on that side. At the end of a week they carried out the same operation on the other side. Neither of the dogs operated upon exhibited tetany following such procedure; and at the end of six weeks a functional test of the efficacy of the transplants was made. Following the excision of the transplants both animals succumbed to death in acute tetany, the symptoms of which appeared two days after excision of the transplanted tissue. A similar procedure carried out in a third dog (six months old), did not result successfully. The animal developed tetany soon after the transplantation and despite the feeding of thyroid tablets died in cachectic condition in about a week. Histologic examination of the transplanted tissue in this case showed it to have undergone necrosis.

Leischner, who was the first to establish the functional proof of parathyroid transplantation, carried out his experiments on eighty rats. In about ten per cent of these animals he was able to transplant parathyroids and have them maintain their function. He chose to place the parathyroids between the peritoneum and the rectus abdominis, or in the muscle itself. Such transplants were made successfully in four rats in which both parathyroids were transplanted with an interval of ten days to a month between the operations. No signs of tetany appeared. From three to six weeks later the portion of the wall containing the transplanted glandules was extirpated and tetany followed the removal. In four other rats both parathyroids were transplanted at the same time and tetany resulted, but after a time it ceased. Then, in three or four weeks, the tissue containing the transplant was removed and a new attack of tetany promptly occurred.

Halsted's transplantation experiments, carried on for a period of two years, show sixty per cent of successful results in autotransplantations with created deficiency. The negative results are of value in bringing out the fact that a parathyroid deficiency must be created by the removal of at least two glands before successful transplantation can be expected. It is to be noted that auto-transplantations were the only ones giving successful results. Isotransplantation which was tried on thirty-eight dogs, was uniformly unsuccessful. The isotransplantations were made into the thyroid, spleen, and behind the rectus abdominis but the isograft did not live in a single instance.

In the first series of autotransplantations by Halsted, five auto-grafts into the thyroid of three dogs gave two successful results; eight auto-grafts into the spleen of three dogs gave only one successful result. Functional proof of the success of these transplantations was not attempted, but microscopically and macroscopically the graft appeared successful.

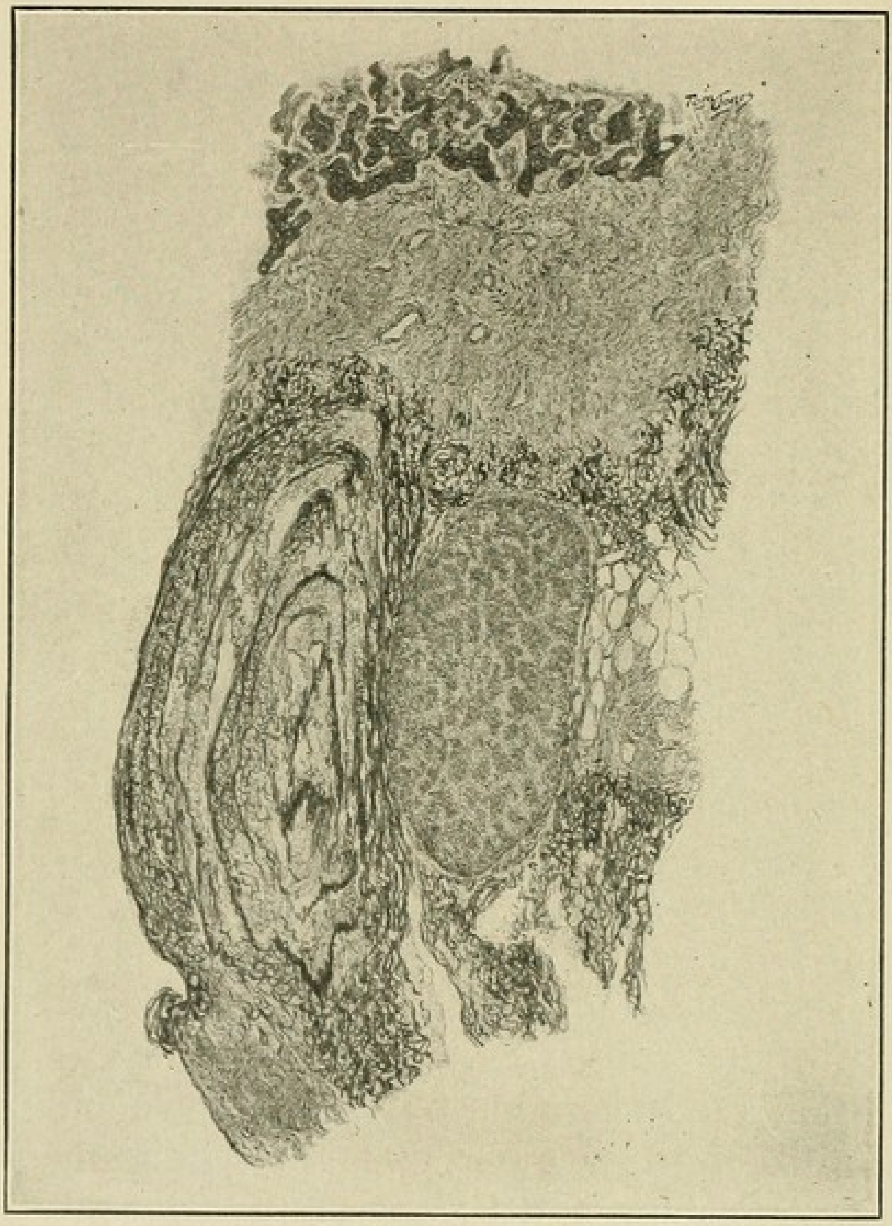


Fig. 77. Transplanted parathyroid glandule in the tibia of a dog.

In the second series, auto-transplantation was made behind the rectus abdominis muscle. Out of eighteen such transplantations in twelve dogs, seven parathyroids were absorbed or necrotic; five to seven lived and performed their function. In two of the dogs the functional test was made. Both these dogs died in tetany after the removal of the sustaining auto-graft. Two other dogs were alive and well after nine and ten months respectively, sustained apparently by a single transplanted parathyroid gland only. Both these dogs developed myxœdema, (the thyroids were removed with the parathyroids) with eczema and some falling of the hair.

In some of Halsted's experiments, when too sudden a deficiency was created, a beginning tetany was tided over by the administration of calcium salts, until the transplanted grafts acquired a circulation sufficient for them to exercise their function.

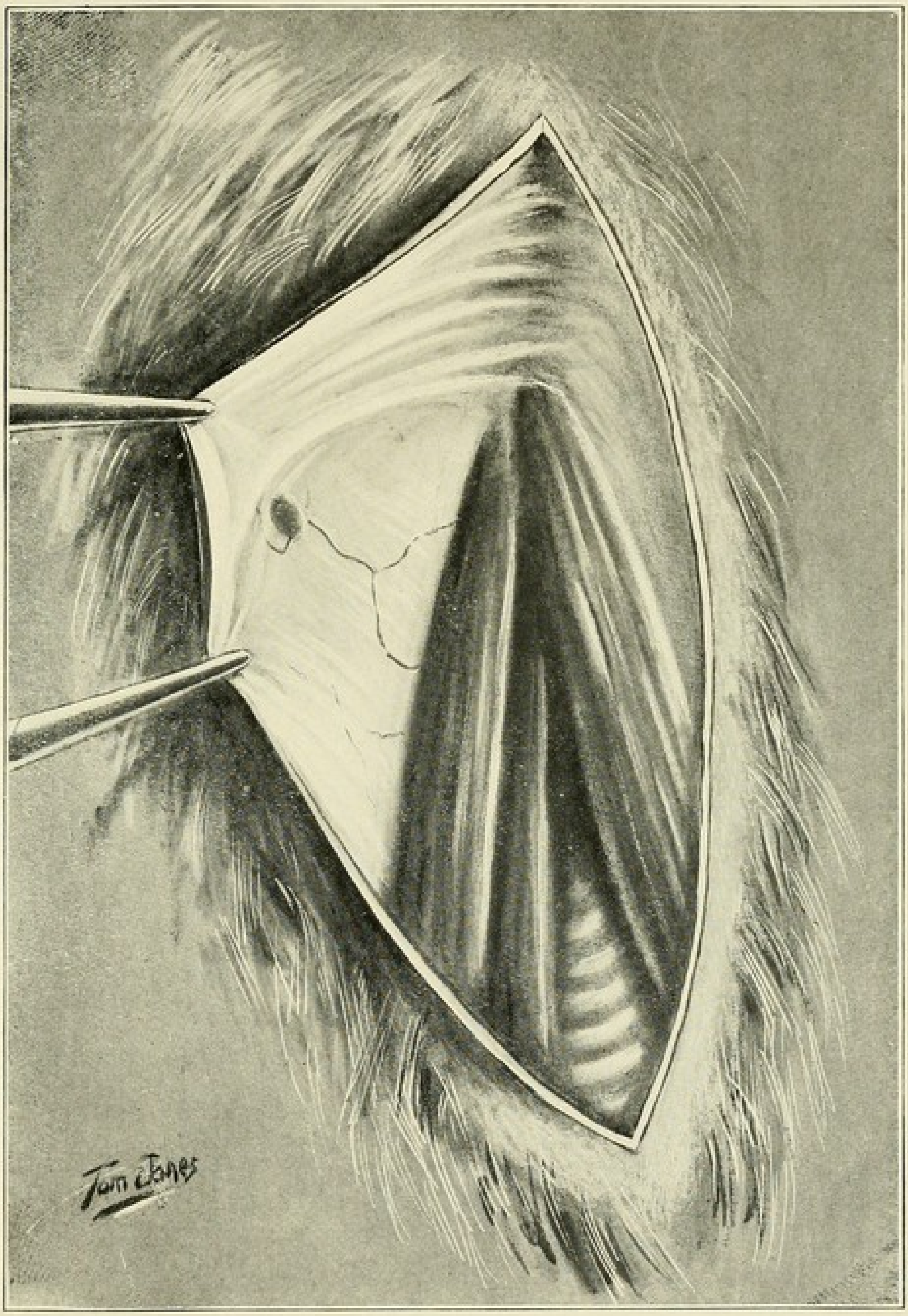
Eiselsberg has reported a case in which a parathyroid was transplanted in a human subject. The patient was a woman, forty-two years old, who for many years had suffered from a fairly severe tetany which followed total thyroid extirpation. She had many times been in the clinic during goitre operations and at last a favorable case was operated upon and a gland was transplanted; this was apparently followed by good results. Von Eiselsberg believes that removal of a parathyroid for this purpose is permissible only when a cyst is taken out of one lobe of the thyroid and the remainder of the organ appears normal so that one can say with some certainty that three parathyroids are left intact. Garre has also reported good results following the transplantation of parathyroid into the tibia in a case of chronic tetany.

The recent thyroid transplantations of Kocher must be taken into account in considering the question of parathyroid transplantation. Kocher's transplantations are made into the bone marrow of the tibia, this bone lending itself best to such an operation. The process is carried out in two stages. In the first stage the marrow cavity is opened, a small pocket formed, and a silver ball about 1x1.5 cm. introduced. The wound is then closed. After two or three days it is reopened, the ball removed and the fresh gland tissue implanted into the cavity thus formed. In this way the author avoids extensive hemorrhage about the implanted tissue, a layer of granulations having formed about the ball. Experimentally, Kocher found that thyroid tissue thus transplanted in dogs proved efficient for the maintenance of life. If the bone containing the transplanted tissue was resected, the animal quickly died with acute symptoms of tetany.

To be especially noted is the fact that in these experiments of Kocher there were no acute symptoms of tetany following the implantation, although thyroid alone was grafted and all parathyroids removed, but as soon as the bone containing the transplanted portion of thyroid was removed acute tetany leading to death resulted. Kocher considers the question of parathyroid tissue having been transplanted with the thyroid in his case, but says that histologically nothing but thyroid tissue was found in the bone.

Thompson, Leighton and Swarts have tried various situations for placing transplanted glandules. The method of Kocher for transplantation of parathyroid into the shaft of the tibia has been attempted, as well as transplantation of thyroid alone in this situ-

PLATE XL



PARATHYROID GLANDULE (WITH BLOOD VESSEL), FORTY DAYS AFTER TRANSPLANTATION INTO THE NECK OF A DOG. THE ANIMAL WAS SUSTAINED BY THIS GLANDULE, AS WAS SHOWN BY DEATH IN TETANY TWENTY-FOUR HOURS AFTER ITS EXCISION.

ation, as the authors could not understand why in the case Kocher reports he should have obtained the same results, including the functional test, for thyroid, that numerous experiments have shown conclusively to depend on parathyroid transplantation.

These authors found that dogs which had been submitted to the tibia operation did not develop tetany although all parathyroids were removed, or transplanted parathyroid had been shown microscopically to have undergone necrosis. The dogs did die finally, however, from cachexia. Moreover, in two animals from which the parathyroids had been removed the tibia operation markedly influenced the tetany parathyropriva even after the dog had developed severe symptoms.

It would seem, then, that there might be some connection between the traumatic injury of bone and the prevention of tetany. In Kocher's case this seemed to be disproved by the statement that when, in his dog, the transplanted thyroid (which was microscopically free from parathyroid), was removed death in tetany resulted. This, if it were true in a number of instances, would be indeed difficult to explain, for the presence of thyroid tissue has never in the least influenced the fatal tetanic results of parathyroid removal which has been practiced so many times.

In the case of Thompson, Leighton and Swarts, the removal of the transplanted thyroid had no effect whatever in the experiment. It is to be noted, however, that these dogs in which a bone transplantation is practiced, although escaping a fatal tetany, usually die in chronic cachexia. These experiments, therefore, influence in no way the well-established fact that the parathyroid glandules are vital organs, but they suggest that the bone operation may serve as a factor in checking the tetany which is usually the most prominent symptom of parathyroprivic death.

One of the most recent contributions to the temporary cure of tetany after loss of the parathyroid glandules has been made by Isaac Ott. This author, who used cats chiefly for his experiments, found that the tetany following complete parathyroidectomy in these animals could be controlled by the administration of pituitary extract. When ten to twenty grains of this drug rubbed up with distilled water was injected there was a replacement of the tremor by steadiness in about three hours. Tetany did not reappear for twenty-four hours. In comparing the effects of calcium lactate and pituitary extract in tetany, it is to be noted that while the action of the former is quicker, the action of the latter drug seems to continue longer.

From all that has gone before we find that tetany, although it is a dramatic event in connection with parathyreoprivic death, is but a symptom, that usually, but not necessarily, accompanies loss of these bodies. We can control tetany after parathyroidectomy, but we cannot maintain life for any considerable time without the parathyroid glandules. Deprived of these vital organs an animal or an individual will die; acutely and convulsively if the deprivation is sudden, slowly and quietly if the loss is more slowly brought about. While in the past investigation has centered itself, naturally, upon the more striking phenomena of complete parathyroidectomy, it is possible that future work may give us a better understanding of the nature of the changes incident to the gradual loss of function of the parathyroid glandules.

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