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THYROID

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THE THYROID

SURGERY
SYNDROMES
TREATMENT

E. P. SLOAN, M.D.

Edited by Members of the Sloan Clinic
GUY A. SLOAN, M.D.; H. P. SLOAN, M.D.; FRANK DENEEN, M.D.;
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And with a Foreword by
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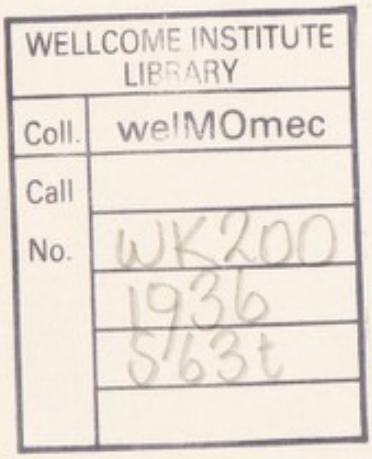
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PREFACE

Among the impulses which carry us forward, none is so vigorous as the yearning for individual self-expression; the desire for creation of something. Perhaps the greatest human happiness is consciousness of worthy personal achievement. Here lies the great urge of the constructive instinct of mankind.

In the field of medicine there are few greater opportunities to satisfy this hunger than afforded in the study of the endocrine glands, of which the thyroid is of prime importance.

I have always believed that a book on goiter surgery should represent as nearly as possible the sum total of present knowledge in both the scientific and clinical phases of thyroid conditions. It proved to be an increasingly difficult task to reach anything approaching an ideal objective: the production of a book which would be complete, and would represent the best modern thought on every aspect of the goiter problem.

I believe that it might be of interest, and of value, to recount some of the ideas and conceptions underlying our work. Many of these conceptions are not found in the literature and I do not sponsor them in any way except to state that they are the results of our personal experience. The manuscript was started in 1927 and, while the book is nearly ready for the publisher, I am still not entirely satisfied with the presentation. The exacting duties of surgical practice must be my excuse for the fact that the book is not as complete as I would wish it.

The book is not intended for the goiter surgeon alone. It is hoped that it will also be of interest and value to the student, to the internist, and to the public health official. The aim of the book is to discuss goiter and its problems from the viewpoint of all whose efforts are directed toward the elimination or improvement of thyroid ailments.

Future thyroid control is the province of preventive medicine and is to be reached through the cooperation of all surgical and medical agencies. The principles of preventive medicine properly applied to the goiter problem can save immeasurably more lives than can the surgeon's art. Goiter crusades consistently and intelligently waged will not only save lives but tend to brighten and glorify life and minimize the individual degradation dependent on chronic goiter conditions.

The entire problem of the mental and physical development of the youth of our land is unequivocally bound up with the management of goiter problem. It is not the object of this work to present plain accepted facts for the proven and the fully accepted facts may be obtained with sufficient readiness from the systematic goiter treatises. The aim of this book is to recount the working theories and conclusions of a surgeon who has devoted twenty-five years of his life exclusively to goiter work.

The book is not encyclopedic, nor is it intended to be. The goiter surgeon is referred to the chapter on surgical anatomy and surgical tech-

nique. It may be that he will not agree with our conceptions of the surgical relationships of the thyroid gland. Every goiter surgeon has a tendency to develop his technique along certain lines, to introduce little innovations and improvements. He finds that this fully developed technique is in *his* hands immeasurably better than any other. The author merely wishes to say that his conception of the surgical anatomy of the neck and his technique, modified in accordance with this conception, has greatly simplified the various thyroid operations he has performed.

The internist too, and the public health worker may find cause to quarrel at our conclusions and with perhaps an even greater show of justice. They may feel that the author is entering dominions foreign to his province and is passing judgment upon things which he is not qualified to judge. The author has always felt that the goiter surgeon should not keep himself aloof; his work is inextricably bound up with the work of specialists in other branches of the profession. The goiter problem is an entity; it represents a field of endeavor which should not be divided and subdivided. There is room enough for all—for the internist, the surgeon, the public health official and psychiatrist to work together harmoniously for the common good. It is for this reason that the author has seen fit to consider at some length the phases of the goiter question which are often not adequately dealt with in surgical treatises.

E. P. Sloan

Bloomington, Illinois, U.S.A.
August, 1935

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B. M. J.

FOREWORD

The study of the thyroid gland in recent years has resulted in great progress. The subject has measurably emerged from the realm of mystery and ignorance to the field of scientific research, and already much that is of practical value can be deduced. The horizon is widening and the future along endocrinic lines seems bright with the promise of unlocking many of the unsolved problems in medicine. Many observers have recorded their findings, and Dr. E. P. Sloan has ably reviewed what has been accomplished by many others and added his own valuable contributions in this volume on THE THYROID. For over ten years he had been gathering material from his wide experience to present in book form. He was in the midst of making arrangements with his publisher when his untimely death suddenly came, and so it was not given him to see this product of his labor in completed form.

Among those to whom one's mind instinctively reverts in a discussion of the thyroid gland and its treatment, is Kocher of Berne, one of the early surgical workers with this member of the internal secretory family. It was the result largely of his studies with Kocher some thirty years ago that Dr. Sloan recognized the thyroid gland as an all important factor in many body functions. It had been my own good fortune to work with Kocher some years previously, while doing post-graduate study abroad, and thus my interest, also, in the thyroid and, later in the whole subject of the internal secretions was awakened. In fact, as early as 1900 I was experimenting with the transplantation of portions of the thyroid gland from animal and from man, when available, in a series of cases of hypothyroidism.

Eugene Hertoghe of Belgium, another pioneer along the lines of thyroid dyscrasias, designated the thyroid gland as the monitor of the internal secretions. He believed that this was the key to the solution of many of the problems of the ductless glands. He early recognized the great susceptibility of the thyroid to infection from many sources, although in 1779 Wilmer of Coventry, England, writing on "The Method of Curing the Bronchocele," quoted several cures, in many of which purging was one of the main essentials, proving that guilt, somehow, was placed on the gastrointestinal tract. Today it is generally accepted that intestinal toxemia is one of the causes in much thyroid pathology. Just before the outbreak of the World War, Hertoghe visited this country and demonstrated some of his epochmaking work in myxedemas. Largely as the result of the great interest he created, the Association for the Study of the Internal Secretions was formed.

Sloan's interest was augmented by these activities, and he applied himself more and more to the thyroid gland. The Sloan Clinic, organized in Bloomington, Illinois, in 1917 became one of the national centers in the thyroid field. It has been estimated that at the end of 1934 over

20,000 cases of goiter had registered at the Clinic, and that operation had been performed upon 15,000 of these. In 1921, having as a vision an organization composed of representatives of all branches of medicine, Dr. Sloan founded a Club of local Doctors who were interested in taking a study trip each year to some clinic. In 1923 he organized a clinic group composed of men who were particularly interested in goiter. From this small nucleus the American Association for the Study of Goiter was formed, and held its first meeting in Bloomington, Illinois, in 1924, with an attendance of 289 members of the medical profession. In 1927 Dr. Sloan organized the American delegation to the first international goiter conference held in Berne, Switzerland.

Perhaps Sloan's greatest contribution to the field of thyroid surgery was his anatomical studies especially with regard to the fascial layers of the neck, with particular reference to their relation to the upper poles of the gland. His method facilitated the avoidance, when ligating the superior thyroids, of injury to the superior laryngeal nerves and to any parathyroid body which might be about the superior thyroid arteries. However, I wish here to interpolate that while he endeavored to limit himself to the thyroid, his scientific mind could not completely cease functioning in other directions, for his original incision of the upper abdomen is considered a real advance in surgical technic.

It is difficult to emphasize sufficiently the particularly outstanding points of this volume on THE THYROID. In it Dr. Sloan deals with the thyroid per se, believing it to be the key to the other glands of the internal secretory system. His survey of goiter morbidity with regard to predisposing causes, types, geographic distribution, will be of interest to the public health worker and the internist. The extensive chapters on symptomatology and diagnosis are readable and practical. The volume is an instructive textbook on the general and surgical anatomy of the neck. The chapters alone, on preoperative care, operative technic, and postoperative treatment, make this publication well worth while. The radiologist will find the results of Dr. Sloan's work with radium and the x-rays herein recorded. The theme of the book, it must be borne in mind, is not only the thyroid, but the surgical thyroid, from experiences gleaned in a surgical clinic, and interpreted by a clear thinking, scientific brain.

The value of the work is greatly enhanced by the splendid illustrations that bring home the cogency of the text and illuminate the entire subject.

The endocrinic field is today receiving the attention of workers in all branches of the healing art. But we are still only on the threshold of our knowledge of the functions of the ductless glands and the treatment of their dyscrasias. The eyes of the medical world are focused on this subject as never before. Experimentation, clinical and laboratory, is being carried on in all countries, and to the list of these earnest, patient seekers after truth of yesterday, today, and tomorrow must be added the name of the author of this volume.

Wm. Seaman Bainbridge

New York City

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THE THYROID

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CHAPTER I

GENERAL ANATOMY AND PHYSIOLOGY

The **thyroid gland,** an organ of internal secretion, has no analogue among the other organs of the body. It is distinctive both in structure and function. The range of variability in the normal gland is amazing and has often proved a trap for the unwary, being responsible for conflicting clinical, as well as experimental, results. The surgeon must be well acquainted with all the variations of the normal before he is fitted to cope with the multiple changes induced by pathologic processes.

The thyroid gland is the largest endocrine gland in the body. It varies in weight from twenty-five to thirty-five grams in the adult, with an average of thirty grams. It is situated in the anterior cervical region beneath the infrahyoid muscles on the anterior and lateral surfaces of the thyroid and cricoid cartilages and the upper part of the trachea. It extends from the junction of the middle and lower third of the thyroid cartilage to the level of the fifth or sixth tracheal ring. It consists in the majority of cases of two lobes and an isthmus. There is frequently a third portion called the pyramidal lobe or process, which arises from the upper surface of the isthmus or, sometimes, from the inner surface of the upper pole of one of the lateral lobes. It may extend upward as far as the hyoid bone.

In its **embryonic development** the thyroid gland originates early in fetal life by a down-growth of epithelium from the ventral wall of the pharynx, between the first and second pharyngeal pouches, forming a stalk. The caudal portion very early becomes solid and either grows downward or is dragged down with the trachea and divides into right and left lobes. The upper portion becomes constricted to form the thyroglossal duct. The lumen of the duct is obliterated during the fifth or sixth week of fetal life, and at birth the duct is represented by a small cord of tissue extending upward from the isthmus, or pyramidal lobe, to the foramen cecum dimple at the posterior part of the tongue marks the site of the former opening of the duct. The right and left lobes of the caudal portion are gradually separated by the increase in size of the rapidly developing trachea and larynx. This leaves only the lateral lobes connected across the trachea, anteriorly, in the region of the third and fourth tracheal rings, by a flattened band of thyroid which forms the isthmus.

Displacement of portions of gland during the course of development may occur. A nodule or even the whole gland may fail to descend and remain at the base of the tongue forming a so-called lingual thyroid. Portions detached during the process of descent may form thyroid nodules along the course of the thyroglossal duct. Segments of thyroglossal duct, failing to become obliterated, may give rise to thyroglossal cysts.

General Structure of the Gland

The thyroid is a ductless organ, the structure of which is modelled on the principle of a compound alveolar gland. It is enclosed in a thin layer of connective tissue which is termed the capsule. This surface capsule is rather a complicated structure. On the anterior surface of the gland it is smooth, peritoneum-like, and composed of more than one layer, but on the posterior surface these layers are not distinguishable. Along the post-thyroid plane of cleavage between the pretracheal and prethyroid fasciae, it is very thin, composed of very loose connective tissue, and does not resemble the smooth peritoneum-like structure found on the anterior surface.

The complexity of this capsule is caused by its various attachments: at the hilus near the esophagotracheal notch, it is fused with and is a part of the pretracheal fascia; anteriorly, it is apparently a continuation of the prethyroid fascia. Over the greater portion of the posterior surface of each lateral lobe, the connective tissue framework of the gland structure is so intimately blended with the dense pretracheal fascia that the capsule cannot be distinguished.

On each side the thick, dense pretracheal fascia forms a supporting pedicle for the lateral lobe. From the pedicles, strands of connective tissue, which hold the vessels and lymphatics, extend into the substance of the gland dividing it into lobules. From these interlobular septa, in turn, arise fine strands of stroma containing the small blood vessels and lymphatics. These, the interfollicular septa, constitute the final subdivision of the stroma and form the connective tissue support for the individual follicles. Very often no definite arrangement into lobules or even into lobes is noted; instead, the connective tissue septa merely divide the gland substance into poorly defined masses of irregular shape and size.

For a general description, because of the complexity of the capsule, we may say that the gland is invested with an outer areolar capsule and an inner true capsule. On section, the outer layer is seen to be made up of flat cells with ovoid nuclei, which accounts for the peritoneum-like structure on the anterior surface, and the ease with which the gland glides about under the overlying tissues. The generally accepted opinion is that thin fibrous septa extend into the gland from the inner portion of this capsule and vaguely mark out lobulated areas. Since the fibers that compose these septa are apparently continuous with fibers of the pretracheal fascia which, extending through the thyroid pedicle, enter the gland at the hilus, it is simpler perhaps to conceive of the septa as beginning in the hilus of the gland and spreading outward, finally ending in the capsule.

Each of the two lobes is about five centimeters in length, three centimeters in breadth, and two centimeters in thickness; the lobes are conical in shape, and for the purposes of study each may be said to consist of an upper pole, a lower pole, and a body; the axis of the upper pole is directed upward and outward; the axis of the lower pole is directed downward and inward. The normal thyroid frequently presents the appearance of the

letter U with the upper poles hugging the lateral surfaces of the thyroid cartilage, the isthmus covering the upper tracheal rings, and the base blunt and rounded with a median indentation molded over the fifth or sixth tracheal ring. In about 15 per cent of the cases, the isthmus, a strip of gland tissue covering the third and fourth tracheal rings, is missing and in this respect the gland resembles the thyroid in the dog.

A cross section of the normal gland reveals a smooth, shining surface which, when minutely inspected with the naked eye, shows areas of colloid collected into small lobules separated by very scanty, thin, fibrous septa. The follicular markings or small areas within the colloid follicles vary in distinctness in proportion to their number and the amount of interfollicular stroma.

Blood Supply

The thyroid is intensely vascular; it probably possesses, in proportion to its size, a richer blood supply than any other organ in the body, and its vascularity is further enhanced by a most complete system of anastomoses. In proportion to its size, it receives five times as much blood as the kidneys and even a larger proportion in comparison with many of the other organs. The rich anastomoses and adaptability to collateral circulation assure to the thyroid an efficient blood supply under practically all circumstances. The activity of the gland will be reduced but it will receive sufficient nutrition for continued function if two or even three of the four thyroid arteries are tied; the four vessels may be ligated without danger of necrosis if the relations of the gland to the surrounding structures have not been disturbed; the collateral supply from the adjacent organs, particularly the larynx and esophagus, will be sufficient to maintain its nutrition.

The Arteries (Pairs)

The Superior Thyroid Artery (A branch of the external carotid)

The Inferior Thyroid Artery (Derived from the thyrocervical trunk, a branch of the subclavian)

The Thyroidea Ima (Derived from the innominate or arch of the aorta; occasionally from the subclavian or common carotid)

The **superior thyroid arteries,** irrespective of changes in size and contour of the gland, are always found at the same location with respect to the larynx and surrounding structures. Each artery averages six centimeters in length and divides into three branches near the upper pole. While the branches are subject to considerable variation in caliber and mode of division, they are usually as follows: One branch, the largest, is the direct continuation of the artery and runs downward and inward over the anterior surface of the upper pole of the lateral lobe and along the upper border of the isthmus and anastomoses in the midline with its fellow of the opposite side. This branch is sometimes called the artery of the isthmus. Another branch, the dorsal, runs behind the posterior border of the upper pole. Its branches supply the posterior portion of the upper

two-thirds of the lateral lobe and form a very rich anastomosis with the branches of the inferior thyroid artery of the same side. This is the most complete anastomosis in the organ, more complete than any transverse anastomosis between the lobes. The third, the external branch, shorter than either of the other two, runs downward externally, and enters the substance of the gland near the upper pole.

The **inferior thyroid arteries** are usually larger than the superiors. On each side one of these arteries, terminal branches of the thyrocervical trunk, passes upward from its origin in front of the vertebral artery to the level of the cricoid cartilage, then turns medially and crosses behind the carotid sheath and the middle cervical sympathetic ganglion and enters the lateral lobe of the thyroid. Near its emergence from behind the carotid sheath, it gives off the parathyroid artery. As it approaches the gland, and sometimes a considerable distance from it, the artery divides into two or more branches that enter the lateral lobe at the junction of the lower and middle thirds of its posterior surface. It supplies the posterior-inferior portions of the gland and anastomoses with the superior thyroid of the same side, and with the inferior thyroid of the opposite lobe. There is considerable variation in the position and distribution of the branches, and the relation of the artery with reference to the lower pole is not nearly as constant as the relation of the superior thyroid with reference to the upper pole. One inferior thyroid artery is absent in about 2 per cent of the cases. In some instances it is absent on both sides.

The **thyroidea ima** is a small artery which is seen only occasionally, perhaps once in ten or twelve cases. It arises from the arch of the aorta, or from the lower part of the innominate, and winds upward in front of the trachea to the lower portion of the thyroid and the isthmus. It is variable in size, and often seems to compensate for the absence of one or the other of the inferior thyroid arteries. It may be bilateral or unilateral.

Arterial Anastomoses.—As already shown, the thyroid arteries are not terminal. The longitudinal anastomoses, particularly the anastomosis between the dorsal branch of the superior thyroid and branches of the inferior thyroid, are the most important. The transverse anastomoses from one lobe to the opposite lobe are seen to exist both in the injected specimen and in the operative field. They are, however, quite variable, and much less marked than the longitudinal.

The Veins

Two or more Superior Thyroid Veins (Tributary to the internal jugular)

Middle Thyroid Vein (Tributary to the internal jugular)

Two or More Inferior Thyroid Veins (Tributary to the innominate vein)

The **veins** are thin-walled, without valves; they are more numerous and less constant than the arteries.

The **superior thyroid veins,** one or more on each side, leave the upper pole in close association with the artery and, together with the lingual and facial veins, drain into the upper part of the internal jugular vein.

The **middle thyroid veins** (sometimes called the lateral thyroid veins), one or more on each side, extend directly outward from the lower lateral border of the thyroid, and empty into the internal jugular. These veins are sometimes torn in operative procedures, causing considerable hemorrhage.

The **inferior thyroid veins,** two or more in number, leave the gland at the lower border of the isthmus or lower pole and empty into the innominate veins.

The **venous anastomoses,** both transverse and longitudinal, are on the surface of the gland within the capsule; the intraglandular anastomoses of large veins are rare, if they occur at all.

Lymphatics

Much remains to be learned concerning the distribution and the function of the lymphatics in the thyroid. Very fine lymph spaces, lying outside the capillaries, form a network about the individual follicle. Some believe that these fine lymph spaces connect directly with the follicle. The lymph is drained from these spaces into lymphatic vessels which lie, with the arteries, in the interlobular connective tissue. The interlobular channels collect into larger trunks and finally unite to form plexuses in the capsule of the gland, from which the lymph is taken by way of the cervical glands to the thoracic and right lymphatic ducts.

Nerve Supply

The nerves are derived from the sympathetic ganglia—middle and inferior cervical—and the superior laryngeal and recurrent branches of the vagus.

Nerves.—According to Berkley (1) the non-medullated nerve fibers arise from plexuses in the course of the arteries. Some of these non-medullated fibers are vascular nerves and terminate in the blood vessels, others form meshes around the follicles. From this perifollicular mesh, Berkley traced terminal filaments, which apparently ended on or between follicular cells. There is, however, need for further research along this line.

BIOCHEMISTRY

Perhaps the explanation for the variability in the structure of the thyroid is to be sought in the great functional activity of the gland. The function varies extensively, depending on factors some of which are familiar to us and others of which are unknown. As the pacemaker of metabolism, the thyroid must meet the most varying demands; a condition which requires a certain amount of morphologic flexibility of thyroid histology.

The physiology of the thyroid gland is a study in itself. The surgeon who undertakes to discuss the subject must confine himself to practical limits and attempt only to summarize and correlate a few facts relating to thyroid function.

Thyroid Substance

Composition

Iodin.—The normal gland has greater iodin content than the abnormal gland. According to Marine (2) the normal thyroid, on the average, contains about 0.2 per cent iodin; the maximum store is 0.5 per cent and the minimum store about 0.1 per cent. The iodin content varies with age and other conditions; it is less in infants and in the aged than in middle life, greater in the female than in the male, greater when the food supply is rich in fat or protein. The iodin content varies with the degree of function and is decreased in conditions which demand increased thyroid function, such as pregnancy, lactation, the menopause, and puberty. The affinity of the gland for iodin is extraordinary. Marine (3) states that the iodin content of the dog's thyroid may be increased several hundred per cent within five minutes after the injection of fifty milligrams of potassium iodid in the femoral vein.

Other Constituents.—According to Bayer (4) 5 grams of fresh thyroid contain 0.00102 gram of pentoxide of phosphorus. Brisson (5) found 0.23 gram of baryta sulphid per two grams of thyroid. Crotti (6) notes an apparent antagonism between phosphorus and iodin.

It is quite probable that further investigation will assign greater importance to arsenic, sulphur, and phosphorus as agents that stimulate and take important part in hormone production.

Active Principles

Various substances have been described as constituting the active principle or principles of the thyroid hormone.

In 1895 Baumann (7) discovered *iodothyrin*, an amorphous substance with an iodin content of about 10 per cent and weighing about 4 per cent of the total volume of the dried gland.

Oswald (8) (1901) isolated two substances: Thyroglobulin and Nucleoprotein.

(a) **Thyroglobulin** is found in the colloid to the amount of several grams and increases as the colloid increases. It may or may not contain iodin. When it does contain iodin, it is called iodothyroglobulin, and the iodin is present in about 0.5 per cent.

(b) **Nucleoprotein** contains no iodin but is rich in phosphorus; it is also found in the colloid.

Thyroxin

In 1914, Kendall (9) isolated from the thyroid a crystalline substance which contains 60 to 65 per cent iodin. In 1919 (10) it was shown to possess the formula $C_{11}H_{10}O_3NI_3$.

This substance, which is obtained by the action of carbon dioxide on the thyroid, was named thyro-oxy-indol, and later thyroxin. It is said to possess all the properties and one thousand times the strength of the dried gland. Its action, according to Kendall, is directly on the cells. It has the

qualities of a weak acid; it is insoluble in water, but soluble in sodium hydroxide. The physiologic activity of thyroxin is supposed to reside in the CO-NH groups. It is credible that thyroxin contains some, if not all, of the active principles of the thyroid hormone. Kendall believes that "thyroxin, when properly combined with protein in the gland, is undoubtedly the only physiologically active substance elaborated by the thyroid."

Thyrom

Although thyroxin is 65 per cent iodin, iodin is not the only active agent. The difference in the physiologic effect of thyroxin and iodin suggests that there must be, besides the iodin, other secretory product or products in thyroxin that complement the iodin. This unknown substance, which for the purpose of discussion the author will call "Thyrom," may be pictured as the active principle contained in the thyroxin molecule that differentiates thyroxin from iodin.

Thyroid Secretion

In physiologic thyroid function the writer sees two or more secretory products: iodized colloid and the element designated above as "Thyrom"; or, otherwise expressed, iodin, colloid, and an undetermined product.

The iodized colloid is secreted into the follicle and, according to generally accepted accounts, remains there in storage ready for use.

Relation of Iodin to Thyroid Function.—While the relation of iodin to thyroid function is very close, it must be borne in mind that the effect of iodin seems largely operative within the gland itself. An essential element, indeed, for the formation of the hormone, it stimulates and takes part in the production of hormone, but must not be identified with it except as a part of the whole. The effect of the hormone is operative throughout the system.

Colloid Secretion.—There are, in general, two theories of colloid secretion, the merocrine and the holocrine. In the merocrine type of secretion, the secretory product is evacuated into the follicle by rupture of the nuclear membrane. The cell is not destroyed; it regenerates and resumes its function. In the holocrine type, the whole cell is used in the process of secretion and is destroyed.

Some authorities favor the merocrine theory and some believe that holocrine secretion is responsible for the production of colloid; that the whole cell, nucleus and cytoplasm, degenerates into colloid substance.

Distribution of Colloid.—The method of distribution of the colloid, like the theory of its secretion, is the subject of considerable difference of opinion. The route of the lymphatics has generally been emphasized. It is held, by those who consider the colloid as the whole of the thyroid secretion, that the colloid is taken up from the lymph clefts and conveyed to the circulation.

Particles of substance that look like colloid have frequently been noted in the lymph clefts between the follicular cells. Thyroglobulin has been demonstrated in the neck lymph. It has not been determined, how-

ever, what processes of metamorphosis the colloid must undergo before it is ready for absorption and assimilation.

The theories of colloid distribution undoubtedly might account satisfactorily for some of the thyroid product. That the full complement of thyroid secretion or the sum of the thyroid hormone is taken up in the manner described above is certainly open to question.

It seems very improbable that the interstitial cells should remain absolutely inactive until such time as they have opportunity to engage in follicle formation. If the follicle is the only secreting unit and the colloid the only product, a large portion of the gland does not function. Furthermore, hyperactive glands are frequently found containing little colloid. It seems more reasonable to grant some degree of function to the interstitial cells with the capillaries as the distributing channels for the secretory product than to assume that colloid is thyroid secretion and that the distribution of colloid to the body by some unknown channels is responsible for thyroid function.

If we can accept the holocrine theory, the functional activity of the interstitial cells offers the best explanation of the therapeutic efficiency of thyroid extracts. Thyroid substance is, with no exception, therapeutically and experimentally more active, uniform, and dependable than any other gland substance. This is readily explained if we can believe that all the cells have secretory function, and that these cells with their full substance, both cytoplasm and nucleus, disintegrate and actually contribute to the elaboration of the secretion.

According to this hypothesis, thyroid gland substance contains thyroid secretion and should suitably replace the normal secretion as it does in myxedema. There seems little doubt that both the capillaries and lymphatics play a part in the distribution of the thyroid hormone or hormones in the system. Reasoning from the clinical and experimental evidence known, it seems reasonable to assume that the secretion of colloid is only one important factor in the elaboration of the thyroid hormone. If this is true, it is logical to assume that there is no direct distribution of unchanged colloid to the general circulation.

We know that the iodin in the food and water ingested is, under suitable conditions, absorbed by the blood stream; that much of this iodin is stored in the colloid of the thyroid vesicles. From this point on, our knowledge as to the mode of distribution and specific action of the colloid is, mainly, in the realm of theory.

Distribution of Thyroglobulin.—Hektoen, Carlson and Schulhof (11), by means of a specific precipitin reaction, have shown the presence of thyroglobulin in the lymph of the thyroid gland and in the lymph of the neck lymphatics, but were not able to demonstrate it in the lymph of the thoracic duct or in the arterial blood. The blood of the thyroid vein was found to give a precipitin reaction with thyroglobulin antiserum, and on the basis of the tests made, Hektoen and his associates concluded that the concentration of the thyroglobulin in the thyroid vein blood is approximately the same as in the thyroid lymph.

Elaboration of Thyroxin.—Once the follicle is formed, its function in

storing colloid is evident, and we are of the opinion that its cells, in addition to secreting colloid, have the function of elaborating thyroxin or converted iodin. It is beyond doubt that iodin plays an essential part in thyroid physiology, but the nature of such a part is not clear. A peculiarity of the follicular cells, that they face two ways—toward the lumen of the follicles and toward the interfollicular space—may mean that the cell can secrete in either direction. In favor of a direct secretion into the blood capillaries closely adjacent to the follicular epithelium is the fact, first noted by Langendorff (12), that the cells have no true basement membrane or membrana propria.

With the blood supply of the gland situated in the interfollicular space and the cells facing either way, it is possible that the iodin is brought by way of the blood stream to the gland where in some way it is taken up by these cells and stored in the colloid of the follicle. If we admit that this is possible, we must admit that it is also possible that these cells may take up thyroxin from the follicle and deliver it into the blood stream.

The exact method of elaboration of thyroxin has not yet been proved. We are satisfied that besides the iodin in the colloid, there must be another product to augment the iodin in order to produce perfect thyroxin. The hypothesis accepted as a working basis by the author is that the follicular cells rupture and release colloid into the follicle. These cells then exfoliate and disintegrate, releasing into the follicle an unknown element which is contained in the nucleus and cell membrane. This unknown element, that the author has called "Thyrom" has a great affinity for, and combines with, the iodin in the colloid, producing wholesome thyroxin; this thyroxin finds its way into the general circulation by way of the blood capillaries. If iodin is not present in the colloid of the follicle, true thyroxin is not formed or elaborated, and the unknown element enters the circulation as a toxic substance. Support is given this theory by the well-known fact that normally the thick colloid in the follicle contains a high percentage of iodin.

Discharge of Thyroxin.—We know little of the mechanism which releases thyroxin to the tissues. Formerly it was thought that the cervical sympathetics had influence as secretory nerves. It has been found, however, that section or stimulation of these nerves has little or no influence on the secretory activity of the gland. It has been noted that transplanted thyroids without any nerve supply functioned efficiently and produced a normal product. We may presume that the agent is something in the nature of a deficiency stimulus. When the thyroxin content in the blood and tissues is insufficient for normal cell metabolism, the thyroid is automatically stimulated to release the hormone until normal cell metabolism is again established.

Conclusions

It seems, in the present state of knowledge, that we must believe either that the thyroid has the faculty of multiple secretion, or that the cell which, according to the holocrine theory, becomes a part of the secretion, contains multiple activating agencies. We cannot conceive of iodin being

the only one. The actions of iodin and thyroxin on the normal individual are in no way similar. We have postulated, therefore, the existence of another product, "Thyrom." This may fuse with the iodized colloid in the follicle, or it may excrete into the capillaries and unite with the iodin in the blood stream to form thyroxin in the circulation. The author ventures to suggest the following hypothesis:

(a) The interstitial cell produces colloid that is stored in the follicle according to the merocrine theory of secretion.
(b) The interstitial cell later becomes a follicular cell and finally exfoliates and disintegrates in the follicle according to the holocrine theory.
(c) The active principle or principles, other than iodin—called by the author, "Thyrom"—originates in the nucleus and cell membrane of the interstitial and follicular cells.
(d) Disintegration of the cell in the follicle liberates its "Thyrom" content.
(e) "Thyrom" has a great affinity for iodin and combines with the iodin of the colloid in the follicle to form thyroxin.
(f) Should there be insufficient iodin in the colloid content of the follicle to complement the "Thyrom" released, it enters the blood stream as an imperfect product.
(g) If iodin is present in the blood stream, the "Thyrom" may combine with it to form thyroxin.

EFFECT OF THE THYROID HORMONE ON THE SYSTEM

While the composition of the thyroid hormone itself is still an open question, we have certain very definite information concerning the effect of the hormone on the system. Our knowledge regarding the function of the thyroid hormone may be said to be of comparatively recent date. Very little was known concerning thyroid function until 1874 when Sir William W. Gull (13) published a paper on cretinoid conditions in women. Kocher (14), in 1883, with his paper on postoperative myxedema, focused the attention of the medical profession on the importance of the thyroid function. Previous to his time goiter was, generally speaking, a deformity rather than a disease and dysfunction of a most important organ.

Marine summarized his position as regards thyroid hormone in the following sentence: "The major function of the thyroid, as far as we know it, is to provide a higher rate of metabolism than would otherwise exist, and for varying this rate"(15).

The influence on metabolism has gradually come to be looked upon as the chief, and by some authorities, as the only rôle of the thyroid hormone. If, indeed, the action of the hormone is directly on the individual cell, as is claimed by many at the present time, it is easy to understand how changes in cell metabolism may account for all the phenomena incident to thyroid dysfunction. The bone changes, the tissue changes, the changes in the genital system and the nervous system in hypothyroid and athyroid conditions are explained by decreased cell metabolism and decreased cellular activity in the bone cell, the tissue cell, the nerve cell, and the genital cell. Combustion in general is slowed up and the changes

seen in the tissues are not specific changes due to a specific hormone; these changes are, rather, the result of incomplete combustion, of smoldering cell activity, with each cell reacting to unfavorable influence according to its type.

In the hyperthyroid conditions, on the other hand, the cell flames, rather than smolders, and this concept of flaming or greatly increased cellular activity furnishes a better picture of the syndrome of diffuse hyperplastic goiter than any other theory.

Endocrine Balance

Thyroid function is intimately associated with the function of the other ductless glands—the pancreas, the adrenals, the hypophysis, the pituitary, the thymus, and the sex glands. Any disturbance in one gland is bound to have some influence on the function of the other glands, and on the endocrine balance in general.

Action of Thyroxin.—Thyroxin cannot by any means be considered identical with the thyroid hormone in its action. Still, it undoubtedly possesses many of the qualities of the normal thyroid secretion. Kendall (16) believes that thyroxin and consequently the thyroid hormone, acts directly on all cells.

Evidence would seem to indicate that thyroxin acts somewhat in the manner of a catalytic agent. The total quantitative amount of thyroxin in the system and the extremely small amount required for adequate function seem to preclude any other explanation. According to figures quoted by Plummer (17) the thyroid delivers approximately 0.33 milligrams of thyroxin daily. The amount of thyroxin in the adult tissues is about fourteen milligrams.

Plummer also notes that "after the administration of a single dose of thyroxin sufficient to bring the basal metabolism to normal, the physiologic status of the thyroidless patient becomes normal in from ten to twelve days, remains approximately normal for ten days, and returns to preexisting status in from five to seven weeks."

The intravenous administration of one milligram of thyroxin elevates the basal metabolism approximately 2.8 per cent. This increase is constant until levels considerably above the normal are reached.

With the normal ration of thyroxin in the tissues and in the gland, normal metabolism results; the cellular anabolism and catabolism are in equilibrium, the weight remains steady over long periods, and the basal metabolic rate remains normal. The balance is very fine, as is shown by the fact that an increase or a decrease of one milligram of thyroxin in the tissues is followed by a rise or fall respectively of about 3 per cent in the basal metabolic rate.

The administration of thyroxin in excess, and over a period of several days, produces a syndrome somewhat similar to that of diffuse hyperplastic goiter. In moderate and repeated dosage: increased pulse, rate, irritability, and increased heat production are noted. With this syndrome

are associated: increased intake of oxygen, increased giving off of carbon dioxide, and increased elimination.

Kendall (16) in a series of experiments on dogs, brought out very clearly the sequence of symptoms due to administration of thyroxin. After subcutaneous injections into animals, little or no effect either on the pulse or the blood pressure is evident for twenty-four or thirty-six hours; after this period the dog appears restless, has slight temperature, and a marked increase in the pulse rate. The severity of the symptoms increases for four or five days and then gradually subsides.

If the animal is injected on successive days, the symptoms already mentioned are much aggravated, and after two or three injections, diarrhea, loss of weight, and tremor are noted. The severity of the symptoms increases and, on the fourth or fifth day, the pulse rate is between two and three hundred and other symptoms are in proportion.

Basal Metabolism and Heat Production.—In addition to the administration of thyroxin, there is other proof that the thyroid is the principal organ concerned in the regulation of basal metabolism and heat production.

(1) After thyroidectomy there is a considerable, sometimes a very great, fall in the basal metabolism. The metabolism rate is below par in hypothyroid conditions, postoperative or otherwise.

(2) If the suprarenals are injured by sufficient, but sublethal injury, a marked increase in heat production ensues provided the thyroid gland is intact. If thyroidectomy has been done previously, the increase in heat production is decreased or abolished.

(3) The normal rise in heat production during pregnancy and lactation is reduced when the thyroid is removed.

(4) In diffuse hyperplastic goiter, the metabolism rate is invariably raised.

In this connection it may be of interest to quote another statement made by Marine relative to the physiology of the thyroid: "Physiologically, the lung has to do with external respiration while the thyroid has to do, in some important way, with internal respiration or the utilization of oxygen by the tissues" (15). The blood transports the oxygen from its reservoir in the lung to its furnace in the cell where it is consumed; the thyroid hormone keeps the furnace going and the flame steady.

Detoxication Theory.—Establishment of the theory of the direct action of the thyroid hormone on cell metabolism would tend to discredit early conceptions such as the detoxication theory. Many authorities have believed and some still believe that the thyroid has an antitoxic action, that the thyroid hormone has the power of neutralizing poisons resulting from metabolic processes. Indeed, some years ago the theory was held that the action of the thyroid was local, and that the blood was cleared of its toxic agency as it circulated through the thyroid.

There seems to be some basis for the detoxication theory in the fact that in thyroidectomized animals bleeding or the intravenous injection of salt solution has a favorable influence on the symptoms of hypothyroidism. It seems more rational to suppose that the poisons eliminated

by these measures are the result of flagging or smoldering cell metabolism than to assume that they are present because they have not been neutralized by some antitoxic property of the thyroid gland. Thyroidectomized animals are said to be more susceptible to infection. This may be true, but possibly the increased susceptibility may be due to disturbed metabolism rather than to any change in the antitoxic property of the blood.

Defense Reaction Theory.—The same argument will apply to the theory that one of the functions of the thyroid is to formulate a defense against bacterial invasion. Correct cell metabolism is the basis of health and is in itself the best protection against bacterial invasion. If the thyroid hormone contained bactericidal or antitoxic properties, it would be logical to suppose that the thyroid gland, where the hormone is prepared, would not be very susceptible to infections. The writer believes, on the contrary, that, considering its efficient blood supply, the thyroid is quite susceptible to infection and that diffuse hyperplastic goiter, for instance, is, in the great majority of cases, an expression of infection. Thyroiditis, also, is more common than generally supposed, and its rather frequent occurrence speaks against the existence of a bactericidal substance in the thyroid gland.

Conclusions

Thyroxin may not be the entire thyroid hormone, but it constitutes an important and essential element of the hormone.

The action of the thyroid hormone, as indicated by the action of thyroxin, seems chiefly concerned with metabolism, and apparently is directed toward the individual cell. The thyroid hormone or some of its constituents act as a catalytic agent in promoting cell metabolism. There is a relationship between the amount of thyroxin in the tissues and the basal metabolism or cellular activity.

Thyroxin is about one thousand times the strength of the gland extract, and its action in general is proportional. Some of the older theories of thyroid function seem untenable. Bacteriolytic and detoxication theories are more rationally explained on the basis of changes in cell metabolism.

As a result of increase or decrease of thyroxin in the tissues, we have increase or decrease in cellular activity, with resultant changes in tissue structure and function.

Obviously, since we do not know the exact composition of the thyroid hormone, we cannot judge of its action or efficiency directly; but appreciation of the scope of thyroid function may be obtained by considering the action of the hormone or hormones: (1) As suggested by the synergistic or antagonistic action of the other glands of internal secretion; (2) As suggested by the action of thyroxin and the result when the thyroid secretion is absent, decreased, increased, or qualitatively changed.

CHAPTER II

ETIOLOGY

A chapter on the etiology of goiter must, in the present state of our knowledge, be an outline of surmise and theory rather than a chapter of demonstrable fact or scientific knowledge.

In the earliest pages of history we find speculation active as to the cause of goiter. Long before the Christian era, public intelligence and popular superstition were concerned with the problem of goiter etiology. In the records of all ages, water and goiter are mentioned together in terms of vague association. The wells, and in some instances the rivers, were blamed, and signs were posted, as on the wells in Chios, warning the pedestrian that the price of a drink was mental dullness. Vitruvius (18), in the first century of the Christian era, writes of a water which he considered goitrigenous as "genus aquae, quam qui bibunt efficiuntur turgidis gutteribus"; "those who drink of it are affected with enlargement of the neck."

Water is still, either in its mineral content or its bacterial contamination, the chief object of suspicion. Theories of varying plausibility concerning the agency in the water which is the direct cause of goiter have been expounded, some of them sustained by apparently convincing experimental or clinical evidence.

The experimental and clinical results, however, have not been uniform in the hands of competent observers. It is, therefore, not possible to state with absolute scientific certainty that any one etiologic factor is of itself the exciting causative agent of any one type of goiter disease.

A thorough discussion of goiter etiology with an exhaustive survey of the literature is a Herculean task and is not practical for the purposes of this book. An attempt will be made, however, to group together in one chapter the significant facts, as far as we know them, on the etiology of the different types of thyroid abnormalities.

ATOXIC CONDITIONS

Sporadic Colloid Goiter

Exception may at once be taken to a distinction between sporadic and endemic goiter. It may very properly be argued that the goiter of puberty, pregnancy, and other conditions of special demand on the system is, in effect, the same simple colloid type as endemic goiter and should be discussed with regard to its etiology under the same heading. In districts where endemic goiter is very prevalent, it is, of course, impossible to make any distinction; but in the districts in which endemic goiter is rare or unknown, it must be granted that the picture as regards

the etiology is slightly different. It is questionable whether the etiologic factor or combination of factors operative in the mild transient goiters of school children in a goiter-free district is the same as that causing the severe persistent goiter of the endemic areas.

Predisposing Causes

Any condition that tends to disturb the mineral balance of the body or promote mineral deficiency may act as a predisposing cause.

1. Infection

   Focal Infections

   Teeth, tonsils, sinus infections, gastro-intestinal derangements, uterine and ovarian disease.

   Systemic Infections

   Influenza, pneumonia, typhoid, rheumatism, measles, scarlet fever, mumps.

   Chronic Infections

   Tuberculosis, syphilis, pyorrhea.

2. Debilitating Influences

   Exhaustion, overwork, prolonged hours of study in the period of adolescence, loss of sleep, excitement, overstimulation, etc.

Physiologic Goiter

In school surveys in comparatively free districts, some enlargement of the thyroid is found in a certain percentage of the girls between ten and nineteen. A large number of these mild goiters clear up spontaneously without any treatment, and this percentage of spontaneous "curves" has suggested and perhaps justified, the term "physiologic goiter."

We know that proper thyroid function including the production of adequate amounts of thyroxin is essential to proper physical development, particularly at the time of puberty. We know that this, particularly in the female, is a period of emotional flux and great physical change, and that the calls on the thyroid to maintain a normal metabolism must be great. In addition to thyroid hyperactivity, there is evidence of increased activity on the part of the other glands of internal secretion, especially the pituitary, adrenals and ovaries. A generalized endocrine stimulation is evidenced by the onset of the menses, the rounding and development of the breasts, the growth of the pubic hair, and other indications of the differential development of puberty. To some, a mild hypertrophy of the thyroid at this time seems normal, as normal as the swelling of the breasts or congestion of the ovary.

There is, however, another point of view. The work of recent investigators, particularly Marine and Kimball (19), indicates that there is a very definite relationship between thyroid hypertrophy and iodin deficiency; that thyroid hypertrophy at puberty is, in fact, in the great majority of cases, an indication of thyroid insufficiency due to iodin deficiency.

There is much evidence to show that goiters of puberty and adolescence can be prevented, in the great majority of cases, by the systematic administration of small doses of iodin, sufficient, theoretically, to maintain the iodin content of the gland at 0.1 per cent.

If, then, the mild goiter of puberty or adolescence in itself is an expression of iodin deficiency, an effort on the part of the thyroid to overcome the effects of this deficiency by hypertrophy, it cannot be considered normal any more than a hypertrophied heart can be considered normal.

Nevertheless, admitting that sporadic adolescent goiter is goiter and not a purely physiologic hypertrophy, it is difficult to place it on the same etiologic plane as the goiter seen in the highly endemic areas. Is the difference in the clinical picture to be ascribed solely to the difference in degree of iodin deficiency in the nutritional supply? Or is sporadic adolescent goiter usually the result of the increased call upon the thyroid in the presence of mineral deficiencies due to inadequate assimilative function, whereas endemic goiter is the result of mineral deficiencies because of inadequate amounts of iodin and other mineral elements in the nutritional supply? Does not the picture fit the known facts? Increased call upon the thyroid and defective mineral assimilation means sporadic goiter. Deficiencies of iodin and other minerals in the nutritional supply of a community means endemic goiter. If in sporadic goiter assimilation improves so that minerals are absorbed and the deficiencies are corrected, before changes in gland structure have occured, the goiter disappears. If the mineral deficiencies in the nutritional supply of the people of a community are corrected, the goiters disappear and the endemic subsides.

Increased call for thyroid function is thought by some to be the cause of adolescent goiter. We must admit the need of thyroid function for differential development, and that puberty and adolescence are periods of developmental activity. But, not all thyroids respond at puberty to increased call by hypertrophy.

Is it not also possible that the increased call is really a deficiency stimulus from inadequate thyroid function—a deficiency in the normal store of thyroxin rather than an increased need of thyroxin? That the thyroxin deficiency overstimulates thyroid activity which in the presence of mineral deficiency results in the storage or accumulation of colloid in the gland? That the retention of colloid in the gland is responsible for the enlargement called colloid goiter?

In support of this theory we might mention the favorable effect upon an early colloid goiter of increasing the iodin content of the colloid by the administration of iodin. If no other mineral deficiencies are present, almost every colloid goiter of recent development will disappear.

But why should colloid goiter usually develop at puberty rather than in early life when thyroid function is so necessary for differential development? In the majority of cases there is every reason to believe that mineral deficiencies were present in early life. The answer seems to us to be in the stage of development of the thyroid gland itself. In early life the follicles are smaller, not so numerous, and the interlobular septa are relatively thicker and stronger. Distention of the follicles with exces-

sive storage of colloid is not so likely to occur as in later life, when increase in size and number of follicles and relative decrease in thickness of interlobular septa have occurred. Changes in the gland structure seem to offer a more plausible explanation for the appearance of colloid enlargement of the thyroid at puberty than the increased call alone.

Other Types of Simple Sporadic Goiter

What has been said of the goiter of puberty may apply equally well to the thyroid enlargements seen during the menopause, pregnancy, and the period of lactation. Do these conditions call for an excessive amount of thyroid secretion or thyroxin so that in an effort to meet this increased demand the thyroid hypertrophies, or is the hypertrophy caused by a deficiency, at this particular time, of iodin or other necessary mineral constituent of the body? The course and development of goiters that occur during the pregnancy is usually similar to that of the same kind of a goiter at other periods of life in the presence of severe mineral deficiencies. It seems quite probable that the colloid goiter that occurs during pregnancy is due to mineral deficiencies from disturbance of assimilation instead of to increased call.

Endemic Colloid Goiter

To those who consider the etiology of endemic goiter a closed chapter, with iodin deficiency as the sole etiologic factor, the definition of McCarrison will be of interest. For a period of several years McCarrison, an officer of the Indian Medical Service, conducted research and experimental work in a district of the Himalayan Mountains which he characterized as "probably one of the purest regions of endemic goiter in the world" (20). He defines endemic goiter as "A chronic infectious disease, occurring in a more or less circumscribed area, and characterized by a non-inflammatory and progressive enlargement of the thyroid gland, which is unattended with marked functional disturbance." Such a statement is indicative of the necessity of approaching this topic with an open mind.

At the present time when goiter surveys and prevention campaigns are matters of great interest, it may be well to consider briefly the question of the prevalence of endemic goiter.

Prevalence

Much remains to be done in the way of determining the present day incidence of goiter. There is great need of further survey work, both in the schools and throughout the adult population.

We know that goiter is as old as history, and we have in the records of the European countries some idea of its prevalence in the past. As early as 1874 France was said to have at least 375,000 people suffering from goiter and over 120,000 cretins, and Italy was said to have over 128,000 goitrous individuals. According to some statistics almost 90 per

cent of the school children of Berne, Switzerland, were goitrous in 1904. In a later survey of the public schools of Zurich, practically 100 per cent of the children were found to have definite enlargement of the thyroid. McCarrison states that in certain villages in the Himalayas two-thirds of the men, women, and children are suffering from goiter, and estimates that in the Indian Himalayas and Europe alone there is a goitrous population of about five million and this estimate is probable ultraconservative.

Geographic Distribution

Endemic goiter is met with in practically every country in the world. According to most writers it is more common in the temperate and subtropical zones; that climate in itself, however, is no deterrent is demonstrated by the fact that it occurs in Siberia, Finland, and northern Canada, and, in the heat of the tropics, in such countries as Ceylon and India, Borneo, Sumatra, Java, and in Central and South America. It has been noted in the Sahara Desert.

What is true of climate is true of topographic considerations. Endemic goiter may be found wherever man can live; McCarrison found it at an altitude of 10,000 feet in the Himalayas; it is found in the mountains, in the plains and, contrary to general belief, it is not uncommon at the seashore.

With this understanding that endemic goiter may occur anywhere, it may be permissible to state that there seem to be certain topographic areas of predilection, and that these areas of predilection in the order of their importance seem to be the mountains, the high plains, and the lake regions.

Mountains.—In Europe, the Alps have been, from the dawn of history, a focus of high endemicity. Goiter is very common in Switzerland, the Tyrol, the Alpes-Maritimes and the Basses-Alpes, and the Savoy. It is met with in the Pyrenees, the Carpathians, the Vosges, and in England in the Cotswold and Mendip Ranges. It is rare in the mountains of Norway and Scotland. In the Orient, it is quite common in the Himalayas; less common in the mountains of Abyssinia and Japan. It is found in many of the mountain ranges of Africa.

On the American continents, it is found in the Andes of South America, and is common in the Rocky Mountain Districts of North America.

Plains.—That goiter is by no means rare in the plains is evidenced by the existence of goiter belts in Ohio, Missouri, Texas, New Mexico, Utah, Dakota, and the northwest states. In Kansas, as revealed by Earle G. Brown's survey (21), a large percentage of the children are affected, goiter is also common in certain districts of Arkansas, Oklahoma, and Nebraska, and in the endemic areas in the plains of Alsace, Piedmont, and Lombardy.

Lake Regions.—River beds and marshy ground have been associated by many writers with the incidence of goiter, as the Struma River in the Balkans mentioned by Crotti (22), and the Guay-qui-raro (thick-

neck maker) River in Brazil. It is also common along the course of the Lena and Obi Rivers in Russia, and in the territory of the Ganges and Brahmaputra in India.

As already mentioned the St. Lawrence Basin and the region of the Great Lakes are goiter belts. The surveys show that goiter is quite common in the school children of Ohio, Illinois, Minnesota, and Wisconsin.

Seacoast.—McCarrison takes some exception to the belief that the seacoast districts are comparatively clear, and mentions as endemic areas such littoral regions as Glamorganshire, the Island of Arran off Algeria, the Ganges Delta, and certain districts on the shores of the Mediterranean (20). Perhaps we might add the northwest Pacific coast in this country.

Goiter in the United States

Surveys have shown that goiter is much more common than had been supposed among the general population of this country, and that our "endemic areas," though for the most part the occurrence is of moderate or mild goiters without cretin accompaniment, may be compared as regards numerical incidence with the severe "goiter districts" of Europe. Bram of Philadelphia states that there are over five million people suffering with goiter in the United States (23), and this estimate, in the opinion of the writer, errs on the side of conservatism.

Montana.—In a survey of Montana school children by the United States Public Health Service in 1924 (24) it was found that of a total of 13,937 children, 3,011 or 21 per cent showed simple goiter. In a group of 9,321 children, 32 per cent of the girls and 13.4 per cent of the boys showed thyroid enlargement. Of 363 high school girls examined in Lewistown, 54.5 per cent had enlarged thyroids. Of the girls of sixteen years of age who were examined, 83 per cent showed definite thyroid enlargement.

Minnesota.—From a survey of 4,061 school children in thirteen localities, Olesen and Clark (25) report that 71 per cent of all the girls showed thyroid enlargement as against 41 per cent of the boys. In one school district, Marble, it was found that only 14 per cent of the girls were free from thyroid enlargement.

Ohio.—In 1924 Robert Olesen (26) made a survey of 47,493 children in the elementary schools of Cincinnati. He found that 33.2 per cent of the children showed thyroid enlargement, 39.8 per cent of the girls and 26.8 per cent of the boys.

Kansas.—Earle G. Brown (21) in a goiter survey of the grade schools of Topeka, Kansas, in 1925 found definite enlargement of the thyroid in 44 per cent of the white girls, 56 per cent of the colored girls, 33 per cent of the white boys, and 16 per cent of the colored boys.

These statistics from different parts of the country show that during the first twenty-five years of this century the goiter problem was of great magnitude in the United States. Following the World War a wave of intense interest in the goiter problem swept the country. The appalling prevalence of the disease as disclosed by the results of numerous surveys by Federal, State, and municipal health departments awakened the

people to the seriousness of the problem. School inspections confirmed the findings of the health departments and brought the problem home to every community. The people became "goiter minded" and since 1925 the incidence of goiter has rapidly declined.

It is certain that a large part of this decline in the incidence is due to the prophylactic measures instituted. We should not forget that there is great need of prophylaxis and treatment during the school years if we are to prevent a high incidence of "goiter hearts" and invalidism in the rising generation, and the gruesome sequelae of cretinism and imbecility in the more distant future. Endemic goiter is apparently an early manifestation, and cretinism a late manifestation, of thyroid insufficiency in a community.

Etiologic Factors

Race

Race, per se, has no influence. The Japanese were said to have some immunity, but the alleged immunity is probably due to the fact that they use seaweed in their diet. The percentage of iodin and other minerals in the seaweed is sufficient to prevent a high incidence of goiter. The incidence of goiter among Japanese living in goiter belts in this country is as large as among the rest of the population.

Sex

Colloid goiter in childhood occurs in females and males in the ratio of four to three; in the teens in the ratio of five to two; in mid-life it has been given as six to one.

In the author's experience the ratio of females to males varies greatly. In his first series of 1000, females predominated in the proportion of ten to one. In his last thousand cases there were 310 males. In areas of mild endemicity, the proportion of males to females has been given variously; one to eight, one to six, one to four and so on. The higher the endemicity, the greater is the proportion of males affected, and in the highly endemic areas the sexes may be affected almost evenly. The high proportion of males affected is said to be more common in the mountainous districts.

Age

Colloid goiter that occurs in endemic form is almost entirely confined to childhood and the teens. Children entering goiter belts from free districts are especially susceptible. In the endemic districts, goiter in very young children is not uncommon. Goiters are occasionally noted even in breast-fed children. McCarrison observed goiter in infants only when the mother had a large and degenerate goiter and lived in a district where the endemicity was high (20). Contrary to McCarrison's observation, the writer has seen twenty-two cases of congenital goiter, and in only one of these was the mother goitrous.

Girls between the ages of eleven and sixteen will show by far the

greatest percentage of goiters. It is found also that as the degree of endemicity increases, the tendency to goiter in the younger children increases so that we must estimate from below the age of eleven, if we are to approximate the true incidence of goiter in one specific community.

Season

According to McCarrison, new cases appear and preexisting goiters enlarge during the spring and autumn months. He has never noted a case which had developed when the temperature was below zero.

Heredity

The factor of heredity is difficult to evaluate owing to the fact that we have to reckon with other influences besides pure biologic transmission. It is not far-fetched to suppose that there exists a predisposition to goiter as to other chronic diseases; that certain families are more sensitive to mineral deficiencies or to specific goiter toxins, if there are such. We do know that goiter in the children is more common when the parents, especially the mother, are goitrous.

Every physician, even in districts where goiter is not endemic, has seen families in which two or more members were goitrous. Many observers see hereditary influence in the "family type" of goiter; that is the type of goiter that appears at the same age in two or more daughters, pursues a similar course and disappears in many cases at about the same time.

An interesting and significant observation, reported by some authorities, is that goiter heredity, apparently operative in an endemic area, disappears after several generations of existence in a free district. However, unless preventive measures are instituted, the direct descendants of goitrous individuals who have moved from a goiter district into a free district are usually goitrous.

Occupation

In the endemic areas, laborers and farm workers seem more affected. In those who move into an endemic district, it has been found that those who work with their hands close to the soil more frequently become goitrous. The social level, meaning presumably the better habits of hygiene, is an important factor. In troops that move into an endemic area, the enlisted men are much more liable to goiter than the officers. Merchants, business men, and clerks who move into a goiter district very frequently remain free from goiter.

Constitutional Predisposing Factors

Whether we accept the mineral deficiency theory or the infection theory of goiter causation, we may safely assume that any condition tending to disturb the mineral balance on the one hand or lessen the resistance to infection on the other, must be considered as a predisposing cause.

Pregnancy

In the district in which the endemicity is not high, the goiter in many cases appears with the first pregnancy and becomes worse with subsequent pregnancies.

Diet

Perhaps the etiologic possibilities of the diet have not received sufficient consideration. We have overlooked to some extent the fact that food is as essential as water; and that, if mineral deficiency is really the exciting cause of goiter, we should scrutinize the menu and study the sources and quality of the food supply in the endemic districts.

This phase of the question was forcibly impressed on the mind of the writer some years ago. During a very dry summer in Illinois the local supply of vegetables was greatly reduced by the drought. Two school districts a short distance apart came under his observation. In one district the children had very little or no green vegetables, fruit, or milk. An inspection made in the following January showed that forty-nine of the sixty-one school children had enlarged thyroids. In the other district five miles away, the people were Germans, had cultivated their gardens intensively, and notwithstanding the drought the children had a fair supply of green vegetables and milk. Only three children out of forty-seven in this school showed any enlargement of the thyroid. The following year, due to a more severe drought, even the industry of the Germans could not save the gardens and pastures. The milk and vegetable supply was extremely limited. By the next January thirty-six out of the forty-nine children had developed a definite enlargement of the thyroid gland.

In the report by the United States Public Health Service of a survey in the Montana school children already referred to (24), some interesting facts are brought out along this line. It was found that goiter was much more prevalent in the isolated rural communities where few vegetables are grown. The supply of fresh milk and fresh meat is also limited. Here, we have a rural community debarred by climate and geographic location from the use of green vegetables. What is true of these communities in Montana is true for most mountain districts, except perhaps some of the well cultivated cantons in the Alps.

The nature of the soil, the difficulties of transportation, and the climate, conspire to make the diet of the mountaineer very deficient in the matter of fresh vegetables and milk, and it is not a far-fetched speculation to suggest a relationship between this peculiarity of diet and the incidence of goiter in mountain districts.

Water

Water has been incriminated by almost every writer from the time of Hippocrates down to the present as the chief agency in the dissemination of goiter. It is difficult to combat the array of evidence in favor of the theory that water is the medium through which goiter is acquired.

Rain Water.—It has been repeatedly shown that even those who reside in endemic districts are often immune if they drink rain water. In a village where part of the inhabitants use the water from cisterns containing rain water, and part use the water from goitrigenous springs, those using the water from the springs develop goiter, while those using the rain water remain free. While this may be true as a rule, it is not universal, and cases are on record where goiter developed even though rain water was used exclusively. Immunity also seems to hold true for those who use wine to a great extent as a beverage instead of water.

Goiter Wells.—The popular belief in the existence of goitrigenous wells in Europe was so profound that the young conscripts were accustomed to drink from them in an attempt to develop goiter and escape military service.

Changes in the Water Supply.—The installation of a new system of water supply offers one of the most conclusive proofs of the connection between water and goiter. A reduction in the incidence of goiter following the installation of a new water supply has been reported from many severely affected districts.

The converse is also true; areas that have been free while using one water supply have become affected when another water supply was substituted. This has been noted several times when, owing to the drying up of the streams, it was necessary to sink wells. Many of those who drank from the wells developed goiter though they had remained free while using the water from the stream.

Epidemics, so-called, have occurred amongst troops, students, and other groups who entered goiter belts from free districts. These epidemics disappeared when the water supply was controlled.

Iodin Supply

It is true that in case after case the water supply seems to have been incriminated; in town after town the population has become goiter free after the installation of a new water supply. Presumably, the virtue in the new water supply was a slightly increased iodin percentage. If we admit this and that goiter is due to a mineral deficiency, we must admit that increased vegetable consumption with increased iodin absorption would have had the same effect as the new water supply and would have rendered the population immune against goiter.

Marine and Lenhart's experiments (27) indicated lack of iodin in the water as the etiologic factor in the production of goiter in fish; one must realize, however, that the fish has no other source of iodin supply except the water, and that in the case of the fish it is probably true that goiter in every instance is a revelation of iodin deficiency in the water.

This reasoning cannot, of course, be applied to man. We can get our iodin ration from the food, and possibly from the air, as well as we can get it from the water.

In regard to these districts where the change of water supply made the community practically goiter immune, it is perhaps safe to assume

that the general dietary was so low in vegetables, fruits, and milk with their iodin content that a water poor in iodin was the last straw; the system already laboring under iodin starvation in the food could not carry on under the additional load of iodin starvation in the water.

If there is enough absorbable iodin in the food, the water supply can remain a matter of indifference as far as goiter is concerned, and as iodin is probably only one of the mineral elements which are deficient, it is more rational and more scientific to attempt to restore the mineral balance of the body by a judicious and well-planned dietary than to bring the iodin content of the water supply up to normal artificially or to correct the deficiency by mass administration of iodin.

The prophylactic administration of iodin in the schools and in the community in general in certain districts is, of course, a necessity at the present time; it should, however, be the aim of the physicians and public health officials to carry on a simultaneous campaign of propaganda and education along the lines of dietetics, so that eventually the iodin pellet may be dispensed with and the public receive their iodin in more natural form.

Hygiene and Climate

All authorities seem to agree that during the first twenty-five years of this century there was an increase of goiter prevalence in this country. The explanation of this may, at least in part, be traced to the change in living conditions during that period.

The children did not have the benefit of as much sunlight as did the children of previous generations. The tenement, the flat building, and the two and three-room apartment supplanted the perhaps poorer but more hygienic home life of earlier years. Enclosed urbanization, crowded workshops, and stuffy offices did for the adult what the flat building did for the child. We became a race of shut-ins, debarred by economic conditions from the sunlight. The beneficent influence of sunlight and the important part that light rays play in the processes of metabolism and especially in calcium fixation was not generally known. The need for iodin, calcium and other minerals had not been widely recognized.

With this idea in mind, let us compare for a moment the goiter incidence during this period in different parts of the west coast. The inhabitants of the northwest portion of the United States, Oregon and Washington particularly, are, as a class, fairly prosperous. They live well and in addition eat large quantities of sea food. There can hardly be any question but that they receive sufficient iodin in their food. Nevertheless, what is the situation as regards goiter incidence? Not only is the region endemic and simple goiter almost the rule in some districts, but the sequence from simple goiter to degenerative adenoma and to toxemia seems to develop more rapidly than in almost any other part of the United States. Why? Absence of sufficient exposure to the influence of the actinic ray seems to be the answer. The climate is sufficiently cool to make fairly heavy clothing comfortable all the year round. This wards off the actinic ray except from the hands and face. Coughs and colds are common although the people live an indoor life.

Let us travel down the coast a little. The goiter incidence remains high until we arrive south of San Francisco. We get to Monterey and find that there is very little endemic goiter there. Finally, we reach Los Angeles, and are told by members of the profession that goiter never develops there; that such goiters as they see are imported. The people in Los Angeles do not receive as much iodin in the food as do the people of Seattle. Yet the people in Los Angeles do not develop goiter. Why? Because the people of Los Angeles do not shut off the influence of the actinic ray with heavy clothing. Many go bareheaded, often with shirt sleeves rolled up and their shirts open at the neck. They live an outdoor life, have sunshine winter and summer, and spend more time in their bathing suits than do the people of most other parts of the United States.

It is probably also true that the quality of the meat and animal products in such a country as southern California differs considerably from the quality of meat and animal products in cold or mountainous climates. It can hardly be supposed that the quality of the meat or of the milk in animals shut up in barns for a large part of the year away from the sunlight, as they are in cold or mountainous climates, can be the same as from animals of a warm climate.

It seems to the writer that the fact that people using a diet largely vegetarian are less susceptible to goiter may, in part at least, be due to climatic influence. No doubt, the vegetables and fruits, as already stated, have an inhibiting influence, but in addition we must recognize the fact that the people subsisting on a largely vegetarian diet are, generally speaking, people who live in warm climates and who are accustomed to long hours of exposure to sunlight.

Goiter certainly does occur in warm climates; even in the tropics. But it must be remembered that the economic condition of the natives of most of the tropical countries is very low and that sunshine cannot alone counterbalance the results of a meager and poorly balanced diet and impoverished living conditions. In the Los Angeles country, we have the counteraction of plenty of sunshine and wholesome food supply —and we have no goiter. In these prosperous north and south sections of the Pacific coast, sunshine may be the factor that explains the prevalence of goiter in Washington and the absence of goiter in Southern California.

Exciting Cause

While practically all proponents of the water theory are agreed that there is a principal medium through which endemic goiter is propagated, there is by no means unanimity of opinion amongst authorities as to the agent or deficiency in the water which is responsible for goiter. Most of the present day writers favor the theory of mineral deficiency. McCarrison (20) ably seconded by Crotti (22), is inclined to the theory of a *contagium vivum* in the water as the exciting cause.

Some men, notably Kocher and Bircher (28), advocated the hydrotelluric theory. Repin (29) advanced the hypothesis of the radio-active qualities of goitrigenous waters.

We will discuss two or three of the more generally accepted theories;

it may be stated, however, that of recent years there are only two theories that meet with acceptance from most recognized authorities: (1) the *contagium vivum* or infection theory as advocated by McCarrison and Crotti and, (2) the mineral deficiency theory, especially iodin, as advocated by Marine and most American writers.

The Hydrotelluric Theory

According to this hypothesis, the cause of goiter is to be sought in the organic or inorganic substances in the water derived from the soil through which the water percolates. It attempts to formulate a relationship between endemic goiter and geologic formations.

As the result of extensive research, H. Bircher (28) came to the conclusion that endemic goiter and cretinism occur only upon marine deposits of Paleozoic, Triassic, and Tertiary periods. Bircher did not attempt to define the nature of goiter toxin, but asserts that it is colloidal in nature and that it is absorbed by the water in its passage through the rocks.

His opinions have not been confirmed by other authorities, with any degree of uniformity; a few agree with him. The majority have found, however, that goiter may occur in the presence of any variety of geologic formation, and that the porosity of the soil which predisposes to stream and well contamination is of more importance than the character of the geologic formation.

Infection Theory

McCarrison (20), as a result of ten years' experimental research work in the Himalayas, finds that water is the common means of transmission, and the goitrigenous effect is due to the presence in the water of a *contagium vivum* or living organism which is the direct or the indirect cause of goiter and its sequelae.

He finds that the excitant cause of goiter may be found in the soil as well as in the water, and to this fact attributes the frequency of goiter among the tillers of the soil as opposed to its rarity amongst merchants and shopkeepers.

He believes that the seat of the infection is in the intestinal tract, and that he has cured endemic goiter by the administration of intestinal antiseptics and lactic acid ferments, and that he has cured cases of endemic goiter by vaccines prepared from the intestinal flora.

The beneficial action of iodin he attributes to its germicidal powers. In support of his theory of infection, McCarrison quotes the incidence of goiter in several villages placed one above the other on the same stream, and finds that the prevalence of goiter in the village increases from above downwards in direct ratio to the degree of pollution of the stream.

His observation is analogous to Gaylord's experiment with the fish tanks, and with about the same degree of incidence. H. R. Gaylord (30) had four fish tanks on the same stream. In the first tank, 3 per cent of the fish became goitrous; in the second, 8 per cent; in the third, 45 per cent; and in the last, 85 per cent.

McCarrison in the support of his theory of infection recounts an interesting observation. Four goitrous individuals from an endemic area moved into a village where, according to all available information, goiter had been previously unknown. Three of these goitrous individuals lived in a house situated at the head of the stream which supplied the village with drinking water. In a few years he made a survey of the village and found a large incidence of goiter, particularly among the children.

In discussing the incidence of goiter in the neighborhood of Madras City he says, "Goiter is unknown as an endemic in this neighbourhood; yet the poverty of the soil in iodine is as great as in some of the most goitrous regions of Himalayan India where the disease and its sequelae prevail with great intensity" (31). He makes the following observations in regard to the incidence in the villages of the Gilgit Fan: "There are nine villages on this fan, eight being situated one above the other on the main water-supply; the ninth is provided with its own supply. Goiter is prevalent in the first eight villages; it does not prevail with equal intensity in all, but shows an increase in incidence from that highest to that lowest on the water-supply. . . . The ninth village (Barmis) situated at the 'handle' of the fan, was goiter-free. It received its water-supply from a spring of exceptional purity, so located with respect to the village and to its irrigated fields that the water in its course to the villagers became contaminated neither from these fields nor by human nor animal excreta. All nine villages have poverty of iodine in the soil as a common feature. . . . It is, I think, equally clear that its essential cause was not the poverty of the drinking-water in iodine, but the unhygienic conditions of life in the villages. Among these conditions bacteriological impurity of the drinking-water was the chief, since the massive ingestion of the unboiled suspended matter in this water caused the disease under experimental conditions in man, despite the use of a drinking-water which contained 1,200 parts of iodine per 100 billion parts of water."

In his experimental work he produced goiter in goats and rats by the administration in their food of fecal material from goitrous subjects, and produced goiter in the human by the administration of the residue left on the candle of a Berkfield filter after infiltration of goitrigenous water.

These findings of McCarrison and other considerations make it difficult to discount the infection theory. The fact that the goiter virus is destroyed by boiling and much influenced by filtration, is, if substantiated by further experimental work, certainly suggestive of an infectious origin.

The influence of three powerful germicides, iodin, mercury, and arsenic, on the course of the disease is still more suggestive. The reported efficacy of thymol and betanapthol in curing the early case can mean only infection. The epidemics and the improvements on change of water supply can be explained on an infection as well as on a mineral deficiency basis.

Analysis of water from goitrigenous regions has not by any means uniformly shown a deficiency of iodin, and this is in favor of the infection as against the mineral deficiency theory.

The hypothesis advanced by Plummer (32) that certain types of

intestinal flora have a limiting effect on iodin fixation or utilization tends indirectly to support McCarrison's contention.

Reasoning from the occurrence of the disease in wild fish, its production in fish-cultural stations; its specific endemicity in certain definite regions and certain troughs of water; the experimental evidence as to its method of transmission; the efficacy of three well-known germicides in the treatment of the disease, iodin, mercury, and arsenic; the influence of filtration upon the capability of water to produce goiter, and the destruction of the agent by boiling, Crotti concluded that the cause of goiter is a living organism (22). He found a fungus consistently present in human goiters and later a similar one possessing the same cultural and etiologic qualities in cabbage whether raw or steamed. He reports the experimental production of goiter in 100 per cent of rabbits in which this fungus was injected. The results were the same whether the fungus was from human goiters or from cabbage.

In 1932, he states as follows, "A further experiment was made, using the cabbage fungus but adding ten minims of Lugol's solution to the drinking water of the rabbits. The iodin did not prevent the formation of goiter, as shown by the postmortem examinations, because 66 per cent of those rabbits had developed as great a diffuse colloid goiter as those in the first series of experiments. In this case, at least, the 'iodin deficiency' cannot be regarded as the cause of the goiter, as all the animals were iodized.

"The fungus belongs to the *genus alternari*. It is well known that this *alternari* sporulates in the spring and summer and comes into a quiescent state in the winter. The fact that the fungus sporulates in the spring and summer may explain why, during these seasons, there is always a recrudescence of goiter. It may explain, also, the summer goiter of visitors who spend a few weeks or months in the summer season in regions where goiter is endemic."

Finally, the type of endemicity with its fluctuation and periods of exacerbation and retrogression is more suggestive of infection than of mineral deficiency.

Theory of Iodin Deficiency

As already stated the beneficial effects of seaweed and sea water in the treatment of goiter have been recognized from time immemorial. It was not, however, until the early part of the nineteenth century that scientific attempts were made to demonstrate an insufficiency of iodin in the soil, water, and food of endemic areas. Prevost (33), in 1830, and Chatin (34) two decades later published the results of pioneer research along this line.

Chatin in 1852 was convinced as a result of his research that goiter was due to iodin deficiency, and claimed to have proved that the soil and water in endemic districts were iodin poor. His work, however, lacked confirmation and no further progress was made in the study of iodin relation to goiter until the discovery by Baumann (35) in 1895 of iodin as a normal constituent of the thyroid. Baumann demonstrated that diseased

thyroid contained less iodin than the normal gland, and that increased iodin intake resulted in increased storage in the thyroid. As early as 1907 Marine (36) held that normal thyroid function is dependent upon a normal amount of iodin in the gland, and in 1916 E. C. Kendall (37) isolated the iodin-containing compound in crystalline form and called it thyroxin.

It is, however, to the splendid research and initiative of Marine and his associates, Kimball, Lenhart, Williams and others, that we owe our present conception of the importance of iodin in thyroid function. Marine in his work did much to establish the theory of a work or compensatory hypertrophy of the thyroid depending upon a relative or absolute deficiency of iodin as the major etiologic factor in goiter production. The modern conception of goiter as a symptom of a specific deficiency disease—in most cases iodin deficiency—is based upon his work. This theory is generally accepted in this country today as the causation of simple goiter. In the course of their work, Marine and his colleagues have presented a mass of evidence that proves without question that whatever the ultimate cause of goiter may be, the immediate factor in colloid goiter causation is usually iodin deficiency.

For convenience it may be advisable to arrange the significant facts that support the iodin theory under three headings: (1) experimental results, (2) therapeutic results, (3) results of water and food analysis.

Experimental Results

Many observers have reported experimental results similar to those of Marine and Lenhart (27) who arrested or prevented the development of endemic goiter in brook trout by adding iodin to the water in a concentration not exceeding one in one million.

Much experimental evidence has been published showing that if part of the thyroid is removed, the amount varying with the species, age, and diet of the animal, the remaining portion enlarges in a compensatory hypertrophy. This, in itself, we know now is an indication of iodin insufficiency. Marine (38) proved this conclusively when he showed that the administration of very small amounts of iodin inhibited compensatory hypertrophy in animals even after three-fourths of the normal gland had been removed.

W. S. Halsted (39) showed that thyroidectomized dogs which were fed during pregnancy on an iodin-free diet gave birth to goitrous progeny. It has been proved that if iodin is supplied to such dogs during pregnancy, the pups will be born free of goiter. Marine (36) was able to obtain from the same animal "alternate litters of goitrous and non-goitrous puppies" by withholding or administering iodin.

Goiter in animals has been arrested and prevented by the administration of iodin. In the Pemberton Valley in British Columbia, the calves, pigs, and other domestic animals were born goitrous; they were either dead at birth or died soon afterwards. Cattle and horses imported into the region developed goiter. It was almost impossible to raise any perfect

animal. Iodin was administered in the feed, and goiter disappeared.

It has been found that after part of the gland is removed there is a constant ratio between the iodin of the residual portion of the gland and the histologic picture; the hyperplasia increases as the iodin content decreases. There is no evidence of compensatory hyperplasia as long as the iodin content in the remaining portion of the gland remains at about 0.1 per cent; when the iodin storage falls below this level hyperplasia invariably occurs. The hyperplasia is controllable by means of iodin, resulting in complete involution with increased colloid, and when sufficient iodin is given, storage results.

The selectivity of the thyroid as regards iodin absorption has been demonstrated by recovering from the thyroid of a dog 18.5 per cent of a dose of thirty-eight milligrams, given as potassium iodide by mouth. This affinity for iodin is even more apparent after intravenous injections.

Histologic examination shows that previous to the development of goiter, or in the very early stages of goiter formation, there is a decrease in stainable colloid, indicating a decrease in iodin storage.

Even in transplanted thyroids the reaction of the gland to iodin sufficiency or insufficiency, irrespective of the location of the transplant, has been demonstrated. Even these transplanted thyroids are capable of storing iodin. This faculty of storing iodin in a gland removed from its normal position in the body and deprived of its normal nerve and blood supply must be regarded as irrefutable evidence of the powerful selective affinity the thyroid cell manifests for iodin.

Marine (36) demonstrated that even in highly endemic areas, animals can be kept normal for long periods of time by means of iodin administration. He carried on experiments along this line in Cleveland where about 90 per cent of the dogs were goitrous. He iodized the mothers to secure normal litters; he then divided the litters. To half of each litter he administered iodin in minute doses. The other half served as controls. The puppies receiving the iodin, one milligram a week, remained free. The others developed goiter. Both sets of puppies lived in the same kennels, under exactly the same hygienic conditions and were fed the same kind of food.

Marine's results have been confirmed by other observers both in this country and abroad, especially in Italy, France, and Switzerland, and we can no longer doubt that iodin deficiency is the most important factor in the immediate causation of colloid goiter. Further research must have as its objective the investigation of the underlying factors in this deficiency and the determination as to the nature of the deficiency and as to whether it is absolute or relative.

Results of Water and Food Analysis

Prevost (33), Chatin (34), and recently McClendon (40) found corroboration for the theory of iodin deficiency in the alleged insufficiency of iodin in the water and food supply available in goiter districts. Fortunately the brilliant work of Marine and his associates is not in need of further corroboration.

The statistics as to water and food analysis in goiter districts and the correlation of these statistics with the incidence of goiter is neither conclusive nor convincing. The reports of analyses submitted by different authorities do not indicate, with sufficient clarity to convince, that the degree of iodin poverty in the water or soil is proportional to the incidence of goiter in the particular community.

Crotti is unconvinced on this point and states, "Analysis has proved that goitrigenous and non-goitrigenous waters frequently contain the same quantity of iodin, and instances are known where water particularly rich in iodin causes goiter, as in the case cited by Chatin at Beaulieu in the Department of Oise" (41).

In this country we find it hard to believe without further evidence that iodin consumption is less in Oregon and Washington, which are endemic areas, than in California and the Southern States which are comparatively free.

Owing to the great diversity of geologic formation with their varying influence on the water supply, the different sources of water supply in any community (river, mountain stream, lake, surface well, artesian well), the great technical difficulties in quantitative analysis for iodin (analysis which reports the iodin in parts per hundred billion), the manifold sources of analytical error in the most competent hands; the correlation of endemic goiter with iodin poverty in soil, food, or water as the sole causative factor must, in the present state of our knowledge, be regarded as a surmise rather than a scientific demonstration of actual fact.

The work of McClendon is usually quoted in support of the assumed relationship between iodin poverty in soil, food, and water, and the incidence of goiter. In his preliminary paper (1923) he stated, "Our results so far have all fallen into line with the idea that there is an inverse ratio between the amount of iodin in surface waters or those of shallow wells or springs, and the distribution of goiter" (40).

In a later paper (May, 1924) he divided the territory of the United States into two sections, and reports that in one section the waters contain from one to twenty-two parts of iodin per hundred billion parts of water; in the other section the waters contain from 23 to 18,470 parts of iodin per hundred billion parts of water (42).

In correlating the results of his analyses with the incidence of goiter as reflected in the data of the draft board, he finds roughly that in that section in which analysis showed from one to twenty-two parts of iodin to a hundred billion parts of water, the goiter incidence was from 5 to 111 military goiters per 1000 drafted men; in the section in which the analyses showed 23 to 18,470 parts of iodin to one hundred billion parts of water, the goiter incidence was from 0 to 5 military goiters per 1000 drafted men. In addition to the technical difficulties already mentioned in estimating the iodin content of water and food stuffs, McClendon in his work had to face another difficulty. The findings of the draft boards cannot be taken, by any means, to indicate the true proportional incidence of goiter for the various districts of the United States. The work of classification was in the hands of hundreds of physicians, from different

parts of the country, whose ideas as to what constituted goiter probably varied within wide limits, and who worked without uniform standards. Indeed, the definition "The military goiter is one too large to button a military collar around," used by the draft board, should be sufficient in itself to throw the whole experiment out.

It must be remembered that only the males were examined, and that in mildly goitrous districts, as we have for the most part in America, the incidence of goiter in the females must be considered the index of endemicity.

We are then forced to conclude that notwithstanding the scholarly research of J. F. McClendon, T. von Fellenberg (43) and others, we have not sufficient evidence at this time to correlate the incidence of goiter with iodin-poor water, soil or food.

Granting that iodin insufficiency is the cause of simple goiter, we still have to find the cause of the iodin insufficiency. Is poverty in the iodin intake always the cause or are there certain endogenous factors that modify or "fix" the iodin in the food and water, and in some way render it unavailable for thyroid function?

If we are willing to concede the possibility of goiter in the face of a sufficient supply of iodin in the food, we have in infection a rational explanation of McCarrison's experiments. **Infection—with the intestine as the site of the infection—and the fixation or utilization of iodin by specific intestinal flora would account for his results and would explain endemic goiter on the basis of iodin deficiency even in the face of a primarily sufficient intake.**

The etiologic sequence of chronic, mild, waterborne infection with secondary insufficient iodin absorption would harmonize many of the conflicting features of endemic goiter. The theory of general mineral deficiency and of the mineral balance would also help us to understand some of the puzzling aspects of goiter.

Theory of Mineral Deficiency

Another phase of the question, which is rarely alluded to, is the importance of the *mineral balance* of the body as a whole. The chemical elements found in the human body other than those which go to make up the carbohydrates, fats and proteins are spoken of as mineral matter, ash or inorganic constituents. Not one of these terms satisfactorily describes the group. For convenience we will speak of them as minerals. Marine's work has had a tendency to focus attention exclusively on the iodin.

It must be recognized that there is a very fine physiologic balance between the different mineral constituents of the blood and tissues, and a very definite relationship between the assimilable mineral content of the diet and the mineral balance of the body. In addition to iodin we must remember that there are twelve other mineral elements necessary for proper bodily function, and that these elements, in the order of their importance, are calcium, potassium, iron, sodium chlorine, phosphorus, sulphur, aluminum, magnesium, silicon, fluorine and manganese. If we

admit that the inorganic salts of these elements, both in the plasma and in the tissues, are in a state of extremely sensitive physiologic balance, and most physiologists believe that this is true, we must admit that their reactions and ratios of absorption and elimination must be correlated and interdependent, and we cannot regard any of them, for instance, iodin, as an autonomous unit.

A few examples may aid in making this point clear. There is evidence to show that the ingestion of abnormal amounts of sodium will result in a reduction in blood calcium. The elimination ratio of calcium and phosphorus is increased by the addition of large amounts of salt to the diet. In hypocalcemia a rise in blood calcium is observed if the patient is placed on a salt-free diet.

Administration of soluble magnesium salts to adult animals causes a loss of calcium. In tetany, the blood calcium is low, about 6.5 milligrams or less. This loss in calcium is immediately signaled as increased electrical irritability; the intravenous injections of strontium or of sodium has a tendency to raise the calcium level in the serum with consequent decrease in the irritability of the tissues.

Sherman found that the chlorin of the blood, in infants, which is normally present to the amount of .505 to .595 per cent sinks with the advance of gastric digestion owing to the increased production of hydrochloric acid in the stomach.

Salvesen (44) of the Rockefeller Institute found that an intravenous administration of calcium chlorid caused a rise in the phosphates of the blood.

Other authorities have also found a definite ratio between the absorption and elimination ratios of calcium and phosphorus.

In addition to the reactions between the minerals themselves, the mineral balance is affected by a host of other factors. To give one example, fat metabolism and calcium metabolism are very closely related.

Disturbance of Mineral Balance

The effect of a disturbance of the mineral balance is shown in such diseases as rickets and tetany. Mineral imbalance is evident in the instinct that sends deer and other wild animals to the salt licks; it is evidenced in a very strange way in osteophagia. During about two months of the year when the grass is very young, the animals haunt the salt licks; during the rest of the time they search out carcasses of skeletons and eat the bone. When calcium phosphate fails to deposit in the bone, there is an overgrowth of cartilaginous tissue at the end of the long bones which causes the all too familiar enlargements of wrists, ankles and rib junctions.

The mineral balance of the body is, then, a very delicate mechanism, and each of its thirteen (or more) constituent minerals must be in some way related to, or dependent upon, one or more of the others.

The writer repeatedly has seen cases in which mineral deficiency as a whole, rather than specific iodin deficiency, seemed to be the cause of goiter. He has seen cases of both simple and exophthalmic goiter, in which iodin medication was ineffective or harmful, which improved

promptly on the administration of calcium, phosphorus, sulphur, or other mineral substances.

As with calcium and phosphorus, it is reasonable to suppose that in the case of iodin also, some of the other minerals act and react either in an adjuvant or inhibitive capacity as regards iodin absorption, assimilation, and elimination.

Catalytic Agents

It is not unreasonable to picture one or more of the minerals playing the rôle of catalyst in iodin metabolism. A catalytic agent may be defined as a substance which, without itself taking part in the process, affects the activity of a chemical reaction. It is termed a positive catalyst when it accelerates the velocity of the reaction and a negative catalyst when it retards the velocity of the reaction.

If we can conceive of one of the other minerals acting in the capacity of catalytic agent in iodin metabolism we can easily understand that mineral imbalance with a deficiency of this particular mineral would result in insufficient iodin assimilation, and we can understand how a substance such as sulphur, apparently quite unrelated to iodin, would have a marked therapeutic result in cases of goiter.

At all events it should be apparent that if we are to discover the fundamental causes of simple goiter, we must extend the scope of our research beyond the limits of mere iodin insufficiency, and include in our study the relations and reactions of the thirteen elements that make up the mineral balance.

Tendency to Mineral Imbalance

If iodin poverty of food, soil, and water is the primary cause of goiter and if the iodin poverty prevails in endemic districts, then goiter in such districts should be universal for all those depending on the same water and food supply. This, of course, is not the case. Some escape and some are affected. To explain this unequal distribution of goiter, "predisposition" is invoked. Predisposition, of itself, explains nothing; we still must reckon with the factors underlying the predisposition. If by predisposition, we mean an inherited physical tendency toward disturbance of mineral metabolism, the term has a meaning. If by predisposition we mean an acquired tendency to mineral imbalance due to infection, particularly of the intestinal tract as McCarrison thinks, or to acute or chronic infections, the term is still significant. There is apparently a hereditary influence in goiter, but this influence, if it exists, must rest on a physical basis and a tendency to mineral imbalance is the most probable physical basis.

The very periods during which goiter is most common, adolescence, pregnancy, and lactation, are the very periods in which the mineral imbalance is most severely threatened, and this fact has some significance.

In conclusion, we may say that we may not always know what is the cause of simple colloid goiter; that we do know that the enlargement

of the thyroid is, in the majority of cases, preceded by and immediately dependent on an insufficient supply of assimilable iodin in the body. While it is generally accepted that the iodin insufficiency is due to decreased iodin intake, there is not sufficient evidence at the present time to warrant the acceptance of this theory as an established fact.

The writer pictures simple colloid goiter as a disease of complex or multiple etiology, with thyroid insufficiency as the exciting cause of the goiter. In the majority of cases the thyroid deficiency is the result of iodin insufficiency from inadequate nutritional supply or it may rest on a basis of general disturbance of the mineral balance, this disturbance of the mineral balance resting, in turn, on the basis of deranged function, particularly of the gastro-intestinal tract, infectious or non-infectious in origin.

Adenomatous Goiter

The great majority of the bases of nodose goiter or adenomas of the thyroid gland are of the variety popularly called colloid adenomas. This group necessarily includes nodular colloid goiter or diffuse adenomatosis, as in our opinion this condition is the early stage of the same process that in later stages is called colloid adenoma.

Nodular Colloid Goiter

The theory that nodular colloid goiter is an advanced stage of simple colloid goiter is supported by the following common observations: An untreated diffuse colloid goiter usually remains smooth and symmetrical and gradually increases in size for several months during which period of time the presence of nodules can rarely be demonstrated. The enlargement usually becomes stationary in from six to twenty-four months and within a few months it is possible to palpate numerous small nodules in the gland. Appreciable reduction in size of the gland may occur coincident with the change from a soft, smooth, diffuse enlargement to a nodular enlargement with increased consistency. In the majority of cases the thyroids removed during the stage of progressive enlargement contain no nodules, those removed during the stage of stationary size contain small nodules or nodes. Even though no nodules are evident upon external examination, they are almost always found in the specimen removed at operation if the colloid goiter has been present for two years or more.

Two or more adjacent nodules may coalesce and form a larger nodule or node that soon becomes surrounded by coarse perilobular fibrosis. Some areas of the gland may return to normal, while the colloid distention of the follicles persists in other areas. In these areas of persistent colloid distention, nodules may form and an asymmetrical nodular goiter is the result. The persistent overdistention of a follicle with colloid seems to be the chief etiologic factor in the development of the individual nodule. Larger nodes are apparently formed by the coalescence of multiple small nodules. This theory explains the origin of the individual nodules and the

appearance of larger nodes but does not satisfactorily explain the thickening and fibrosis of the stroma found immediately surrounding the larger nodules. Much evidence that thickening and fibrosis of the stroma surrounding the larger nodules does occur is furnished by the reports of many observers. It may be that a simple tumefaction, by its bulk, by pressure, or by its disposition within the gland, does result in perinodular fibrosis.

However, simple tumefaction in limited areas does not seem a sufficient explanation for the diffuse fibrosis that is found in almost all untreated nodular goiters of long standing. In goiters in which adequate treatment has been instituted, during the second or transitional stage, the progress in the development of the nodes does not seem to be altered by the treatment, and the perinodular fibrosis occurs the same as in the untreated ones. The diffuse fibrosis in areas somewhat removed from the nodules is not so often seen.

It seems that we must look for some other factor than the presence of nodules for an explanation of the cause of the general fibrosis. The author suggests that perhaps the diffuse fibrosis may be the result of continued overstimulation from the same thyroxin deficiency that was the etiologic factor in the production of the simple colloid goiter. Clinical observation seems to show that there are three stages in the progress of a simple colloid goiter. The first is marked by symmetrical increase in size over a variable period of time. The second or transitional stage is marked by stationary size, the appearance of palpable nodules, and a gradual increase in consistency. The third stage is marked by increase in size of the nodules and perhaps by a relative decrease in the size of the rest of the gland. The term simple colloid goiter is applied to those in the first stage, nodular colloid goiter to those in the second stage and multiple adenoma to those in the third stage.

Multiple Adenoma

In the third stage the same etiologic factors that produced the nodular colloid goiter produce further increase in the size of the nodules. As the nodules enlarge they may retain their individual characteristics, in which case, each one remains spherical or oval in form or they may coalesce and form large nodes or so-called adenomas or several of them may preserve their individuality but be grouped together and form a mass that on external examination appears to be a single adenoma.

This type of thyroid enlargement occurs most frequently in the third and fourth decade of life, and more often in women than in men. About 50 per cent of the patients with this condition are between the ages of thirty and fifty when they present themselves for examination. Perhaps 95 per cent of multiple adenomas are of the colloid type and in about 75 per cent of these, a history of colloid goiter can be elicited. Even in those in which such a history is lacking, it is highly probable that an unrecognized colloid goiter with persistent colloid areas preceded the development of the colloid adenomas which were discovered much later.

Multiple adenomas that are not of the colloid variety originate from new growths, embolisms, cysts from apoplexy or hemorrhage in the gland, or, in rare cases, are the result of cystic degeneration surrounding a fetal adenoma.

Primary Adenoma

The term primary adenoma is usually applied to a localized enlargement that occurs in a supposedly normal gland.

The etiology is sometimes indefinite. In some cases it is due to a hematogeneous, fatty, or septic embolism. In the author's experience he has seen seven cases that occurred following fractures. Two of these originated from septic emboli from compound infected fractures. The other five occurred following simple fractures and were non-septic in character. He has seen five cases in which the adenoma developed during convalescence from abdominal operations. On account of their external resemblance to adenomas, they are often classed as primary adenomas. They are not true adenomas but are, in fact, localized processes produced by the normal defense reaction of the gland. A small area of gland in which colloid distention persists may undergo nodular formation, apparently resulting in a primary adenoma, but on removal of such an adenoma its colloid character is manifest.

There is little to be said with regard to the etiology of true adenomas of the thyroid. No satisfactory explanation of their origin has been presented. The same may be said of the other neoplasms sometimes found. New growths found in the thyroid gland present no particular features which would indicate that their etiology differs from that of those found in other organs.

In the small group of fetal adenomas the histories usually date back to early childhood and while there is no general acceptance of the theory advanced by Wölfler (45) that these adenomas are of embryonal origin there is reason to support the belief that they originate during fetal life.

Thyroiditis and Strumitis

The thyroid is subject to the same infections as the other ductless glands. The arrangement of the lymphatics in the gland appears to protect it from lymph-born infections. In spite of the fact that it is frequently attacked by blood-born infections, abscess formation is rare. This is explained by its bountiful blood supply. During the acute stage of an inflammatory reaction the activity of the gland, as indicated by the basal metabolism rate, is lowered. Repeated infections are followed by fibrosis the same as elsewhere. The effect of inflammatory reaction upon the secreting unit is a subject of controversy. The author is convinced that in some cases a severe inflammatory reaction destroys the ability of the cell to secrete normal colloid.

TOXIC CONDITIONS

Diffuse Hyperplastic Goiter

(Graves' disease, exophthalmic goiter)

Before we enter the well-trodden arena of conflicting theory and attempt to discuss the various hypotheses as to the exciting cause or causes of hyperplastic goiter, it may not be amiss to review briefly a few of the facts regarding distribution and incidence.

Geographic Distribution

Some authorities find that diffuse hyperplastic goiter or Graves' disease is comparatively rare in regions of endemic goiter. This, certainly, cannot be said to apply to the region of the Great Lakes or to the states of Oregon and Washington in this country. In England, according to Campbell (46), it is more common on the seacoast. In this country, this type of goiter is found both at the seacoast and inland, at high and low altitudes, and it seems as if geographic or topographic factors have little to do with its incidence.

Etiologic Factors

Race.—As far as we know, no race is immune. It seems to be a common belief that the incidence of this disease bears some relation to the degree of civilization. It is less common in the negro than in the white race, and among the whites is more common in the Hebrew.

Sex.—The incidence is greater in the female. Some writers give a proportion of eight females to one male. In Bram's (23) experience males were affected in the proportion of twenty-five males to one hundred females. In our experience when the incidence of hyperplastic goiter is relatively low, males are affected in about the proportion of one male to seven females. But when the incidence is relatively high, the ratio of males to females becomes higher. As an example, the accompanying table shows the ratio of males and females with this disease who presented themselves for examination over a period of eight years.

	Males						Females						
	A	B	C	D	E	Total	A	B	C	D	E	Total	Total Cases
1918	3		2	3	4	12	26	27	24	11	3	91	103
1919	14	6	17	9	8	54	29	18	26	29	14	116	170
1920	37	19	16	17	22	111	22	9	36	15	19	101	212
1921	16	11	9	28	7	71	19	2	34	22	14	91	162
1922	6		12	17	2	37	31	22	13	15	4	85	122
1923	2		16	9	4	31	49	28	14	11	6	108	139
1924	6	5	4	15	9	39	74	44	27	9	4	158	197
1925	4	28	42	23	8	105	33	24	49	32	19	157	262
Total	88	69	118	121	64	460	283	174	223	144	83	907	1367

Classified in columns A B C D E according to the degree of severity.
(A—Mild, E—Severe)

Age.—Diffuse hyperplastic goiter is seen at all ages. The greatest incidence comes between twenty and forty. This is the period of greatest stress and strain when the metabolic balance, particularly in the female, is strained to the utmost.

Cases of congenital exophthalmic goiter are on record. Klaus (47) reported a case of Graves' disease in an infant nine months old. Dinsmore (48) has reported from the Crile Clinic 105 cases of hyperthyroidism in children; the proportion was one to four (twenty-one boys to eighty-one girls). Lewis (49), in a summary of 1512 cases operated on at the Mayo Clinic, reports five cases of exophthalmic goiter in girls under ten. Banett believes that the ratio of children to adults is one to fifty. Buford (50) reports an operation for exophthalmic goiter in a girl of six. Fernandez-Sanz (51) reports acute Graves' disease in a woman of eighty-two. Sattler (52), in a compilation of 3477 cases of exophthalmic goiter, reports 184 cases in children, or an incidence of 5.2 per cent. Of the 184, eleven, four boys and seven girls, were under the age of five.

In the last few years, the writer has seen twenty-one cases of severe hyperplastic goiter in children under the age of ten. Five of these twenty-one were under five years of age. It would seem from these figures that this disease in children is more common than has been supposed, and that many of the cases escape detection.

Heredity.—In most cases of diffuse hyperplastic goiter, no hereditary influence can be traced. There are, however, numerous examples to indicate that heredity may have some influence. Cheadle reports four cases in one family. Bumstead (53) reports a family in which four sisters were affected. Souques and Lermoyez (54) in 1918 reported seven cases of exophthalmic goiter, among the sixteen members of one family, in three generations. In the case reported by Osterreicher, (55) the mother was hysterical; of her ten children, eight developed exophthalmic goiter.

Probably the history of nervous instability, autonomic imbalance, hysteria, and similar conditions in the parents is of more importance than the idea of a goiter per se. In other words, it is a neuropathic rather than a goiter heredity.

Mental States.—Worry, grief, mental exhaustion, labile emotional states, shock, and fright are often given as factors of importance in the etiology of Graves' disease. Fright, particularly, is frequently reported as the exciting factor. Repeated instances are quoted in which the onset of symptoms is dated from the occurrence of some incident which frightened or shocked the patient. A railroad accident, a sudden death in the family, financial catastrophe, anything, in short, that tends to a sudden upset of the nervous equilibrium is reported as the exciting cause. The fright preceded the flare-up of the symptoms in the picture; therefore the fright is ipso facto the cause of the disease.

Of a thousand people in train accidents or shipwrecks, perhaps one develops hyperplastic goiter. Why do the others not develop it? Why does he develop hyperplastic goiter? The fact is, he does not develop it, he was already suffering with this disease in a mild or at least in an unrecognized form. Careful history would elicit in most cases the fact that

he had been nervous, emotional, irritable for some time. The shock or fright had, at one and the same time, the effect of focusing the attention of the patient on his symptoms, and of intensifying and crystallizing those symptoms into the full-blown picture of hyperplastic goiter or Graves' disease.

The tendency to worry, the nervous instability, the emotional lability, the hypersensitiveness, the autonomic imbalance, are, in the writer's opinion, more often a result than a cause, predisposing or otherwise, of this disease.

Predisposition.—The importance of personal predisposition or personal susceptibility is emphasized by some writers. This again seems, in final analysis, a confusion of issues. Instead of surmising that an individual with nervous and psychic instability is "Predisposed to Graves' disease," we should rather suspect that he is already suffering from the effects of mild dysthyroidism.

Exciting Cause

In a review of the theories as to the exciting cause of hyperplastic goiter, we are confronted with a rather unusual situation. Usually, in discussing the active cause of disease, we are limited to two considerations—the exciting organism (or inorganic poison) and the pathogenesis. To these two in the case of hyperplastic goiter, we must add a third consideration. We must add the consideration of the organ involved.

Extraordinary as it undoubtedly is, there is not even today universal agreement as to the organ involved in this disease. In the past, a great variety of organs have been incriminated: the thymus, the adrenals, the sympathetic nervous system, the coronary arteries, the parathyroids, the pituitary, the central nervous system, and others. There are some who believe that the changes in the thyroid are secondary, and that the primary involvement is elsewhere.

In our review, then, we must take cognizance of three factors: (a) organ or system involved; (b) causative agent; (c) pathogenesis.

Organ or System Involved

Parathyroid Theory.—This theory is now only of historic interest. It was advanced at about the same time by Gley (56), Edmunds, and Moussu (57). Edmunds found in the thyroid of parathyroidectomized dogs a hyperplasia similar to that after partial thyroidectomy.

The histologic findings have not been confirmed, and the symptom complex of parathyroid dysfunction is entirely different from that of hyperplastic goiter.

Cardiovascular System.—Friedreich considered Graves' disease as due to enlargement of the coronary arteries, and Stokes (58) considered it as a cardiac neurosis. These hypotheses, in view of our present knowledge, are untenable.

Thymus.—In a large proportion of cases, thymic enlargement is noted in cases of Graves' disease. In a series of 100 autopsies in cases of

exophthalmic goiter. Blackford (59) at the Mayo Clinic found the thymus hypertrophied in practically all the patients under forty and in about 50 per cent of those above this age.

On the clinical side, the author has seen three cases in which thymectomy for the relief of pressure and respiratory symptoms from an enlarged thymus was necessary some years after subtotal thyroidectomy had relieved the patient of the symptoms due to hyperplastic goiter.

Extract of the thymus, however, both in the human and the experimental animal has proved innocuous, and all modern proof is against the thymus as the seat of the trouble.

Thyro-Pancreatico-Adrenal Theory.—Physiologically it seems to be true that the thyroid enhances the function of the adrenals and antagonizes the action of the pancreas. In hyperplastic goiter there is often indication of disturbed carbohydrate metabolism, and in myxedema there is the opposite condition, an increased tolerance for sugar. Chvostek (60) convinced himself that, in a few cases of Graves' disease, he saw amelioration of the symptoms after he had given extracts of the pancreas. Lesions of the pancreas have been reported in patients dead of Graves' disease.

Crile (61) places considerable importance on structural changes in the adrenals. In exophthalmic goiter, he sees an involvement of the Kinetic System as a whole (brain, muscles, suprarenals, liver, thyroid) with the thyroid as the "activator" of the system. Various other pluriglandular theories, such as the thyrogenital and thyropituitary hypotheses, have been advocated assigning the chief causative rôle to derangement of function in one or the other organs of internal secretion.

Concerning all these theories, one can only say that in hyperplastic goiter there is very likely to be disturbance in the function of one or more of the other glands of internal secretion. In a meshed gear one tooth alone does not break. In the endocrine balance, we may assume that the secretions and functions of the glands interlock with a more scientific and balanced nicety than do the toothed wheels in a gear. If one gland is thrown out of function, the gland with which it is "geared" is also disturbed in function. Here, of course, the comparison ends, as the resiliency of the endocrine system provides that the secondary gland disturbance may be of any degree of intensity.

Our problem is to locate the primary "break." There is rather convincing evidence for some of these pluriglandular theories, but the combined evidence of clinical, experimental, and pathologic research indicates with a reasonable degree of certainty that in this disease the thyroid is the bellwether of the endocrine insurgents and that the other glands follow in the path of endocrine imbalance. Thyroid dysfunction is the cause; general or other endocrine dysfunction is the effect.

Neuropolyglandular Theory

This hypothesis is favored by many of the recent writers. To the thyroid is assigned the chief rôle in the pathogenesis of hyperplastic goiter, but secondary rôles of importance are assigned to the nervous and poly-

glandular systems. Pathologic changes in the thyroid is the most important link in the polyglandular chain. Its pathology repercusses upon the other organs of internal secretion which, in turn, react upon the thyroid, hence a vicious circle.

Bram's position is evidenced in his definition: "Graves' disease is a chronic, rarely an acute dysfunction of the entire chain of endocrine organs and of the vegetative nervous system, characterized by persistent afebrile heart hurry, tremor, increased basal metabolism, loss in weight, weakness, emotionalism, dermographia, a relative immunity to cinchonism, and usually also by a swelling of the thyroid and exophthalmos" (62).

The position that this disease is a neuro-endocrine dysfunction is well taken, but after all, the neuropolyglandular hypothesis is a story of etiologic sequence and pathogenesis rather than strict etiology.

There must be a starting place, a primary impetus to dysfunction in some organ; some tooth in the gears must break first. It is not reasonable to suppose that several endocrines and the sympathetic nervous system are simultaneously disturbed in function without a primary cause.

There must be a pacemaker in endocrine dysfunction and that pacemaker, according to the evidence available, is the thyroid.

Neurogenic Theories

Section of the restiform bodies, according to some investigators, results in exophthalmos, tachycardia, thyroid enlargement, asthenia, and related symptoms. These findings have given rise to the **bulbar theory.** Similar experiments in the hands of other authorities have failed.

According to the **sympathetic theory,** sympathetic excitation causes exophthalmos, lowering of sugar tolerance, increased basal metabolism and cardiovascular symptoms. This symptom complex is, of course, very suggestive of hyperplastic goiter. However, pathologic lesions have only rarely been found in the sympathetic ganglia in this disease; lesions are uniformly found in the thyroid. This would indicate that the primary involvement is in the thyroid. No one denies the close relationship between the adrenal function and the sympathetic nervous system, but all indications emphasize the sequence—thyroid first, sympathetic second.

Thyrogenic Theory

Clinical, experimental, and pathologic evidence all point to the thyroid as the seat of the primary disturbance.

The surgeon has perhaps the best opportunity to evaluate the importance of the thyroid in hyperplastic disease. He finds that ligation of the thyroid arteries brings about marked improvement in many of the cases. Injection into the gland of hot water, carbolic acid, or alcohol in many cases brings about marked temporary improvement. Removal of any appreciable amount of gland substance is followed by definite improvement. He finds that any procedure which tends to reduce the intensity of thyroid function tends to improve the condition of the patient.

The thyrogenic origin of hyperplastic disease is occasionally impressed on the mind of the physician, who in a mistaken diagnosis or otherwise submits a patient with this disease to injudicious therapy with thyroid extract. Doses of thyroid extract which are harmless in the normal individual may produce decidedly undesirable results in the patient with hyperplastic goiter. The recurrence of the symptoms after operation, synchronous with increase in size of the remaining portions of the thyroid, is a further indication of the origin of the disease.

In the writer's experience, in cases of true diffuse hyperplastic goiter, amelioration of symptoms invariably follows removal of thyroid substance. The degree of improvement is in direct ratio to the amount of gland removed.

Experimentation shows that a picture closely resembling this disease can be produced by the administration of thyroid extracts or juices, particularly extracts or juices from toxic glands. Some authorities deny that real hyperplastic goiter can be produced in experimental animals. However, most of the symptoms can be elicited: tachycardia, sweating, tremor, nervous and mental instability, and gastro-intestinal disturbance.

In every case of this disease subjected to operation that characteristic hyperplasia may be found in some portion of the specimen removed. It may be that a large percentage of the total volume of the gland is normal. If the gland is carefully sectioned, however, areas will be found in which the typical hyperplastic changes are evident. The increased vascularity of the thyroid, the increase in the size of the vessels, the adhesions frequently noted, also point to the thyroid as the primary seat of the disease.

The cause of the thyroid dysfunction or thyrotoxicosis is, therefore, the primary etiologic factor of this disease. Since thyrotoxicosis is always accompanied by and doubtless is preceded by the characteristic hyperplasia, we may assume that the cause of thyrotoxicosis is secondary to the cause of hyperplasia. If it is true that during various periods of life the normal thyroid gland responds physiologically to increased stimulation by hyperplasia, and then involutes to the resting stage when the demand is decreased, should we not consider the extreme degree of hyperplasia in the diseased thyroid—malignancy and specific infections excepted—as the result of overstimulation?

Reasoning from the standpoint of the pathologist who sees in hyperplasia the chief evidence of gland activity and also the chief evidence of disease, this would appear to be obviously true. But from clinical observation, it seems certain that disease of the thyroid gland accompanied by extreme degrees of hyperplasia may and often does occur when no functional deficiency can be suspected. In fact, in the great majority of cases of the disease known as diffuse hyperplastic goiter all the clinical facts obtainable seem to show that it has appeared in a gland that until recently has been functioning normally. So the conclusion is warranted that hyperplasia can result from etiologic factors other than deficiency stimuli. The fact that mild hyperplasia accompanies the reaction of the gland to a deficiency stimulus, does not establish the theory that all hyperplasias are the result of deficiency stimuli.

Some authorities claim that intoxication by phosphorus and other chemicals, as well as intoxication of intestinal origin, can result in thyroiditis followed by hyperplasia. There is considerable evidence to show that changes in the gland accompanied by moderate or even severe degrees of hyperplasia may be prompted by bacterial toxins or other poisons, but cases presenting the possibility of such an origin are rare.

Infection as the Causative Agent

In the opinion of the writer any agent capable of producing an inflammatory reaction that changes the structure of the cells so that the secretion of colloid is checked may be the causative agent. Infection—local, focal, or general—is, of course, the most probable cause. As the result of the thyroiditis, hyperplasia occurs, the secretion of iodized colloid is checked, and hyperplastic goiter follows. In other words, infection is the exciting factor of hyperplastic goiter in the great majority, if not in all, of the cases.

There is much evidence in favor of this belief. DeQuervain (63) for instance, found that injection of bacterial toxins caused a marked hyperplasia of the thyroid tissue. Vincent and Jolly (64) have demonstrated that thyroidectomized animals are more susceptible to infection.

McCarrison (20) has long been an advocate of the infection theory in goiter. In 1914 Rosenow (65) isolated a non-hemolyzing streptococcus from the thyroid gland in twenty-five of thirty-two cases of thyroid enlargement, most of which were of the exophthalmic type. Vincent (63) and others have noted the thyroid enlargement that is often present in acute articular rheumatism. Beebe (66) found a history of repeated attacks of tonsillitis in 40 per cent of his hyperthyroid cases. Charles Mayo years ago noted the relationship between hyperactivity of the thyroid gland and focal infection. Numerous other writers might be quoted who have by clinical observation and animal experimentation secured evidence indicating that infection is a most important factor in the etiology of hyperplastic goiter.

It may be of significance that in the first description of exophthalmic goiter ever published (by Parry in 1819) it is mentioned that the symptoms appeared subsequent to a cold and rheumatic fever. Parry's exact words are as follows: "This malady to which I allude is enlargement of the thyroid gland. The first case of this coincidence which I witnessed was that of Grace B., a married woman, aged thirty-seven, in the month of August, 1786. Six years before this period she caught cold in lying-in, and for a month suffered under a very acute rheumatic fever; subsequently to which, she became subject to more or less palpitation of the heart, very much augmented by bodily exercise, and gradually increasing in force and frequency till my attendance, when it was so vehement, that each systole of the heart shook the whole thorax. Her pulse was 156 in a minute, very full and hard, alike in both wrists, irregular as to strength, and intermitting at least once in six beats. The part swelled was the thyroid gland. The carotid arteries on each side were greatly distended;

the eyes protruded from their sockets, and the countenance exhibited an appearance of agitation and distress, especially on any muscular exertion, which I have rarely seen equalled" (67). Since the time of Parry various infectious diseases have been mentioned occasionally in clinical reports as preceding or initiating this disease, but the significance of such histories has attracted little attention.

In 154 out of 237 cases of thyroiditis seen by the writer diffuse hyperplastic goiter developed within five to thirteen months after the infection had subsided. In none of these cases was the pulse or metabolic rate higher during the course of the infection than that to be expected from the fever present. In twenty-three of these the basal metabolic rate was found to be below normal and the pulse rate 88 to 99 in from four to six weeks after the patient's recovery from the acute thyroiditis.

In a great majority of the cases of hyperplastic goiter seen by the writer, the patient has presented such a definite history of a preceding infection that the probability of the infection being the cause of the disease could not be ignored. In some instances, the interval between the infection and the development of the goiter was rather long. It is owing to the fact that the symptoms of thyrotoxicosis do not appear until some weeks after the acute infection has subsided that the history of the previous infection is not more often noted. We frequently see a typical hyperplastic goiter that has obviously followed a preexisting strumitis.

The tenderness frequently present over the thyroid, the presence of adhesions, even in cases which have not been subjected to x-ray treatment, the leucocytic infiltration and the slight rise of temperature, point to infection as the causative agent.

As to the infections that may be causative in this disease, gastrointestinal infection is considered of great importance by McCarrison (68), Lane (69), Bainbridge and others, and perhaps it is often an etiologic factor, but the evidence that any organism that may cause thyroiditis may be the exciting cause of this disease is too strong to be ignored. There is no specificity in thyroid infections.

Thyroid Dysfunction

Most authorities are agreed that the thyroid secretion, increased or qualitatively changed, is the most important, if not the sole agency, in the production of the symptoms of thyrotoxicosis. There is no universal agreement as to the manner in which the thyroid secretion in hyperplastic goiter varies from the normal. Two of the theories most commonly held, we will consider briefly: (a) Hypersecretion of normal thyroid secretion—hyperthyroidism; (b) Qualitatively changed secretion in normal, increased, or even decreased amounts—dysthyroidism.

Hyperthyroidism

This theory assumes that increased amounts of normal thyroid secretion are thrown into the circulation and that this increase in thyroid secretion, or in its active element thyroxin, is responsible for the sequence

of symptoms—tachycardia, tremor and nervous symptoms, increased metabolic rate, and other symptoms.

In support of this theory the effects of the administration of thyroid extracts or thyroxin are quoted. Undoubtedly, the administration of such substances does induce some of the symptoms seen in hyperplastic goiter but the true picture of this disease has rarely if ever been produced experimentally in the human or in the animal in the laboratory.

In the second place, the theory of a pure hypersecretion involves a contradiction; it postulates that a gland which has undergone pathologic changes, which has varied structurally from the normal, can and does produce a normal secretion. If we admit this hypothesis, we must admit that the histologic change in cell structure from low to cuboidal to columnar is of no significance, that the decreased iodin content of the gland is of no significance, that the decrease or absence of colloid is of no significance, and that consequently the colloid has no function and can safely be dispensed with. Unless we can admit that a definitely pathologic gland can produce normal secretion, we must abandon the hypothesis of a pure hypersecretion as the cause of hyperplastic goiter.

Dysthyroidism

The theory of a qualitatively changed secretion answers the various questions of the pathogenesis of hyperplastic goiter or Graves' disease better than any other hypothesis.

It is difficult to explain through the medium of any other theory some of the results seen after thyroidectomy. The author has found that when, in an operation, any considerable portion of the gland is left in one place, a recurrence is to be expected. He finds that the recurrence of the symptoms in such cases is in proportion to the degree of recurrent thyroid hyperplasia. Very often the size of the remaining portion is small; the symptoms, nevertheless, may be quite severe. It is difficult to believe that so small a portion of the gland could produce enough normal secretion to cause symptoms of such severity.

When, instead of leaving a sizable portion of the gland in one piece, he leaves a thin layer or tiny particles of gland tissue scattered over the course of the excision, the writer finds that recurrence is very rare. Why? Because the gland tissue near the surface of the gland in the region of the thyroid pedicle, almost always appears to be, and doubtless is, normal or sufficiently free from the characteristic changes usually spoken of as hyperplasia. This area free from hyperplasia is usually very thin and when thick pieces of gland tissue are permitted to remain, some "hyperplastic" tissue is left and the dysthyroidism recurs.

The dysthyroidism theory is the only one so far suggested that properly correlates the pathologic and clinical picture in hyperplastic goiter. We often see cases in which the symptoms are quite severe, and yet on histologic examination only small areas of hyperplasia are found. A vitiated secretion from these small areas is the logical explanation of the clinical syndrome.

As further evidence Marinesco (70) and other observers have found, by complement fixation method, that the secretion in this disease is qualitatively changed. Experiments, such as those carried out by Klose (71), demonstrate this fact. Instead of the extracts, Klose used the juice expressed from the thyroid gland. With the juice expressed from toxic goiters, given by intravenous injection, he produced the symptoms of thyrotoxicosis. The juice from normal thyroids was innocuous, even in large dosage.

Combined Hyperthyroidism and Dysthyroidism

There is no way of proving or disproving this hypothesis. It may be that hypersecretion may accompany dysthyroidism, but hypersecretion, alone, cannot explain hyperplastic goiter.

The Author's Hypothesis

As regards the exact pathogenesis of the dysthyroidism, the authorities are in disagreement and the definite solution of this problem does not seem near at hand.

The pathologists tell us that in hyperplastic goiter there are certain changes in the gland—decreased colloid and iodin content, change in the follicular cells from low to cuboidal to columnar, hyperplasia of the interstitial tissue, epithelial proliferation and degeneration and infolding processes into the follicle.

The histologists for the most part do not find much individual variation in the structure of the cell, follicular or interstitial. Some find two types of cell—the chief, and the colloid, and some discuss various types of "secretion antecedents."

We cannot believe that, in a gland as intricate structurally and physiologically as the thyroid, the secretion is limited to iodized colloid—to one or even two products.

Kendall (37) found the active agent thyroxin, which is about 65 per cent iodin, but did not explain the other 35 per cent of the thyroxin molecule. We have suggested the term thyrom to designate the activating substance in this 35 per cent and we find much clinical and physiologic evidence of the existence of this hypothetical product.

Clinical Observation

The symptoms of iodin poisoning and thyroxin poisoning show two entirely distinct clinical syndromes. In iodin poisoning, we see sneezing, coryza, bronchitis, conjunctivitis, headache, and skin eruptions. The catarrhal symptoms are predominant. These symptoms are certainly not the same as the typical picture of thyrotoxicosis.

Let us now administer considerable dosage of thyroid gland to a normal individual. What are we likely to see? Tremor, nervousness, tachycardia, palpitation, loss of weight, asthenia, and increased basal metabolism. This is an entirely different picture—a picture of hyperthyroidism. The thyroid must contain besides the iodin product another thyroid secretory product equally or even more active.

Physiologic Evidence

Secretion and storage of iodized colloid as the sole physiologic function of the thyroid is too simple, and its very simplicity is an argument that it is not the entire picture. We are quite convinced that, in addition to the iodized colloid, there is another product derived, perhaps from the same cell that secretes the colloid; that this product is also secreted into the follicle and there undergoes processes of fusion with the iodin in the colloid, and that this combination, and not either part of it, is the normal activating unit of the thyroid hormone. In the normal thyroid, the iodin of the iodized colloid combines with the undetermined product, thyrom and normal thyroxin is produced. If the iodin storage in the colloid is sufficient, there is no excess of free thyrom.

In hyperplastic goiter, the secretion of iodized colloid is checked by the cell changes incident to inflammation. There is marked evidence of extreme hyperplasia. All are agreed on the decreased colloid content. The secretion continues, but there is evidence that it is qualitatively changed. It is the belief of the writer that the iodized colloid is decreased, while secretion of thyrom continues. The thyrom, or undetermined product, thrown out of partnership with the iodin, is thus released in a free state into the blood stream and provokes the train of symptoms that we see in hyperplastic goiter.

The favorable results from iodin medication in this disease seem to favor this hypothesis on the following basis. During the administration of iodin the excess of thyrom combines with the iodin in the blood stream and is converted from a toxic substance into a wholesome hormone, thyroxin.

Causation of Cardiovascular Symptoms

Cardiac Changes

None of the numerous theories that are advanced to explain the extraordinary involvement of the cardiovascular system in diffuse hyperplastic goiter are quite adequate. One of the most acceptable hypotheses is that the toxemic content, of the qualitatively altered thyroid secretion, acts on the myocardium and results in a pathologic change, in the heart muscle, which is responsible for the tachycardia and other cardiovascular symptoms. While this theory seems to be supported by the clinical evidence presented by the condition of patients seen late in the course of the disease, the early symptoms point to involvement of the endocardium with disturbance of the sinus node as the primary factor in the production of the tachycardia.

Another theory is that the cardiac changes are due to the effects of the qualitatively changed thyroid secretion upon the nervous system. One of the functions of the vagus nerve supply to the heart is that of inhibition. By others, the tachycardia and other heart changes are attributed to stimulation of the sympathetic system by the thyroid toxin.

The extreme vascularization of the thyroid in hyperplastic goiter

with the consequent dilation of the blood vessels is also given as a cause. It is claimed that the highly vascular thyroid acts as a "shunt," short-circuiting the flow of blood to the neck and head and consequently increasing the load upon the heart.

Blood Findings

Epinephrin is said to be increased in the blood of some patients with this disease. This finding is in harmony with the hypothesis that the adrenal system is frequently involved. Hyperglycemia is frequently noted and the diminished carbohydrate tolerance often seen in hyperplastic goiter is indicated by the blood examination. Weltman and others have found that the cholesterol content of the blood is diminished. The writer places much emphasis on this finding as well as on other evidence of disturbed cholesterol metabolism.

Causation of Exophthalmos

There are various theories as to the causes operative in the production of the exophthalmos. According to some of the older writers, a gradual increase in the deposit of fat behind the eyeball is responsible for the protrusion. According to others the intense congestion of the retinal vessels and of the other vessels in the posterior part of the orbit is the causative factor. It may easily be seen how a chronic venous congestion of the orbit would produce some protrusion of the eyeball.

Contraction or irritation of Landstrom's or of Müller's muscle are also given as possible causes. It is, however, to the probable influence of thyrotoxicosis on the sympathetic system that we must look for the most feasible explanation. It has been shown experimentally that stimulation of the cervical sympathetic produces, in some instances, exophthalmos of various degrees. Section of the sympathetic has improved or decreased the degree of exophthalmos and this operation has been practiced to relieve severe cases of exophthalmos that threatened vision.

The fact that "burned out" areas are nearly always found in glands removed from patients with exophthalmos suggests to the writer that the exophthalmos may be due to a product elaborated only in burned out tissue.

Causation of Gastro-Intestinal Symptoms

The etiology of the digestive derangements encountered in hyperplastic goiter or Graves' disease is not agreed upon. Some attribute a large percentage of the gastro-intestinal disturbance to a vagus stimulation which produces hyperacidity and the pyloric spasm, vomiting and diarrhea seen in a crisis. Probably much of the trouble is due to disturbances caused by the greatly increased food consumption attendant upon the greatly accelerated metabolism.

TOXIC ADENOMA

Relation to Hyperplastic Goiter

Is toxic adenoma (secondary Basedow, secondary toxic goiter, Basedowified goiter, adenoma with hyperthyroidism) a distinct clinical entity? Much has been said and written concerning this point.

Plummer (32) was the first to insist on a definite distinction in classification between hyperplastic or exophthalmic goiter and toxic adenoma. He emphasized the difference in onset and clinical course in the two conditions and brought out the fact that exophthalmic goiter has certain symptoms, in some degree peculiar and characteristic, and that the same is true, to a certain extent, of toxic adenoma. Other writers, for example Crotti (22) and Allen Graham, claim that both conditions are merely "clinical variations of a single disease" (72). Graham points out the fact that frequently cases present all the symptoms and signs of exophthalmic goiter and nevertheless have adenoma in the thyroid. He points to the similar reaction to iodin medication often observed in the two conditions as proof of the unity of the two types of thyroid disease.

It seems to the writer that much of the discussion is futile. After all it is not material whether we consider hyperplastic goiter and toxic adenoma as "clinical variations of a single disease" or as two distinct clinical entities. We find varied and inconstant pathologic lesions, at least to a certain degree, in both conditions, and we also find atypical and abortive types of the disease; consequently there is a varying and inconstant clinical picture in either condition and we must therefore expect to find, and do find, a certain overlapping of symptoms. There is, however, sufficient difference in the general character of the symptoms, sufficient variation in the course of the disease in the two conditions to warrant separate consideration of toxic adenoma—whether as a "distinct clinical entity" or as a "clinical variation" is of no great consequence.

Two Types of Toxemia in Toxic Adenoma

It seems to the writer that much of the confusion has arisen from the fact that there are two types of toxemia in the class of cases popularly called toxic adenoma. One form of toxemia is that which comes from absorption of degenerated products, or the débris from hemorrhages, within degenerated areas in the adenoma itself. This form of toxemia presents symptoms quite similar to those of an anaphylactic reaction due to absorption of foreign protein.

There is, however, another and very distinct type of toxemia found in certain cases of toxic adenoma. The toxic symptoms of this group are quite similar to those of hyperplastic goiter or Graves' disease and there is much evidence to indicate that they are directly attributable to localized areas of the same type of hyperplasia that is productive of hyperplastic goiter.

In another group of cases, the two types of toxemia are present at the same time—or the thyrotoxemia from hyperplastic changes in the gland

was preceded by the toxemia from absorption of degenerated gland products.

A brief discussion of the two types of toxemia mentioned is in order.

Anaphylactic Toxemia

It is recognized that in a certain number of cases of toxic adenoma there inevitably develops within the gland itself areas of degeneration and disintegration. These areas are at times quite extensive and it is only natural to assume that the absorption of the products of extensive degeneration must be accompanied by symptoms other than those of thyrotoxicosis. Our clinical observation has supported this assumption. We note, in these cases, symptoms directly referable to the absorption of protein substances from the broken down tissue.

That the symptoms suggestive of anaphylaxis are due to the absorption of protein substance from broken down gland tissue seems to be borne out clinically by the following facts:

(1) After removal, degenerated areas are always found in the adenoma.

(2) The removal of the adenoma always gives relief.

(3) Many of these cases respond favorably to desensitization by repeated injections of small doses of foreign protein; the symptoms are aggravated by large doses.

(4) The symptoms are intensified in many cases by the administration of drugs that have a tendency to increase sensitization, such as iodin, strychnin and adrenalin.

In a large proportion of cases of the anaphylactic type there are found intrathoracic projections and many are classed as retrosternal. It may be that undue pressure in these abnormal positions has a tendency to cause degeneration of the adenomatous tissue.

Thyrotoxemia

The etiology of the thyrotoxemia seen in toxic adenoma is the same in every respect as the etiology of primary hyperplastic goiter or Graves' disease. When the symptoms due to this form of toxemia are quite pronounced the case is usually called a secondary Basedow or secondary exophthalmic goiter in contradistinction to the typical primary hyperplastic goiter. While the cardinal symptoms are by no means the same in degree as those seen in typical primary hyperplastic or exophthalmic goiter, the etiology is the same. The variation in manifestations is explained on the basis of the histologic and anatomic changes in gland structure already present at the time the hyperplastic changes occur.

DEGENERATION IN THE THYROID GLAND

Degeneration as an individual entity is dependent upon some underlying factor. True it may occur rather suddenly in a previously healthy thyroid gland, but some change in the parenchyma of the healthy gland

starts the degenerative process on its course. Such a change is more likely to occur in a diseased gland and especially in old nodose goiters in people past middle life. In our experience, the incidence of degenerations is about three times as great in women as in men. This is probably related to the similar higher incidence of nodose goiter in women than in men, and to the effect of menstruation, pregnancy, and the menopause upon diseased glands.

It has been noticed that people who live in the Alps and other high mountainous regions, and particularly those who are subject to frequent change in altitude, are most often affected by cystic and other degenerative changes in the thyroid gland. There may be some connection between this incidence of degeneration in the goiters of people subject to change in altitude and the apparent high incidence of degeneration in the goiters of those who indulge in strenuous physical exertion.

In general we may state that degeneration occurs in a previously healthy thyroid gland, in one harboring infection, in an adenomatous goiter, and in neoplasms of the gland.

In a previously healthy gland the direct etiologic factor is usually found to be a thrombotic vessel with resultant anemic infarcts, or an acute infection with abscess formation. While degenerations from these causes are very rare, we feel that they do occur and should be mentioned.

In chronic infections of the thyroid, regressive changes to a very mild degree are noticed, but these degenerative changes do not differ from those found in similar infections involving other parts of the body and the etiology is entirely dependent upon the type and severity of the inflammatory reaction. In the usual simple thyroiditis there is only a mild degeneration, if any, while in tubercular thyroiditis there is marked caseous degeneration. There is also a form of non-specific thyroiditis, simulating a tuberculous process with giant cell formation, in which a marked degree of degeneration is seen.

A thyroid gland which is the seat of nodulation or so-called adenomas is the one which is most subject to degenerative changes. In fact, the interpretation of benign degeneration in the thyroid is confined almost wholly to the various retrogressive changes which follow the development of nodes or adenomas. It may be said that the exciting etiologic factor in this process is pressure, because the distended follicles compress the blood vessels in the interfollicular fibrous tissue with resultant anemia to the parts affected. Similarly the follicles fuse to form large spaces filled with colloid in which the contents are poorly supplied with blood vessels and subject to pressure necrosis.

Degenerations dependent upon a neoplasm in the thyroid gland are similar to the degenerations of neoplasms found in any other part of the body. In the true adenoma, degeneration is very likely to occur within the tumor growth, which is usually poor in blood supply as compared with the normal profuse vascularity of the thyroid gland. In the solid carcinomatous type, degeneration rarely occurs, unless it is late in the disease as is seen in similar carcinoma found elsewhere. In the papillary adenocarcinoma, however, degeneration occurs quite frequently and

comparatively early in the disease. It is possible that the vascularity is in some way associated with this degeneration, because this type of malignancy is very vascular.

MALIGNANCY OF THE THYROID GLAND

The etiology of malignancy in the thyroid gland presents no appreciable difference from the etiology of similar types of tumor found elsewhere in the body. Here, as in any other tumor, the theory that embryonal cells, more than any others, possess the essential factors of tumor growth, while not universally applicable, is perhaps the most important fact in our knowledge of tumor genesis. It is not universally applicable because it has its defects. It has been shown that the mere presence of embryonal cells is not sufficient to account for their growth to tumor formation; it has further been shown that tumors grow where probably no embryonal cells exist. In an attempt to show how tumors arise from cells which are neither originally misplaced nor essentially embryonal, another theory, known as tissue tension, had its inception. This theory assumes that cells are capable of growing indefinitely unless restrained by another type of cell. To prove this assumption are offered the astonishing regenerative powers of injured tissues, the hypertrophy of the pregnant uterus, and the almost unlimited reparative capacity of injured or transplanted epidermis, suggesting that normal cells, although restrained by organized forces of other cells, are capable of unlimited growth in proper environment. These theories apply to malignancy of the thyroid gland just as they do to malignancy of any other organ.

The most significant fact in regard to its etiology is that in 94 per cent of the malignant specimens, removed at operation, the malignancy is found to have originated in an old true adenoma or in a so-called colloid adenoma. This tends to support the theory that primary malignancy does not occur in a normal gland, but in one which has previously been the seat of some form of goiter.

Additional evidence in this direction is afforded by the fact that carcinoma of the thyroid usually develops within a preformed nodule. Very early focal hyperplasia of the follicular cells is also often seen in thyroid carcinoma, especially in papillary adenocarcinoma. This view is in accord with the usual clinical history that some benign disturbance or overgrowth has for a long period preceded the malignancy. At least it is quite evident that some abnormal condition precedes the malignant tumor.

Some observers think that true adenomas, especially when associated with colloid adenomas, are quite apt to become malignant. There is much evidence to support this belief. Thirty-eight per cent of all the malignancies found have apparently originated in true adenomas. As true adenomas are found in only about 5 per cent of all nodular goiters, this makes the incidence of malignancy in true adenomas about thirty times as great as in the so-called colloid adenomas. This may be due, in some measure,

to the fact that true adenomas are usually of slower growth and have been present longer than colloid adenomas. In many instances when both types of adenomas are involved in the process, it is difficult to determine whether the malignancy first occurred in the true adenoma or in the so-called colloid adenomas. We are inclined to believe, therefore, that in the thyroid, as in any other gland, any benign tumor may after variable periods of time prompt the development of malignancy.

CHAPTER III

PROPHYLAXIS

Today, goiter prevention offers physicians and public health officials a greater opportunity than any other field in preventive medicine. In the campaign against tuberculosis, heart and contagious diseases the public health officer is confronted by a prolonged fight, measured in generations; he must be prepared for rather discouraging annual expenditures and unremitting effort, and a reward of only mediocre success. If a fraction of the time, money and energy spent in these health measures were extended in the direction of goiter prevention, the beneficial results, comparatively, would be multiplied many times.

It seems inconceivable that communities and their health leaders, thoroughly awake to the dangers of one health menace, should be indifferent to the dangers of another menace no less serious. This is particularly surprising in view of the fact that the goiter problem offers such splendid and incontrovertible returns on the effort invested. The results from well directed efforts are promptly evident and will be in direct ratio to the amount of time and energy expended.

There is great and indeed urgent need for adequate and efficient preventive measures. It is conservatively estimated that there are today over five million people in the United States suffering from goiter. This exceeds the estimated number of people suffering with tuberculosis and cancer combined. More important to us in America, from the civic and the public health standpoint, than the mere number of goitrous individuals, is the possibility of a greatly increased incidence of cretinism and the milder degrees of subnormalcy in the future. If we may judge from the experience of European nations, five generations of goitrous forbears imply a high incidence of cretinism. In the ninth generation nearly 100 per cent of the offspring are cretins or cretinoids and the family becomes extinct.

The discovery that colloid goiter heredity is not the cause of retarded differential development but that both colloid goiter and subnormalcy are different manifestations of thyroid deficiency increases the importance of prophylactic measures. A reduction in the incidence of colloid goiter will necessarily be accompanied by a reduction in the incidence of subnormalcy from hypothyroidism. A smaller number of colloid goiters in any community in this decade will make for a smaller number of adenomatous goiters in the next decade; similarly, the smaller the number of goiters in this generation, the smaller will be the number of subnormals from retarded differential development housed in state institutions in the following generation. Marine and his coworkers have shown beyond question that simple endemic goiter is the most easily preventable of all the serious diseases which afflict humanity (73).

The indications for prophylaxis are the presence of goiter, or symptoms of retarded development from hypothyroidism, in the family or community. Even slight indications for treatment should be followed by the therapeutic test. The patient should be placed upon prophylactic doses of iodin and the results obtained in the course of a few weeks will make the differential diagnosis. Institution of prophylactic treatment upon the earliest indication of thyroid insufficiency will do more toward the prevention of goiter than exhaustive efforts directed towards accurate scientific diagnosis.

SURVEYS

Value of Surveys

A well planned preliminary survey, applicable to groups rather than individuals, is the essential factor in appraising results of prophylaxis in goiter. By "survey" we imply not only the survey of the school children, which is usually made and offers a very good index of the goiter incidence of the community, but also the study of all the possible factors in the particular community which might bear etiologic relationship to the goiter incidence—the mineral content of soil, food and water; housing and hygiene; heredity, and other factors. A food deficiency, temporary or permanent, due to geographic, topographic or seasonal factors may, in a certain locality, prove the sole causative factor. If this is discovered and remedied, the entire endemic goiter problem for the particular community is solved.

A well conducted survey will determine to what extent prophylaxis is needed in that particular community. It may indicate, in the highly endemic districts, need for a generalized prophylaxis of school children of all ages and both sexes. In another instance, the school survey might indicate that treatment of girls ranging in age from eleven to sixteen will be sufficient. When the survey shows that the endemicity is mild, group prophylaxis is frequently unnecessary. Attention may be confined to such children as show evidence of goiter and the individual cases treated.

Group Examinations

Periodic examinations of groups, particularly school children, are of greatest importance in goiter prophylaxis. In order to follow some form as a basis of judgment and at the same time prepare proper statistics, uniformity in standards and classification is necessary. The examiner, even though he follows a form, should exercise his best diagnostic ability by inspection, palpation, thyroid measurements, and observation of general behavior. The varying degrees of thyroid enlargement encountered are usually arranged in a simple classification and denoted by the signs "normal," "one plus" and so on. It may also be advisable to include notes on the type of goiter, presence or absence of thyrotoxicosis, basal metabolic estimations and other special findings.

Reexaminations at least twice a year are of the utmost necessity for intelligent evaluation of the results of treatment. The subsequent

examinations should, when practicable, be made by the same physician who made the first one. While the results of such surveys are by no means uniform, they are the best available index of the prevalence of goiter in a community.

PREVENTIVE MEASURES

Surgery

A chapter on prophylaxis is not complete without a word concerning the prophylactic value of timely surgery. In many instances the surgeon's knife is the only instrument of prophylaxis—if we are allowed to include under the term prophylaxis the prevention of thyrotoxicosis, cardiovascular changes, and other serious conditions. The removal of an adenoma, which we are convinced will sooner or later become toxic, is a sound measure of prevention. Adenomatous goiters, which have been present for a considerable time, should not be permitted to remain after the patient is thirty or thirty-five years of age. Early diagnosis and early thyroidectomy are the best measures of prevention so far as the distressing complications seen in the late thyrotoxic case are concerned.

Correction of Constitutional Defects

We are too apt to think of iodin and nothing but iodin when we consider the problem of goiter prevention. We must consider the individual as an individual and be on the lookout for possible constitutional factors that may have etiologic significance. This search for an underlying constitutional basis is particularly important in the matter of sporadic goiter, for presumably the patient is receiving as much iodin in his food and drink as his neighbor. A thorough physical examination is indicated in every case, to determine the presence or absence of gastrointestinal derangements, chronic or focal infections, mineral imbalance, or hypothyroidism. The writer has repeatedly seen cases of sporadic goiter clear up quickly and definitely on the discovery and correction of some constitutional disturbance. Presumably, the same measures that were successful in causing the disappearance of the goiter would have prevented its appearance if administered in time.

Improvement in Living Conditions

In considering prophylaxis attention should be called to general considerations such as diet, hygiene, housing, and habits of living. A simple change in the nutritional supply may convert a goitrous into a comparatively non-goitrous district. In goitrous areas it has been demonstrated that laborers, farm workers, and people living under adverse hygienic and economic conditions are most prone to goiter. Animal experiments demonstrate that animals kept in dirty cages develop goiter more readily than animals kept in hygienic living quarters even though the diet is the same in the two instances.

Change of abode may be considered when discussing prophylaxis. In this country, even in the "goiter belts," the condition is rarely serious enough to call for a change to a goiter free district. In Europe, it is advisable, in certain instances, to suggest a prophylactic migration, particularly if both parents are goitrous or if there is a severe goiter history in the family.

Iodin in Prophylaxis

Iodin is, in the present state of our knowledge, the most potent agent in the prophylaxis of simple goiter. Reference has already been made to Marine's experiment in goiter prevention in the schools of Akron, Ohio (74). The period of observation in this experiment was thirty months, and two grams of sodium iodid was given in a period of two weeks twice yearly. Of a total of 4495 normal pupils observed, 2190 took the prophylactic treatment and only 5 developed enlargement of the thyroid; of 2305 untreated pupils, 495 showed thyroid enlargement.

Previous to this in France and elsewhere in Europe during the early part of the last century, experiments in goiter prevention were undertaken (75). Iodized salt was used but owing to the high iodin content (from 0.1 to 0.15 gram of iodin per kilogram of table salt) accidents occurred and the experiment was discontinued. Some experiments made in French schools around 1860 promised a fair degree of success. Again, the dosage was too great and the work was not pursued.

Following in the footsteps of Marine, the European physicians, particularly the Swiss, introduced the administration of iodin in minute doses as a prophylactic measure in school children with highly satisfactory results. In 1918 Klinger initiated his campaign to eliminate goiter in Switzerland. Instead of the sodium iodid preparation used by Marine, he used a chocolate coated tablet containing five to ten milligrams of iodin, giving one tablet each week throughout the school year. He established this system of prophylaxis in the Cantons of St. Gali, Zurich, and Berne, and continued the work over a period of three years with eminently satisfactory results. More recently the Swiss Goiter Commission has instituted school prophylaxis along these lines as a public health measure for the entire country.

Methods of Administration

We must keep clearly in mind the distinction between prophylaxis and treatment. A dose that would be quite adequate for prophylaxis would be of no value in treatment. Since the demonstration by Marine and Kimball of the prophylactic value of small doses (76), various modifications in the method of administration have been advocated. It has been suggested, for instance, that one drop of the syrup of ferrous iodid or of hydriodic acid for each year of age be given three times daily for two or three weeks twice a year. Others advise the administration of the prophylactic dose daily during alternative months.

Perhaps no preparation is better and certainly none is more popular

than Lugol's solution. The only objection to its use is that it is frequently distasteful to children. Tablets, especially if they are almost tasteless, are less objectionable to the average child than liquid medicine. Recently the chocolate coated iodin tablet, first introduced abroad, is being used extensively in this country. The tablets in common use contain about ten milligrams of iodin and are administered once a week to each child for whom prophylaxis is indicated.

In our experience the form in which the iodin is given is of little consequence. Only a small amount is required but it must be supplied over long periods of time. We have found tablet triturates of iodoform to be well tolerated, and as effective as any other preparation of iodin. The tablet of 1/10 grain corresponds in effect to 5 minims of Lugol's solution. If smaller doses are desired, the tablets containing 1/50 or 1/100 of a grain may be prescribed.

Individual Prophylaxis

Group treatment cannot be exact in its application, therefore individual prophylaxis is essential for maximum results. The responsibility for individual prophylaxis rests upon the practicing physician, hence much of the success of goiter prophylaxis is in his hands. When obvious symptoms of goiter have appeared, the most favorable time for prophylactic measures is past.

There is especial need of prophylaxis during three life periods—fetal life, adolescence, and pregnancy. Experimental and clinical work has shown the necessity of furnishing sufficient iodin in the nutritional supply during these life periods. It has been clearly demonstrated by animal experiments that if iodin is efficiently administered to the mother during pregnancy, the offspring will be born goiter free and may be kept so even in a heavily goitrous district (76). In the human more consideration must be given to thyroid deficiencies than to iodin deficiencies if we wish the child to attain perfect differential development. There is much evidence to show that, by prophylactic measures in childhood and youth, goiter can be almost entirely prevented in the periods of puberty and adolescence. The development of goiter in the pregnant mother can usually be prevented, but the prevention of an increase in size or of the onset of toxicity in a goiter that is already present may be difficult or impossible.

Group Prophylaxis

Manifestly it is impossible, through the private physician or through health agencies, to reach every individual in the community with prophylaxis. Consequently, the experiment of group prophylaxis has been tried and the success or failure of these experiments has been a subject of considerable discussion.

Water Iodization

McClendon (77) believes that iodization of the water in endemic districts is an efficient means of supplying the iodin deficiency. He holds

that one-tenth of a pound of sodium iodid per million gallons of water is ample for purposes of prevention. Water treated on this basis will contain one part of sodium iodid to about one hundred million parts of water. In his opinion the iodization may be continuous or intermittent, the dosage being of course proportionately increased when it is intermittent.

An experiment in water iodization was carried out in Rochester, New York. For several years the entire water supply of the town was treated twice yearly with 21 administrations each of 16.6 lbs. of sodium iodid. This treatment produced an iodin concentration of between 14 and 28 parts per billion.

Notwithstanding the fact that some experts consider water iodization as a method that will solve the problem of mass prophylaxis, the consensus of opinion seems to be that the objections to this method are too serious to be readily overcome. When we consider that less than 0.5 per cent of the iodized water is used for drinking purposes, we must realize the enormous waste in the process. All of the rather expensively treated water except 0.5 per cent is used for such purposes as bathing, laundry, washing the automobile or mopping down the front steps. The enthusiastic advocates feel that even so the iodin is not wasted; that it is taken up in the air and breathed into the lungs; that it gets into the soil and increases the iodin content of the vegetables. Such hypotheses are too nebulous for serious consideration. It must be admitted that the greater part of the water, as far as prophylaxis is concerned, is wasted and this waste in itself constitutes the first serious objection to the procedure.

Even if the iodin content of the water is up to the requisite level, there can be no assurance that the individuals in the community who need iodin will drink sufficient water to supply their iodin deficiency. For instance, in Rochester it is estimated that in accordance with the results of water analysis, each person in the town receives approximately 3.1 milligrams of iodin per year. Water analysis, however, does not compel the individual citizen to drink the water. Some drink more, some drink less, and it is common experience that the poorer and laboring classes—who, we are led to believe, are more susceptible to simple goiter—drink comparatively little water. The dangers incident to water iodization are also concerned with a possibility of awakening toxicity in adenomatous glands, although it is doubtful whether this is a real danger under a scientific and careful plan of water treatment.

Iodized Salt

The method of prevention through the medium of iodized salt is open to some of the objections operative in the case of iodized drinking water. It is difficult or impossible to gage the dosage; people use salt in amounts that vary greatly. Many people object to the use of salt and only consume it in prepared foods—in bread for instance, where the taste is hardly perceptible—while others like their food richly salted. Furthermore, the amount of iodin in the food ingested is not an index of the amount absorbed and assimilated. The iodin in the salt may be released in cooking or it may combine with starch and form the insoluble iodid of starch.

According to some observers there is danger of arousing toxicity in adenomatous glands. How far this danger can be averted by keeping the iodin content of the salt below prescribed limits, is the point on which the safety of this procedure must rest. The salt must, on the one hand, contain sufficient iodin to supply the physiologic needs; the iodin content, on the other hand, must not be so high as to harbor the threat of toxicity for goitrous individuals. Will it be possible in the preparation of a salt to strike the happy medium between these two extremes?

The problem would be greatly simplified if we could estimate, even within very wide limits, the amount of salt consumed per day or per month by the individual. This being impossible, we can hardly say that the use of iodized salt for prophylaxis rests on a scientific basis. It is today, however, the best medium for mass prophylaxis at our disposal, and as such is worthy of further study and trial.

CHAPTER IV

PATHOLOGY*

NORMAL STRUCTURES OF THE THYROID GLAND

Introduction

To properly discuss existing pathology in the thyroid gland, its histology and function as seen in the non-diseased specimen should first be considered. Upon the stage of activity—with resultant morphology of the individual cells which comprise the histologic unit—will depend the rational interpretation of what may or may not be considered pathological.

The writer has been long convinced that the wide range of histologic variation in the thyroid is not fully appreciated. The experimentalist, if he is to secure reliable results, must bear in mind the fact that each thyroid is, within limits, an individual unit with an individual standard, and other glands should not be considered pathologic because their histologic structure varies in a slight degree from any one individual type.

The follicles have not the fixed character of the kidney tubules for example. The lining epithelial cells have no membrana propria; they are not walled off definitely from the surrounding structures; they may easily participate in the formation of new follicles.

The interstitial cells are not morphologically differentiated from the cells lining the follicles. It is possible that they take part in the formation of new follicles. If this theory is correct, any of the parenchymatous cells in the thyroid may take part in follicle formation and presumably in secretory activity. This is flexibility in the highest degree.

Histologic Variation

Crawford and Hartley (78) of the Pharmacology Department of the University of Edinburg found such a wide variation in the histologic picture, in the normal rabbit, that they considered it impractical to use the healthy thyroid of a normal animal as a control in their experimental work. They found, in every case examined, that the histologic picture in the healthy thyroid was the same in both lobes of the same rabbit. In studying the influence of the autonomic nervous system on thyroid function, they were in a position to do their experimental work satisfactorily

* The author is greatly indebted to his colleague, Dr. Benjamin Markowitz, for his assistance in preparing the materials for the chapter on Pathology and for supplying the illustrations for this chapter.

on one lobe and use the other lobe of the same animal as a control. As this is a point of considerable importance and one which is usually not sufficiently emphasized, the original report is quoted as follows:

"A number of experiments were performed to study the normal histology of the gland in the rabbit under conditions similar to those which prevailed during our experiments. The striking feature of these observations was the marked differences which were seen in different rabbits, although in all the animals the histologic picture was the same in both lobes. All these observations were made at the same period of the year so that a seasonal variation could not explain the differences. . . . In some animals the acini were large and filled with colloid which stained well, while in others the acini were very small and contained much less colloid."



FIG. 1.—Schematic Drawing of Normal Adult Thyroid Follicle.

Within the interfollicular stroma are found small groups of interfollicular cells which in morphology and staining characteristics do not differ from those lining the follicles. The number of these interfollicular cells varies according to age. They are most numerous during late fetal life and infancy and normally decrease with age, except during the periods of puberty, pregnancy, and menstruation. In the normal adult gland those cells found between the follicles are most likely the result of tangential sections across the follicle. Lymphoid cells, composed of small scattered foci, are normally found within the stroma. Under certain conditions, associated with general over-growth of lymphoid tissue, the lymphoid cells of the thyroid stroma may undergo marked hyperplasia with development of typical lymph gland structure.

The Follicle

The follicles are made up of irregular, rounded, or oval spaces of variable dimensions lined by a single layer of low cuboidal or, at most, cuboidal epithelium, and filled with colloid. Such an individual follicle represents the ultimate histologic unit of the gland. It is composed of a sac lined by a single layer of thin, flat, endothelial-like epithelium, enclosing the colloid substance. Slight infolding of the epithelium or increase in the size of the individual cell may be noted, but the structure of the individual follicle is always an epithelial sac—composed of a thinned-out epithelial sheet the thickness of only one flattened cell—within which colloid is contained. These follicles do not branch or join others but are

entirely discontinuous and separate individual units. Whether large or small, they are normally completely filled with colloid, and there is sufficient space in the gland for each follicle to become normally distended without causing irregularities in the shape of other follicles by pressure.

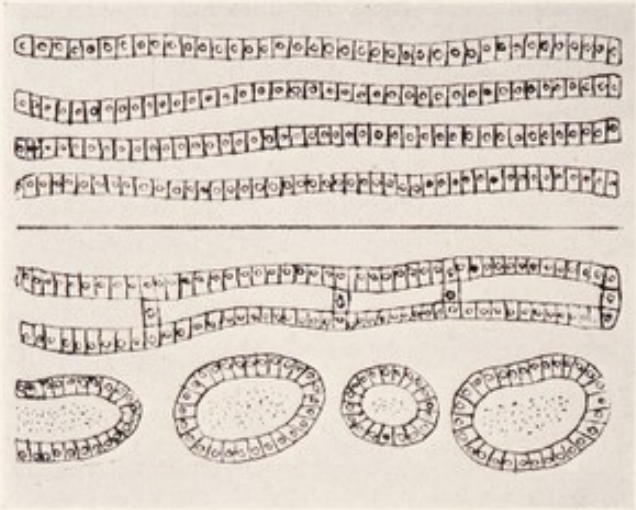


FIG. 2.—Schematic Drawing of Development of Follicle.

Williamson and Pearce (79) have described this unit as consisting of long twisted cylindrical columns of epithelium bounded by a fibro-elastic capsule surrounded by a serous cavity in which the epithelial columns are suspended. They state: "Concisely stated therefore, the functional gland unit of the thyroid organ is essentially a lymphatic sinusoid in which float columns of epithelium enmeshed by a highly specialized plexus of blood capillaries." The accuracy of this conception, however, has not been definitely established. In fact Rienhoff (80) has refuted this conception by a method of maceration and microdissection particularly applicable to the study of the individual follicle. He found that the ultimate histologic unit of the gland was this individual follicle, varying greatly in size and shape, but that it is a definite and distinct epithelial sac enclosing the colloid, instead of twisted columns of epithelial cells floating in a fluid. These follicles are very irregular varying from that of a perfect sphere, through all stages, to that of almost a perfect cube. The outstanding characteristics of the normal thyroid gland are, the great preponderance of the small follicles over the larger ones and the fact that they are all complete, distinct and fully differentiated histologic units. They are lined by a single layer of low cuboidal epithelium in contradistinction to the high cuboidal or columnar epithelium found in hypertrophy.

Development of Follicle

These follicles are formed, we believe, from the original cords of cells with which the thyroid of the embryo is almost solidly packed. In the new-born very little, if any, follicular formation is seen; the cells are in solid cords. Later these cords assume an arrangement in rows. The follicles occur by formation of a tubular growth of these rows of cells with ingrowth of certain cells of the tube meeting the cell opposite and causing the tube to be divided into segments. Each segment then fills with colloid, as it enlarges, and forms a follicle.

Norris (81) has shown that in the fetal thyroid a primary set of

follicles develops as solid masses of cells from the ultimo-branchial body at a very early stage, probably the first month. From these another set of follicles is formed later by a process of budding from the primary follicles. He finds that this secondary formation begins at about the third month, becomes very pronounced between the fourth and sixth months, and then ceases entirely—that during the later stages of development new follicles are formed only from preexisting ones, instead of from fetal rests, as contended by Wolfer (82) in his theory regarding the formation of fetal adenomata. Colloid makes its appearance at about the end of the second month, but towards the end of fetal life a desquamation of the lining cells occurs, the lumen of the follicles becomes filled with cells and the gland presents a solid appearance.

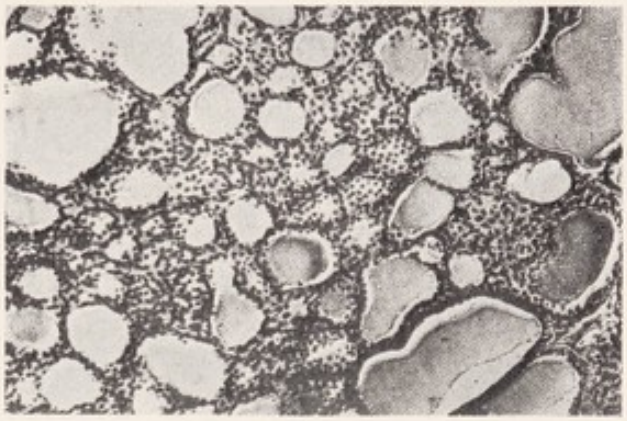


FIG. 3.—Normal Thyroid Gland.

Murray (83) contends, and his contention is supported by Boyd (84), that this solid appearance and absence of colloid is seen only after death, largely the result of post mortem disintegration; that the colloid of the thyroid of the new-born becomes vacuolated and disappears soon after the death of the infant; that the epithelial cells are then detached and fill the follicles resulting in the picture of only solid clumps of cells as seen at post mortem. To support this explanation he has shown that if the thyroid of a newly born child is fixed in solution immediately as soon as death occurs, it is found to be composed of small vesicles lined by cuboidal epithelium and containing large amounts of colloid.

Gross Appearance

A cross section of the normal gland reveals a smooth, shining surface which when minutely inspected with the naked eye shows areas of colloid collected into small lobules separated by very scanty, thin fibrous septa. The follicular markings or small areas of colloid follicles vary in distinctiveness according to their number in proportion to the interfollicular stroma.

Microscopic Appearance

A microscopic section of the normal human thyroid gland would then give the picture of various sized and shaped follicles lined by a single layer of epithelial cells and filled with colloid; and a variable amount of interfollicular tissue made up of the fibrous septae separating the follicles in which are imbedded loose interfollicular cells. A large number of these cells between the follicles may be the normal picture, depending upon

the diameter through which various follicles have been cut; maximum or minimum diameter will present larger or smaller follicles in the picture. Large groups of cells may represent a tangential section through the dome of an underlying follicle. Follicles cut through their domes, so that the lumen is not shown, cause these interfollicular cells to be seen.



Fig. 4.—Vertical Cross Section of Colloid Goiter.

The type and amount of colloid contained within the follicle will also vary in the normal picture. Frequently the central portion of the follicle may contain a spherical portion of deeply stained colloid while the peripheral area may contain very lightly stained thin colloid, or no colloid at all. It is assumed that the older or central portion which stains with hematoxylin is the colloid first secreted, and the peripheral portion which takes the eosin stain or fails to stain is colloid of more recent secretion.

PHYSIO-PATHOLOGY

The Individual or Follicular Cell and Its Life Cycle

The individual cell of thyroid function, the cell which undergoes hypertrophy and hyperplasia with increased thyroid activity, is the cell which lines the follicle. This individual or follicular cell is the essential factor in thyroid physiology and pathology. This cell has a definite life cycle from its early development, originating from the cords of cells of the new-born, to the stage of exhaustion, desquamation and finally absorption, with periods of remission in the interim.

The variations in the thyroid during the physiological processes seen from the new-born to the adult resting gland depend upon the life cycle of the individual cell. In disease the process seems to be somewhat similar but greatly exaggerated, with subsequent departure from the normal.

In the normal thyroid it is described as a cuboidal cell, with its nucleus near the base, and its cytoplasm clear. This picture varies slightly depending upon the degrees of activity to which the thyroid is subjected. With a decrease in iodin intake and increase in colloid storage this cell loses its cuboidal shape and becomes rather flat, the nucleus seems to make up almost all of the cell, and the cytoplasm is barely seen. This cell is seen in the resting or inactive stage.

The normal resting cell is very easily stimulated, especially by iodin. When this occurs the cell becomes higher, is described as definitely cuboidal, the nucleus assumes a higher position, and the cytoplasm is rather granular; it is the active cell. The cell at this stage is found where there is a slight glandular hypertrophy, or a mild degree of increased stimulation such as occurs during puberty, menstruation and pregnancy. Frequently in late adolescence, in a patient in whom hyperthyroid symptoms are quite pronounced, this type of cell is seen without true hypertrophy of the gland.

With further stimulation this cell becomes high cuboidal, slightly irregular, the nucleus assumes more of a central position and the cytoplasm is quite granular. This stage is typical of true hyperplastic goiter with its clinical symptoms of thyrotoxicosis. A later stage, which marks the extremely active state of the cell, is seen when it becomes columnar, irregular, with central large hyperchromatic nucleus, coarse granules in cytoplasm. An increase in their number causes rows of those cells to be pushed within the lumen of the follicle. This is the cell of extreme hyperplasia found in the type of gland termed exophthalmic goiter, hyperplastic goiter, Basedow's or Graves' disease; it may, however, be found without exophthalmus in definite hyperplastic goiters.

Following this stage of extreme hyperplasia is the stage of vacuolation. Here the cell is still quite tall, the nucleus is somewhat irregular and eccentric, and in the cytoplasm are seen many non-staining vacuolated spaces. This marks the beginning of the cell's cessation of activity. The final stage is the stage of exhaustion, in which the nucleus is barely seen, the cytoplasm poorly stained, and the cell flat and devoid of all signs of activity. Following exhaustion, in which the cell has already spent

all its ability to activate the gland, comes desquamation; the cell disintegrates, is desquamated, thrown in with the colloid and resorbed.

The response of follicular cells in the same gland to any stimulus varies with the stage in which the cell is found in the evolutionary process of thyroid physiology and pathology. Iodin affects the cell differently in each stage, but in general it accelerates the life cycle, and produces greater activity. It stimulates the resting cell quite markedly, has little or no effect on the active cell, and pushes the extremely active cell of true hyperplastic goiter to its final stage of exhaustion.

Storage and Secretion

Once the follicle is formed, its function is storing colloid, and we are of the opinion that its cells, in addition to secreting colloid, have the function of elaborating thyroxin or converted iodin. It is beyond doubt that iodin plays an essential part in thyroid physiology, but the nature of such a part is not clear. A peculiarity of the follicular cells, that they face two ways—toward the lumen of the follicles and toward the interfollicular space—may mean that the cell can secrete in either direction. In favor of a direct secretion into the blood capillaries closely adjacent to the follicular epithelium is the fact that the cells (first noted by Langendorff (85)) have no true basement membrane or membrana propria. With the blood supply of the gland situated in the interfollicular space, and the cells facing either way, it is possible that the iodin is brought to the gland by way of the blood stream and there a portion of it is taken up by these cells and in some way converted into thyroxin while the surplus is stored in the follicle.

Elaboration of Thyroxin

The exact method of elaboration of thyroxin has not yet been proved. We are satisfied that in addition to the iodin in the colloid, there must be another product to augment the iodin in order to produce perfect thyroxin. The hypothesis accepted as a working basis by the author of this book, is that the follicular cells rupture and release colloid into the follicle. These cells then exfoliate, and disintegrate, releasing into the follicle an unknown element contained in the nucleus and cell membrane, This unknown element has a great affinity for, and combines with, the iodin in the colloid, producing wholesome thyroxin which finds its way into the general circulation by way of the blood capillaries. If iodine is not present in the colloid of the follicle, true thyroxin is not formed or elaborated, and the unknown element enters the circulation as a toxic substance. Support is given this theory by the well known fact that normally the follicle is filled with a thick colloid material containing a high percentage of iodin.

Active and Resting Stages in Various Periods of Life

The thyroid of the new-born is very active and in some ways sharply resembles the active hyperplastic thyroid of Graves' disease. It is a tu-

bular gland characterized particularly by large numbers of closely arranged cuboidal cells which are packed with granules. There is a definite amount of intercellular stroma which divides the gland into circumscribed lobules, each lobule containing many follicles filled with colloid. This histologic picture considered as a physiological process in the new-born is seen in the thyroid gland of abnormally increased activity of later life, at which time it is considered pathological.

Following the activity of infancy, the thyroid gland gradually assumes a resting stage, during which the closely packed cells show a small degree of follicle formation, and these follicles contain colloid. The large number of closely packed or cords of cells found in infancy normally decrease and the follicles apparently increase in size and number as the child grows older. Until puberty is reached the gland is not very active, as shown by colloid storage and decreased cellular activity. At this period however the gland again becomes active. The colloid is decreased in amount and thinner, the cells lining the follicles become higher—high cuboidal with a marked increase in number—and are found to be quite granular.

The increased number of follicular cells causes a relative decrease in colloid containing follicles, the interfollicular stroma becomes more vascular, and the entire gland assumes the appearance of secretory rather than storage function. During this period, known as puberty, the variation in the microscopical picture, which we accept as evidence of increased activity of the gland, is sometimes more pronounced than that usually found in glands from older patients presenting definite symptoms of thyrotoxicosis. The increased activity of the gland at this period sometimes exceeds even the normal limits of this stage, causing the patient to present symptoms of thyrotoxicosis. It is usually in the later period of puberty and in early adolescence that this occurs and it is commonly called "adolescent goiter." The adolescent goiter is popularly understood as the goiter of late puberty, and is a hyperplasia which marks the final step in the increased activity of puberty.

In adolescence, the thyroid gland again reverts to a resting stage during which the increased number of follicular cells found at the time of puberty are replaced by follicles which contain a considerable amount of colloid. The cells of the follicles, which were high cuboidal during the active stage of puberty, become flat and less granular. In later adolescence and adult life this resting stage becomes intensified, the follicles are filled with colloid, the cells are flat and show a dense oxyphilic cytoplasm, and the stroma is very scant. This presents the picture of the adult resting gland. A normal increased activity of the thyroid gland is also elicited by pregnancy and menstruation. While the increased activity at these times may not be so marked as in infancy and at puberty it is considered a physiological activity.

Hyperplasia and Its Relation to Disease

The hyperplasia of the increased activity, in the newborn, at puberty, during pregnancy and in a lesser degree during menstruation, is consi-

dered physiological. The same histological changes, in a greater degree, are found in the diseased hyperfunctioning thyroid. It is quite possible that the same degree of hyperplasia which would be interpreted as normal in infancy or puberty would be evidence of disease in adult life. Hyperplasia presents the same histological picture wherever found; the degree of hyperplasia determines the category in which the thyroid is placed. Histologically the hyperplasia from physiological stimulation resembles that of the extreme hyperplastic goiter except that it is very much milder in degree, is very early arrested, and followed by the colloid resting state.

The pathologist, because hyperplasia is in evidence, must take cognizance of it even if it is physiological and compensated by the resting stage. The clinician usually fails to recognize this stage of hyperplasia and interprets only the extreme or pathological increased activity as true hyperplasia.

During the stages of increased activity we have histological evidence of hyperplasia which may be briefly stated as follows: The epithelium lining the follicles becomes taller, the nucleus occupies a more central position and mitotic figures are seen. The cytoplasm stains feebly and contains many granules which often cause the cell to bulge and are probably pro-secretion products. The number of follicular cells is increased and there is a relative decrease in colloid.

Mild or physiological hyperplasia, which is immediately followed by the resting stage, shows no increase of these follicular cells to the degree of papillary formation. Where hyperplasia continues, however, and is not followed by the resting stage, these cells continue to increase in size and number. The follicle enlarges in order to accommodate the cells, yet there is a resultant decrease in size of the follicular space. Soon, the proliferating epithelium is seen to project into the follicular space in the form of processes or papillae until the follicle assumes a solid appearance. During this time the colloid becomes vacuolated, thinned, and finally disappears. The entire gland shows greatly increased vascularity, with areas of cellular solidity replacing the areas of colloid containing follicles.

Resting Stage

During the resting stages we have the opposite picture. The epithelium lining the follicles is low and flat, and no proliferating buds are seen projecting into the follicular space. The follicles are filled with colloid which appears dense and stains intensely with eosin. There is an even picture of follicles, lined by a single layer of cells, filled with colloid and separated only by a thin strand of connective tissue.

As these two stages—active and resting state—normally follow each other during life, the gland maintains a certain equilibrium in which physiological hyperplasia is followed by the physiological resting stage and the gland possesses the accepted normal picture. The evolution of goiter pathology may bear some relationship to this physiological process.

These periods of physiological activity and reversion to the resting stage may be compared with the greatly increased activity and resultant excessive hyperplasia followed by the subsequent stages of involution,

of the diseased thyroid. In one we have physiological activity within normal limits and always followed by the resting stage; in the other, increased activity of disease, exceeding normal limits but not always followed by reversion to the resting stage. The first meets the necessary demands by simple hyperplasia and reversion to normal; the latter, unable to meet the necessary demand even by extreme degrees of hyperplasia evidencing an extreme degree of over-activity, and unable to revert to the normal resting state.

If physiologically, during various period of life, the thyroid gland responds to increased stimulation by hyperplasia, and then involutes to the resting stage when the demand is decreased, should we not consider the diseased thyroid, excepting malignancy and specific infections, as a constantly recurring process of over-stimulation with hyperplasia, from whatever cause, with subsequent involution? This will be further discussed in thyroid pathogenesis, where the various subdivisions of the numerous existing classifications will be treated as one continuous process in the dysfunction of the thyroid gland.

PATHOGENESIS OF GOITER

The term goiter is applied to any enlargement of the thyroid from whatever cause. Loosely used it may be made to include any disease or dysfunction of the thyroid; dysfunction including hypofunction as well as toxic, diseased or hyperthyroid states. At this writing we prefer to separate the functional disturbances—the usual goiter types—from inflammatory and tumor disturbances.

Goiter due to functional disturbances is usually divided into certain classes and each class considered as a separate disease, whereas it is quite probable that insofar as thyroid dysfunction is concerned we are dealing with only a single morbid state in various grades of progression or regression.

In goiter production the enlargement is caused by hyperplasia as the primary step. Simple or very mild hyperplasia, found during physiological periods of activity, is followed by involution to the resting stage, during which there is a production of colloid sufficient to meet the necessary demand, and the metabolic equilibrium depending upon thyroid secretion is properly maintained. If the mild hyperplasia is not followed by involution to the resting stage (evidencing the possibility that the thyroid is not meeting the body demands), the stimulation continues and hyperplasia increases past the physiological limit. If then, the demand is finally met, and involution does occur, a resting stage is reached wherein the production of colloid, in proportion to the hyperplasia, has also passed the physiological limit—excessive storage of colloid with enlargement of the gland is the result. This is termed colloid goiter.

It is reasonable to assume that marked distention of the follicles over a considerable period of time may produce thinning of the interfollicular septae, with possible damage to the secreting cells or interference with the blood supply, resulting in various pictures of thyroid

dysfunction. This may be the explanation for mild simple colloid goiters, of recent appearance, disappearing with no further symptoms under medicinal treatment. Those that have been present for a considerable period of time are not so successfully treated.

In cases where the mild physiological hyperplasia is not followed by the resting stage, and even at a later stage, when the increased hyperplasia which has passed the physiological limit is still not followed by the resting stage with production of colloid goiters, the hyperplasia continues unarrested. The whole gland is involved, and all the gland substance is undergoing marked hyperplasia with no focal areas growing more rapidly than others. Should this process continue uninterruptedly it results in a diffuse, even, and smooth enlargement of the entire gland, showing extreme hyperplasia, and produces the marked symptoms of the goiter which is clinically termed exophthalmic, Graves' or Basedow's disease. At any period during this hyperplasia stage, however, the process may be arrested, either by medication or bodily adjustment, with resulting focal areas of circumscribed hyperplasia. The arrest does not occur over the entire gland diffusely; certain areas do not undergo involution as quickly as others and these become surrounded by the involuting areas which by colloid production exert sufficient pressure to form circumscription.

As this process continues involution follows hyperplasia and the various types of goiter pathology are only stages of this hyperplasia-involution cycle. While both of these conditions are listed under, and are the essential phases of thyroid pathology due to disturbed function, we are principally concerned with hyperplasia because production of this hyperplasia underlies all the following processes.

The cause of goiter should be dependent upon the cause of the hyperplasia. While we cannot definitely establish such a cause, it is certain that a close relationship exists between goiter and iodin deficiency. This deficiency may be prompted by bacterial toxins which so effect the thyroid gland that it cannot assimilate the iodin even if present in sufficient quantity. From a clinical standpoint we have noticed that the histological picture, of the glands of a large majority of the toxic goiter patients, presents evidence of pre-existing thyroiditis. The usual thyroid infection is a non-suppurative process and the symptoms of pain, inhibited head motion, and "stiff neck" are to be considered. From a pathological standpoint we cannot completely disregard the later indications of thyroid infection: a marked increased vascularity with dilatation in all blood vessels, even the capillaries (pulsations seen clinically bear some relationship to engorgement of vessels, and increase in elements of dilated vessel walls). The increase in cellular stroma; the cellular hypertrophy and hyperplasia of the parenchyma; the presence of loose, possibly wandering cells; the areas of marked lymphocytic hyperplasia; the production of young fibrous cells with definite increase in fibrous tissue—all bear evidence favoring thyroiditis as a possible existent factor.

Cole and Womack (86) have shown that the microscopic findings, in thyroid glands removed from dogs dead from acute infections, show

desquamation of the follicular cells into the follicle with disintegration of the protoplasm of the cell. The remaining cells lose their cuboidal shape, become columnar, and in many cases there is a piling up of the follicular cells with papillary infolding such as is seen in the human exophthalmic goiter. This work is strongly indicative that the thyroid gland takes an active part in the mechanisms combating general diseases in the human body, especially fevers and acute infections. It is also indicative that infection attacking the gland itself is subsequently related to goiter. It concurs with previous work in which lesions of the thyroid, produced by infections, strongly resemble the microscopic picture seen in exophthalmic goiter in man.

This first step of hypertrophy is the starting point in goiter pathology, and is comparable to the compensatory hyperplasia evidenced in an animal when a large part of the thyroid is removed. Withholding iodin completely from the food of an animal produces the same hyperplasia; this too we think is a compensatory hyperplasia. Gaylord (87) produced a similar process in fish by keeping trout in a series of tanks each of which drained into a tank below and the proportion of goiter increased in each successive tank. McCarrison (88) has shown that a diet containing an excess of fat will result in thyroid hyperplasia even though the animal is supplied with an abundance of iodin. We must content ourselves then with the idea that a possible multiplicity of factors are responsible for goiter development.

We believe this hyperplasia is a compensatory one. With the lack of iodin the thyroid is called upon to supply more iodin, in the form of thyroxin, to the body and draws upon the reserve supply accumulated in the follicles. The follicular cells undergo what is usually termed "work hyperplasia" because the process goes on with the normal work of the thyroid under physiological stimulation. This same process is seen in the various forms of goiter, and except for the altering types of reaction in given cases, we believe to be of essentially the same nature.

The natural result of hyperplasia is involution, which is the opposite process and is responsible for the return of the thyroid unit to its normal state. Between these two processes is found a resting stage at which time some sort of an equilibrium is established and results in the return of the gland to the condition nearest normal that such a gland can assume. From a physiological point of view we might consider such a gland normal because the process which brought it to the resting state is purely a physiological one, the same as occurs during normal periods of thyroid hyperfunction.

From an anatomical point of view it is abnormal, and the extent of the abnormality depends on the size of the gland and the number of times it has undergone hyperplasia and involution. In the very early case there is a uniform increase of colloid within the follicles, resulting in a diffuse enlargement of the whole gland.

Viewed histologically we find this to be the resting stage between hyperplasia and involution. This is readily seen by administering iodin to and producing involution in the thyroid of an animal and then dis-

continuing the use of iodin which results in the reappearance of hyperplasia. This process of involution occurs in two ways—either as a result of exhaustion as seen in the experimental animal and often called "burnt out," or as a result of replacing the lack of proper iodin content which presumably induces the hyperplasia. It seems to follow that as long as there is an abundant supply of iodin the gland functions normally, but as soon as this supply falls below a certain level, increased activity and hyperplasia are necessary to meet the metabolic demand.

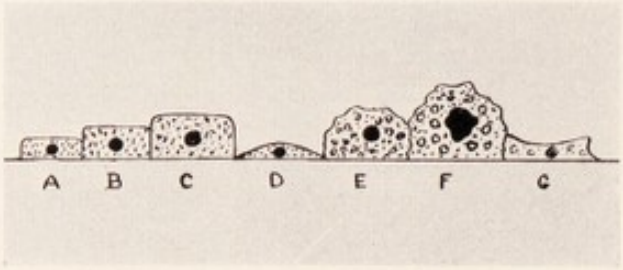


FIG. 5.—Phases of Cell Activity (A–G).

As involution is the necessary complement of, and has the opposite result from hyperplasia, so does the histological picture of the former characterize the stage of hypoactivity while that of the latter the stage of hyperactivity; between these is the colloid resting stage. In the colloid resting stage the traces of former hyperplasia can be seen in the form of very small epithelial projections into the lumen of the follicles, but, in the main, the follicles are dilated and filled with colloid so that the lining epithelium is flattened. The individual cell shows evidence of only slight activity, with no evidence of proliferation. In involution the follicles show very low flattened and supposedly exhausted cells which are in a state of inactivity. The vascularity of the gland is decreased while the stroma is increased with formation of many bands of fibrous tissue irregularly distributed throughout the gland. These bands finally circumscribe irregular areas of gland substance producing lobulated masses which resemble tumors and are often incorrectly called adenomas. These lobules are for the most part made up of colloid which at a later stage may go on to liquefaction and degeneration. In this manner a diffuse goiter is changed to a nodular one.

As these two counter actions occur, not all portions of the gland are involved, and those that are involved are not acted upon to the same degree. Rienhoff (89) removed a portion of the thyroid in a small number of cases of severe Graves' disease, administered iodin for about two weeks, and then removed the remaining portion of the gland. Prior to the use of iodin those glands presented the usual diffuse picture characteristic of exophthalmic goiter. After the use of iodin the diffuse picture was replaced by one composed of various sized nodules definitely circumscribed. Some of these circumscribed areas already contained a watery colloid material such as found in the cystic formation of long standing colloid goiters.

Microscopically, the change varied from a slight to a very marked degree. Even where only a slight change was noted, the dominant factor was the attempt of arrested growth with involution characterized by formation of circumscribed areas showing colloid instead of proliferating

epithelium—a definite reversion towards normal even though the normal was not reached. In cases with a marked degree of involution, the change was not uniform being extreme in some places, moderate in others, and in still others, practically absent. In the same gland then may be demonstrated hyperinvolution, involution and hypoinvolution. This brings out the fact that while, even in extreme hyperplasia, reversion to normal is attempted, the true normal is never reached and hyperplasia never completely arrested. Likewise, in the same specimen we may find various pictures of hyperplasia, normal, and exhausted or degenerated areas.

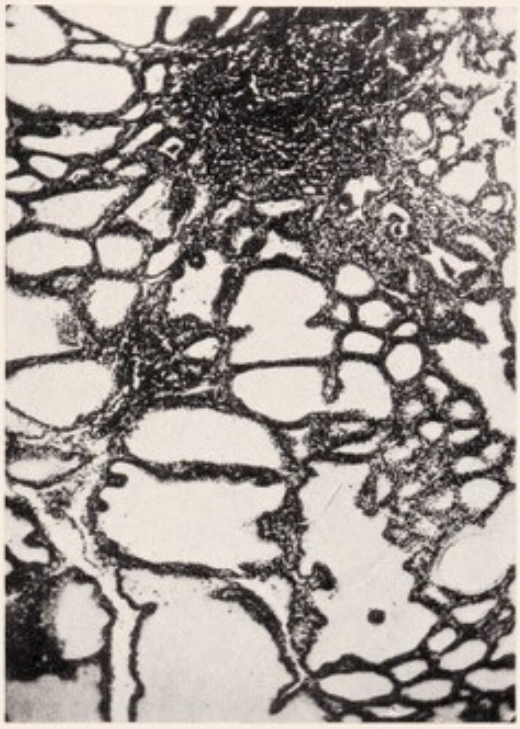


Fig. 6.—Diffuse Hyperplastic Goiter (Exophthalmic Type) showing Involution and Colloid Storage.

The process is quite a rapid one when produced by the use of iodin but very slow, extending possibly over a period of years, when produced as a result of natural exhaustion, of "burning out" process. In either case the hyperplastic cells of the follicles are seen to recede, there is formation of colloid, follicles are distended and intervening walls give way with resultant fusion, making circumscribed areas of colloid; the fibrous septae are greatly thickened, and because this process is not diffuse, but occurs in certain areas, it results in large colloid spaces surrounded by fibrous tissue with pressure upon and finally obliteration of the surrounding structure. While such an area is definitely encapsulated and completely separated from the rest of the gland, we still do not consider it colloid adenoma as it is commonly called, but rather a nodose or circumscribed colloid goiter.

The same thing but with a different picture occurs in focal areas where involution did not take place. Here the follicles remain small and closely packed because they do not become distended with colloid, and form small nodular masses of packed cells corresponding to the usual description of what is commonly called fetal adenomata.

In the microscopic picture of this natural or "burning out" process we can more readily see the slow but progressive changes from hyperplasia to involution and on to exhaustion. From the stage of colloid containing follicles to their complete degeneration many variations are seen: areas still showing colloid here and there, but in the main showing all types of regressive changes such as swelling and desquamation of follicular cells, formation of epitheloid cells, lymphocytic infiltration, and fusing together of desquamated swollen epithelial cells to form giant

cells. Sometimes fibrous and plasma cells are found. All of these may simulate the picture of a tuberculous process. We agree with the opinion of Jaffe (90) that some of the tuberculous thyroids reported may be in this stage of involution and degeneration. It occurs to us that this picture may have some relation to the infection theory advanced regarding the production of goiter.

In examining a large number of goiters, from patients with toxic symptoms in some of whom exophthalmus occurred, we find that hyperplasia in many cases is not general but restricted to certain areas. Further, that hyperplasia is very marked in some areas, less marked in other areas, absent with formation of colloid in others, and in various degrees of exhaustion to desquamation in still others. Thus in a single specimen we may find all degrees of hyperplasia from the resting colloid state to involution and degeneration.

In the areas of marked involution or hyperinvolution, the follicles become so distended that the intervening walls give way and several follicles are blended into one large colloid filled cavity. Over a period of years, as this process goes on, the septae separating the lobules become very thick and form definitely encapsulated colloid areas. Unless there is an acute exacerbation of hyperplasia, the involved tissue keeps going through the same cycle each time until by pressure necrosis and hemorrhage, liquefaction takes place. With each successive step of involution the nodule becomes larger, and points further toward degeneration. In such a case, a number of sections taken from various parts of the gland or from various parts of the same nodule show many stages of this hyperplasia involution process. Within the nodule itself hyperplastic changes may start over again at any time. Some of the follicles, although found in a nodule with marked hemorrhage, may show active budding. Several buds may arise from the same follicle, some showing solid masses of cells, others showing a definite lumen representing a new formed follicle. Then too, the nodule per se may have lost all evidences of previous hyperplasia, but other areas of the gland may show greater or less degrees of hyperplasia or lack of involution, termed by Rienhoff "hypoinvolution" (91).

Marked circulatory disturbances are noted in these focal areas of hypo and hyperplasia. There are seen large numbers of dilated thin-walled vessels from which we presume the hemorrhage, which is so frequent, takes place. In these hemorrhagic areas the colloid becomes thinned and liquefaction results. These are the areas outside of the nodes, which resist the process of involution. This explains why a patient may still have symptoms of thyrotoxicosis even though large areas of the gland are non-secreting. Similarly this can explain the toxic symptoms which often accompany the seemingly harmless, so-called adenoma. In sectioning a large number of fresh thyroids removed at operation this observation is very striking. Frequently a very large, lobulated and cystic goiter, of perhaps fifteen or twenty years standing, will be removed only because the patient first began to present symptoms of thyrotoxicosis within the last year prior to operation. On examination of this specimen

we usually find in this large seemingly harmless, and very often markedly degenerated colloid nodular mass, areas of hypoinvolution (where hyperplasia persisted instead of being followed by involution) or small areas of meat-like fresh hyperplastic thyroid tissue entirely separated from the main tumor mass.

In such a case the original hyperplasia which commenced many years before was gradual in its onset and in each area the hyperplasia was followed, until a year ago, by involution or hyper-involution. With this process continuing in different areas over many years, the patient never developed symptoms of thyrotoxicosis, because involution or hyper-involution immediately followed the hyperplasia, until the major portion of the gland was finally transformed into a large irregular degenerated nodular mass. Finally an area of the gland within the tumor mass failed to undergo involution and the symptoms of thyrotoxicosis appeared.

In the latter case the areas of hyperplasia are separate and distinct from the tumor mass and the symptoms are similar to that found in the usual thyroid of hyperplastic or exophthalmic goiter. It develops in a patient who has an old colloid nodular goiter. Instead of progressing in the manner the previous hyperplasia did, this one varies in that the hyperplasia is rapid and involution does not occur—the hyperplastic process continues without reversion toward normal colloid storage.

From this we conclude, at least in the light of present goiter etiology:

These colloid nodular goiters or so-called colloid adenomata are the result of degeneration dependent upon hyperplasia followed by involution and hyper-involution.

The so-called toxic adenomata differ from the non-toxic colloid nodular goiter only in that they contain areas of hypo-involution, in which hyperplasia was not followed by involution.

The so-called toxic adenomata are frequently not toxic per se, in which case they are pathologically the same as the non-toxic type, but are associated with hyperplasia in a separate portion of the thyroid not included in the encapsulated lobulation in which rapid hyperplasia with no attempt at involution occurred.

We think it is quite evident that similar factors are involved in the production of both hyperplastic and colloid types of goiter. The simple colloid goiter is only an end result of a hyperplastic goiter in which the hyperplasia is mild and not rapid in its cause; involution occurred and a condition resembling the normal state resulted. The nodular colloid goiter is of similar origin, but differs in that the hyperplasia-involution cycle occurred only in certain areas. The toxic nodular goiter or toxic adenoma is also of the same origin, but here, while the hyperplasia-involution cycle occurs, there are a few areas of hypo-involution or those in which hyperplasia persist. The true hyperplastic or exophthalmic goiter is one in which there is marked and very rapid hyperplasia not followed by any form of involution—unarrested hyperplasia.

We must add, with regard to adenomas, that not all thyroid nodules or nodular goiters found are of the origin here contended. Less than twenty per cent reported by Rienhoff, and in Lewis' series eight per cent,

are likely true enoplasms and deserve the term adenomata. Their character, however, differs from the encapsulated areas here described. The encapsulation does not make true tumors, but the internal structure does. Microscopically, this group shows masses of epithelial cells forming very early follicles which show no lumen; these cells are in strands which anastomose with each other. The blood vessels are quite abundant but nowhere is there evidence of open hemorrhage. The hyperplasia-involution process is not seen at any stage, nor is there any evidence of lone hyperplasia. These are true adenomata definitely neoplastic in character, and therefore of entirely different origin than the various types of goiter developed through the pathogenesis here described.

GOITER PATHOGENESIS AS ONE CONTINUOUS PROCESS

Approach to Classification

The consideration of the *modus operandi* of goiter pathology usually results in a goiter classification which is in accordance with the mode or path the goiter is alleged to have traveled. The construction of a classification which will be acceptable to both pathologist and surgeon seems rather difficult. This is easily explained by the fact that the histological findings very often fail to coincide with the clinical picture. It would be a comparatively simple problem if the different types of goiter represented distinct clinical entities, and the histological findings coincided with those of the clinician.

Two Main Types in Classification

One of the simpler classifications is the one offered by Marine (92) in which he divides the diseases of the thyroid, due to disturbances of its functions, into two groups: (1) Thyroid insufficiency and (2) Exophthalmic goiter. These two groups are popularly designated hypo- and hyperthyroidism, even though they very often overlap. Such a classification is acceptable, and for many years has been, if we base our findings on clinical examination and disregard the histological examination. From a clinical standpoint most of the classifications offered would be acceptable and offer an advantage by emphasizing definite, prominent, clinical groups through the use of terms such as toxic, exophthalmic, non-toxic, adolescent, etc. This would lead us to believe that these groups represent different diseases, or at least separate and distinct disease states which bear little or no connection with each other. From both histological and clinical points of view, considered as aids to each other, it seems much more likely that the various states of goitrous disease are not a series of separate types of goiter, but rather a continuous process of stages of progression or regression and more often both.

From the very origin of the embryonal formation of the human thyroid to the time the gland reaches maturity of adult life, we are normally dealing with colloid storage on the one hand and lack of colloid with hyperplasia on the other. During the various periods of life, such as pregnancy, puberty and adolescence, the human thyroid normally

changes in texture, depending upon the stage of development, and these changes are brought about by virtue of increased or decreased activity. With increased activity, as is normally seen at puberty and pregnancy, we see histologically, a marked decrease in colloid containing follicles and a definite increase in the number of cells making up the follicles, with hyperplasia of these cells. With decreased activity we see the opposite histological picture; decrease in number of follicular cells and marked colloid storage in the follicles.

There is reason to believe that this normal process is the basis, in its simple form, of disturbed thyroid function resulting in many various stages or so-called goiter types. With thyroid insufficiency we have one extreme while with marked toxic or exophthalmic goiter we have the other extreme. The possibility of these various types of goiter being but various stages of a single morbid process is seen more easily in goiters between these two extremes.

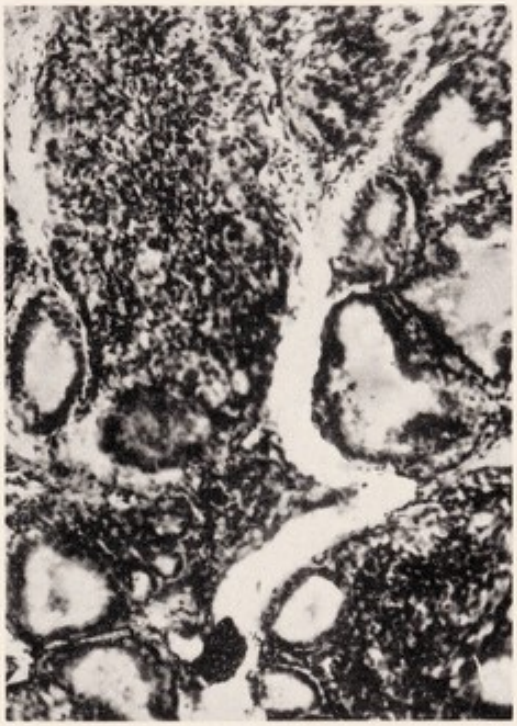


FIG. 7.—Involution and Hyperplasia.

Thyroid Insufficiency

Colloid Goiter

In the colloid goiter we find what the name indicates; an excessive collection of colloid in the follicles with thinning of interfollicular septae. The gland shows little or no signs of activity but presents the picture of the resting state. Many of the patients show only mild symptoms, while others complain only of thyroid enlargement with no general disturbance. Those that do present symptoms sometimes give some clinical evidence of increased thyroid activity but are usually found to have a decreased metabolic rate. The gland is essentially enlarged due to increased colloid content of the follicles.

The cells lining the follicles are flattened, the interfollicular septae are thin and stretched and the number of follicular cells is less than normally found. The picture, in general, is one of rest and decreased activity, yet in certain areas we find small buddings or plications with some irregularity of the follicular cells and generalized increased vascularity. These findings are most likely remnants of preceding hyperplasia and testify in favor of increased activity with hyperplasia being followed by excessive amounts of colloid, and storage of this colloid in the dilated

and hypertrophied follicles of simple colloid goiter. Here is seen some overlapping of the hypo and hyperthyroidism. With single hyperplasia we have the latter, while during the colloid resting state or in colloid goiter we have the former.

This may be taken as evidence that hyperplasia is the initial reaction of the thyroid parenchyma to whatever the cause may be of disturbed thyroid function and goiter. Because under certain physiological body changes and at certain periods of life we find similar hyperplasia followed

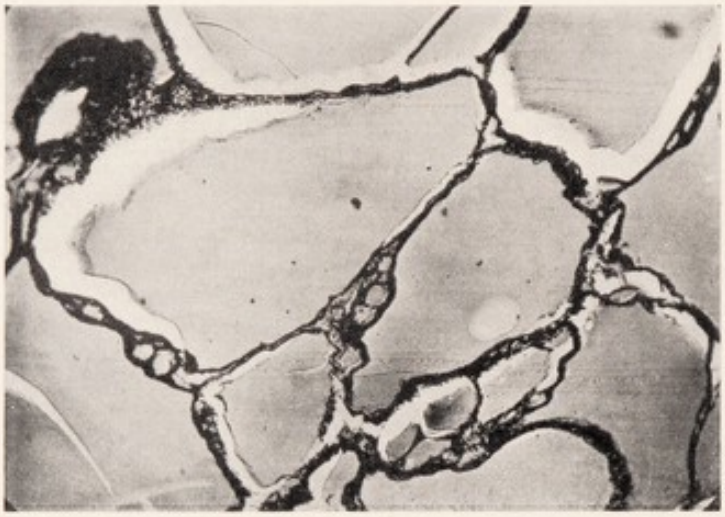


FIG. 8.—Colloid Goiter Showing Large Follicles.

by the resting colloid state, it is reasonable to assume that the simple colloid and adolescent goiters are dependent upon the same process, but have assumed somewhat greater proportions.

Nodular Colloid Goiter

This colloid type appears as a more or less uniform enlargement and in early life is called adolescent goiter. The name implies merely the time of life it is most frequently seen. Histologically it differs from the colloid goiter of later life only in that the latter is less diffuse and shows a tendency to irregular formation with circumscribed nodules. There is reason to believe that these nodules are formed by more rapid growth of certain areas, as contended by Hertzler (93).

The development is supposedly brought about by continuous successive exacerbations (hyperplasia) and remissions (colloid storage) and very often this increased, considered physiological, growth is associated with pregnancy. It cannot be overlooked that this point may have a marked relationship to the comparative rarity of this nodular colloid type of goiter in the male. With the formation of nodules, the term adenoma is applied, but it is difficult to conceive of such a goiter being a true tumor because the development does not begin at one point and extend from this point as tumors do, but all parts of the gland take part in this

process with certain areas growing more rapidly than others. The disturbance does not seem tumorous, but functional and the degree of this functional disturbance is seen in the anatomical structure of the gland.

Irregular Hyperplasia and Involution.—The development of nodular goiters by a process of increased growth in certain areas, irregular hyperplasia and involution, isolation, complete circumscription and final encapsulation is borne out by considerable evidence and many investigators support this view. (Rienhoff (91), Graham (94), Hertzler (93).) That such a process occurs in the thyroid gland is given support by the transition from apparently normal non-nodular thyroid tissue to nodular goiter as seen in the glands of individuals approaching, or who have already attained, adult life. This is particularly seen in females where hyper-function of the thyroid occurs at certain periods as a physiological phenomenon. This process, with its end result of nodule formation, presents its most complete anatomical picture in regions in which goiter is endemic.

Since the probability exists that simple colloid goiter is preceded by diffuse hyperplasia which is arrested and results in the colloid storage state, we take the next step in which nodulation in its earliest stages is considered. Here a single localized area of hyperplasia failed to become arrested and failed to recede to the colloid resting state. Within this area there is a formation of new follicular structure with increasing lack of orderly arrangement, and failure of development of the stroma that characterizes normal thyroid tissue. Further proliferation of tissue within this localized area continues, causing it to increase in size and with increasing growth more and more pressure is exerted upon the surrounding tissue. In the immediate periphery atrophic changes occur and replacement fibrosis, of the portions undergoing atrophy, isolates this area of irregular hyperplasia. As the process continues the zone of replacement fibrosis becomes compressed and consolidated, completely circumscribing and finally encapsulating a mass of proliferating thyroid tissue. Histologically the early changes of hyperplasia seen in non-nodular thyroid bear a marked resemblance to the early encapsulated mass, which speaks very strongly in favor of these changes being transitional stages of the same process.

Degeneration.—The hyperplasia within the circumscribed or nodular area is subject to the various changes found in diffuse hyperplasia and it is easily possible that this hyperplasia may be arrested at any time. If so, this may explain the great variety of anatomical changes occurring within the nodule. The goiter in which there are many of these nodules (which histologically show evidence of considerable hyperplasia) is evidence of continued focal growth with lack of arrest; this type is rare compared to the type showing arrest and changes of involution occurring within the nodule. More often we find evidence of arrested hyperplasia followed by retention of colloid within the circumscribed area. Further changes may take place; the arrested area if deprived of blood supply may result in a form of atrophy with formation of fibrosis. If the process of degeneration continues the area becomes hyalinized and finally calcified or even ossified.

Instead of lack of blood supply there may be hemorrhage into the nodule, after hyperplasia has been arrested, in which case the colloid becomes thin and watery and with continued hemorrhage complete liquefaction takes place. Finally a completely encysted area containing a dark hemorrhagic liquefied sort of colloid may result. Formation of definite cysts filled with various types of degenerated colloid and hemorrhage are often seen. Because many of these stages may be seen in the same goiter it is quite reasonable to assume that this is one continuous process in thyroid dysfunction.

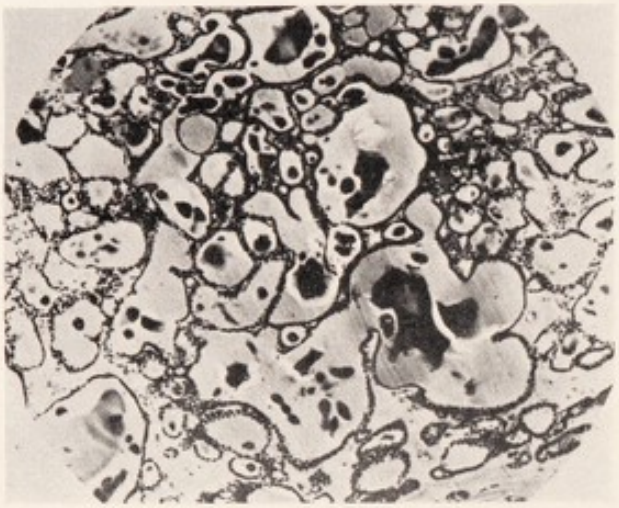


Fig. 9.—Diffuse Colloid Goiter.

Diffuse Hyperplastic or Exophthalmic Goiters

Diffuse Hyperplastic Goiter

In the goiter with diffuse hyperplasia we do not find much evidence of the colloid resting stage, but rather marked activity of the gland. This type is associated with constitutional disturbances. If the patient has been known to have had a goiter previous to the onset of symptoms the clinician applies the term "toxic adenoma"; if the patient gives no history of previous goiter the term "exophthalmic goiter" or "Graves' Disease" is applied. Both of these terms serve as an aid and offer an advantage in establishing a clinical entity, but fail in properly classifying the goiter as to its pathological findings. The histological picture is essentially one of cellular proliferation and in the advanced case there is actual papillary formation. True, we may find many areas in which the colloid follicles, the contained colloid and the interfollicular stroma are in normal relationship as found in the normal thyroid; a few areas may even show some evidence of the colloid resting state in which the follicles are dilated and filled with colloid to their utmost capacity, but this is merely further evidence that this condition, while it may suggest a separate entity by its clinical manifestations, is only part of some progressive and continuous process.

Should hyperplasia continue unarrested we have a very rapid process with very marked clinical manifestations. The hyperplasia continues diffusely throughout the gland and the process of resting stage and involution with resultant changes is completely absent. The onset and continued growth are both very rapid and there seems to be complete absence of thyroid readjustment such as occurs in arrested hyperplasia and involution; a diffuse hyperplastic goiter commonly called Graves' disease by the clinician is the result.

In this particular type, probably more than in any other, we find the histological picture in agreement with the clinical symptoms. The con-

tinued hyperplasia, evidencing marked cellular activity, is manifested clinically by the usual symptoms of a very active goiter. The pathologist, even here however, cannot make an interpretation relative to the symptoms which this increased activity may produce. For instance, he cannot say whether or not exophthalmus is one of the clinical symptoms, no matter how marked the hyperplasia is on histological examination; nor

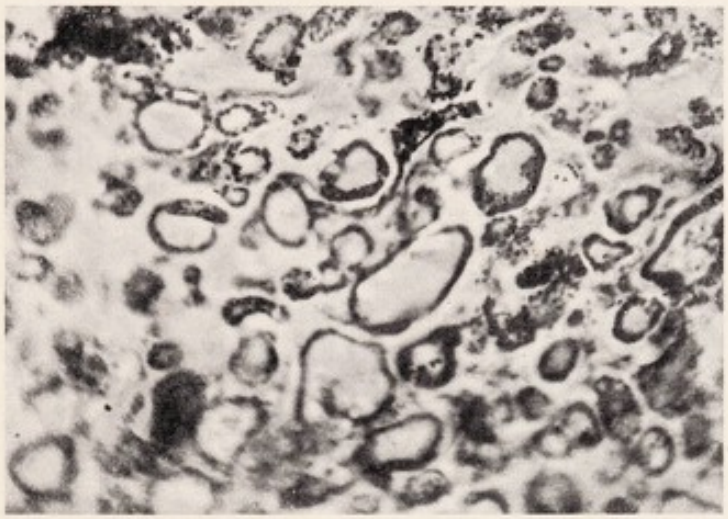


FIG. 10.—Nodose Goiter.

can he state the degree of toxicity such a histological picture may produce. The terms "exophthalmic," "toxic" and the like are not the best ones to be used in giving a pathological interpretation. Instead we prefer to report the hyperplasia as the essential finding and by way of further explanation state the degree as slight, moderate or very marked hyperplasia, and whether or not it is sufficiently marked to produce papillary infolding.

Occasionally the patient may withstand the bodily abuse by the unarrested hyperplastic thyroid and the process continues until there is cellular exhaustion. Without arrest the cells continue in their active hyperplasia until completely exhausted. The high granular active cell becomes flat and inactive and is finally desquamated and absorbed. This is commonly referred to as the "burned out" gland; while the patient survives there is always marked pathological change with its accompanying symptoms of hypothyroidism having followed hyperthyroidism.

Hyperplasia Reverting to Colloid Goiter

With the ability of adjustment possessed by the animal body it is quite conceivable that the demand may finally be met with a proper supply, but only after hyperplasia had progressed to a stage which is above that found in the normally functioning thyroid. With the demand met, the gland begins its usual process of reversion to normal but because hyperplasia has already passed the stage of normal thyroid function, this reversion imitates and simulates, but never reaches the normal. It as-

sumes the resting state, but because the hyperplasia had exceeded its normal limits, the resting state is now also abnormal in that an overabundance of colloid has been produced. There is a marked increase in colloid content of the follicles, and a simple colloid goiter results. Assuming this process to be the one involved, that of simple hyperplasia beginning in the normal thyroid gland which when arrested, results in a simple colloid goiter, we must admit the possible existence of a relationship between hyperplasia, colloid goiter and normal thyroid function.

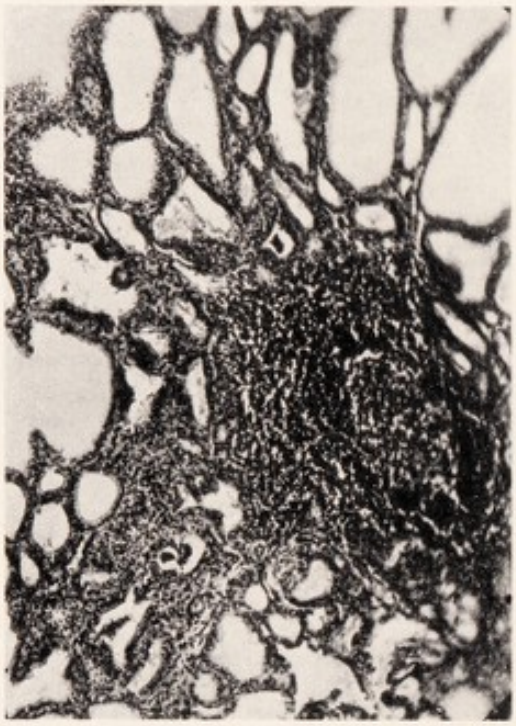


FIG. 11.—Diffuse Hyperplastic Goiter.

Hyperplasia Reverting to Nodular Colloid Goiter

The ability of bodily adjustment may fail in some instances and in these cases the intermediate stage of colloid goiter is not seen. The simple hyperplasia of normalcy is not followed by the normal resting stage nor is the hyperplasia slightly in excess of normal followed by the colloid goiter, but the hyperplasia continues unarrested. The demand apparently cannot be supplied, but nature is not deterred in her efforts to maintain a metabolic equilibrium and the thyroid gland in its attempt to function in its specialized capacity continues its increased activity with resultant diffuse hyperplasia.

At any stage before exhaustion, in this progressive hyperplastic course, a readjustment may assert itself and a resting state results. The gland then assumes a resting state, related to the normal, but only as close to the normal as possible, depending upon the degree of the preceding hyperplasia. Mild hyperplasia with proper adjustment results in simple colloid goiter, and the greater the preceding hyperplasia the greater will be the resultant colloid goiter. If the preceding hyperplasia is only of the mild type which produces no clinical symptoms, the arrested state will result in simple colloid goiter which is usually smooth and diffuse. If the preceding hyperplasia has passed this stage and has produced clinical symptoms the arrested state will result in circumscribed areas of colloid with possible nodular formation as compared to the smooth and diffuse simple colloid goiter. The circumscription is due to increased fibrous connective tissue in the interfollicular stroma forming connected strands which completely enclose areas of more rapidly growing colloid containing follicles.

These nodular colloid goiters differ from the simple colloid goiters

only in that the preceding hyperplasia had been farther progressed before it was arrested, and in the former there is much more histological evidence of the preceding hyperplasia. When arrest of the hyperplasia did occur the process is somewhat more intricate than that which results in the colloid goiter. It is highly probable that the hyperplasia continues for a longer period, or grows much more rapidly in certain areas with the production of the nodules at these points.



FIG. 12.—Diffuse Hyperplastic Goiter (Exophthalmic) Showing Papillary Infolding.

Such a picture may be seen in the thyroid of a patient who showed marked symptoms of hyperthyroidism, but who was given iodin for ten days or two weeks prior to operation. If, in such a case, iodin is continued over a long period of time a diffuse hyperplastic goiter may be changed to a nodular colloid goiter which still shows areas of hyperplasia. The natural process of readjustment or arrest of the hyperplasia seems to present a similar picture but is apparently much slower in its course.

The cellular proliferation in the gland, with or without papillary infolding, is usually associated with the symptoms of toxicity found in toxic goiters. In a general way it may be stated that the severity of the toxic symptoms bears a direct proportional relationship to the degree of cellular proliferation. It is a mistake, however, to assume that the entire gland of a patient presenting symptoms of thyrotoxicosis is made up of proliferating follicular cells. In many cases the larger part of the cut section is made up of small colloid follicles and very little active cellular proliferation. In other cases the larger part of the gland is made up of active cellular proliferation with marked papillary infolding. In the majority of operative cases, which are preoperatively prepared and given iodin, a part of the gland is made up of old colloid follicles associated with formation of new follicles some of which show active cellular development and papillation. The varying degree of colloid containing areas in this proliferating type of goiter may bear some relationship to the other types of goiters in which cellular proliferation is not the outstanding finding. Similarly the varying amount of cellular proliferation in the nodular colloid goiter or so-called "toxic adenoma" may bear a like relationship to the diffuse hyperplastic goiter with moderate colloid containing areas.

In studying a larger number of goiters one finds that the dividing line between diffuse hyperplastic or exophthalmic goiters and toxic nodose goiters or the so-called toxic adenomas may be only the route the gland has traveled in this process of hyperplasia-involution cycles.

Continuous unarrested hyperplasia with little or no evidence of involution results in diffuse hyperplasia of the exophthalmic type. Hyperplasia followed by involution and constant repetition of this process by some not definitely known stimulation results in the nodular from of goiter, the toxicity of which may depend upon the degree of suddenly developed hyperplasia which is not counteracted by involution. In many of these cases, if a careful history is taken, the toxic type will be found to be an acute exacerbation of an old chronic state rather than a new or distinct process.

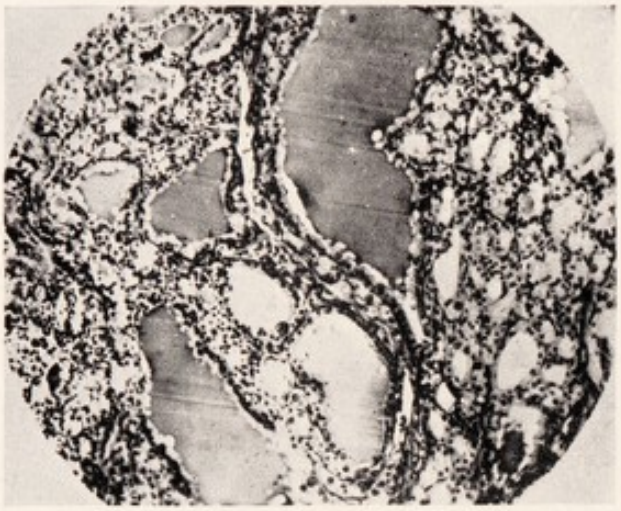


Fig. 13.—Diffuse Hyperplastic Goiter (Exophthalmic Type) with Areas of Colloid in Which Exhausted and Degenerate Cells are Seen.

It seems that greater clarity is achieved by considering this toxic nodular form of goiters as one of the variations in this continuous hyperplasia-involution process instead of separating them from old pure colloid or nodular colloid and degenerated goiters. All goiters may therefore be considered as various stages with individual variations of a single thyroid disease. In conformity with this conception the various groups or types of goiter, malignancy and infection excepted, listed in the following classification may be looked upon as the various stages in the development of goiter due to thyroid dysfunction, instead of separate types or kinds of goiter.

GOITER CLASSIFICATION

Tabulation of the essential pathology existing in the various types or stages of goiter is attempted in the following classification. Goiters are usually divided in three main groups, namely: colloid, adenomatous and exophthalmic goiters. These are regarded as being distinct entities, but from a pathological point of view this is far from satisfactory. These names are purely clinical and have little or no pathological connotation except the adenoma but even this term is unjustified because the nodules described under this heading are not true tumors in the pathological sense. A pathological classification should attempt as closely as possible to give the actual condition of the diseased thyroid.

If serial section is made and a number of blocks from each thyroid, in a series of cases, are studied it is surprising to find how varied are the lesions in any one gland. Even in the normal gland, at certain periods of life, areas of hyperplasia can be found. In a simple colloid goiter, in which the gland is supposed to be completely at rest, areas of hyperplasia can

nearly always be demonstrated if proper search is made. In nodular goiters, or so-called adenomata, where well-developed nodules form a striking gross feature, localization and partial encapsulation can be found in areas in which, to the naked eye, the enlargement is diffuse. Finally, in exophthalmic goiters which are characterized by diffuse general hyperplasia, colloid areas indicating involution are found in almost all cases.

It may therefore be stated that, in a single section, areas characteristic of normal thyroid, colloid goiter, exophthalmic goiter and nodular or so-called adenomatous goiter may be seen. The anatomical picture will most likely depend upon the existing stages between the processes of the hyperplasia-involution cycle, upon the extent or proportionate degree to which the hyperplasia has progressed before involution has occurred, and upon the degree of localization of this hyperplasia-involution process.

For the purpose of description, the following outline of goiters, divided essentially into functional, inflammatory and tumor disturbances and arranged with reference to origin, may be used.

THYROID ENLARGEMENT

1. Functional Disturbances.
   - A. *Diffuse goiter.*
     1. Diffuse colloid goiter.
     2. Diffuse proliferating goiter. (Some forms of adolescence.)
     3. Diffuse hyperplastic goiter. (Exophthalmic.)
     4. Diffuse goiter of myxedema. (Exhaustion fibrosis.)
   - B. *Nodose goiter.*
     1. Nodose colloid goiter.
     2. Nodose colloid goiter with fibrosis.
     3. Nodose proliferating goiter. (Adenoma).
     4. Nodose hyperplastic goiter. (Exophthalmic or adenoma—or both.)
2. Inflammatory Disturbance.
   - A. *Thyroiditis.*
     1. Acute non-specific.
     2. Chronic non-specific.
     3. Tuberculous.
     4. Syphilitic.
     5. Strumitis.
3. Tumors.
     1. Adenoma.
     2. Carcinoma.
     3. Benign metastasizing goiter.

The following illustration of the functional disturbances of the thyroid gland, outlined according to the probable pathogenesis, is an aid in determining the modus operandi of the various goiter types.

For clinical description, this classification, which is essentially a pathological one, could be used by merely adding a clinical descriptive term. Whether diffuse colloid or diffuse hyperplastic the words toxic, exophthalmic or the like could be added. Similarly the nodular goiters

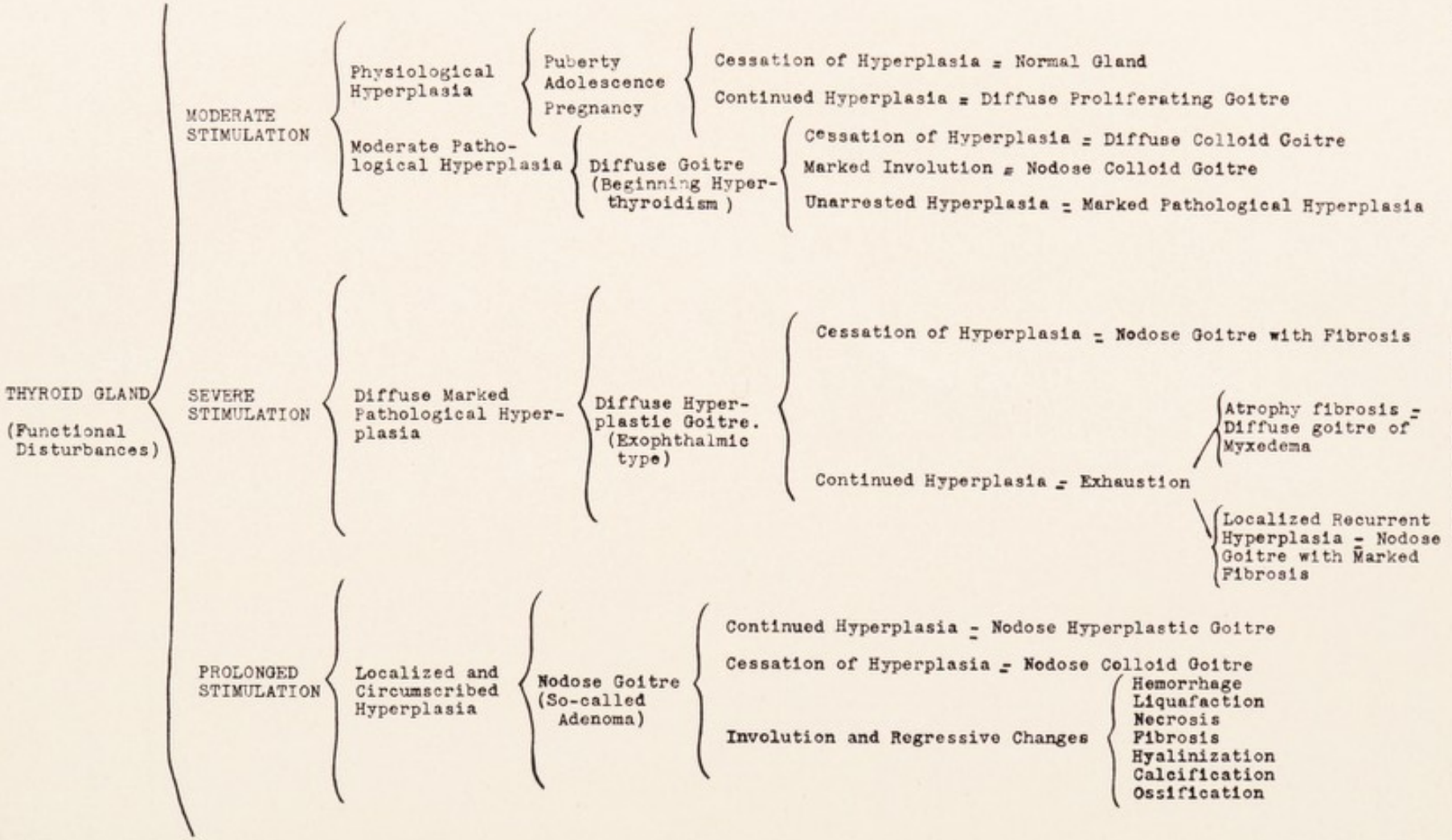


FIG. 14.—The Production of Goiter.

could be designated clinically and at the same time be as far as possible in accord with the pathological findings. A nodular colloid goiter can be so called instead of being misnamed adenoma, and a nodose hyperplastic goiter could be called a nodular toxic goiter or if found with exophthalmus could be called a nodular exophthalmic goiter instead of the misnamed toxic adenoma.

We are using the term stimulation for purpose of description in the absence of any definitely known etiology. Whatever the cause (mineral deficiency, infection, etc.), of the production of goiter, we use the term stimulation merely to indicate that which produces the gland activity. In functional disturbances of the gland the original process begins with hyperplasia of the secreting cells of the follicles which is well termed as increased glandular activity. Without definite knowledge of what produces this activity we use the term stimulation to indicate that which prompts the gland to begin its abnormal course. We can, therefore, associate the physiological or mild hyperplasia of puberty, adolescence, and pregnancy with what may be termed as moderate or mild stimulation. Cessation of this mild stimulation results in involution with subsequent normal gland while continuation of this stimulation results in the various forms of hyperplasia with corresponding goiter types. Severe stimulation may follow the moderate stimulation or may begin as severe, with resultant rapid growth without involution and production of the exophthalmic type of hyperplastic goiter. Prolonged stimulation produces localized and circumscribed areas of hyperplasia and is attended with involution resulting in the corresponding type of nodose goiter or so-called adenoma.

Whatever produces the increased glandular activity, hyperplasia is most likely the keynote to the beginning of thyroid dysfunction and the degree of stimulation with its counteracting involution will determine the type of goiter. There is reason to believe that the various types of goiter are dependent upon one continuous process which differs only in its degree, intensity and conditions characteristic of the individual patient.

INFLAMMATORY DISTURBANCES

In inflammatory disturbances of the thyroid gland the picture differs from the various types of goiter produced by functional disturbances. While no hard and fast rule can definitely separate these two conditions it will simplify discussion to classify infections of the thyroid gland as distinct from thyroid dysfunction.

Acute Thyroiditis

Acute thyroiditis is sometimes difficult to demonstrate unless a pyogenic abscess is found in the thyroid. There is, however, a thyroiditis which histologically presents leucocytic infiltration, marked accumulation of lymph cells forming definite lymph follicles, and in general shows the picture indicative of an inflammatory process.

The fact that many patients complain of symptoms which are clinically described as those of thyroiditis a few months prior to the time they become afflicted with acute hyperplastic goiters, lends some evidence to the theory of a relationship between infection and the excessive hyperplasia of acute thyrotoxicosis.

Specific Infections

In specific infections of the thyroid gland such as syphilis or tuberculosis the histologic picture is similar to that found in any other organ harboring disease of the same origin. There is, however, a form of marked

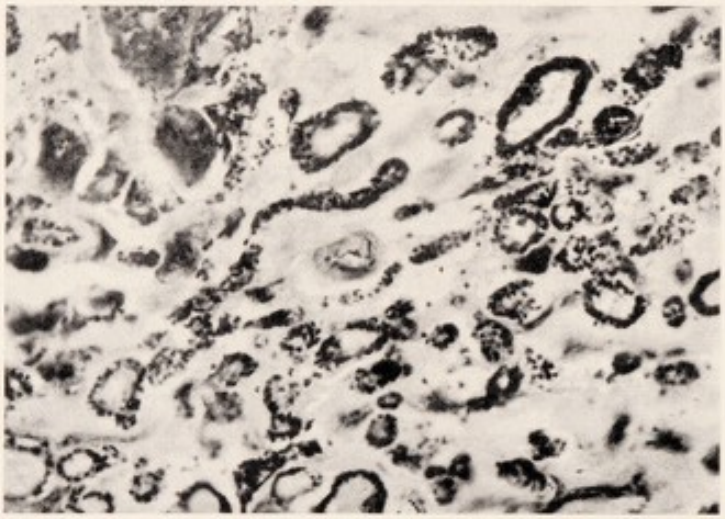


FIG. 15.—Nodose Colloid Goiter Showing Both Cords of Cells and Follicle Formation (So-called Fetal Adenoma).

involution found in certain types of goiter, in which the degenerative process simulates and is often mistaken for tuberculosis of the thyroid gland.

Strumitis

In strumitis we see the same histologic changes of inflammation which, instead of occurring in the normal gland and presenting the picture of thyroiditis, occur in an abnormal gland or some form of goiter due to functional disturbance. The normal gland was first subjected to some thyroid dysfunction and this goiter was further the seat of an inflammatory process.

In Riedel's strumitis there is a very marked production of fibro-blasts and fibrous tissue, resulting in a diffuse fibrosis of an ordinary strumitis. The gland is extremely hard and firm, and on cut section presents a grayish white surface indicating the extremely large amount of fibrous tissue.

Tumors

Adenoma

The type of thyroid adenoma about to be discussed is not to be confused with those thyroid nodules or nodular goiters, often called colloid adenomas, whose origin in connection with the processes of the hyperplasia-involution cycle has already been traced. Both varieties show encapsulated areas, but the question as to whether they are true tumors or not, depends, not on the encapsulation but on the internal structure. A large percentage of the nodes and clinically benign "tumors" reported as adenomas of the thyroid gland are of the colloid type formed during the involution stage of the hyperplasia-involution cycle and are not true tumors. Less than 20 per cent of the cases reported by Rienhoff and only 8 per cent of those reported by Lewis exhibited the characteristics of true neoplasms and deserve the term adenoma.

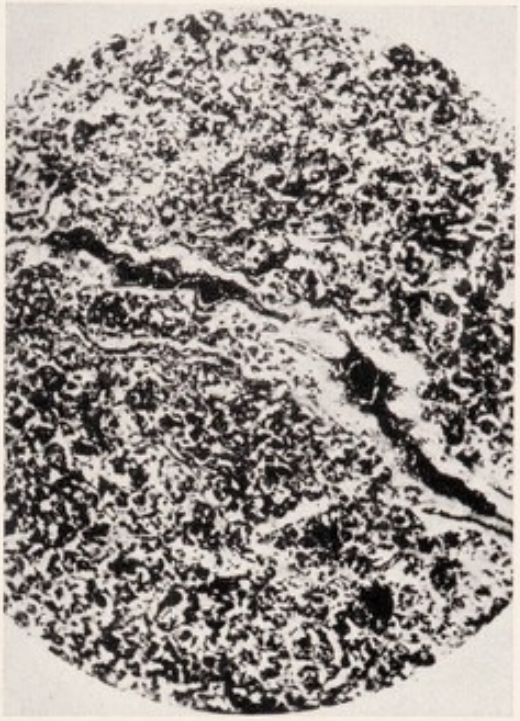


FIG. 16.—Thyroid Adenoma. Cords of Cells with no Attempt at Follicle Formation.

True Adenoma

There is, however, a true adenoma found in less than 5 per cent of all completely encapsulated nodules of the thyroid gland. Microscopically these tumors show masses of epithelial cells in strands and cords, sometimes anastomosing with each other, but nowhere is there seen any lumen formation of the normal thyroid follicle. The blood vessels are quite abundant but nowhere is there evidence of open hemorrhage. The hyperplasia-involution process is not seen at any stage nor is there any evidence of hyperplasia.

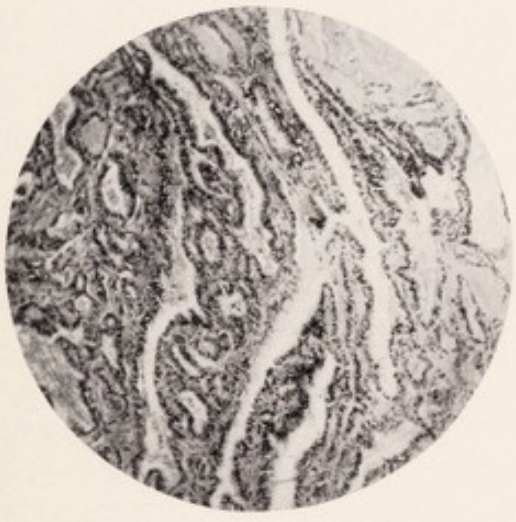


FIG. 17.—Papillary Adeno-carcinoma —Rapidly Growing Malignant Cells Forminal Papillae.

The entire picture somewhat resembles that of the gland of the embryo, and differs definitely from that seen in the non-tumorous nodule where all stages of the func-

tional thyroid cycle are seen. The neoplastic character of the true adenoma is established by the embryo-like cords of cells with no tendency to lumen formation in contradistinction to the various stages of follicle formation and regressive changes found in nodose goiter with encapsulated nodes.

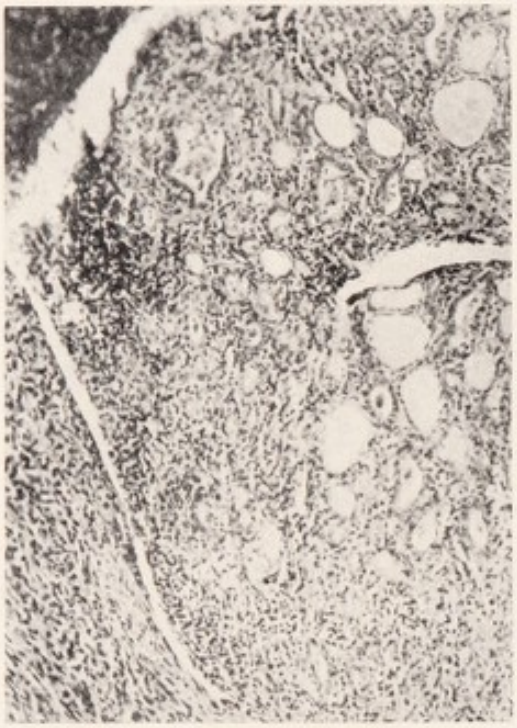


Fig. 18.—Infiltrating Carcinoma of Thyroid.

Carcinoma

In carcinoma of the thyroid many transitional stages of different tumor processes are seen. For this reason the distinction between carcinoma, adenocarcinoma, and the so-called malignant adenoma is far from clear-cut and often differentiation is exceedingly difficult. When, however, the tumor cells assume a definite glandular formation the neoplasm is referred to as an **adenocarcinoma.** In this type we sometimes find these malignant cells growing very rapidly and producing papillae which invade the stroma in the form of finger-like projections. The invasion of the stroma by the tumor cells is usually quite discernible and the term papillary **adenocarcinoma** is applicable.

In addition to the solid groups of atypical infiltrating cells which distinguish these tumors as true carcinomas, we find gross anatomic changes such as infiltration of stroma and blood vessels with formation of local and general metastases.

Grossly, thyroid carcinoma presents a firm encapsulated mass which in all likelihood develops from some preceding pathologic growth of thyroid dysfunction. Whether the malignancy develops in a normal gland is doubtful. Something precedes the malignant tumor and it is highly probable that the vast majority of carcinomas of the thyroid gland originate in nodose goiters. The carcinoma grows steadily and diffusely until it invades the capsule and surrounding structures. First there is local invasion and finally metastases. Sometimes metastases may occur very early, during the time of local invasion, in which case the original tumor may remain small while diffuse and extensive metastases develop. When metastasis is late the original tumor may grow to considerable size and produce pressure symptoms.

Metastases

Metastasis takes place mainly through the blood vessels, less often through the lymph channels, and sometimes through both paths. It is

possible that in those cases in which it takes place through both channels, the blood stream is the local avenue through which the malignant cells find their way to the lymphatics and are disseminated to other parts of the body by way of the lymph stream. Because of the great vascularity and the many blood spaces in the thyroid gland we presume that metastasis usually takes place through the blood stream. The bones are most frequently the site of involvement, and the metastatic growths appear at epiphyses or along sutures, producing large encapsulating tumors. When metastasis takes place through the lymph stream the course taken is found to follow the lymph node chains; for example, the cervical nodes, the pulmonary hilus, and the mediastinal and perigastric nodes, from which—still following the lymph vessels—the metastasis frequently extends into the liver.

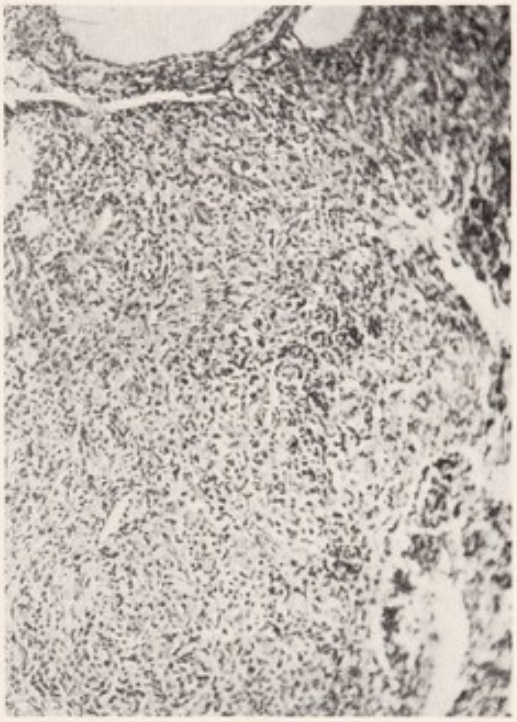


FIG. 19.—Infiltrating Carcinoma Showing Solid Masses of Malignant Cells.

Microscopically, the stroma, which is an extremely vascular network, encloses follicles and cavities formed by follicles breaking into each other; into these project many papillary strands of epithelial cells. These cells are cuboidal or columnar, the nuclei are large and hyperchromatic and the cytoplasm takes a clear or acidophilic stain. Colloid, if present, is very scanty. There is marked increase in the number of cells with decrease or absence of colloid.

In the variety sometimes referred to as solid carcinoma very few or no follicles are seen; the picture is one of solid masses of malignant cells.

On the whole we must say that the microscopic diagnosis of carcinoma of the thyroid is sometimes very difficult. The histologic picture is not always reliable. A post-mortem examination sometimes reveals positive evidence of a malignancy which could not be definitely diagnosed during life.

Sarcoma

Sarcoma of the thyroid is reported almost as frequently as carcinoma. We believe, however, that these tumors are wrongly interpreted, since the gross and microscopic pictures fail to show definite or distinct variation from carcinoma. The majority of these tumors or possibly all of them are varieties of carcinoma in anaplastic form.

Benign Metastasizing Goiter

The tumor type which presents the greatest question is the benign metastasizing goiter. When the thyroid is the seat of a primary carcinoma, interpretation of the condition presents little difficulty. There are cases, however, in which normal thyroid tissue, or thyroid masses presenting the picture of a colloid goiter are found as metastases to other organs. These cases have been described as benign metastasizing goiter although some critics credit the existence of the condition only to the imagination of the writers. We, however, have seen such a case in which huge masses of tissue were found in the abdomen at postmortem which on microscopic examination presented the picture of a colloid goiter similar to the section made from the thyroid gland, and we are satisfied that such benign metastasis did occur.

CHAPTER V

SYMPTOMATOLOGY

BASAL METABOLISM

A book on goiter, even from the pen of a surgeon, would not be considered complete without some discussion of basal metabolism, especially since there is some difference of opinion as to the true value of metabolism tests in the investigation of thyroid conditions.

Development of Science

Metabolism is the term commonly used in referring to the combined processes of the "building up" (anabolism) and "tearing down" (catabolism) of the body tissues. The study of energy intake and output and of what happens to each particle of food that we ingest forms the basis of physiologic chemistry. Though a great army of men and women supplied the stepping stones in this field it would be an injustice to the science of metabolism as well as to the science of nutrition not to mention the names of Lavoisier (96), Pettenkofer and Voit (97), Lusk (98), Benedict (99), DuBois (100), Boothby (101), and Atwater (102). These leaders and their contributions stand out in this great masterpiece—the development of the science of metabolism.

The early investigations in this field were made in the study of the chemical processes that occur in the body in the utilization of foods. Recognition of the significance of oxygen in this process was followed by the discovery of the constant ratio relation of heat production to metabolic activity. The first attempts at estimating the rate of metabolic activity were made by the difficult process of measuring the rate of heat production and utilizing the rate as an index of metabolic activity. In the middle of the last century the constant ratio of oxygen consumption and carbon dioxide production to metabolic activity was discovered.

Complicated appliances for the measurement of heat production, of oxygen consumption, and of carbon dioxide production were constructed. Better methods of calculating the metabolism from the respiratory exchanges demonstrated that metabolism is affected in varying degrees by fever, exercise, digestion, exposure to cold, and even by different foods.

It was discovered that there is a fairly constant minimum of normal metabolism, for animals of the same species possessing the same physical characteristics; that the minimum rate is not only fairly constant in the same individual but is relatively constant for all other normal individuals of the same sex, age, and size in the same species. This minimum rate, obtained when the body is at complete rest, is termed basal and is used as a basis for the determination of the variations produced by different physiologic states. The variations from this estimated normal in the

basal rate, dependent upon disease, exercise, or other factors, are stated in terms of percentages. The estimated normal basal rate is designated by zero (0), increased rate by "plus" (+), and decreased rate by minus (−), followed by the percentage of variations from zero or normal.

Simplification of Methods

In 1895 Magnus-Levy (103) established the fact that the measurement of the basal metabolism is of great clinical service in determining activity of the thyroid gland. Unfortunately however, the apparatus available at that time was expensive and difficult to manipulate. Correct interpretation of the results of the determination of metabolism was even more difficult—first, because of the lack of accepted standards for the normal basal rate in different types of individuals and, second, because of difficulties entailed by the numerous measurements and complicated mathematical calculations required for the estimation of the blood and muscle content of the body—the data upon which the early standards for the actual basal rate were founded.

The discovery that the surface area is proportional to the protoplasmic mass of the body and the acceptance of the surface area as the basis for the estimation of the standard rate of metabolism greatly simplified the procedure. The final step in the simplification of methods was the acceptance of height and weight as the most important factors in the estimation of the body surface area, and the preparation of charts by means of which the normal basal rate and the variations therefrom, stated in terms of percentages, can be found at a glance. Improved apparatus and the development of simplified technic has made possible the enormous amount of research work that has been done in recent years in the study of the relation of various factors, such as digestion, drugs, muscular exercise and disease, to metabolism.

The estimations of the total metabolic rate were found to be equally dependable whether made by means of the measurement of heat production, oxygen consumption, or carbon dioxide elimination. The development of accurate, dependable, comparatively inexpensive apparatus for the measurement of the rate of oxygen consumption has had much to do with the present day acceptance of the rate of oxygen consumption as an index of the total metabolic rate. The possibility of an error of 1 or 2 per cent in the estimation of the actual consumption of oxygen and an error of as much as 20 per cent in the estimation of the surface area of the body by means of charts is admitted; but the fact that clinicians find basal metabolism determination indispensable in their work indicates that the modern methods for the estimation of the metabolic rate are of sufficient accuracy to be of value.

Metabolism in Thyroid Disease

Determinations of the variations of the basal metabolic rate from the normal basal rate are of great service in the diagnosis and differentiation of thyroid conditions. They are of value furthermore in preoperative

prognosis, in helping to formulate the indications for operation, and in estimating the progress of treatment. It is for these reasons that the subject of basal metabolism has a place in the discussion of thyroid problems. In thyroid conditions the importance of the estimation of the basal metabolism is confined to the determination and interpretation of the actual basal metabolic rate as compared to the estimated normal basal rate. The means and methods for arriving at this estimation are widely known (100).

Normally man consumes oxygen and a certain amount of food, which, when properly assimilated, go to make up the various body tissues. These tissues are constantly giving off waste products and tissue proteins which are replaced by the utilization of the ingested food. A balance between this building up (anabolism) and tearing down (catabolism) is maintained in the normal individual, and the weight curve does not fluctuate a great deal, in the average adult, unless influenced by excesses in either diet or physical exertion. The individual eats such an amount of food as is demanded by the body and this amount is in proper proportion to the production of energy.

In thyroid disease, an abnormal factor comes into play and the normal balance between anabolism and catabolism is disturbed. The effect of the thyroid hormone on the body is seen in the increased catabolism. In hyperthyroidism, the greater the hyperfunction of the gland, the more the catabolic processes exceed the anabolic. The oxygen consumption will be above the normal for a given height, weight, and age, and the metabolic rate will be correspondingly high.

The converse is true in cases of hypothyroidism. With decreased thyroid function catabolism is retarded, oxygen consumption is below that normally demanded by the body and the metabolic rate is low.

Whatever the mechanism, the result of the determination of the basal metabolic rate is a very good index of the activity of the thyroid, and, if studied carefully in connection with the clinical picture, will enable the clinician to evaluate the extent to which the dysfunction of the thyroid is responsible for the condition of the patient. The metabolic rate determination is the best guide we have for determining the status of a definite thyroid case, or detecting thyroid disturbance in the borderline case. Whenever there is the slightest doubt as to the correctness of the estimation, the test should be repeated under favorable circumstances.

SIGNS AND SYMPTOMS OF ATOXIC GOITER

Simple Colloid Goiter

The symptoms of simple colloid goiter are usually only those occasioned by the enlargement of the gland. The gland is always enlarged and soft, altering the contour of the neck. Variations in the size of the gland, chiefly due to the amount of blood within the organ, may be noted from day to day. The enlargement is diffuse, symmetrical, and well rounded; sometimes a cyst-like resistance due to increased tension may be evident upon palpation.

Patients with extreme enlargement of the gland sometimes complain of respiratory disturbances upon exertion. The intensity of these symptoms is greater when the enlargement has been of rapid growth. Pressure symptoms, such as coughing attacks, hoarseness, disturbances of deglutition, and distention of the superficial cervical veins, indicate that a portion of the gland has become retrosternal or intrathoracic.

As a rule the pulse rate is not directly affected to any great degree, yet owing to muscular weakness it may be abnormally increased upon exertion. The basal metabolism rate is usually normal or below normal.



FIG. 20A.—Simple Colloid Goiter.

The general condition is not greatly disturbed although the patient often complains of restlessness, insomnia, and a feeling of exhaustion. Mental symptoms are mild or absent, and yet inability to concentrate, mental sluggishness, memory defects, and even intellectual weakness are not infrequently noted.

Nodular Colloid Goiter

The symptoms of nodular colloid goiter are identical with those of simple colloid goiter except that nodules are present in the gland. From inspection, the gland in this variety usually appears to be as symmetrical, smooth and well-rounded as in simple colloid goiter. Upon palpation, however, small nodules may be felt in the gland and some increase in consistency noted. The outlines of the gland are more clearly marked than in simple colloid goiter. The nodules are, as a rule, symmetrically and diffusely distributed throughout the gland but are more easily palpable near the upper poles.

Multiple Adenoma

Constitutional symptoms are absent in multiple adenomas as in simple colloid goiter. Variations in the size and shape of the gland are the characteristic symptoms. The gland is usually asymmetrical with marked change in contour. Tumors in the gland are evident upon palpation. Pressure symptoms are often present.



FIG. 20B.—Exophthalmic Goiter.

Primary Adenoma

The signs of primary adenoma, early in its course, are an asymmetrical localized enlargement with tenseness, some tenderness on palpation, and marked change in contour of the gland. Later in its course, after the swelling has subsided and the tenderness on pressure has disappeared, the symptoms differ in nowise from those of any other atoxic adenoma.

Fetal Adenoma

The signs of fetal adenoma are almost entirely confined to the change in contour of the gland. When seen early in life, a unilateral enlargement is usually present that in appearance and on palpation resembles the enlargement of one lobe of an early colloid goiter. When seen later in life the tumor is usually found to be upon the surface of the gland and easily outlined by palpation.

DIFFUSE HYPERPLASTIC GOITER

(Graves' or Basedow's Disease)

In 1835, Robert Graves (104) of Dublin described a classical case of diffuse hyperplastic goiter. He defined clearly the cardinal symptoms of the syndrome, which was later to bear his name, with the exception of the tremor. He described the nervousness, the tachycardia, the weakness and languor, the exophthalmos and other eye symptoms, and the loss of weight.

Our task of recitation of the symptomatology would be very easy indeed if every case, or even the majority of the cases we see in practice, conformed to the clinical picture as painted by Graves.

Diffuse hyperplastic goiter, or to use the more familiar clinical term, Graves' disease, is the full expression of thyroid dysfunction along certain lines. It is comparatively rare. In other words, the atypical, abortive or fruste types of exophthalmic goiters are more common than the classical type as described by Graves.

In a disease in which no two sufferers present clinical pictures that are even approximately the same, it is impossible to furnish an account, no matter how elaborate, which will fit every case or even a majority of cases. We must content ourselves with sketching merely the broad outlines: first of the typical case of hyperplastic goiter and next of the various atypical forms.

Onset

In the majority of cases diffuse hyperplastic goiter develops in the decades between twenty and forty, and very frequently during periods of peculiar stress and strain; at puberty, or in women during a menstrual period, at the time of the menopause, or following pregnancy.

The history of onset with shock, so often quoted, is open to considerable doubt. It is true, in many instances, that the shock or fright first drew the attention of the patient, family, or friends to the condition. However, the shock merely aggravated the already long-existent condition. Probably the patient who developed exophthalmos subsequent to shock or fright, had, previous to the shock, all the cardinal symptoms of Graves' disease except noticeable exophthalmos.

The onset differs from case to case, but the first symptom noted in the majority of the cases is slight palpitation and barely noticeable dyspnea on exertion. Languor and weakness are usually the first symptoms observed; in other instances nervousness without apparent cause and protracted insomnia usher in the syndrome.

Frequency of urination, both by day and by night may be troublesome and constitute the first symptoms. Night sweats, so severe and constant as to raise suspicion of tuberculosis, are sometimes noted quite early.

In some instances, gland enlargement of moderate degree is noted first and may be evident for some time without the patient being conscious of subjective symptoms.

Cardinal Symptoms

The characteristic symptoms in the sequence in which they are most frequently seen may be listed as: tachycardia, increased metabolic rate, tremor, loss of weight, thyroid enlargement, and exophthalmos.

Frequently several months are required for the patient to exhibit the complete sequence. However, it is not unusual for a patient to develop these symptoms, definitely and in rotation, within two weeks from the time that he first suspected that something was wrong. Usually in the writer's experience, when such a rapid sequence occurs, the first symptom, the tachycardia, appears about three weeks after the subsidence of an attack of some infection such as influenza, diphtheria, or severe sore throat.

Tachycardia.—Tachycardia probably deserves first place among the symptoms of hyperplastic goiter. An increased pulse rate, which is greatly augmented on excitement or exertion, is noted early in the course of the disease. It is practically uninfluenced by rest and is not amenable in any great degree to digitalis medication. The pulse is usually full and bounding, and the rate varies from 100 to 160. The pulse is regular early in the disease and in fact, continues regular until myocardial changes occur.

A marked degree of tachycardia may be present and still the patient may not complain of palpitation. On the other hand, with a moderate or mild tachycardia, palpitation may be troublesome; may in fact be the symptom that first brings the patient to the physician's office.

Thompson (105) described the tachycardia very well indeed when he says: "The Graves' pulse never calms down, however quiet the patient may become. It runs as fast or faster than in any fever or inflammation, by day and by night, and also in sleep, with less change at each counting over long periods than in any other affection."

Increased Metabolic Rate.—The tachycardia is usually evident for some time before significant change in the metabolic rate is evident and the rise in the basal metabolic rate usually occurs at the time that tremor makes itself manifest. In the mild or borderline type of case, the metabolic rate is changed so slightly that its estimations are of little or no significance.

The Goetsch or Adrenalin Test.—This test, proposed by Goetsch (106) for determining the presence or absence of thyrotoxemia in borderline cases, is based upon the reaction to the hypodermic administration of adrenalin. It cannot be relied upon as a test for thyrotoxemia but is of value as an indicator of the sensitiveness to adrenalin. This may be of great importance if the use of adrenalin is contemplated in local anaesthesia.

The test is based upon both skin and constitutional reactions. To test the constitutional reaction 7.5 minims of a 1:1000 solution of adrenalin is injected hypodermically. A positive reaction is marked by a rise in blood pressure of 10 to 50 mm., a rise in the pulse rate, flushing and other symptoms of thyrotoxemia. If the test is positive a reaction appears within a few minutes and subsides within two hours.

To test the skin reaction, one minim of a 1:4000 solution of adrenalin is injected indermically. A positive reaction is more likely to be obtained if such an injection is made in three or four places. At the site of injection, a white area, surrounded by a zone of pink, appears, which, in the normal individual disappears in thirty to forty minutes. If the test is positive, the disappearance of this zone of reaction is delayed. A disappearance



Fig. 20C.—Cystic Goiter.

time of one and one-half to two and one-half hours is considered as positive evidence of thyrotoxicosis.

Tremor.—The tremor is quite characteristic; in fact a differential diagnosis can often be made by discovering very slight tremor such as that of one finger. The character of the tremor is quite similar to that seen in the course of the acute febrile diseases such as typhoid fever.

Tremor is usually best seen in the extended hands having the fingers separated. It is also noted in the tongue when the tongue is protruded. Sometimes the lips are affected; sometimes the whole head. In severe cases it may be said that the tremor is universal, as palpation of the muscles in any part of the body elicits a "trembly" sensation. At times the patient has subjective cognizance of the tremor and feels "trembly all over."

Loss in Weight.—Quite early in the disease there is loss in weight despite increased appetite. The patient may consume 4500 to 5000 calories per day and still lose six or seven pounds a month. Some loss of weight usually occurs following the appearance of tachycardia, increase in metabolic rate, and tremor. The loss in weight usually precedes the appearance of exophthalmos and is in proportion to the severity of the thyrotoxemia. In the more severe cases as much as 20 per cent of the usual body weight may be lost within a few weeks. This is especially true if a gastro-intestinal crisis occurs.

The loss of flesh is usually ascribed to the increased metabolic rate, the explanation being that tissue is burned up in the body more rapidly. There is, however, usually a disturbance of the digestive and assimilative functions, and a disturbance also of the other metabolisms in the body, such as the carbohydrate and protein metabolisms. These disturbances taken with the increase in general metabolism account for the rapid loss of weight.

When weight has been lost during an acute exacerbation, it is unusual for a patient to gain back all he has lost even if the remission of the

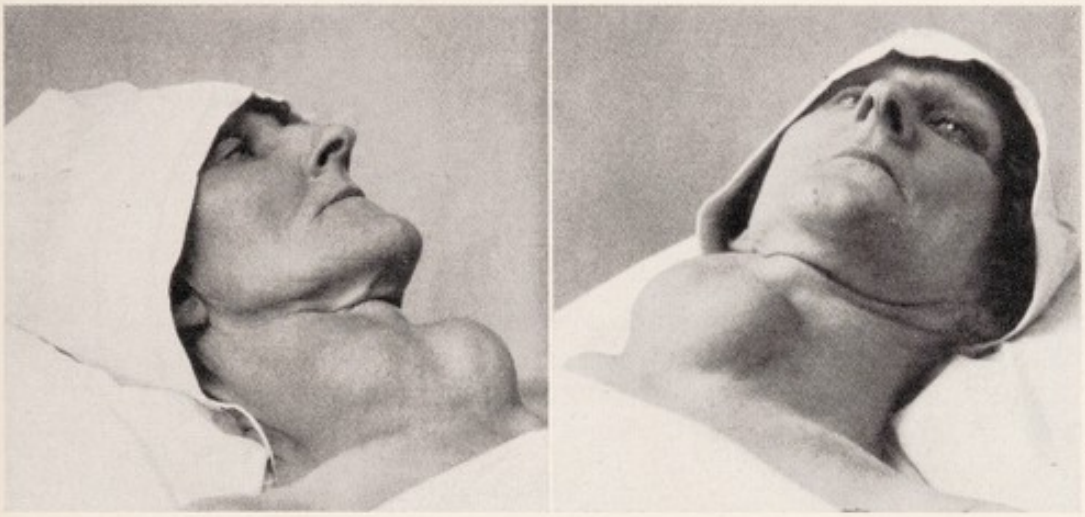


FIG. 20D.—Nodular Colloid Goiter.

toxemia is prolonged. If 20 per cent of the lost weight is regained during a remission, it must be considered satisfactory. During the next exacerbation the patient will probably lose about half as much as before, and the final result, after the second exacerbation, will be a loss of 25 per cent or more of total body weight.

Thyroid Enlargement.—Thyroid enlargement is not often noted as an early symptom. Hyperplastic goiters of three times the size of the normal gland are rare and in about 15 per cent of the cases there is no visible enlargement of the neck.

The enlargement, as a rule, is diffuse and affects both lobes and the isthmus. The size of the thyroid in hyperplastic goiter is subject to distinct fluctuation at times, increasing, for instance, at the time of menstruation and during pregnancy.

The thyroid in this disease is quite vascular. The whole gland at times is seen to pulsate; the carotids and even the superior thyroids are seen to beat violently. Thrills and bruits are present over the carotids. In some cases the vascularity is so great that the thyroid is like a sponge and may be reduced in size by mere squeezing.

Early in the course of the disease the gland is usually soft; later, palpation reveals it as elastic and firm; later still in the advanced stages, with the occurrence of marked fibroid changes in the thyroid substance,

there is distinct sensation of hardness. Slight tenderness is sometimes noted over the thyroid particularly in the early cases.

Exophthalmos.—Exophthalmos occurs in about 60 per cent of the cases. It is seen during the first three months of the disease in only about 40 per cent of the cases.

Preceding the exophthalmos in many cases, a peculiar stare is noted. This becomes quite marked at times and taken in conjunction with the symptoms of nervousness and psychic instability, may cause some concern as to the patient's mental condition.

The protrusion is usually bilateral, but in the exceptional or occasional case may be unilateral. Frequently the exophthalmos is more marked on one side than on the other. No definite relationship seems to exist between the intensity of the symptoms and the degree of exophthalmos.

Course of Diffuse Hyperplastic Goiter

The patient may go through life without much detriment to his health, and except for the fact that he is nervous and perhaps temperamental, he may not show much evidence of thyroid disease. Usually the disease progresses slowly until all of the symptoms are present and primary exacerbation occurs. In the primary exacerbation the symptoms gradually become more definite, the tachycardia increases, a rise in the basal metabolism rate occurs. The palpitation becomes more noticeable, tremor and nervousness appear, and the clinical picture of the disease is complete. It is not unusual for this primary exacerbation to continue over a period of several months and finally culminate in an acute condition, the crisis.

Second Exacerbation

The primary exacerbation is often followed by a period of remission in which there is distinct amelioration of the symptoms. The tachycardia improves, some gain in weight is noted, and there is an upward trend for a period of several months. Then a second exacerbation of less severity is noticed. Even though the second exacerbation is less severe the patient is physically less competent to deal with it. The many months of thyrotoxicosis will have left an indelible impression on the physique of the patient. Evidence of cardiovascular disturbance is almost always present, the nervous and mental symptoms are in many instances pronounced, and the patient is in a poor condition to resist a second attack of the thyrotoxemia. The patient may recover though with still further impairment of heart and nervous system.

Later Exacerbations

Exacerbations, usually of less severity and of shorter duration, follow the second one at irregular intervals. Exacerbations may result from infection, overexertion, undue mental excitement, or excesses of any kind. They may also follow emotional insult, such as shock or fright.

Late Course

In rare instances, spontaneous recovery—or apparent recovery—occurs. It is hard to believe that a patient could withstand the severe toxemia of hyperplastic disease for several years without irreparable damage to his physical structure. Even if its toxicity does abate, the disease leaves the patient with an impaired cardiovascular and nervous system. If the entire thyroid substance is not either completely destroyed by the disease or "burned out" the patient is likely, on some provocation, to suffer a reactivation or recrudescence of the thyroid condition. If the thyroid substance is burned out, hypothyroid symptoms may be superimposed on the residual thyrotoxic syndrome.

Systemic Involvement in Diffuse Hyperplastic Goiter

The effects of hyperplastic disease are so wide-spread in the organism that it is impossible to give even a fair account of the condition without considering the effect of thyrotoxicosis in each system separately.

The Respiratory System

A slight hacking cough sometimes accompanied by hoarseness is often a mild but annoying symptom of thyrotoxicosis. Asthma is sometimes present associated with and may be aggravated by the thyrotoxicosis. Widal and Abrami (107) described a number of cases in 1924 in which asthma was cured by thyroidectomy.

In the early stages of thyrotoxicosis dyspnea is not common but in the later stages, if myocardial degeneration or congestive heart failure occurs, dyspnea or orthopnea may become distressing. The milder degrees of thyrotoxemia are usually accompanied by an increased respiratory rate but the patient is not conscious of it. With increasing thyrotoxemia the respiratory rate rises. Irregularity in respiratory rhythm may occur in any stage of the disease. It is usually observed in the sequence of shallow breathing, apnea, deep breathing. Diminished vital capacity is often present in the later stages by shallow breathing, and diminished ability to hold the breath. The ability of the patient to voluntarily reduce his respiratory rate for a period of five minutes is markedly reduced by thyrotoxicosis.

Respiratory Rate Test

This test is based upon the difference in the ability of thyrotoxic and normal persons to control their respiratory rates. A normal individual is able over a period of five minutes to reduce his normal respiration rate about six or eight per minute. The thyrotoxic individual is unable to reduce his usual respiratory rate, when at rest, more than three or four respirations per minute over the same length of time.

The resting rate is best obtained while the patient is asleep. The minimum voluntary rate is best taken by placing a watch upon the patient's chest and while pretending to count the pulse the patient is

urged to breathe as slowly as possible. By observing the rise and fall of the watch the respirations are counted. The test is obviously of more value if the patient is under the impression that his pulse rather than his respiration is the subject of investigation.

This test may be of value in the absence of facilities for metabolic rate tests, but is of more value in confirming the accuracy of the basal metabolic rate determination than in the differential diagnosis between thyrotoxicosis and other conditions.

Cardiovascular System

The cardiovascular system is, in most instances, the one most severely involved in thyrotoxicosis. As already noted, one of the first, if not the first symptom in this disease is increased heart rate and palpitation. The palpitation is often paroxysmal and particularly troublesome at night. The heart pounding frequently prevents sleep, particularly if the patient sleeps on the left side. At times the patient complains of pain, often vague and indefinite, in the precordial region. The pounding of the heart is reflected in the peripheral circulation. The apex beat is often displaced downward and to the left and is forcible and heaving. The carotids and the thyroid vessels show marked visible pulsation. The head, in fact, may be seen to vibrate synchronously with the pulse. Capillary pulse is frequently noted.

Inspection shows the displacement of the apex. The impulse is diffuse and forcible. **Palpation** occasionally reveals a thrill over the apex. A thrill over the carotids and superior thyroid vessels is sometimes present, but, since it is not constant, its absence is of little diagnostic importance. **Percussion** shows an increase in the size, particularly of the left ventricle. The transverse diameter of the heart is increased. Later, as dilatation occurs, there is definite dullness to the right of the sternum.

On **auscultation** the heart sounds at the apex are loud; the first tone is particularly loud and snappy. Later, as dilatation occurs, the first sound becomes weaker. A functional murmur is often heard in the pulmonic area. In late cases, a systolic murmur at the apex transmitted to the axilla is sometimes noted, which together with the hypertrophy to the left, indicates the true mitral insufficiency. Extrasystolies, auricular flutter, and fibrillation are not uncommon in late cases.

Fluoroscopy in the early stages of the disease shows the borders of the heart clearly outlined. Little, if any change in size or symmetry, can be observed. The rapidly increased contractions as seen under the fluoroscope are perhaps best described by the phrase, "heart hurry." One gets the impression that one contraction must "hurry" to get out of the way of the next.

Later, if the thyrotoxicosis continues, we have the progressive signs of cardiac embarrassment, dilatation and finally failure. Widening and change of contour of the aortic and auricular shadows are followed later by an enormously enlarged heart shadow with indistinct margins.

The pulse rate is rarely lower than 100 or 110 when the patient is at rest, even in the comparatively early stages. Later in the course of the



FIG. 20E.—Multiple Adenoma.

disease the pulse rate is nearly always found to be 120, 130, or even 150. It is still further increased by exertion or excitement and is usually proportionate to the increase in basal metabolism. The tachycardia is comparatively uninfluenced by sleep and is often as high in the morning before arising as in the evening. Later, auricular flutter and auricular fibrillation appear and then the pulse becomes quite irregular and is often difficult to count.

The heart is the true criterion of prognosis in hyperplastic disease. The severity of the disease is reflected in the degree of involvement of the cardiovascular system. As the heart improves, the other symptoms improve; as the severity of the cardiovascular involvement increases, the other symptoms also become aggravated. The nervousness, the insomnia, the mental unrest—all become intensified as the cardiac symptoms increase.

Blood

Red Cells and Hemoglobin

Changes in the number of blood cells have been reported at various times. True enough, a very mild decrease in erythrocytes is often found, but it is neither constant nor significant. In a given case of hyperplastic goiter, there is such great change in the normal metabolism that a mild change in the number of red cells is negligible and of no diagnostic import.

The hemoglobin, as a rule, is found to be in direct ratio to the number of red cells. In cases in which the number of cells is decreased, the hemoglobin is proportionally lower and vice versa.

White Cells

The white blood cell count in hyperplastic goiter was the subject of considerable discussion for many years. Theodore Kocher (108) was the first to give detailed study to the blood picture in this disease, and in 1908 reported some interesting and, as he claimed, very characteristic findings. He established to his own satisfaction, and to the satisfaction of most others interested in the subject at that time, that the blood picture in this disease presents quite distinctive features. He found that the total number of white blood cells is low, dropping to 4000 or less per cubic millimeter. With this leukopenia he reported a relative increase of lymphocytes which often reaches 40 to 70 per cent and a corresponding decrease of polynuclear leukocytes which may drop as low as 30 per cent.

The reason for this reported change in the blood picture was not definitely established; some thought the thymus rather than thyroid dysfunction was responsible. The blood findings are not of as much significance in hyperplastic goiter as would appear from the attention they have received.

Early Leukocytosis

The experience of the writer with respect to the blood findings in goiter varies, particularly in one detail, from the traditional picture as just

given. We usually find, quite early in the course of the disease, a mild leukocytosis. Hyperplastic goiter, in many instances, is due to an antecedent thyroiditis accompanied by leukocytosis. By the time the case first comes under observation, the infection and the inflammatory condition of the gland usually have subsided and little if any leukocytosis is present.

Eosinophils

Eosinophilia is mentioned by some writers, but is not a constant finding and has no definite significance.

Coagulation

An increase in the coagulation time in hyperplastic goiter, referable to a decreased fibrinogen and calcium content, has been reported by numerous writers. In the writer's experience, on the contrary, the coagulation time is 20 to 25 per cent less in the average goiter case than in other surgical cases. This observation is made in a general clinic where the number of goiter cases amounts to approximately 50 per cent of the whole number of cases which appear for examination.

The writer has observed also that the viscosity of the blood varies with the stage or duration of the disease. In the early stages, the viscosity is less than normal; while in the case which has lasted over a considerable period, it is higher. A very marked increase in the degree of viscosity is, in our experience, of serious portent.

Blood Pressure

The blood pressure in hyperplastic goiter is subject to some variation. In a general way the blood pressure findings resemble those seen in cases of aortic regurgitation. The systolic pressure is elevated, the diastolic pressure lowered, pulse pressure is increased. These blood pressure findings are not by any means constant. A definite hypertension is present in some instances, but a careful investigation will usually show that the hypertension preceded the thyrotoxicosis. The blood pressure in the late cases, in the presence of severe myocardial change or decompensation, may be low.

Sensory Disturbances

Pruritus

Pruritus, probably due to the sweating and other vascular change, is sometimes a persistent and troublesome symptom. The itching may be quite generalized and is, apparently, not related to any local disease of the skin.

Headache and Tinnitus

Considering the general condition of the patients and the neuropathic history that is frequently present, headache is not as frequent as

one might expect, and in most instances is not unbearably severe. The headache is sometimes frontal. It is often one-sided and resembles migraine to some extent. The severity of onset and the vomiting are usually lacking, although attacks of true migraine do occur occasionally. Noises in the ears are a frequent complaint.

Vague Pains

Vague, fleeting, ill-defined pains are characteristic of hyperplastic goiter. They are rather frequently referred to the muscles of the neck, the finger tips and toes. Numbness and tingling are noted at times. Neuritis is occasionally present and may be quite severe.

Eye Findings

The importance of the eye symptoms of hyperplastic goiter have been, in the past, unduly stressed. The eye findings are not by any means constant, and, when they are present, they usually develop late in the course of the disease.

Exophthalmos

The subject of exophthalmos has already been discussed. Other less important eye signs may be recognized; most of them are known by the names of the men who first described them.

Eye Signs

Dalrymple's Sign.—One of the first signs to be observed is the Dalrymple sign. Normally with the eye looking straight forward the eyelids, both upper and lower, touch the cornea or cover a small portion of its surface. The palpebral fissure is just wide enough so that the margin of the lids touches the upper and lower edges of the cornea.

When the Dalrymple sign is present there is widening of the palpebral fissure; the lids are more widely separated so that a band of sclera is to be seen between the upper or lower lid and the edge of the cornea. When the sign is markedly positive, a band of sclera is visible both above and below the cornea. The Dalrymple sign is not dependent on the degree of exophthalmos and is sometimes present when no exophthalmos is noted. This condition of a widened palpebral fissure is seen not only in hyperplastic goiter but also in fright or shock, in apoplexy, and in various other brain diseases. The band of white sclera above and below the cornea with the widened palpebral fissure results in the peculiar expression of the eyes which is called the "stare."

Von Graefe's Sign (109).—Von Graefe's sign is only observed in the rotation of the eyeball from above downward. To elicit this sign the patient is requested to keep his head immobile and to look forward and upward at the finger of the examiner. The finger is then brought slowly downward. As the eye follows, there is a lagging of the upper lid in relation

to the upper edge of the cornea. As the movement continues, a band of sclera is seen above the cornea and this band often becomes wider or more pronounced with the rotation of the eyeball.

The "Hitch" Sign.—The "Hitch" sign, described by Solomon Solis-Cohen, is merely another expression of the Graefe sign. The upper eyelid stops suddenly in its downward course, pauses for a fraction of a second, then suddenly resumes an uneven or "staggering" descent.

Stellwag's Sign (110).—The Stellwag sign refers to decreased frequency in the act of winking. The normal individual winks about ten times a minute. In Graves' disease a whole minute may pass without winking. It is frequently noted and may be an early sign. It is often absent, however, and is not deserving of too much significance from a diagnostic standpoint.

Möbius' Sign (111).—The Möbius sign refers to insufficiency of combined convergence in Graves' disease. If the eyes are focused on an object held some distance before the patient, horizontal with the line of vision and midway between the eyes, it will be noted that as the object is brought closer, the eyes lose their power of double convergence at a greater distance than normal. One of the eyes usually follows the object, the other diverges and wanders without the occurrence of double vision.

Gifford's Sign (112).—Gifford in 1906 called attention to the difficulty in everting the upper lid on account of its retraction and rigidity.

Rosenbach's Sign.—This sign is usually noted when marked tremor is present. To elicit it, the patient is asked to close the eyes gently as though in sleep. When the eyes are closed a fine trembling of the upper lid is noted.

Retinal Indications

Slight attention has been paid by most observers to the ophthalmoscopic findings in the retina. In toxic goiter, distended retinal arteries are nearly always found. Becker has reported arterial pulsations of the retina in six out of seven cases. In the characteristic picture of the retina in toxic goiter cases, the blood vessels seem to lie on the retina like ropes upon a floor. They stand out more plainly and appear to be more tortuous than on the normal retina. Increased pulsation of the retinal vessels is sometimes noted. Choked disc is rarely seen.

Sequels and Complications

Owing to the exposure resulting from the exophthalmos, with the consequent diminution in the sensibility of the cornea, complications are frequent and at times serious. Conjunctivitis and keratitis in varying degrees of severity are often noted. In severe cases in which the eyelids cannot be closed, the cornea is exposed day and night over a considerable period of time and corneal ulceration of varying degrees of severity may result. Cases of panophthalmitis as a result of the corneal ulceration, necessitating the enucleation of one or both eyes, have been reported.

Gastro-Intestinal System

Appetite

In the early cases, loss of appetite is sometimes noted; it is more usual, however, to find that the appetite is normal or even increased. Often, both in the early and late stages of the disease, the appetite is ravenous and the desire for food insatiable. The large amount of food taken may have a deleterious effect on the digestive processes.

After the digestive disturbances have been present for a considerable time, the appetite frequently becomes capricious and unreliable. The patient eats ravenously one day and will not touch food the next. Sometimes the patient develops diet vagaries and expresses a desire for quaint or unusual combinations of food. Arnold Jackson (113) has called attention to this peculiarity and has compared it to the dietetic vagaries observed in pregnant women. In some instances the patient eats frequently, though the amount of food consumed each time may be small and the total amount consumed in the twenty-four hours may not be excessive.

The writer has noted that when a patient with a goiter of long standing develops an unusual and abnormal appetite, it usually means that the goiter has become toxic.

A large amount of drink as well as food is also frequently taken and this may in part explain the persistence of the polyuria that is sometimes noted.

Digestive Disturbance

It will frequently be found, upon careful questioning, that mild digestive disturbances have been present long before any other symptoms of the disease were noted. For months or years before the apparent onset of the disease, the patient may have been subject to transient attacks of diarrhea, the cause of which could not be discovered. Hyperacidity is often one of the early symptoms of thyrotoxicosis. It is usually accompanied by increased appetite. Pyloric spasm is, as a rule, a later symptom and occurs only after indigestion and derangement of the gastric function have existed for some time. The combination of increased appetite, hyperacidity, and pyloric spasm frequently presents a syndrome that may easily be mistaken for gastric ulcer.

Diarrhea

Diarrhea may be one of the earliest symptoms. It may likewise continue with more or less periodicity throughout the course of the disease; the movements do not usually contain mucous, pus, or blood, or show other evidence of an inflammatory origin. The diarrhea is very refractory to modes of treatment usually effective in diarrhea. The absence of signs of disease of the intestinal tract, points to nervous involvement as the causative factor. It has been suggested that the diarrhea is due to the effect of a qualitatively altered thyroid secretion on the vague and sympathetic.

Nausea and Vomiting

There is something distinctive in the vomiting spells of hyperplastic goiter. They are often cyclic and appear suddenly, not being preceded by nausea. During the period of a crisis the vomiting may be severe and uncontrollable. As in the case of the diarrhea, it is usually very refractory to treatment but in severe cases may lead to exhaustion and death. On the other hand nausea of greater or less degree may be present for months without any tendency to vomiting spells. It may have no relation to meals but frequently leads to a greatly decreased appetite and loss of weight.

There is still room for much work on the subject of gastric chemistry in this disease. Many writers note a decreased acidity and undoubtedly a hypochlorhydria or an anachlorhydria may result in some instances. In the experience of the writer a hyperacidity with definite spasticity is the usual finding.

Genito-Urinary Symptoms

Kidneys

Most authorities are agreed that no kidney lesions are seen, in hyperplastic goiter, which are directly traceable to the disease. Albuminuria does at times occur but is usually mild in degree and unaccompanied by casts or changes in the blood pressure. Later in the course of the disease if cardiac decompensation occurs, kidney changes, secondary to this condition, will be noted.

Polyuria

Polyuria is often observed and usually does not rest on a genito-urinary basis. The frequency is sometimes more marked at night and the patient's sleep is considerably broken. In the case of one physician that came under our observation, the polyuria was the first symptom that drew his attention to his condition. He had to get up four times or more every night to urinate, was losing weight, and was decidedly nervous. As there was no evidence of nephritis and since he also had a greatly increased appetite and at times a transient glycosuria, his condition was diagnosed as diabetes and he was treated accordingly over a period of years.

The thyroid swelling was very mild in degree. In fact, he had never noticed it himself. Within a short time after the thyroidectomy, he gained in weight and polyuria, which had been his most troublesome symptom, had completely disappeared.

NEUROMUSCULAR SYSTEM

The nervous system, motor, sensory and psychic, is markedly involved in every severe case of hyperplastic goiter.

Neuromotor Changes

Tremor has already been described. To recapitulate briefly, it is fine and rapid, about eight to twelve a second and is practically always present; it may be limited to the hands, but is often noted in the tongue and in severe cases may involve practically all the muscles of the body. It is a tremor of striated muscles and is continuous.

It is not known whether the tremor originates within the muscles or whether it is a result of remote nerve stimulation. It has been suggested that the origin is in the neuromuscular junction. Again, some believe that the interfibrillar nerve cells in skeletal muscular tissue and in the heart muscle are responsible. The tremor of thyrotoxicosis is a toxic tremor, and seems intensified in goiter patients who have been addicted to the use of alcohol.

In the majority of cases, the reflexes are greatly increased. Occasionally, however, they may be diminished.

Twitchings, purposeless movements, and generalized trembling are frequent. Marked motor excitation and restlessness without a cause are often early symptoms. The patient twists and turns, changes position frequently, and is never physically at rest.

Psychic Disturbances

It may be said without fear of contradiction that there is some degree of psychic or emotional disturbance in every case of hyperplastic goiter. Even in the undeveloped or *fruste* type of the disease, the conspicuous features of the clinical picture are the mental instability, change in disposition, and irritability. In the advanced stages of the disease, the severity of the psychic disturbance is much intensified. Temperament, emotionalism, nervousness, "nerves," are the terms used both by the patient and his friends to describe his condition.

The patient apparently enters upon a new mental life. His disposition changes. Perhaps heretofore of a placid temperament, he becomes restless, dissatisfied, anxious, tense, sleepless, irritable, suspicious, and hysterical. The writer emphasizes the importance of the symptom which he terms "restlessness without a cause." These patients evince an anxiety, a restlessness, and can offer no logical explanation for their state of mind. This symptom, in one heretofore placid, should evoke suspicion.

The patients mentally dissatisfied are never happy. No matter what they are doing, whether engaged in occupation or recreation, they want a change. They have no zest for living, complain of boredom, and feel that nothing is worth while. Their jerky cerebration is reflected in their conversation and it is often difficult to keep up with them as they hop in scatter-brained fashion from one subject to another. The mental condition of such patients is very well described by Reynolds as "mental chorea," or again by Crotti (114) as "cerebral diarrhea."

Vagaries

The patients are quite subject to vagaries. They travel from physician to physician, develop unfounded antipathies for a certain physician and refuse to go back to him. They have crying spells without cause, and develop fads and fancies about diet and about their condition. Frequently the patient has a nameless dread or apprehension even though he is not greatly concerned over his disease or physical condition. It is very unusual for a patient with hyperplastic goiter to be able to give any foundation for his fears.

The peculiar appearance of the eyes—the exophthalmos or stare, the restlessness, the changes in character and disposition which has been noted, convince relatives and friends that the patient is mentally unbalanced or "queer." The unfortunate victim of hyperplastic goiter is thus frequently stamped as mentally irresponsible for months or even years before his true condition is recognized.

Melancholic States

Occasionally conditions bordering on true melancholia are seen. The patient may be taciturn, moody, sulky, and is apt to resent friendly advances or attempts to draw him into conversation.

He is disinclined to sustained effort either physical or mental. He may be apathetic and remain for long periods in the same attitude or posture; at times his behavior is somewhat suggestive of dementia praecox. The memory is often unreliable, owing rather to a lack of power of concentration than to any mental defect.

Phobias and obsessions are not uncommon in hyperplastic goiter but, because in most cases they are mild in character, their existence in the generalized emotional tumult is frequently overlooked by patient and physician alike. Sometimes very definite phobias and impulsions are noted. Suicidal impulses, homicidal attempts, anxiety syndromes, such as fear of sudden death or fear of being crushed in theaters, are not unusual complications of crisis.

Insomnia is one of the most constant and distressing nervous symptoms in this disease. The patient does not experience that sensation of pleasant weariness that precedes repose. The mental and physical hyperactivity, which is characteristic of the daylight hours persists. The patient's mind "races"; thoughts chase each other through his mind and tumble over each other in a maze of kaleidoscopic confusion. His mind pictures are brilliant and ever changing, too variegated to allow slumber.

The nocturnal persistence of physical or motor activity of the daylight hours is also disturbing. The patient tosses and turns in the bed. He is restless and constantly changes position. The frequency of micturition and the heart pounding make him more restless still; he turns on the light and tries to read; he finds he is too tired for this, but still not tired enough or rather not sufficiently worn out for sleep. It seems often that sleep only comes when the point of utter exhaustion is reached. The morning finds him bleak, irritable, and unrefreshed.

The next night is a repetition of his sufferings, and so on for months. It is small wonder that his mentality, character, and physique break down under the strain.

Hysteria, neurasthenia and similar nervous conditions are occasionally noted. What relationship exists between these and hyperplastic goiter is not definitely settled. Has the nervous instability some influence as a causal factor in the production of hyperplastic goiter? Are the constitutional factors that predispose to one, the same that predispose to the other? Has the thyrotoxemia awakened a dormant neuropathic tendency? We can readily understand how a prolonged toxemia might easily provoke an explosion of a latent neurosis.

Delirium is often noted in severe cases—in those that present crises, and occasionally in those in which operation has been done. The delirium somewhat resembles delirium tremens; the patient frequently has delusions of hearing and of vision, imagines friends and acquaintances are present, and talks to them. It is apparently a toxic delirium, incoherent, without fixed delusions or hallucinations.

While **insanity** and other forms of severe mental disease occasionally occur, the wonder is that under the circumstances they do not occur more frequently. When we take into account the prolonged and exhausting insomnia, the severity and duration of the other nervous symptoms, the continual strain, tenseness and anxiety, we may well wonder that so many of these sufferers succeed in remaining on the right side of the rather indefinite line which separates sanity from insanity. Indeed it is probable that many of these cases are borderline cases, in the full meaning of the word. However, the incidence of toxic goiter is no greater among the insane than among the sane and hyperplastic goiter is rarely noted as the sole etiologic factor in the development of insanity.

Muscular Weakness

As a result of the gastro-intestinal, cardiovascular, and nervous involvement, patients often become very weak.

The muscular asthenia is very marked and, at times, is the outstanding feature of the syndrome. The muscular involvement is particularly noticeable in the case of the quadriceps muscles, and the weakness of these muscles is easily demonstrated by asking the patient to step up on a chair. In the later stages of the disease, the patient will not be able to perform this maneuver without grasping the back of the chair to help himself up, no matter how great an effort he makes.

REPRODUCTIVE SYSTEM

Sexual Appetite

In the early stages, sexual desire sometimes is greatly increased. This is perhaps more true of the male than of the female. It is an expression of the greatly increased metabolism and the marked nervous

excitement. In women in whom amenorrhea has occurred, sexual desire is frequently greatly decreased or absent. At times, the greatly increased nervous excitation may lead to vaginismus and dyspareunia.

Menstruation

Amenorrhea sometimes appears early and may have been present for some time before any other symptoms of the disease are noted. As in tuberculosis and other wasting diseases, the disturbance of the normalcy of the menstrual flow is usually proportional to the severity and duration of the disease. In mild cases in which the thyrotoxicosis is not marked, the menstrual flow may continue normally over prolonged periods of time. As the thyrotoxicosis increases, marked weakness and emaciation appear and the menstrual flow becomes scanty and finally ceases. This amenorrhea may persist for a long time if the condition of the patient remains unimproved. However, in cases in which operation is performed, and in such cases as improve under medical treatment, the menstrual flow recommences and in a short time is again normal.

The Skin in Hyperplastic Goiter

In hyperplastic goiter some rather characteristic skin changes are noted. The skin is moist and warm in all cases of hyperplastic goiter during the active stage. Flushing is common—is noted objectively by the observer and complained of subjectively by the patient. In many instances, hot flashes are frequent and annoying.

Hyperhidrosis

Sweating or hyperhidrosis is the rule. The tendency to profuse perspiration is at times very troublesome. It is both local and general, that is to say, profuse perspiration over the whole body is common, but certain areas, such as the palms of the hands, are more subject to sweating. The palms of the hands are almost continuously moist and give an unpleasant clammy sensation upon shaking hands.

Night sweats similar to those seen in tuberculosis are not unusual. They may recur night after night, are usually not amenable to treatment, and may cause great weakness and prostration.

Day or night the patients are apt to complain of excessive warmth. They require fewer blankets at night and less clothing in the day time than the average individual. They frequently, even in the coldest weather, sleep with the limbs uncovered. Erythema is common, sometimes almost entirely covering the chest and back, and, in fact, any part where the clothing presses.

Dermographism

Dermographism is seen quite frequently and is an expression of the vasomotor instability present in the disease.

Pigmentation

Pigmentation, varying from a slight localized mottling to a discoloration as diffuse and as extensive as that found in mild Addison's disease is seen in 50 per cent or more of cases. It is strongly suggestive of involvement of the adrenals. When it is patchy and localized, it is more frequent in the exposed regions, such as the neck, face, or arms.

Urticaria

Urticaria is not uncommon in hyperplastic goiter but when present is even more transient in character than the ordinary urticaria.

Other Skin Changes

Many other skin conditions occur as occasional complications. Scleroderma, psoriasis, acne, eczema, angioneurotic edema, pityriasis are seen occasionally. It is doubtful whether they have any special significance. Jaundice is seen occasionally. Myxedematous skin changes are infrequently seen, and occur only when the thyroid is burned out and when the picture of myxedema is superimposed on the syndrome of hyperplastic goiter.

Hair and Nails

In many cases of hyperplastic goiter, after the condition has lasted some time, the hair becomes dry and lusterless. It falls out abnormally and alopecia is not at all uncommon. The hair of the arms and chest, the eyebrows and eyelashes likewise become thin. The finger and toe nails grow brittle and break easily.

Atypical Forms of Hyperplastic Goiter

Acute Hyperplastic Goiter

The terms "acute hyperplastic goiter" and "acute Graves' disease" should be limited to cases that have been acute from onset and these are not very common. Occasionally the term is applied to patients who are suffering with the chronic type of the disease and who are in crisis. The crisis is manifestly an acute exacerbation of a chronic condition and consequently the term "acute Graves' disease" is incorrect and misleading. Sudden stormy exacerbation in an individual, who has been suffering from a latent form of thyrotoxicosis, may be occasioned by physical or psychic shock, severe infection, exhaustion, or intoxication, and if the earlier symptoms have gone unrecognized, the case may present all the appearance of one primarily acute from the start.

Onset.—The onset, in the case of primary hyperplastic goiter that is really acute, is rapid; the symptoms appear suddenly in an individual previously in fair health. Nausea, vomiting, and diarrhea may occur as the first symptoms. The palpitation may be extreme and cause great discomfort.

Pulse.—The pulse may be 130, 160, or more, and occasionally a slight irregularity is noted. An increase in pulse pressure is the rule.

Exophthalmos.—Exophthalmos or a pronounced stare usually appears in these acute cases within a few weeks. In some instances it is very marked and immediately attracts the attention of the physician.

Loss of Weight.—The loss of weight is rapid and extreme. A third of the body weight may be lost in a few weeks. Perhaps in no other condition is there such a serious loss of weight in so short a time. In extreme cases half the body weight may be lost within a comparatively short time.

Nervous Symptoms.—A marked tremor, usually in the form of a trembling generalized over the entire body, is observable. Hallucinations and obsessions are present at times. Delirium is common and may be violent and prolonged. Mania is not unusual and true psychoses are occasionally found.

Temperature.—In severe cases the temperature is usually elevated one or two degrees within the first week or two and remains constant unless lowered by hydrotherapy or other means. A further rise in temperature is an indication of the development of complications.

Basal Metabolism.—A rise of 60 to 90 per cent in the basal metabolism rate is not unusual. The rate sometimes is plus 100 or even more.

Course.—Nausea, vomiting, trembling, delirium, and restlessness lead to a perversive and severe emaciation and exhaustion. The patient may die within a few days. Sometimes the symptoms become less intense and the patient develops the chronic form of the disease with recurring exacerbations at irregular intervals.

Hyperthyroid Temperament

The French writers particularly stress the "hyperthyroid temperament." The condition so designated is, however, probably a reflexion of slight thyroid dysfunction. By the term hyperthyroid temperament, the writer understands the temperament or character noted in a certain type of individual with nervous instability not at all uncommon in everyday life. Perhaps "hyperthyroid temperament" and the term temperamental as usually understood, may be considered as synonymous. The individual with hyperthyroid temperament is mentally and physically active, even to the point of restlessness. He—or more frequently she—is emotionally labile, prone to extremes of joy or sorrow, tears or laughter. She is ambitious, energetic, fretful, envious, impatient, and discontented. Physically she is often above the normal in stature, thin, with sparkling eyes. She has initiative but usually lacks in self control and mental and emotional stability.

Fruste Type of Hyperplastic Goiter

Incidence.—The fruste, the incomplete or borderline, type of hyperplastic goiter is probably much more common than is usually supposed. Undoubtedly there are many individuals suffering from an abortive or undeveloped type of this disease who do not feel sufficiently ill to consult a physician. When they do consult a physician complaining of vague,

fleeting, indefinite symptoms, they are rarely diagnosed as fruste types of hyperplastic goiter. They are told that they are run down, nervous, or neurasthenic, and receive tonics and an admonition to get plenty of rest, and to build up. They are frequently told that they are threatened with tuberculosis and in some cases sanitarium care is advised which, incidentally, is a good prescription even though the basis of the trouble has not been recognized. They are frequently classed as neurotics by the physician and sometimes as pests and hypochondriacs by others.

In some instances a single symptom of hyperplastic goiter may be present and even this may not be fully developed. For instance, nervous instability and slight evidence of autonomic unbalance may be the only suggestions of an underlying dysthyroid diathesis. A woman patient may complain of hot and cold flashes, be subject to spells of exaltation or depression, may blush rapidly, and be easily embarrassed. She complains of excessive cold sweating, particularly of the hands, is energetic and ambitious at times, but the energy and ambition are sporadic and not of sufficient driving force to carry her over a subsequent period of depression. Consequently, she starts many things and finishes few.

This is probably due to the fact that, owing to the mild thyrotoxicosis, she is incapable of sustained effort. It may be said in passing that in many of these mild forms of hyperplastic disease, positive diagnosis is impossible. At most, we can merely surmise that a fruste type of hyperplastic goiter exists, and base our therapeutic action and regimen accordingly. When we tell these patients that they are run down and need a rest, a vacation, we are giving them the best possible advice and undoubtedly many unrecognized early cases of this disease clear up, or at least improve, under this treatment.

To date, laboratory procedures have not helped us in the diagnosis of these early cases as much as they have in the more developed ones. Later perhaps, with greater refinement in technic, laboratory tests may be the means of uncovering many of the cases now unrecognized.

Varieties

The more common varieties of the fruste type of hyperplastic goiter are those associated with:

1. The age periods of stress and strain.
2. Cardiovascular symptoms.
3. Permanent "larval" conditions.
4. Pulmonary tuberculosis.

The Variety of Fruste Type in the Age Periods of Stress and Strain

The variety of the fruste type in the age periods of stress and strain is found in connection with the simple goiter of puberty, pregnancy, and perhaps the menopause. The usual symptoms that indicate the existence of a mild type of hyperplastic goiter are as follows: The pulse is rapid, palpitation is complained of, the patient is irritable, restless without

cause and suffers from insomnia. In the goiter of adolescence particularly, we often note an eager, anxious, dissatisfied expression, coupled with a barely noticeable stare. In addition, there may be unexplainable diarrhea, or alternating constipation and diarrhea, sweating, and hot flashes. Most of these incomplete forms disappear spontaneously, or after a short period of general dietetic and hygienic regimen. It is quite likely that in association with simple goiter some slight hyperplasia has taken place which supplies enough qualitatively changed secretion to produce vague temporary symptoms of mild hyperthyroidism. These glands, already probably slightly hyperplastic, are, in the experience of the writer, especially susceptible to infection and the writer recalls many instances of such fruste types of this disease which developed the full-blown syndrome of hyperplastic goiter subsequent to the occurrence of a local or general infection.

The Cardiovascular Variety

The cardiovascular variety is particularly important as many cases are treated over a period of years for cardiovascular disease that are really cases of a very mild hyperplastic goiter. The writer has seen case after case of mild hyperplastic goiter in which the thyroid disease was overlooked for years because of the predominance of the cardiovascular symptoms. That the condition in these cases was due to goiter, was proved repeatedly by the results of operation. Besides these cases in which the cardiovascular symptoms predominate, there are many cases in which the heart symptoms are persistent but never seem to become severe. There is a persistent tachycardia without discoverable cause, and an increase in the pulse pressure. In addition to these mild cardiac symptoms there may be some evidence of nervous instability, but beyond this no further sign of thyroid disease. In fact, in many of these cases that are recognized, the thyroid disease would never have been discovered but for the occurrence of a gradual increase in the symptoms.

The Permanent Larval Variety

The permanent larval variety embraces a rather large class of mildly hyperthyroid individuals who present some evidence of hyperplastic goiter in its early stage. The disease for some reason does not progress and apparently may remain indefinitely in this larval state. There is slight thyroid swelling; the thyroid is small soft and vascular, and a bruit may in some instances be heard over the gland; the tachycardia is mild but persistent. There is a tendency to sweating; perhaps a slight stare. There may be a slight rise in the metabolic rate. These patients seem able to remain at their occupation and perform fairly satisfactory work over prolonged periods.

The writer is inclined to believe that in this type of larval hyperplastic goiter only small areas of the gland are affected. Either the virulence of the infection was not sufficient to cause generalized or diffuse involvement of the thyroid in the infectious process or the specific re-

sistance of the gland was, for some reason, sufficient to prevent structural change in the thyroid except in certain areas.

These patients may, indefinitely, exhibit the picture of the fruste type of the disease. They may, however, with great suddenness, develop all the symptoms of a classical case of hyperplastic goiter. The exciting factor in the exacerbation may be additional infection, shock, fright or exhaustion.

The Variety Found with Tuberculosis

In this important and sometimes rather confusing group of cases, pulmonary tuberculosis is associated with symptoms of hyperplastic goiter. In many instances it is difficult to say whether the hyperplastic goiter in association with the tuberculosis process is of the larval type or not. This is owing to the fact that the interaction and mutual relationship of the two diseases blurs the syndrome of the coexistent goiter.

TOXIC ADENOMA

(Secondary Hyperplastic goiter)
(Secondary Basedow's disease)

The symptoms and physical signs of toxic adenoma vary with the type and stage of development of the adenomas or nodes present at the time that toxic symptoms appear. The manifestations of each of the two types of toxemia described in the chapter on Etiology are different and distinct. However, there are characteristic features that, at least from the clinical standpoint, justify their joint classification.

The gland is always enlarged and usually nodose and asymmetrical, the adenomas or nodes being multiple and of considerable size. The symptoms of primary hyperplastic goiter have already been considered. The difference in the symptomatology of this disease and secondary hyperplastic goiter or toxic adenoma will be quite evident after a consideration of the following points relative to the symptoms and course of toxic adenoma.

Onset

According to the histories given by our patients the average age at which the enlargement was first noticed is nineteen and a half years, while the average age at which toxic symptoms appeared is thirty-nine years. In other words, an average of eighteen and a half years elapse between the appearance of the goiter and the development of toxic symptoms. This is the first point of variation we note from the course of topical hyperplastic goiter, the symptoms of which usually appear with, or soon after, the appearance of the goiter.

The onset of toxicity in toxic adenoma is usually slow and insidious, becoming evident after the so-called simple adenoma has been present for a number of years. The symptoms of the onset of the toxemia are often vague. A mild tachycardia with some dyspnea and palpitation may be present. Mental and physical activities require greater effort than

usual. Languor and weakness may be marked. Gastro-intestinal disturbances are occasionally noted.

While the average age at which toxemia develops is older than is usual in diffuse hyperplastic goiter, the writer has repeatedly seen patients with adenomatous goiter in which thyrotoxicosis developed at a comparatively early age. In a series of 3458 cases of toxic adenoma, 48 were patients under 20 years. It may be of interest to note that in this series the thyrotoxemia developed; during the course of a coexistent pulmonary tuberculosis in 14 cases, following attacks of influenza in 623, following mumps in 2, and following severe sore throat in 423.

Chief Symptoms

The chief symptoms in toxic adenoma are by no means identical with those seen in primary hyperplastic goiter. Nodes or adenomas in the gland, and thyrotoxemia are always present.

Cardiovascular Symptoms

There is frequently a predominance of the cardiovascular symptoms with an abeyance of the nervous and mental symptoms. The tachycardia is usually of mild degree and lacks the persistence and intensity of the tachycardia in primary hyperplastic disease. It may not be constant and at times may disappear almost completely. In the early cases, the pulse rate is often between 90 and 105; the rhythm is regular and the first sound accentuated. The cardiovascular symptoms exist for a considerable period of time without causing the patient much alarm. Except for dizziness, occasional palpitation, and some dyspnea the patient may feel fairly well. Even in advanced cases there is rarely the degree of tachycardia observed in primary hyperplastic goiter. The pulse rate is seldom above 120 to 130 except in paroxysmal attacks. Attacks of palpitation become more frequent and more troublesome as the disease progresses and sooner or later arhythmia develops. This is usually a late symptom, occurring spasmodically at first and later becoming constant. Auricular fibrillation is common in the late stages. As the heart condition becomes worse, edema supervenes and may become generalized.

The **heart sounds** in toxic goiter are characteristic, but difficult to describe. The first sound is accentuated and slapping. The second sound is frequently muffled and indistinct, particularly during a remission.

Blood Pressure.—Hypertension is common late in the course of the disease. Following the onset of toxic symptoms, the systolic pressure rises and the diastolic pressure falls. Later both rise, and blood pressures of 160 to 170 systolic and 100 diastolic are often found. This may be compared with the characteristic blood pressure of primary hyperplastic goiter, which often runs around 135 or 140 systolic and 60 or below diastolic.

Thyroid Tumor

The thyroid swelling in toxic adenoma is usually large and irregular but may be small. It lacks the symmetry, pulsation, and compressibility

of the thyroid in primary hyperplastic goiter. Usually no thrill nor bruit can be discovered. The goiter has usually been present over a long period of time.

Nervous and Mental Symptoms

Tremor is frequently absent. When present it is usually much coarser than the delicate tremor seen in primary disease. The mental symptoms, as compared with those seen in primary disease, are mild and usually are not of much consequence. The persistent insomnia and the psychoses often seen in primary hyperplastic goiter are very rare indeed.

Eye Findings

The presence of eye symptoms is usually emphasized as an important point in the differential diagnosis between primary hyperplastic goiter and toxic adenoma. It must not be forgotten, however, that pathologic eye conditions are frequently absent in primary hyperplastic goiter or may occur late in the disease. Furthermore, it can scarcely be denied that exophthalmos and other eye complications do occasionally develop in typical cases of toxic adenoma.

It may be said, however, that in typical toxic adenoma, the exophthalmos and the related eye findings are quite rare, and the presence or absence of such signs is of some importance in the differential diagnosis of toxic adenoma and primary hyperplastic goiter.

Gastro-intestinal Symptoms

Constipation is often present. Loss of appetite is frequently complained of. The acute gastro-intestinal attacks noted in primary hyperplastic goiter are rarely seen in toxic adenoma. Frequently a normal amount of food is taken and the weight remains normal over a prolonged period of time. As the disease progresses and the thyrotoxemia increases, weight is lost, but it is a gradual loss and the extremely acute wasting sometimes noted in primary disease is rarely seen.

Basal Metabolism

Taken on the average, the basal metabolic rate is considerably lower in toxic adenoma than it is in primary hyperplastic goiter. The patient may be very ill with marked symptoms of thyrotoxemia and severe cardiovascular disturbances and still show only slight rise in the basal metabolic rate. It is also noted that a rise in the basal metabolic rate in toxic adenoma is not always associated with the same severity of symptoms that a similar rise in primary disease would imply.

There is striking lack of uniformity in the curves of basal metabolism in these cases of toxic adenoma. In the early stages of the thyrotoxemia in the mildly toxic cases, there may be slight or no elevation of the metabolic rate and a marked increase in the later stages. In some severe cases the rate is plus 30, even plus 50 over long periods. In other instances the increase in the metabolic rate is mild throughout the whole course of the disease.

Course

The onset of the disease is insidious. Slight palpitation, dizziness, or precordial pain may be the first noticeable symptom. As the condition progresses, the cardiovascular or nervous symptoms may become predominant. Endocardial change occurs early in many instances. Later there is marked tendency towards myocardial change. Dyspnea on exertion and palpitation become more troublesome. The area of cardiac dullness is increased and organic murmurs at the apex are noted. Functional murmurs at the base are quite common.

Owing to the insidious onset, considerable cardiac damage may result before the condition is diagnosed. The damage is usually of an organic nature and is sufficiently advanced in many cases to detract from the beneficial result of operation. Unless performed early, removal of the adenoma, while it does remove the cause of the thyrotoxemia, cannot be expected to repair a heart that has suffered severe structural damage. However, surprising beneficial effects are sometimes observed.

In proportion to the duration and the severity of the thyrotoxemia the tendency to hypertension becomes more marked. There is a rise both in the systolic and diastolic pressures. Associated with the hypertension there is usually, as might be expected, some degree of cardiac hypertrophy and myocardial change. Both the hypertension and myocardial change are usually quite evident by the end of the third year after the onset of toxicity. It may be said that at this period the best time for operation has passed, though even at this stage removal of the goiter may still be productive of very great benefit.

Auricular flutter and extrasystole occasionally are seen. Evidence of decompensation may soon become apparent. Arhythmias may develop; auricular fibrillation is quite frequently noted. Later passive congestion and edema develop, and, at this stage, operation is not only attended by a higher mortality, but is frequently followed by only partial relief with many residual symptoms. While the patient with severe cardiovascular damage may improve with the removal of the offending goiter, very often the patient, whether operated on or not, is doomed to a life of partial disability.

Types of Toxic Adenoma

Although clinical findings in toxic adenoma are varied and diverse the patient will be found to belong in one of the following four, rather loosely defined, groups:

(1) Cardiovascular Group: Mildly toxic chronic cases exhibiting few acute symptoms at any time, but with severe cardiocirculatory involvement late in the progress of the disease.

(2) Anaphylactic Group: Cases with adenomas, usually rather large, with symptoms of definite thyrotoxemia, and, in addition, symptoms definitely suggestive of an anaphylactic reaction.

(3) Hyperplastic Group: This group includes a series of cases of adenomatous goiter in which a clinical syndrome similar to that of hyperplastic goiter appeared after or secondary to the adenoma.

(4) Mixed Group: The individuals in this group present a variable combination of two or more of the essential features of the above clinical syndromes.

Cardiovascular Group

This group included the largest number of cases; namely, 1432 of a total of 3458 cases of toxic adenoma. The essential feature is the predominance of the cardiovascular symptoms. The symptoms and course of the cardiovascular changes have already been described.

Anaphylactic Group

In the anaphylactic group 514 of the total of 3458 cases were included. In a number of cases of toxic adenoma, areas of degeneration and disintegration within the gland itself develop inevitably. These areas are at times quite extensive and it is only natural to assume that the absorption of the products of extensive degeneration must be accompanied by certain symptoms over and above the mere symptoms of thyrotoxicosis. This assumption is supported clinically by the frequent observation of symptoms directly referable to the absorption of protein substances from the broken-down tissue. In other words, we note symptoms distinctly suggestive of an anaphylactic reaction. Among these may be mentioned dermographia, urticaria, respiratory paroxysms, paroxysmal tachycardia, digestive disturbances, slight jaundice, vomiting, diarrhea, puffy face and swollen eyelids.

This type of toxemia, although representing a large percentage of the toxic cases, has not been observed by us except in the presence of degeneration with destruction of gland tissue in some portion of the gland. Frequently the complete picture does not develop until evidence of absorption of degenerative products has been present for some time.

The rôle of *iodin in the aggravation of anaphylactic symptoms* has been demonstrated clinically. All the instances of thyrotoxemia, induced by iodin, that we have seen were in patients in this anaphylactic group. In all cases with preexisting adenoma in which symptoms of toxicity were resultant on the administration of iodin, it was found that areas of degeneration had existed in the adenoma and that symptoms suggestive of anaphylaxis formed part of the picture of the thyrotoxicosis. In 187 of the 510 cases in this group the history reads, "The acute symptoms appeared after administration of iodin." In 146 of the remainder the history showed that thyrotoxicosis had already been present but had been intensified by the administration of iodin. Symptoms of thyrotoxicosis developed in 152 of the cases in the group during pregnancy and three months after delivery in 49 cases. In 19 cases the toxicity appeared to be the direct result of the injection of various substances into the tumor.

Hyperplastic Group (Secondary Basedows)

This group included 647 cases. All these cases presented clinical symptoms suggestive of hyperplastic goiter. While marked exophthalmos

was shown in only forty-seven cases, tachycardia, palpitation, faint tremor, loss of weight, increased appetite, muscular weakness or fatigue, and moderately increased metabolism were present in all of them. While there is still some doubt in the present state of our knowledge as to the exact pathogenesis of this condition, the weight of evidence seems to indicate that the symptoms are directly attributable to areas of excessive hyperplasia in the gland.

The writer is of the opinion that in some instances of toxic adenoma a localized excessive hyperplasia occurs successively in separate areas of the gland, and that the variation in the symptoms present are due to the different stages of hyperplasia in the various areas. In such cases the typical syndrome of primary diffuse hyperplastic goiter is not observed and in the presence of an adenoma the condition must be classed in the general group of toxic adenoma, notwithstanding the fact that the toxic symptoms may be due to hyperplasia.

Mixed Group

Of the total of 3458 cases of toxic adenoma, 865 were classed in this fourth or mixed group. In 722 of these 865 cases, symptoms common to both the cardiovascular and hyperplastic groups were present. In 143 cases there were symptoms common to all three other group types of toxic adenoma: namely, the cardiovascular, anaphylactic, and hyperplastic groups. Symptomatology in this fourth type of toxic adenoma is of necessity quite varied and precludes definite descriptions. In some instances the symptoms typical of the cardiovascular group are in the ascendancy with, however, mild symptoms of hyperplastic goiter. In other instances the hyperplastic symptoms are predominant. The symptoms are suggestive of hyperplastic disease, but, in addition, there is the adenoma, and the urticaria and other anaphylactic phenomena suggestive of degenerative processes within the adenoma.

SYMPTOMS OF OTHER THYROID CONDITIONS

MALIGNANCY

Age Incidence

Malignancy in the thyroid occurs, as would be expected, comparatively late in life; it is quite common in women at the time of the menopause. The most common period of onset lies between the ages of 45 and 65. About 25 per cent of the malignant goiters occur in the age period between 65 and 75. This applies to goiters that are diagnosed as malignant before removal. If we consider cases in which the condition is apparent only at operation, we must place the most common period of onset at a considerably earlier age. Occasionally malignancy occurs in young adults but very rarely in children.

Onset

The symptoms of onset may be mild, particularly when the malignancy is associated with the menopause, and considerable time may elapse before the condition is diagnosed. In the great majority of cases a goiter has been present for years, the patient is accustomed to the deformity and the goiter gives no concern. Suddenly an increase is noticed in the size of the gland without apparent cause. The rate of growth may be extremely rapid, the tumor reaching in a few weeks such size as to cause marked pressure symptoms and even spasms of suffocation.

Symptoms

Dysphagia is often severe and troublesome. It is due to spasm of the muscle fiber of the wall of the esophagus as well as to pressure and consequently even the swallowing of liquid may be difficult and painful.

Cough and Choking Spells.—A severe barking cough is often present and is not usually amenable to medication. Much more distressing than the cough are the choking spells that are sometimes present. These become worse as the pressure on the trachea and the involvement of the nerves become more marked. The spells become more frequent and severe, and eventually the patient is almost continually gasping for breath.

Aphonia.—Hoarseness is often present in varying degree. Severe involvement of the recurrent nerves may lead to complete aphonia.

Pains.—Owing to inclusion of the cervical and brachial plexuses in the malignant process, neuralgic pain is common. This pain is often sharp, shooting in character, and is referred to the ear, neck, fingers, arm or shoulder.

Fixation or rigidity of the spine from about the third cervical to the third dorsal is sometimes a very prominent symptom. This rigidity is not a result of metastatic extension of the malignant growth, but is due to an effort of the patient to secure ease by procuring immobility of the cervical structures through muscular rigidity or fixation.

Constitutional Symptoms.—Weakness, loss of flesh and tachycardia are noted. The loss of flesh at times may be pronounced and rapid, but often is not of great diagnostic significance owing to the fact that a similar loss of weight is encountered in hyperplastic disease. In malignancy, even in the early stages, the voracious appetite often observed in hyperplastic goiter is not noted. As the disease progresses, the complexion becomes sallow; the extremities are commonly cold.

The patient sits still and breathes as though conscious of the act of breathing, thus giving the impression of voluntary respiration. Respiration is usually slow and the patient can be induced to breath at as low a rate as can the normal individual. There is lacking the warm skin, the active capillary circulation, the restlessness without a cause, and the higher metabolic rate, usually present in thyrotoxicosis.

Thyroid Dysfunction

Symptoms of thyrotoxicosis are sometimes noted. Tremor, tachycardia, even exophthalmos may be observed. Malignancy may occur in an old hyperplastic goiter, and the symptoms of malignancy will, in this case, be superimposed upon the syndrome of Graves' disease. In other instances the malignancy may occur in a burned-out thyroid. The patient may have had hyperplastic goiter for years and the active symptoms may have almost completely disappeared owing to the destruction of gland substance. One or more residual symptom, such as exophthalmos or slight tremor, may remain and to these are added the hardening and fixation of the gland, the muscular rigidity, the dysphagia, the pain, and the aphonia characteristic of thyroid malignancy.

Objective Findings

Many cases of early malignancy yield no definite evidence on physical examination. Indeed, in only too many instances the diagnosis is made on postoperative examination of a section of the gland.

Hardness.—Only a slight sense of resistance or hardness is noted in the early stages; the skin is still freely movable over the gland and there is no one finding sufficiently distinctive to establish a diagnosis of malignancy. The resistance of the gland gradually increases until finally a boardlike hardness develops. Hard circumscribed nodules are sometimes observed.

Immobility.—Lack of mobility in the thyroid tumor, indicated by the fact that the thyroid does not move up and down freely in the act of swallowing is soon noted. Later, complete fixation occurs and the thyroid does not move at all during swallowing. The skin is often still freely movable over the platysma, but the muscles are rigid. The muscular rigidity is often very definite and simulates the rigidity of the abdominal muscles in the presence of an acute infectious process within the abdomen.

Course

The course of the disease in thyroid malignancy varies considerably. In some instances the onset and course of the disease are acute. This is particularly true in young subjects. In such cases, sometimes within even a couple of weeks, the symptoms are pronounced and the stage of the disease apparently well advanced. The trachea and esophagus may be severely involved in the malignant process even at this early date, and severe dysphagia and dyspnea or even choking spells may be observed. There is rapid extension of the process and death may result in a couple of months, or even sooner. Usually, however, the course is subacute. There is gradual weakness, loss of weight, and, as the process extends, there are pressure symptoms such as dyspnea, choking spells, and dysphagia. As the nerves also become involved, there is hoarseness and aphonia. The pain on swallowing becomes extreme and the patient finally becomes disinclined even to attempt to take food. Rapid and extreme emaciation results and the course is rapidly downward.

Extension and Infiltration.—As the disease progresses, extension with infiltration of the surrounding structures is noted. The trachea and esophagus are involved. The malignancy may extend into the tracheal walls and even occasionally perforate through. The esophagus may be severely compressed by the constantly tightening grip of the tumor, and extreme dysphagia and finally starvation may result. Definite extension of the malignancy to the surrounding structures is noted at about the time that the pain is observed to be more or less constant.

If the patient survives long enough the skin becomes infiltrated, swollen, and adherent to the deeper tissues. The superficial veins are often engorged and prominent. The carotid sheaths are often involved in the malignant process and also the laryngeal, vagus, and sympathetic nerves. Extension to the lymph-nodes is common and the cervical nodes and later the mediastinal nodes are affected. Thrombosis of the great vessels in the neck is not infrequent, and occasionally even a subclavian or a jugular vein is thrombosed.

Metastases.—Metastases are not infrequent and very often go unrecognized. Secondary metastatic processes from the thyroid are more common in the bones, and the skull, sternum, pelvis, humerus, mandible, and femur. The viscera are also at times involved in secondary growth of thyroid origin, and the stomach, liver, intestines, mucous membranes, as well as the skin may be affected.

The secondary growths are often definitely cancerous in structure. Occasionally the metastatic growth, on histologic examination, reveals no evidence of malignancy, and has the appearance of normal thyroid tissue. Whether the normal thyroid is capable of producing metastases in other organs or structures must be considered extremely doubtful. Probably all those secondary thyroid deposits in distant organs should be considered malignant.

This belief is further strengthened by the fact that frequently normal and cancerous thyroid tissue are found together, in varying proportions, in the same metastatic process. It is quite possible that many of the metastatic growths composed of so-called normal thyroid tissue would present some histologic evidence of malignancy if removed at a later date.

THYROIDITIS

Inflammation of the thyroid, both acute and chronic, is quite common. In about 60 per cent of thyroids examined at postmortem areas of inflammation are observed. Inflammation developing in a previously normal gland is termed thyroiditis; in a gland which has already become goitrous, it is called strumitis. Although it is usual to make a distinction between the suppurating and non-suppurating types of acute thyroiditis, both types may be looked upon as merely different stages of the same condition. The factor of suppuration depends to a large extent on the etiologic agent. Thus, thyroid inflammation due to measles or rheumatism does not end in suppuration; if, however, the thyroiditis is secondary to puerperal fever, typhoid or scarlet fever, suppuration is more likely

to occur. Thyroiditis may or may not be accompanied by disturbance of the endocrine system.

Acute Thyroiditis

Onset

In severe cases the onset is often sudden and stormy. A severe chill, accompanied by a sharp rise in temperature, is often the first symptom. If there is no definite chill, there may be chilliness and pain in the region of the thyroid. Some discomfort upon swallowing, attributed by the patient to a mild sore throat, is often an early symptom.

Symptoms

Pain.—The pain as a rule is not severe and may be confined to the region of the thyroid, but often radiates to the shoulder and the back of the neck. It is frequently referred to the ear and occasionally to the tonsillar region. The most frequent symptom complained of is earache. In case the inflammation is limited to one lobe, the pain may be restricted to the affected side of the neck. There is some tenderness on pressure and the patient seeks relief by striving for relaxation of the overlying muscles. Mild but sharp pains radiate to the ear, shoulder, and jaw upon swallowing.

Dyspnea and Dysphagia.—Owing to the pain and pressure from the tumor and the rigidity of the surrounding muscles, swallowing may be difficult and quite painful. Usually, however, there is only a sense of tightness or fulness in the throat, due to rigidity of surrounding structures and perhaps to pressure on the esophagus. Dyspnea may be pronounced, and coughing spells may become troublesome in severe cases. Due to pressure on the trachea and the laryngeal nerves, or if the infection extends to the larynx, hoarseness is also noticed at times.

Constitutional Symptoms.—There is great variability in the constitutional symptoms due to inflammation of the thyroid gland. In the great majority of cases the thyroiditis occurs at about the time that some infectious disease, such as influenza, measles, scarlet fever, or severe pharyngitis, is subsiding. Consequently, the slight rise in temperature and pulse rate, the local pain and tenderness, and the rigidity of the cervical muscles are either overlooked or ascribed to the antecedent infection.

When the inflammation is severe, the constitutional symptoms may be pronounced. In addition to those provoked by infection, there are frequently symptoms indicative of disturbance of thyroid function.

During the acute stage of thyroiditis, even in the presence of slight fever and increased pulse rate, the basal metabolism rate is rarely above normal. As the thyroiditis subsides, the pain, tenderness, and muscular rigidity in the cervical region disappear; the temperature and pulse rate return to normal; and the basal metabolism rate usually drops below normal for a period of about two weeks. If no great damage to the gland has occurred, and no iodin deficiency is present, the basal metabolism

rate will promptly return to normal. However, in more than 50 per cent of the cases of definite thyroiditis that we have seen, the return to normal is not so satisfactory. The pulse rate remains high or drops only to return again to a point above normal. Tremor, loss of weight, and nervousness appear. The basal metabolism rate goes above normal, flushing of the skin, and, finally, eye symptoms appear and complete the picture of fully developed hyperplastic goiter.

Objective Findings.—The swelling is often unilateral but may be bilateral. The isthmus usually seems to be free. At first, the lateral lobe is hard and easily palpated; later, due to rigidity of the overlying muscles, it apparently decreases in size and becomes tender. The tenderness is pronounced at times and the slightest touch may provoke severe pain. In some rare instances the surrounding tissues become infiltrated and the entire front and sides of the neck become swollen. Movement, active or passive, provokes pain and is likely to induce coughing or choking spells.

If the process goes on to suppuration, the lobe involved enlarges, and finally a definite node area may show fluctuation.

Chronic Thyroiditis

To most writers chronic inflammations of the thyroid are typified by syphilitic and tuberculous thyroiditis. There are, however, other forms which are of importance.

Syphilitic Thyroiditis.—Probably this type of inflammation is more common than is generally supposed. Little if any investigation has been made of the possible presence of thyroiditis during the acute stages of syphilis. Most of our knowledge of syphilitic conditions of the thyroid is drawn from a study of the glands removed from patients in the tertiary stages of syphilis. Information as to whether or not syphilitic thyroiditis was present in the early stages of thyroid disease cannot be gained by the study of a gland removed after marked structural change has already taken place.

Tertiary syphilitic lesions may occur as gummata or may be evidenced as diffuse sclerosis of the gland. The sclerosis may be unilateral or bilateral, and may result in a hard resistant goiter. The hardness is emphasized by most writers as one of the characteristics of this type of goiter and frequently leads to an erroneous diagnosis of carcinoma. The fact that a goiter may be due to tertiary syphilis should be borne in mind, and while the condition is comparatively rare, it should not be forgotten that in a few instances an energetic course of antisyphilitic treatment may obviate the necessity of operation.

With regard to the occurrence of pain our experience is at variance with that of most writers. We have found that syphilitic thyroiditis is usually accompanied by vague pain which is often dull, intermittent, slightly aggravated by swallowing, and frequently referred to the auricular region or to the angle of the jaw. Frequently there is a feeling of discomfort or pressure in the neck. Slight tenderness upon palpation can be elicited over the entire anterior cervical triangles. Difficulty may be ex-

perienced in outlining the gland by palpation on account of the rigidity of the muscles. Evidence that the thyroiditis is of syphilitic origin is furnished by the prompt response to antisyphilitic treatment.

Ligneous Thyroiditis.—This form of thyroiditis was first described in 1896 by Riedel (115). It occurs most often in young individuals who were previously in excellent health. The onset may be rather acute; the patient may suddenly become aware of dyspnea of varying degree. He may then notice a change in the contour of the neck. The patient sometimes complains of a feeling of discomfort such as that caused by a foreign body in the throat. Dyspnea due to the compression of the trachea between the lobes of the gland may make its appearance and may be progressive and at times alarming. Hoarseness and aphonia are occasionally noted, but are usually absent. Occasionally the thyroid is tender and severe lancinating pains are complained of.

Well marked thyroid enlargement is usually present. The contour of the swelling may be smooth and even, or slightly nodular. The swelling may be confined to one side but is usually bilateral. On palpation the gland is well defined, but hard and rigid and usually densely adherent to the trachea, esophagus, muscles and other adjacent structures. The rigidity and fixation of the surrounding structures often makes it impossible to distinguish the borders of the thyroid. The growth, however, does not invade surrounding structures.

Frequently, owing to immobilization of the larynx, the tumor does not move with deglutition and when it does it has a peculiar, vertical rotating motion. The skin and superficial structures are freely movable, but frequently appear thickened and somewhat infiltrated. As a rule, fever is absent and constitutional symptoms are slight or absent. There are no toxic symptoms, and the patient's metabolic rate is not elevated. Loss of weight and some nervousness are at times noted but, in the absence of an increased metabolic rate, cannot be construed as evidence of thyrotoxemia. At times a leukocytosis of moderate degree is present.

Tuberculous Thyroiditis.—Some instances of persistent chronic thyroiditis are tuberculous in character. The lobe, or sometimes the whole gland, undergoes lardaceous change. In other instances, localized tuberculous lesions are noted.

The frequency of involvement of the thyroid in tuberculosis is not sufficiently appreciated by the majority of writers. Neither the specialist in tuberculosis nor the thyroid surgeon place sufficient importance on the possible secondary changes in the thyroid gland in the course of pulmonary tuberculosis.

Chagas' Thyroiditis.—According to Chagas (116), who first described the condition in 1907, this type of thyroiditis is due to a parasite. The disease, he states is sometimes acute, particularly among children, and is accompanied by thyroid swelling, high fever, and severe constitutional symptoms. The patient may die in two or three weeks. In the subacute or chronic form seen in older persons, the constitutional symptoms are much less marked, but a goiter, often extremely large, results. Symptoms of hypothyroidism or myxedema may be associated with the goiter.

Toxic Thyroiditis.—Toxic thyroiditis is rather a vague term. It may be applied to inflammatory thyroid change resulting from toxins, chemical or bacterial, as opposed to inflammatory thyroid change resulting from actual implantation of organisms in the thyroid substance. Chemical toxins or poisons, such as turpentine, iodin and phosphorous, may undoubtedly cause a thyroiditis, but thyroiditis of such origin is rare. As an example of toxic thyroiditis, the mild inflammatory swelling seen in many cases of pulmonary tuberculosis may be mentioned. In these cases no tuberculous lesions are noted in the thyroid and the changes that are seen in the gland, with the resultant symptoms, must be considered a result of the prolonged tuberculous toxemia.

Aberrant or Abnormally Located Goiter

Aberrant thyroids may be found at the foramen cecum or at any location along the original course of the thyroglossal duct even as low as the arch of the aorta. They are found frequently at the base of the tongue, in the submaxillary region, and more rarely in the lateral anterior cervical region or within the trachea.

Undoubtedly many cases of accessory thyroids are never recognized as such. The accessory thyroid functions as thyroid tissue and is subject to the same hyperplastic or degenerative changes as the normal gland. The accessory thyroid may develop colloid or hyperplastic changes with symptoms corresponding to the type of the disease present in the particular case. Unless an obvious tumor is present an accessory thyroid can seldom be diagnosed before operation.

Lingual Goiter

Not so long ago this type of aberrant goiter was considered an exceedingly rare condition, in fact, a medical curiosity. In more recent years, due to the greater frequency of laryngoscopic examinations and perhaps also to the greater publicity given the subject, many cases are recognized.

Onset

The onset is insidious and in many instances the goiter remains unobserved over a long period of time. The increase in the intensity of the symptoms is very gradual. The condition is more common in females than in males and is most often discovered at about the time of puberty.

Symptoms

There may be some slight difficulty in swallowing and coughing spells are occasionally noted. If due to hemorrhage the increase in the size of the goiter is sudden; there may be extreme dyspnea. Speech disturbance is occasionally noted. The possibility of constitutional symptoms in cases of lingual goiter may be questioned, yet instances have occurred in which symptoms of thyrotoxicosis seemed directly attributable to hyperplastic change in a lingual goiter.

Objective Findings

The tumor is usually located in the middle line, in the neighborhood of the foramen cecum. It varies in size from that of a marble to the size of a small hen egg. The tumors are usually rounded or lobulated and highly vascular. If cystic degeneration occurs, the consistency of the tumor is, as a rule, elastic, but fluctuation may be noted. It is sometimes large enough to be evident to direct vision, but the smaller lingual goiters are only discovered through the medium of the laryngoscopic mirror.

A small lingual goiter may remain latent throughout life and cause no symptoms of any kind. On the other hand, owing to hemorrhage, cystic degeneration, or other reasons, it may suddenly enlarge and cause severe symptoms, such as extreme dyspnea, speech disturbance, and dysphagia. It occasionally happens that the lingual thyroid is the only source of thyroid hormone and the surgeon must assure himself of the presence of thyroid tissue elsewhere before he undertakes the radical excision of a lingual goiter.

Aberrant Thyroid Tissue in the Trachea

This is a rare condition, but a number of cases have been reported. The thyroid tissue in most cases reported was located approximately at the level of the first tracheal ring. A gradually increasing dyspnea, which eventually becomes paroxysmal, is the most characteristic symptom. Laryngoscopic examination, in suitable cases, will reveal the tumor mass.

Aberrant Thyroids in the Thorax

Aberrant thyroids are occasionally found in the chest cavity. They rarely, however, reach a sufficient size to cause symptoms, and are merely pathologic curiosities.

Intrathoracic Goiters

Considerable confusion exists with regard to the terms substernal and intrathoracic. Perhaps in the majority of goiters classified as intrathoracic or substernal, it would be more proper to say that the portions in the chest are merely intrathoracic projections from the cervical goiter. Rarely, can the goiter be said to be a misplaced thyroid, completely intrathoracic.

A substernal or partly intrathoracic goiter is, as the name implies, only partly within the thorax and usually the greater part of the goiter is located above the thoracic aperture.

In a third type of goiter, the diving goiter, or the **goitre plongeant** of the French writers, the tumor mass is sometimes above and sometimes below the manubrium sterni, sometimes entirely cervical, sometimes almost entirely intrathoracic. During a severe coughing spell, the goiter suddenly appears above the clavicle and quickly subsides into the thorax again as the coughing spell disappears. At first an intrathoracic goiter is merely substernal and moves with deglutition. Gradually it sinks deeper

and deeper into the thorax and with increase in size may become incarcerated there. In the case of increase in size from hemorrhage or cystic degeneration, grave pressure symptoms appear. In other instances, the increase in size is less voluminous and more gradual and the pressure symptoms are of lesser severity. In some instances the goiter is at times forced above the clavicle in paroxysms of coughing and vomiting.

Onset

The onset is frequently associated with an interesting history. The patient may have had a large goiter for years. Suddenly it disappeared and the patient considered himself well but he became dyspneic and subject to substernal pain, vertigo, headache, and other symptoms.

Symptoms

The sequence and the severity of the symptoms depend, to a large extent, on the size and location of the intrathoracic goiter, and also on the type of change which has taken place (hyperplastic or degenerative) giving rise to pressure symptoms or thyrotoxemia.

The intrathoracic goiter is mechanically similar to a mediastinal tumor and presents much the same symptoms. But in addition to the simple pressure symptoms of mediastinal tumor, may be noted, usually in the third decade, symptoms of hyperplastic disease and at any time respiratory obstruction of lesser or greater severity from curvature or flattening of the trachea.

Dyspnea is often pronounced and intractable, particularly so if the tumor is large or so situated as to press directly on the trachea. The dyspnea may be gradual in onset, or may be sudden and paroxysmal if the tumor suddenly increases in size or changes position so as to cause direct pressure on the trachea. A sudden increase in dyspnea is frequently noted following sudden movements of the head or neck. Other movements, on the contrary, which manipulate the tumor so as to relieve the pressure on the trachea, bring ease to the patient. Pronounced dyspnea, associated with cough and inspiratory stridor, often presents a picture resembling asthma and patients with intrathoracic goiter are occasionally treated as asthmatics over prolonged periods of time. Owing to the pressure both on the trachea and the great vessels, the patient finds it extremely difficult to adapt himself to a comfortable position for sleep, and in many instances he finds it impossible to lie in the recumbent position and spends the night in an arm chair. In the advanced cases, there are sometimes severe paroxysms of choking which greatly alarm the patient.

A characteristic, brassy **cough** is frequently present. The character of the cough closely simulates the cough due to aneurism. Sometimes the patient has been treated for a long time for bronchitis and similar conditions; the cough, however, has resisted all treatment and it may be this symptom of persistent, intractable cough which first draws attention to the possibility of the existence of an intrathoracic goiter.

According to some writers **dysphagia** is not a common or troublesome

symptom. In the writer's experience, however, dysphagia of varying degree has not been infrequent.

Hoarseness and Aphonia.—Hoarseness due to pressure or an irritation of the recurrent nerves is frequently present and total loss of voice may occur.

Symptoms Due to Pressure on the Large Vessels.—Owing to pressure on the vessels and consequent impaired circulation, we often note headaches, tinnitus, epistaxis, cyanosis, and vertigo.

Constitutional Symptoms.—Constitutional symptoms due to hyperplastic or degenerative change in the intrathoracic goiter may be present. These, in addition to the serious symptoms due to pressure, aggravate very considerably the condition of the patient. The constitutional symptoms, referable to thyrotoxicosis, have already been described and need no further discussion here.

Objective Findings

The most constant symptom is the characteristic posture. The head is held forward but tilted slightly backward with the shoulders forward and slightly raised, increasing the curve of the upper dorsal and cervical spine. In the attempt to enlarge the upper thoracic aperture, the ribs are held rigidly upward. This position of the head and shoulders relative to the thorax is maintained constantly in an effort to relieve respiratory obstructure.

Marked dyspnea is often apparent; orthopnea may be present. Cyanosis of the face and neck is frequently noted. Some edema of the face, neck, and upper extremities may be seen. These signs, due to interference with the circulation, are a further indication of circulatory disturbance. Clubbing of the finger tips is sometimes noted.

A medusa head (dilated superficial veins of the chest and neck) is frequently noted. This is particularly true if the intrathoracic goiter is of long standing. In these instances the external and anterior jugulars are markedly dilated. The superficial mammary, epigastric, intercostal, and other veins are also enlarged.

The suprasternal notch is effaced. There may be slight bulging of the sternum; some ptosis of the larynx and restriction of the laryngeal movements are noted. The ptosis and restrictions in the laryngeal movements are of considerable clinical significance. Sometimes laryngeal movement is completely abolished, the larynx becomes immobile or fixed due to the dragging effect of a large goiter. This immobility or fixation is of importance in the differential diagnosis between intrathoracic thyroid tumor and other types of mediastinal tumors.

The auscultatory findings will vary greatly with the size and location of the tumor. In some instances there is definite bronchial breathing. In other instances, if a main bronchus is completely compressed, there may be total absence of breath sounds over the affected area.

The heart findings are often very definite and suggestive. Associated with intrathoracic goiter, we frequently note the condition termed the mechanical goiter heart. In addition to this condition we may note the cardiac finding, secondary to a thyrotoxicosis.

CHAPTER VI

DIAGNOSIS

CONSTITUTIONAL CHARACTER OF THYROID CONDITIONS

The surgeon is inclined to confine his attention to the thyroid tumor in the neck. He is apt to see in the thyroid swelling, merely an indication for surgical interference, and to overlook the fact that goiter is an indication of a constitutional disease. The internist on the other hand sometimes loses sight of the local pathology in his tense interest in the constitutional manifestations of the disease. Thyroid hypertrophy can no more be considered a local condition than can cardiac hypertrophy. The thyroid enlargement is an indication of a constitutional want, and, consequently, should be considered an indication of constitutional disease, or constitutional inferiority.

The so-called physiologic goiter is an indication of the presence of a deficiency stimulus to which, during those periods of life characterized by unusual stress and strain, the thyroid responds by hypertrophy. The chief manifestations of dysthyroidism are general and not local. Consequently, the surgeon should devote considerable study to the general constitutional trend, as well as to the thyroid swelling itself, while the internist should bear in mind the possibility of actual pathologic changes in the gland. To assure a diagnosis based on complete data, a careful analysis of the personal and family history should first be made. A general physical examination should follow, including a careful examination of the local condition of the neck.

CASE HISTORY

The importance of a detailed history cannot be overestimated. Discussion of the actual details will not be necessary here but time used in history taking is well spent, and will bear fruit a hundredfold. The use of a record sheet, designed for recording in brief form the data considered of importance in every case of thyroid disease, not only facilitates consideration of the results of the various examinations, but encourages uniformity of procedure and statistical study. The following outline has been used by us for several years.

GENERAL EXAMINATION

It is not necessary to discuss the procedure of a general physical examination. It is sufficient to say that in all goiter cases special attention should be directed to the cardiovascular system. The signs suggestive of

No._____

REGISTRATION BLANK

THE SLOAN CLINIC
BLOOMINGTON, ILL.

NAME_____ Date_____ 19____

Address _____

Family Physician_____ Address_____

Nearest friend_____ Address_____ Tel._____

Occupation _____ Age_____ Married or Single_____

Height_____ Weight_____ Date of marriage_____

Has your weight recently increased?_____ Or diminished?_____ How much_____

Ages of Children _____ Menses _____

Have any of your blood relations ever died of Heart Disease, Consumption, Cancer, Goiter, Stomach or Female Trouble?_____

Have you ever had Rheumatism, Difficulty in Breathing, Palpitation of the Heart, Fistula, Syphilis, Difficult Urination, Stricture, Ulcers, Varicose Veins, Appendicitis, Asthma, Epilepsy, Rupture, Diphtheria, Diabetes, Flu, Pneumonia, Scarlet Fever, Typhoid, Jaundice, Tonsilitis?_____

What other sickness, disease or injury have you ever had?_____

Have you ever undergone a surgical operation?_____ When?_____

For what?_____

Are there any defects or deformities of any kind?_____

History of present attack—time, cause, manner of attack, previous treatment. (Give description in your own way, briefly, but clearly)_____

Special Examinations

History
Physical Examination
Surgical Examination
Re-Examination
Eye, Ear, Nose, Throat
Biliary Drainage
Gastric Analysis
Bacteriological
Sputum—T. B.
Sugar Tolerance
Respiratory Tolerance
Basal Metabolism
Sp. Fluid

Gynecological
Rectal
Goiter
Obstetrical

X-Ray—Fluoroscope: Goiter, Heart
" Stomach
Part
Skiagraph: Part
Stomach
Complete Intestinal Tract
Kidney, Ureter, Bladder
Treatment
Part
Dose

Urological

Urine—Routine
Microscopical
Special

Kidney Function (Phenolsulph)

Blood—W.B.C., R.C.B., Diff.
Hgb.
Coag.
Wasserman
Widal
Chemical: Sugar, Non-Prot.
Nitrog. Urea
Uric Acid

General Examination by Dr._____

REMARKS:_____

Provisional Diagnosis _____

Advised: Operation_____

X-ray—Radium _____

Medical _____

Referred to_____ for_____

Final Diagnosis_____

Charge to_____

Responsible for Acc't_____

Referred by Dr._____

FIG. 21.—Registration (History) Blank.

goiter heart have already been discussed and, in the absence of other definite cardinal symptoms, will frequently confirm the diagnosis of thyrotoxicosis. Estimation of the blood pressure and examination of the blood are of value.

The usefulness and limitations of basal metabolic tests have already been discussed. Other diagnostic procedures are occasionally of some use in the differentiation of thyroid conditions. Prominent among these is the Goetsch (117) test. While the value of this test has undoubtedly been exaggerated, it has its field of usefulness.

EXAMINATION OF THE LOCAL CONDITION OF THE NECK

Technic of Examination

Inspection.—The patient should be seated on a revolving stool in a good light, opposite the examiner. Inspection will usually reveal any tremor, pulsations over the carotids, eye signs and definite thyroid enlargement which may be present. Note particularly whether the thyroid tumor moves with deglutition. The presence or absence of collateral circulation, bulging in the suprasternal notch, or pulsation of the vessels, should be noted. Inspection will also reveal valuable information as to the character of the swelling—whether there is a symmetry indicative of colloid or hyperplastic goiter, or an asymmetry suggesting primary or fetal adenomas or goiters which have undergone degenerative processes.

Palpation.—The technic of palpation varies with the examiner. Many surgeons prefer to carry out this procedure from the front, resting the hands and fingers on the shoulders of the patient, and palpating the thyroid with the thumbs. The writer secures better results by standing behind the patient, allowing the thumbs to meet over the cervical spine, placing the fingers of one hand on each side of the neck and pressing gently downward and backward. Palpation of the upper poles and isthmus is best managed by inclining the patient's head gently forward. Palpation of the lower poles is facilitated by requesting the patient to swallow or cough. A substernal prolongation may be noted and even the presence of an intrathoracic goiter may be recognized. If the patient is requested to cough or swallow while the neck is flexed anteriorly, palpation may reveal valuable evidence as to displacements of the trachea.

Palpation affords the best means of estimating the consistency of the thyroid and outlining its margins. The normal thyroid is soft and elastic. The colloid goiter is of approximately the same consistency, but at times gives a sensation approaching fluctuation. In the later stages, certain areas of the gland may become harder.

In thyroiditis the upper poles are sharp to palpation, and, as a rule, are easily outlined by the exploring fingers; the rigidity of the entire gland is evident to the experienced examiner.

In about half of the cases with thyrotoxicosis and no evident enlargement of the thyroid, the experienced examiner will recognize by

palpation that the gland is slightly nodular or that it is harder and perhaps more rigid than the normal gland. Often this increase in consistency is of as much clinical significance as is an evident increase in the size of the gland.

Pain and sensitiveness of the thyroid are only rarely encountered. If the patient complains of pain as the gland is being palpated, it is more often due to rigidity of the surrounding tissues than to tenderness in the thyroid itself. This sensitiveness of the surrounding tissues on palpation is usually present in the acute stage of thyroiditis or strumitis, in ligneous thyroiditis, in abscess of the gland, and in malignancy. Tenderness over the thyroid is often a transient symptom. It usually disappears as the acute inflammatory stage of thyroiditis subsides and is therefore absent at the time that thyrotoxicosis develops. Small goiters are often more sensitive to ordinary manipulation than large ones.

While on the subject of tenderness, it may not be amiss to speculate for a moment on the absence of pain in thyroid conditions. In no other group of diseases accompanied by such gross pathologic changes, inflammations, and degenerations, and complicated by severe systemic effect, is pain so seldom a symptom. Intrathoracic goiters, misplaced goiters, or very large goiters, may cause discomfort from pressure upon adjoining structures, but rarely give rise to pain. Abscess of the gland is occasionally accompanied by pain, particularly upon motion. Dull aching pain is sometimes present in the late stages of malignancy, after the malignant process has encroached upon the nerves. It is rather extraordinary, however, that the frequent inflammatory and degenerative processes of the thyroid are not accompanied by pain and it is probably owing to the absence of this symptom in the history that the occurrence of previous thyroid inflammation is not more frequently surmised.

As an outstanding exception to the absence of pain in thyroid conditions, the writer notes that slight pain or tenderness is a constant symptom of syphilitic thyroiditis. In fact, we have come to the attitude that goiter in the early stages, accompanied by pain, should always suggest the possibility of a syphilitic origin.

Mobility is more important from the point of view of surgical treatment than from the point of view of diagnosis. Palpation should determine more easily than inspection, whether or not the goiter follows the excursion of the larynx during deglutition. In the case of malignancy, owing to fixation to the surrounding structures, the up and down movement will probably be limited. It may also be difficult to elicit this movement in the case of a very large, or a substernal, or intrathoracic goiter. A substernal goiter may sometimes be palpated above the suprasternal notch during swallowing.

Mensuration.—There is no method of mensuration that can be considered thoroughly satisfactory. Owing to differences in the shape and size of the neck and variations in the location of the larynx and thyroid, mensuration by means of a tape measure is obviously unsatisfactory and indefinite. Measuring the breadth of the gland or the height of the lobes

by calipers or by other means is also subject to considerable error and the element of personal equation is of significance.

Considering the many variable factors, it is doubtful whether sufficiently accurate results can be obtained to justify an intricate system of mensuration. The writer believes that, both for private record and public health work, a simple plan of estimating the degree of thyroid enlargement should be adopted.

In the United States Public Health Department reports of thyroid surveys, Olesen grades goiters according to size, in the following manner:

(1) Very slight enlargement
(2) Slight enlargement
(3) Moderate enlargement
(4) Marked enlargement
(5) Very marked enlargement

Such a classification will be found satisfactory for average purposes.

Percussion.—Percussion is particularly useful in indicating the possible presence of a substernal or intrathoracic goiter.

Auscultation.—Auscultation over the carotids and over the thyroid in cases of hyperplastic goiter will often reveal the bruit characteristic of this condition. Auscultation may also serve to discover pressure on a large bronchus, which would suggest the existence of an intrathoracic goiter. Finally, auscultation may reveal the characteristic heart finding of thyrotoxicosis. It is an important factor, which may point the way to diagnosis of this condition, even in the absence of other cardinal symptoms of thyrotoxemia.

Laryngoscopic Examination

Laryngoscopic examination should reveal any twisting or displacement of the larynx or a possible deformity of the upper section of the trachea. It is also of value in disclosing evidence of disturbed function of the recurrent laryngeal nerve, such as the presence of partial paralysis of one or both vocal cords. Any disturbance of this important nerve may easily be attributed to faulty technic if the operator has failed to discover it preliminary to operation. Even if it is possible to show, subsequent to operation, that the nerve disturbance is functional and not due to operative injury, it is often difficult to convince the patient or the patient's family that the operator and the operation are not to blame for the condition.

X-ray Examination

X-ray examination should not be neglected. A fluoroscopic examination may reveal the presence of an intrathoracic or substernal goiter. It may show an aortic aneurism or constriction and displacement of the trachea; S-shaped curvature of the trachea is frequently observed. In case of toxic adenoma, a greatly enlarged cardiac shadow will frequently be seen. More important still, the fluoroscope will show the heart in action and give accurate visible evidence of its size, shape, and position.

SIMPLE COLLOID GOITER

The history is of importance. This type of goiter occurs most commonly in adolescence and sometimes during pregnancy. It is very common among school children in endemic areas. When occurring sporadically, the diagnosis may be more difficult.

Physical examination reveals a gland symmetrically enlarged smooth, and soft. Evidence of an underlying condition due to mineral deficiency is frequently noted. A school child, with moderate or extreme enlargement of the thyroid, may manage to keep up with his class work, but he is usually retarded and sluggish both in the athletic, and in the social phases of school life.

Simple colloid goiter complicated by strumitis makes it difficult to differentiate between this condition and diffuse hyperplastic goiter. The pulse rate may be accelerated and the basal metabolism rate may be slightly increased but the absence of other local or constitutional signs of hyperplastic goiter usually makes the differentiation clear.

NODULAR COLLOID GOITER

The diagnosis of nodular colloid goiter implies, of necessity, the previous existence of a simple colloid goiter. Physical examination reveals a gland fairly symmetrical, smooth, and well rounded. On inspection, the thyroid swelling presents all the appearance of a simple colloid goiter. Palpation, however, reveals greater solidity in the consistency of the gland. There is not that suggestion of a soft or fluctuant sensation that is felt in colloid goiter. In addition to the increased hardness, palpation determines the presence of small nodules, more evident in the upper poles than elsewhere.

The onset is gradual, as is to be expected when we consider that the nodular colloid goiter is, strictly speaking, merely a stage in the process of evolution of a simple colloid goiter into an adenomatous one. If it is possible to observe this course of development from the simple colloid, it will frequently be noted that, as the stage of nodular colloid is reached, the size of the gland is apparently decreased. Nodular colloid goiter is usually seen a little later in life than diffuse colloid goiter but is rarely seen after twenty-five. Constitutional symptoms are absent and the metabolic rate is a little below normal.

ATOXIC ADENOMA

The colloid type of multiple adenomas shows all stages of degeneration, from abnormal colloid storage to hyalinization and calcification. In an extremely large percentage of this type possibly 90 per cent, we find a history of the sequence—simple colloid, nodular colloid, small adenomas, and finally, multiple adenomas. Those in whom the typical history is lacking are frequently vague in regard to previous enlargement or other symptoms and, in most cases, the negative history is not conclusive.

It should be remembered that nodular colloid and multiple colloid adenoma represent different stages of the same condition. Multiple adenoma is more apt to be asymmetrical, for the adenomas in certain portions of the gland develop more rapidly than in other parts. Degenerative changes, including cyst formation, are more common than in the case of nodular colloid. The asymmetry and marked enlargement very frequently results in definite change of contour of the neck and occasionally some pressure symptoms are observed.

The diagnosis of multiple adenoma not of the colloid variety must be made from the history and the presence of the various types of tumors in the thyroid.

PRIMARY ADENOMA

The character of the onset and the history of the etiologic factors will usually determine this diagnosis. The onset is often sudden; frequently, as a result of septic, fat, or blood embolism, a localized swelling occurs in some portion of the gland, accompanied by symptoms of localized infection. A nodule remains after the swelling subsides. The onset may be noted in the course of some infectious process, such as septicemia following abortion, postpartum infection, or abscess of the lung. It may also follow fractures or operations. The history which shows an existing infectious process or a recent fracture or operation, followed by the sudden appearance of thyroid swelling accompanied by tenderness, in a previously normal thyroid, is characteristic. If (within the course of a few weeks) the swelling subsides, the tenderness on pressure disappears, and a smaller, more definitely circumscribed tumor remains, the diagnosis is confirmed.

There is another variety of primary adenoma in which the onset is more insidious. This type often develops during pregnancy or is associated with some other etiologic factor. The adenoma is due to the presence of persistent colloid distention in localized areas of the gland; its course is regular, progressive, and continuous, and it is liable to degenerative change. Definitely walled off cysts are rare in this type of primary adenoma, and, when they do occur, the increase in the size of the gland is neither so sudden nor so marked as in cases of primary adenoma due to embolism, in which cyst formation is common.

FETAL ADENOMA

Fetal adenoma is often first noted as a diffuse swelling of one lobe, or sometimes the isthmus; this swelling tends to localize in a definite palpable tumor of firm consistency. The tumor is round or ovoid, painless, and mobile. The thyroid in fetal adenoma is asymmetrical. The tumors when multiple, are sometimes found in both lobes of the thyroid, but they usually develop at different times in different locations. They are more frequently found in the lower pole, but may appear in any part of the gland. More often they are located near the anterior surface than in the posterior or lateral portions of the gland.

Fetal adenomas in early life are often situated in about the center of the gland. As enlargement occurs, pressure causes absorption of the overlying gland tissue, and the adenoma grows or is propelled to the surface of the gland in much the same way that a fibroid tumor makes its way to the surface of the uterus.

Fetal adenoma is differentiated from other adenomas by its onset comparatively early in life, its slow growth, the character of the mobile ovoid tumor, and finally, by the demonstrable fact that the tumor, by slow growth and resultant pressure necrosis of surrounding tissue, has made its way out to the surface of the gland.

DIFFERENTIAL DIAGNOSIS OF ATOXIC THYROID SWELLINGS

In the differentiation of these conditions, the history is of great importance. While the differentiation of atoxic thyroid swellings is of value and interest, it is more essential to be certain that a thyroid swelling is atoxic, than to determine the particular group of atoxic thyroid tumors to which the goiter in question belongs.

A simple goiter may digress from one class into another, and eventually develop symptoms of toxicity. During certain stages in the evolution of the disease, it is not only difficult to determine to what class of simple goiter the case belongs, but it is hard to know whether symptoms of toxicity are present. The chief conditions to be differentiated are cysts of the thyroglossal duct, sebaceous cysts, and fat.

Thyroglossal Duct Cysts.—The thyroglossal duct extends from the foramen cecum to the thyroid, but only as far as the isthmus. These cysts, which are due to a failure of the duct to close, are almost always located at a point in the neck above the thyroid and in, or near, the midline. They rarely extend down to the suprasternal notch.

Sebaceous Cysts.—Sebaceous cysts should cause no difficulty in diagnosis as they do not move with deglutition, and are more superficial than other types. They are more often found over the region of the carotid triangle than over the thyroid region.

Fat.—Adiposity, with large deposits of fat in the transverse supraclavicular fold, particularly in short necked people, may lead to an erroneous diagnosis of goiter. Careful examination will show that the mass of fat does not move with deglutition, and, if the muscles are relaxed, the normal thyroid may be felt beneath.

Thyrotoxicosis

The diagnosis of the different conditions due to thyroid dysfunction constitutes a field that is still rich in possibilities. Doubtless, as time goes on, refined laboratory procedures will simplify greatly the diagnostic difficulties now encountered in the recognition of the milder forms of thyroid dysfunction.

No one will experience any difficulty in the recognition of the typical case. It is in the atypical forms of thyroid disease that the diagnostician

will frequently find himself at sea. In such cases the physician will have to depend on experience and clinical judgment rather than on laboratory routine and instruments of precision. To the differential diagnosis of obscure thyroid conditions may be applied the phrase credited to the late John B. Murphy, "Cortical cells are of more importance than instruments of precision."

Metabolic Rate in Diagnosis

The value of basal metabolism tests has perhaps been overestimated. It is true that as a means of gaging operative risk, and from the point of view of prognosis in general, basal metabolism determinations are of considerable importance. The hope that they would prove to be an accurate means of measuring the degree of the thyrotoxemia and would be a dependable guide for the detection of abnormal thyroid conditions has not been fulfilled.

In the severe cases of hyperplastic goiter, the metabolic rate is greatly elevated; but in this type of case, clinical examination without recourse to laboratory procedure will reveal the nature of the disease. It is in the milder forms of the disease that basal metabolic estimations are of little or no value. The increase in the metabolic readings is so slight as to be without practical significance.

Some physicians place great importance on the results of the metabolic readings and will not diagnose a thyrotoxic condition in the presence of normal metabolic rate. Similarly, they will make a diagnosis of hypothyroidism on one or two metabolic readings, will immediately start thyroid medication, and report that after a few days the metabolic rate has returned to normal. Doubtless many such cases are accurately diagnosed, but it is also true that, in some instances, the alleged hypothyroidism is due to faulty technic in estimating the metabolic rate rather than to faulty thyroid function. When we consider the possible percentage of error that may creep into metabolic estimation, even in the hands of capable observers, we must be awake to the possibilities of mistake from this source and not be too dogmatic in the interpretation of the findings.

In view of the wide margin of error it is difficult to accept the belief of Kessel, Lieb, and Hyman (118) that a case should not be diagnosed as true hyperplastic goiter unless the metabolic rate is repeatedly and definitely elevated. We have no absolute proof that a disturbance of metabolism must be considered the first symptom, or the primary disturbance, in all cases. It may very well be that the condition or conditions, described as *autonomic imbalance* by Kessel, Lieb, and Hyman, really mark the first stage of hyperplastic goiter and that the rise in the metabolic rate is merely evidence that the disease is progressing beyond this stage.

It is hard to believe that a raised metabolism in itself could be the first development in hyperplastic goiter. An elevated metabolism is in the nature of an effect rather than a cause, and it is only natural to suppose that some working factor must have been operative and must have preceded the elevation in the metabolic rate.

It is only by this hypothesis that we can explain the many abortive or fruste types of hyperplastic goiter that undoubtedly occur. It is justifiable to make an analogy between tuberculosis, diagnosed exclusively on a positive sputum, and hyperplastic goiter, diagnosed exclusively on a raised metabolic rate. Do not the cases of tuberculosis with a positive sputum and the cases of hyperplastic goiter with raised metabolic rate really represent disease conditions that are no longer in their incipiency?

TOXIC ADENOMA

The diagnosis of thyrotoxicosis, associated with, or secondary to, adenomatous goiter, constitutes the diagnosis of toxic adenoma. The differential diagnosis between toxic adenoma and hyperplastic goiter will be discussed under differential diagnosis of hyperplastic goiter.

DIRECT DIAGNOSIS OF DIFFUSE HYPERPLASTIC GOITER OR GRAVES' DISEASE

The direct diagnosis is made on the history, the character of the onset, and the presence of all or some of the chief symptoms of the condition. These points have been covered in the chapter on Symptomatology and will be only briefly reviewed here.

History

Heredity has only slight influence. The history of hyperplastic goiter in another member of the family may help confirm the diagnosis in a doubtful case. A mild antecedent thyroiditis, which perhaps the patient will recall only as a little stiffness in the neck muscles, difficulty in swallowing and some pain and tenderness over the thyroid, should receive particular attention. A history of the chief symptoms (tachycardia, exophthalmos, nervousness, and tremor) is very significant—not so much of the onset of hyperplastic goiter, but of a hyperplastic goiter that has already been existent for some time.

Character of Onset

The very vagueness of the early symptoms is often significant; no one symptom is sufficiently developed to be extremely obvious. Definite sequence is marked by a gradual, but steadily progressive change in the patient. The barely noticed palpitation, the nervousness without a cause, the tachycardia without a heart lesion, the loss of weight without apparent reason, the insomnia without basis, all appearing consecutively and without pain or worry; the gradual psychic changes, the talkativeness, the emotionalism, the exaltation and depression, completely change the character of the individual. It is the ensemble of a changed personality with slight, indefinite, apparently inexplicable physical ailments, that draws the attention to the possibility of an early hyperplastic goiter.

Characteristic Symptoms

If all or most of the chief symptoms are present no one will experience difficulty in making the diagnosis. No clinical picture is more definite or clear-cut than the well-developed, typical case of hyperplastic goiter. It is even more characteristic than the picture of far advanced tuberculosis, and, once seen, is not soon forgotten.

The characteristic symptoms on which a diagnosis of diffuse hyperplastic goiter is based are: *tachycardia, increased basal metabolism, tremor, loss of weight, thyroid tumor, and exophthalmos.*

It is the exception rather than the rule to find all these cardinal symptoms present at the same time. Frequently a diagnosis must and readily can be made on the presence of two or three of the leading symptoms. While there is no question of differential diagnosis in a typical case of this disease, there are atypical forms that are easily confused with many other conditions, and a brief résumé of a few of these conditions with some differential points may be of interest.

DIFFERENTIAL DIAGNOSIS OF DIFFUSE HYPERPLASTIC GOITER

Autonomic Imbalance

Some writers, particularly Kessel, Lieb, and Hyman (118), emphasize autonomic imbalance as a distinct clinical entity. This condition may present all the signs and symptoms of a hyperplastic goiter with the sole exception of a raised metabolic rate. With the onset of a definitely elevated metabolism, the case of autonomic imbalance becomes a case of hyperplastic goiter. To the writer this distinction seems to be made between two stages of the same disease rather than between two different conditions. Consequently, it does not seem logical to attempt a differential diagnosis between autonomic imbalance as such and hyperplastic goiter, a condition which is always preceded by autonomic imbalance.

Simple Thyroid Enlargement

It may seem, at first glance, that there is not much possibility of confusing simple thyroid enlargement with diffuse hyperplastic goiter. In certain cases of simple goiter, particularly at puberty and during pregnancy, there may be considerable similarity between the two conditions. At puberty, and in some individuals in pregnancy, there is noticed some nervousness, palpitation, tachycardia, flushing, and occasionally a slightly raised metabolism. There may be at times even a suggestion of the stare of a slight exophthalmos. Sometimes there are mental and psychic changes, very suggestive of hyperplastic goiter.

Careful study of the history and detailed examination will usually clear up the case. The goiter may be of long standing and not reveal the bruit and the extreme vascularity of the gland noted in diffuse hyperplastic goiter. Loss of weight with increased appetite, which is rather characteristic of hyperplastic goiter, is absent. The increase in metabolic

rate is mild, and never reaches the level seen in a developed case of hyperplastic goiter. This feature, however, cannot be emphasized as of diagnostic significance, for in many cases of hyperplastic goiter the basal metabolism is only moderately elevated; if the cases are seen during a period of remission, the basal metabolism may even be found to be normal.

It must be remembered that a case of simple goiter during the strain and stress incident to puberty or pregnancy, may develop a fruste type of hyperplastic goiter subsequent to a mild infection. The case of simple goiter which, during periods of strain, shows symptoms that are very suggestive of the milder forms of this disease—even including a slight exophthalmos—can hardly be explained on any other hypothesis.

Toxic Adenoma

This is one of the conditions that is most frequently confused with diffuse hyperplastic goiter. According to some writers the two conditions, diffuse hyperplastic goiter and toxic adenoma, are identical. We agree that the toxemia encountered in a large percentage of toxic adenoma cases is the same as that encountered in all cases of diffuse hyperplastic goiter. There are, however, a sufficient number of differential points to justify us in classifying them as separate conditions. There are differences also from the point of view of prognosis and treatment which necessitate a separate classification for each condition.

A few of the differential points between toxic adenoma and primary diffuse hyperplastic goiter may be listed as follows: The onset of toxic symptoms in the case of toxic adenoma usually occurs many years after the presence of an adenoma has first been noted: in the majority of instances of primary hyperplastic goiter, symptoms of thyrotoxicosis precede the enlargement of the gland and, in almost all cases, are definitely developed within six months after the thyroid tumor has been observed. The goiter in toxic adenoma is larger and usually nodular, asymmetrical, and more irregular than the goiter in diffuse hyperplastic goiter while in the latter the thyroid tumor is symmetrical, compressible, and reveals the characteristic bruit. The heart changes in toxic adenoma tend more towards myocardial degeneration and show more tendency to become permanent. Increase in blood pressure is not unusual. In hyperplastic goiter, a lowering of the diastolic pressure and slight, if any, rise in systolic pressure is noted with consequent increase in pulse pressure. The loss of weight in diffuse hyperplastic goiter is usually much more striking and rapid than in toxic adenoma. The exophthalmos and stare, characteristic of established diffuse hyperplastic goiter, are quite rare in toxic adenoma. Some authorities assert that eye findings are never noted in toxic adenoma. This view seems extreme. The writer has seen definite eye signs in a small percentage of cases that were unquestionable cases of toxic adenoma.

The course of the disease is also different in the two conditions. The crises characteristic of diffuse hyperplastic goiter are not often seen in cases of toxic adenoma. The course of toxic adenoma is less stormy; it

progresses insidiously and usually with much greater damage to the cardiovascular system than in the case of diffuse hyperplastic goiter. Frequently, by the time the patient with toxic adenoma reaches the surgeon, the heart and vessels have been sufficiently damaged to make the results of operation doubtful in the extreme. The fine fibrillary tremor noted in cases of diffuse hyperplastic goiter is usually slight or absent in toxic adenoma. The basal metabolism in toxic adenoma rarely reaches the extremely high level noted in severe cases of diffuse hyperplastic goiter. This distinction is of no avail in the individual case, as, in a few toxic adenoma cases, the basal metabolism rate is moderately high and, in some cases of hyperplastic goiter the basal metabolism is only moderately elevated.

Pulmonary Tuberculosis

Atypical cases of hyperplastic goiter are frequently diagnosed as pulmonary tuberculosis. The differentiation between these two conditions is extremely important and sometimes difficult. Appreciation of the possibility of the presence of atypical toxic goiter will cause it to be recognized.

Addison's Disease

The great muscular weakness and pigmentation of Addison's disease occasionally give cause for confusion with hyperplastic goiter. The pigmentation in Addison's disease is more marked and more generalized. The eye findings of hyperplastic goiter are lacking. The basal metabolic rate is not increased, the weakness is more marked, and the downward course of the disease is more definite. The absence of tachycardia in Addison's disease should prevent an error in diagnosis.

Neurasthenia

Neurasthenia shows many of the symptoms characteristic of hyperplastic goiter. The neurasthenic is emotionally unstable and complains of gastro-intestinal disturbance, insomnia, languor, and occasionally, of loss of weight. She frequently displays tremor, but it is not the fine, rapid tremor of hyperplastic goiter. The exultation and talkativeness, characteristic of hyperplastic goiter, are also lacking. The psychic disturbance tends more towards melancholia. The basal metabolic rate is usually unchanged, or at least is not consistently elevated on repeated estimations. The increased pulse pressure of hyperplastic goiter is not noted. The tachycardia is not persistent and is less noticeable in the morning after a night's rest. This is in contradistinction to the persistent tachycardia of hyperplastic goiter which is little changed by sleep or digitalization.

Hysteria

In hysteria, at times, there are mental changes suggestive of hyperplastic goiter. There is emotional lability, obstinacy, perverted appetite, and restlessness. In addition, there are the pseudoparalysis and abolished

pharyngeal reflexes, characteristic of hysteria. The tremor, when present, is more coarse; the heart action is normal, or only slightly increased in rate, and is decreased by repose. The hysteria is amenable to suggestion. It is more frequent to diagnose a case of hyperplastic goiter as hysteria than to make the reverse mistake. The vagueness of the symptoms in hyperplastic goiter, the restlessness without a cause, the insomnia, the crying spells, the emotional change, are suggestive on superficial examination of hysteria. The raised metabolic rate, the vascular thyroid, the persistent tachycardia, and the loss of weight will make the diagnosis.

Cardiac Conditions

While a case of typical primary diffuse hyperplastic goiter cannot, in itself, be confused with cardiac disorders of other origin, it is nevertheless true that certain cases of hyperplastic goiter, in which the toxic symptoms are more or less submerged and in which the cardiac symptoms predominate, are sometimes treated as cases of primary heart disease. It may not be possible always to avoid this mistake for the patients are frequently seen late, after decompensation has occurred, and severe cardiac symptoms so dominate the picture that the thyrogenic origin of the condition escapes recognition. The exophthalmos and other eye symptoms may be slight or absent and the thyroid may show very little enlargement. Often, the only symptom that should draw attention to the possibility of the presence of thyrotoxicosis is a tachycardia that persists notwithstanding digitalization.

Malignancy of the Thyroid

Thyroid malignancy occurs at a more advanced age than hyperplastic goiter. In malignancy the thyroid tumor is less mobile or even definitely fixed. The surrounding tissues are infiltrated. Metastases and secondary glandular involvement are usually late symptoms but may appear early. Symptoms of thyrotoxicosis occasionally occur in the course of the malignancy, but they are seldom severe and the metabolic rate, as a rule, is not appreciably changed. It is usually in an adenoma of long standing that malignancy occurs. A sudden increase in size of an adenoma, with some pain and difficulty on swallowing, in a patient advanced in years, should draw the attention of the observer to the possibility of malignancy.

Syphilis of the Thyroid

Syphilis of the thyroid, either secondary or tertiary, should not cause much difficulty. The history of an initial lesion, the presence of secondary or tertiary lesions elsewhere, and the positive Wassermann should establish the diagnosis.

Diabetes

In diabetes, as in hyperplastic goiter, we note an increased appetite with loss of weight, muscular weakness, nervousness, depression, and polyuria. Glycosuria, a characteristic symptom of diabetes, is not in-

frequently present in hyperplastic goiter. The glycosuria, however, is constant, more pronounced and accompanied by hyperglycemia in diabetes, but intermittent and mild with no increase in blood sugar in hyperplastic goiter. The metabolic rate is only slightly elevated in the early stages of diabetes and is later decreased; in hyperplastic goiter, the increasing metabolic rate is constant. Loss of energy is an early and characteristic feature of diabetes, and muscular weakness of hyperplastic goiter. Tachycardia, tremor, and eye symptoms are pronounced in hyperplastic goiter and absent or mild in diabetes.

Acute Surgical Conditions in the Abdomen

During the crisis of diffuse hyperplastic goiter, the severe gastrointestinal symptoms may be suggestive of acute surgical conditions in the abdomen. The intense nausea and vomiting, abdominal tenderness, and prostration may at once suggest an obstruction or an acute inflammatory abdominal condition. However, distension and rigidity are usually absent; constipation is not present, and there is no leukocytosis.

The temperature frequently noted in the crises of hyperplastic goiter may be an additional confusing factor. A careful history will probably show that the patient has been ill for three months or more with progressive loss of weight, and has complained of palpitation, nervousness, insomnia, and dyspnea; careful physical examination may show a moderately enlarged vascular thyroid, tachycardia, possibly some eye signs, and if an estimation of the basal metabolism is possible, it will usually be found that the rate is greatly increased.

Chronic Alcoholism

Chronic alcoholism in a comparatively young subject may develop a picture suggestive of hyperplastic goiter. This is due to the emotional lability, irresponsibility, and lack of moral control that characterize certain cases of hyperplastic goiter. Occasionally, particularly in male subjects, these two conditions may be associated.

While tremor, tachycardia, emotional lability, and insomnia are often found in alcoholism, this condition may be differentiated from hyperplastic goiter by the absence of eye symptoms, an increased metabolic rate, and enlargement of the thyroid gland. The tremor in alcoholism is coarse and slow compared to the rapid, fine tremor of hyperplastic goiter; the pulse rate is changeable, especially as it is decreased in the morning, as compared to the almost constant tachycardia of the latter disease.

Paroxysmal Tachycardia

This condition, as far as the pulse findings are concerned, may, during an exacerbation, resemble hyperplastic goiter. There is, however, a history of good health between the paroxysms of tachycardia. The absence of enlargement of the thyroid, and rise in the metabolic rate should make the diagnosis.

Gastritis

Cases of hyperplastic goiter in which nausea, vomiting, and abdominal distress were the prominent symptoms, have been diagnosed as gastritis and valuable time lost in instituting treatment for the thyrotoxicosis.

Insanity

In some cases of hyperplastic goiter, particularly of the acute type, syndromes, suggestive of the major psychoses, may be observed. There may be delirium, mania, or symptoms of dementia praecox. Psychoses may occur coincidentally with hyperplastic goiter. It is reasonable that in some instances patients suffering from hyperplastic goiter, with its tendency to psychic disturbance, will, during the progress of the disease, develop insanity.

Pernicious Anemia

The extreme weakness, the tachycardia, the dyspnea, and cardiac disturbance of pernicious anemia may be suggestive of hyperplastic goiter. Examination of the blood smear will make the diagnosis.

Chlorosis

Young girls with chlorosis may present a moderate enlargement of the thyroid gland. Nervousness, tachycardia, amenorrhea, palpitation, and dyspnea on exertion may be associated with this enlargement. The low hemoglobin index and the negative response to iodin and thyroid therapy will establish the diagnosis.

Menopause

The nervous phenomena of the menopause, the hot flashes, the mental anxiety, and the insomnia, which are often noted at this period may suggest hyperplastic goiter. The situation may be peculiarly confusing if the patient has a simple adenoma. Prolonged observation and repeated estimations of the metabolic rate may be necessary before a diagnosis can be reached.

Dysentery

Occasionally a case of hyperplastic goiter is diagnosed during a crisis as dysentery. The diarrhea and gastro-intestinal disturbance are responsible for this error. Other symptoms of hyperplastic goiter will be noted on close observation and no specific organisms will be found in the stool.

Formulation of the Diagnosis

In the formulation of the diagnosis better results are obtained by following some definite plan of procedure. In our clinic the complete diagnosis is formulated from a consideration of the determinations made under the following headings:

1. The presence or absence of goiter
2. Type of goiter present
   - Simple Colloid
     - (Adolescent Goiter)
     - (Goiter of Pregnancy)
     - (Endemic Goiter)
   - Non-Toxic Nodular Colloid
   - Non-Toxic Multiple Adenomata (Nodose Goiter)
   - Non-Toxic Fetal Adenoma
   - Toxic Nodular Colloid
   - Toxic Multiple Adenomata
   - Toxic Fetal Adenoma
   - Primary hyperplastic goiter or Graves' Disease
   - Intrathoracic and misplaced goiters
   - Inflammations
   - Degenerations
   - Malignancy
3. Stage of development (early, advanced, late)
4. Severity (mild, moderate, severe)
   - Non-toxic—as measured by cardiovascular changes, pressure symptoms and visceral damage
   - Toxic—Degree of intoxication as measured by cardiovascular symptoms, basal rate, physical examination and visceral damage
5. Complications
   - Cardiovascular
   - Renal
   - Mental
   - Gastro-intestinal
   - Hypertension
   - Valvular conditions
   - Any concurrent disease as:
     - Syphilis
     - Diabetes
     - Anemia
     - Tuberculosis
     - Abdominal or pelvic disease

CHAPTER VII

PROGNOSIS

Considering prognosis from the standpoint of the goiter problem as a whole, what does the future hold, in the way of threat or promise, regarding the menace of goiter to the community? To date, as a nation, we have escaped to a large extent the unwelcome results of thyroid dysfunction which tend towards race deterioration. The curse of cretinism and cretinoid degeneration has touched us very lightly. But the future will not hold similar immunity from these conditions if the increase in the incidence of goiter is not checked.

Statistics show an annual increase in the number of deaths from cardiovascular disease. There is much evidence to show that the mortality rate from this cause can be materially reduced by the early recognition and proper treatment of thyroid disease.

In the individual case the prognosis, to be of practicable value as a basis for the proper management, must include the prognosis **without** treatment as well as that **with** treatment. The **difference** between the two constitutes the chief indication for treatment.

SIMPLE COLLOID GOITER

Factors Influencing Prognosis

We are apt to consider the outlook for simple colloid goiter in too sanguine a manner. It is true that in many cases, particularly in children, the goiter disappears spontaneously, yet we cannot guarantee a spontaneous cure in every case. Colloid goiter is not physiologic; it is a compensatory hypertrophy to meet a deficiency. It is usually seen in periods of stress or strain such as puberty, adolescence, and pregnancy, and prognosis will be influenced by certain definite factors.

It is possible that a deficiency, which we think is general, may be corrected by a fortuitous change to a diet richer in iodin and other minerals. In such a case, the goiter will disappear and the patient will undergo a "spontaneous cure," which is not truly spontaneous. The "cure" must be attributed to the correction of a mineral deficiency, resultant on higher mineral intake in the food. The correction and cure are brought about in exactly the same way as though the proper dosage of iodin had been therapeutically administered.

Epidemics of simple goiter occurring in restricted areas may be similarly prognosticated. If temporary etiologic factors are overcome, the majority of the goiters will disappear spontaneously. In two such epidemics among school children that came under the notice of the writer,

the incidence of goiter was reduced by 65 per cent within two years after the nutritional supply was improved.

In other instances the "cure" may be explained on other grounds: the patient, having passed the critical period of stress or strain, or having overcome the effects of some intestinal derangement, may become able to assimilate the elements necessary for a relative increase of thyroid hormone. The thyroid, relieved of the deficiency urge, reverts to normal size.

Some colloid goiters will not revert to the normal state. There must always remain an element of doubt which prevents us from giving a uniformly good prognosis in all cases of simple colloid goiter.

The period of time over which a goiter has been present is of importance in forming the prognosis. Other factors being equal, the longer a simple goiter has been present, the poorer the chance for a complete return to normal. A series of cases in the writer's experience illustrates the importance of the duration factor. The first group comprised the patients who had been suffering with simple colloid goiter for more than a year when they came under observation. In this group the obvious enlargement of the gland disappeared within two years in 14 per cent of the treated cases and in 2 per cent of the untreated cases. In the second group, the patients with goiter of less than one year's duration, 91 per cent of those with treatment and 37 per cent of those who refused treatment, made complete recoveries.

Reduction in size of a goiter must not be considered a cure; as a matter of fact, reduction in size which is accompanied by formation of nodules is an unfavorable symptom. Very large goiters seldom completely revert to normal. These large glands, distended with colloid to an extreme degree, are also more liable to toxicity. The small goiter that shows even slight evidence of asymmetry or irregularity in outline also offers a poor prognosis as far as complete return to normal is concerned. As a general rule, the principle may be formulated that the longer the duration of the goiter, the worse the prognosis.

The prognosis is unfavorably influenced by many associated conditions. Chief among these is a history of a high incidence of goiter or other endocrine disorders in the family.

According to our experience simple goiter is quite apt to persist in girls who suffer from delayed or scanty menstruation. This type of goiter also persists in a large majority of obese patients with low metabolic rates; those that do return to normal, do so very slowly.

The smooth simple goiter occurring during the early months of pregnancy is more amenable to treatment than that occurring during the later months. If the goiter has been present in a previous pregnancy, the prognosis, for return to normal, is poor.

Prognosis Without Treatment

Simple colloid goiters of small size and of recent appearance disappear without treatment in 60 to 70 per cent of the cases except during

endemics. Those that appear at puberty are more likely to disappear spontaneously than those that appear in childhood or in adolescence. In those that appear after maturity, the incidence of spontaneous complete disappearance is not more than 20 per cent. The chances that the goiter will disappear spontaneously are lessened by extreme degrees of enlargement, unfavorable environment, and a high incidence of simple colloid goiter in the family or in the community. Large goiters rarely disappear; the colloid degeneration, at least in some areas, persists. During endemics the percentage of spontaneous recovery is only 20 to 30 per cent.

The prognosis in the case of endemic goiter is changed for the better if the patient leaves the goitrous district, and is more influenced by the institution of treatment than is sporadic goiter.

Prognosis With Treatment

The improved prognosis of simple colloid goiter under treatment is demonstrated well in Marine's (119) excellent therapeutic experiment in the public schools of Akron, Ohio. He made his observations over a long period of time on two large groups of children. To one group he gave sodium iodid; the other group remained untreated. Of the 1182 children with thyroid enlargement who took the iodin, 773 showed definite decrease in the size of the thyroid. Of the 1048 children with thyroid enlargement who did not take the sodium iodid, only 145 showed improvement. This would point to the fact that not all colloid goiters respond to iodid treatment even though there is reason to believe that the thyroid enlargement is due to mineral deficiency.

The goiter of puberty occasionally shows that there is, even early, some constitutional as well as local disturbance. The patient complains of tachycardia, a little restlessness, dyspnea on exertion, and is overemotional. Properly treated, this type of goiter usually returns to normal within a year. Not infrequently however, the nervousness, emotionalism, and other symptoms increase and the patient is soon definitely on the road to thyrotoxicosis.

If proper medical treatment is instituted within three months of the appearance of the thyroid enlargement, the incidence of complete recovery in colloid goiter can be raised to 90 to 95 per cent. The prognosis is dependent upon the early recognition of the condition and the institution of appropriate medical treatment before the gland has become greatly enlarged. If the enlargement has been present for six months or more the prognosis is less favorable; even a moderate sized goiter which has been present for nine months or more rarely disappears completely. In some instances, despite all treatment, the goiter persists and changes in size from time to time—particularly during periods of menstruation or during pregnancy—and finally undergoes nodular and degenerative changes. The prognosis therefore should be guarded in every case of simple goiter, particularly during puberty or pregnancy.

NODULAR COLLOID GOITER

The variety of nodose goiter that we call nodular colloid goiter represents the first step in the degeneration of the simple colloid goiter and consequently offers a poorer prognosis. It is the second stage in the course of a persistent, simple, smooth, diffuse, colloid goiter. Definite degenerative change has already taken place in the thyroid tissue and consequently it can hardly be hoped that medicinal, dietetic, or hygienic treatment can have much influence in restoring the normal structure of the gland. The nodules may be expected to increase in size and to coalesce forming larger ones.

Toxicity develops in this type of goiter more frequently than in the diffuse colloid type. However, a nodular colloid goiter may remain practically stationary for years and may give little trouble, except possibly from pressure symptoms. The best prognosis in nodular colloid goiter is offered by medical treatment followed at the appropriate time by surgery.

ADENOMATOUS COLLOID GOITER

The so-called multiple colloid adenoma, a later stage of colloid goiter, offers, without surgical intervention, a still poorer prognosis. In this type of goiter, the nodes or adenomas have attained a considerable size and the chances of toxicity are much increased. The immediate prognosis in cases of atoxic type is not poor. In the absence of toxicity, the patient may go through many years and even through life with good health.

Until such time as toxicity appears, the disadvantages or dangers are mechanical rather than systemic, and neither cosmetic nor mechanical considerations play a great rôle in casting the horoscope of a patient suffering with adenomatous goiter. In estimating the prognosis, the threat of possible toxicity at a later date is of much greater import. The sword of Damocles is ever hanging over the head of the patient with well-developed adenoma. In our experience over 70 per cent of the patients with this type of goiter develop symptoms of toxicity sooner or later; there are few who do not develop them within fifteen or twenty years of the time that the thyroid swelling is first observed.

Prognosis, as to cure, in this type of goiter, under medical or expectant treatment alone, is of course hopeless. With timely surgical treatment, however, the prognosis is excellent.

TRUE AND FETAL ADENOMA

What has been said of adenomatous colloid goiters applies as well to true and fetal adenomas. While true adenomas are not so likely to undergo retrogressive changes as the adenomatous colloid types, the prognosis without surgical intervention is just as unfavorable. In this type of adenoma, as well as in fetal adenoma, prognosis with surgical removal is excellent.

TOXIC ADENOMA

FACTORS INFLUENCING PROGNOSIS

After the adenoma has become toxic, what is the prognosis? Is it better or worse than that of diffuse hyperplastic goiter or are the conditions identical and to be considered as such?

To answer the second question first, we believe unquestionably that each of the two conditions has its own specific prognostic outlook with features specifically its own.

Speaking first in generalities, it is safe to say that the prognosis as to complete restoration to health should be guarded in every case of adenomatous goiter with toxicity of long standing. If we could determine in each case the duration of the toxicity, we would have a much firmer foundation upon which to build a sane prognosis. The duration of the toxicity is important both from the therapeutic and prognostic angle.

In formulating a prognosis in a case of toxic goiter we must have in mind the following considerations:

(a) The duration of thyroid enlargement and the known duration of toxic symptoms
(b) The type of toxic adenoma present
(c) The amount of demonstrable visceral injury present
(d) Complications
(e) Age

We must next compare the prognosis with medical or expectant treatment against that with surgical treatment.

Duration

From the histories we obtained in a series of 1300 patients with toxic adenoma, the average known duration of the adenomatous goiter prior to the onset of the thyrotoxemia was seven years and three months. Conditions that were apparently the sequellae of mild intermittent thyrotoxemia of long duration were present in many of these cases that had only recently been diagnosed as toxic. In no case in which the adenomatous goiter had been present for more than five years were cardiovascular symptoms absent. A history was given of more than four months of non-surgical treatment by 834 of these 1300 patients. In 114, the occurrence of a reduction in size of the goiter was reported but in no case was credible evidence of an alteration of the course of the disease presented. As has already been stated, the longer the toxicity has been operative, the worse the prognosis. Early diagnosis is the ruling consideration; the chances for complete restoration to health are dependent on the timeliness of the diagnosis, while the amount of permanent visceral damage will vary directly with the tardiness of the diagnosis.

The prognostic features in each type of toxic adenoma in the following classification are different and will be discussed separately:

The cardiovascular group
The anaphylactic group
The hyperplastic group
The mixed group

Cardiovascular Group

From the point of view of subjective symptoms alone, many patients in a cardiovascular group seem to offer an excellent prognosis; as a matter of fact it is only on the evidence of cardiovascular degeneration, objectively determined, that a true prognosis may be based. The results of surgery in our own series of cardiovascular cases have demonstrated that it is in this type of case that early diagnosis is particularly essential. In those instances in which operation was postponed until the most favorable time had passed, the myocardium had sustained permanent damage and complete recovery was not to be expected. It is true that in many of the patients an undoubted improvement took place after thyroidectomy, yet, to be in a position to promise a practically complete restoration to health, early operation is absolutely necessary.

Anaphylactic Group

In a series of 3455 cases of toxic adenoma we were able to classify 514 in the anaphylactic group. The chief interest in this group was our observation that the course and the prognosis were often markedly influenced in an unfavorable direction by the administration of iodin injudiciously given. In 187 of these cases acute toxic symptoms were first noted subsequent to the administration of iodin. In 146 other cases an already existent thyrotoxicosis was intensified by iodin. On the whole we estimate that, with surgical treatment the prognosis in this type of case is better than in the cardiovascular type.

Hyperplastic Group (Secondary Basedow)

In this type of case the patient is aware of the existence of the goiter and on the appearance of the toxic symptoms usually seeks relief.

Results obtained with 647 cases in a series of 3455, in which the thyrotoxemia had appeared after the adenomatous condition, suggest that with early diagnosis and prompt surgical relief a good prognosis is justified.

Mixed Group

The multiplicity of symptoms presented by patients in the mixed group would suggest a poor prognosis. Experience has shown, however, that in this group of cases the chances for ultimate recovery are better than in the cardiovascular group. The prognosis as regards operative mortality is better than in the hyperplastic group. As in the other groups, for a good prognosis, early diagnosis and prompt treatment are requisites.

Visceral Damage.—The intensity of the toxemia as indicated by the basal metabolism rate is not very valuable in estimating the prognosis in the usual case of toxic adenoma. The amount of visceral damage is of more importance. This is best determined by physical examination, blood pressure estimation, cardiograms, x-ray and fluoroscope, and laboratory procedures.

Age.—As a general rule, the older the patient the older the adenoma, and the less favorable is the prognosis. Some of the worst cases which we have seen have been old women who had had goiter "all their lives"; had been ailing for years, and had neglected to summon medical aid until a particularly "bad spell" brought them to the doctor.

In the cases observed in our clinic, toxicity (determinable) developed at the average age of thirty-seven. Youth, however, is no protection against a severe course in a case of toxic adenoma. In our series, forty-eight patients, many of them severely toxic, were under twenty.

PROGNOSIS UNDER DIFFERENT TYPES OF TREATMENT

The prognosis of atoxic adenoma is not good, by any means. The patient is constantly menaced with the possibility of toxicity. With the actual development of toxicity, the outlook is more threatening. There is much evidence to show that there is very little that we can do in a medical way for the patient with toxic adenoma except as a preoperative measure. The prognosis of the average case of toxic adenoma under medical treatment is unquestionably poor and the prognosis will be improved only in proportion to the promptness of surgical intervention. The prognosis with surgical treatment, however, is excellent. In no other class of cases are satisfactory results so often obtained as in toxic adenoma cases.

DIFFUSE HYPERPLASTIC GOITER

In estimating the prognosis, we must bear in mind that this condition is a chronic disease subject to severe exacerbations. The outlook may appear quite different, depending on whether we see the patient during a quiescent interval or during an exacerbation. We must not only consider the degree to which the patient is affected at the time of examination, but must also take into account the length of time he has been suffering from the disease, and whether or not it has left any indelible marks on his physique. We must consider too what the future, with or without surgical intervention, holds for him; we must judge whether the disease has practically burned itself out and has placed him on the road to the so-called spontaneous cure, or whether the most stormy phase of the disease still confronts him.

Acute Type

In some cases the disease is acute from its onset and is attended by no remissions. The extremely great hazard consequent to operation, contra-indicates major operative procedures. A gastro-intestinal disturbance that prevents the maintenance of a high degree of nutrition usually complicates and makes medical or expectant treatment very difficult. If the gastro-intestinal efficiency will permit of a high caloric intake, the outlook for the patient is more favorable. The prognosis is usually grave whatever the treatment.

The Chronic Form

In the usual or chronic form the prognosis is quite favorable with surgical intervention; with expectant treatment it is variable, though most frequently poor. In any case of diffuse hyperplastic goiter, or Graves' disease, the prognosis should always be guarded. We are too often inclined to consider as cured a patient who by operation or otherwise is relieved of most of the distressing symptoms. We are apt to overlook the fact that residual damage persists. May we then speak of a complete "cure" in a well developed case of Graves' disease?

The course and prognosis of hyperplastic goiter is analogous in some respects to pulmonary tuberculosis. In both of these diseases the possibility of permanent cure may be questioned. Though the tuberculous patient may be apparently well and able to return to his work without discomfort, there remains the possibility that the disease is merely arrested. Clinical experience has shown that many of these arrested cases break down when subjected to any unusual stress or strain. Is it not reasonable to place the patient who has been afflicted with a well-developed case of hyperplastic goiter in a similar status? Although the patient may be symptomatically and subjectively well, after a technically efficient thyroidectomy, there remains in almost every case a certain amount of residual visceral damage. In the milder forms of the disease, the chances of permanent visceral change remaining after an efficient subtotal thyroidectomy are greatly reduced.

FACTORS INFLUENCING PROGNOSIS

Degree of Development.—We may include with the mild types offering a favorable prognosis the many individuals who suffer from abortive forms of thyrotoxicosis which may never have been diagnosed. In individuals with the so-called hyperthyroid temperament, the outlook with regard to average health and life expectancy is good. These hyperthyroids, although they are excitable, over-active, restless, and given to psychic explosions, manage as a rule to accommodate themselves to their environment.

The outlook in the fruste forms is similarly quite favorable; many cases of this type go unrecognized. The undeveloped or evanescent form of Graves' disease frequently noted in girls at puberty subsides quickly as a rule and the patient may never again be troubled with symptoms of hyperthyroidism. Many of these cases diagnosed as fruste are in reality cases in the very early stage of hyperplastic disease and this possibility should be kept in mind when rendering a prognosis.

Antecedent or Coexisting Disease.—We often fail to realize how greatly the prognosis in goiter is influenced by preceding or coexisting diseases. We have repeatedly seen patients who failed to be completely relieved after thyroidectomy but made satisfactory recovery as soon as diseased tonsils, appendix, or gallbladder were removed. A focus of infection seems, at times, to be a considerable factor in stimulating activity or even provoking exacerbations. This is particularly true of influenza.

Experience has shown us that patients with goiters of the hyperplastic type, when attacked by influenza, usually react most unfavorably; too often such a combination proves fatal. Similarly, when thyroid disease follows influenza, it usually manifests itself in a very severe form. Any association of these two diseases speaks for a very grave prognosis.

Although tuberculosis is usually a serious complication, it sometimes happens that mild cases of Graves' disease, when associated with tuberculosis, may be benefited or even arrested as a result of the routine rest and hygiene applicable to the treatment of tuberculosis.

Diabetes mellitus occurs as a complication in only 3 to 5 per cent of the cases of diffuse hyperplastic goiter and in these the prognosis is very unfavorable. While the definite association of these two diseases is rare, the transitory or alimentary glycosuria noted in this disease is often mistaken for a true diabetes, and, if the patient is placed on a diet suitable to diabetes, the prognosis will be very unfavorably influenced.

Pregnancy.—Spontaneous abortion or premature labor is not an infrequent occurrence in the more serious cases of hyperplastic goiter. It is safe to say that most cases of hyperplastic goiter are aggravated by pregnancy. While the prognosis for both mother and child is unfavorable, it may be improved by thyroidectomy performed before the fourth month of pregnancy.

Personal and Constitutional Factors.—Hyperplastic goiter, at least in so far as the medical treatment is concerned, is a rich man's disease and unless the patient can be relieved of economic worries and lives a life of ease and comfort, he will not make satisfactory progress. Unpleasant associations in the home, disturbing economic problems, and lack of adaptation to environment will act as obstacles to recovery. Removal of the causes of these psychic disturbances will have a favorable influence on the prognosis. A similar qualification may be made in regard to physical conditions. The individual who has always been anemic, undernourished and of frail physique, will react very poorly when subjected to the added strain of Graves' disease.

Stage of the Disease.—From the statistics available, it would appear that the first year of Graves' disease is the period associated with the largest mortality. At this time the first serious flare-up is seen and, if untreated, this exacerbation may result fatally. Death occurring after several years may be due to the associated degenerative processes common in hyperplastic goiter rather than to the disease itself.

Age.—It has been said that, in the case of children, the severity of the disease varies in indirect ratio to the age of the patient. In our experience the very severe and the very mild cases of Graves' disease are in about the same ratio in children as in adults. We are under the impression, however, that the disease usually runs a more rapid course in children.

Timely Diagnosis.—Of great importance in prognosis is the relative time of diagnosis. The earlier the diagnosis, the better the prognosis. This is true whether the case is to be treated surgically or medically. The patient in whom thyrotoxicosis is determined early offers a better prognosis even under medicinal treatment. Most surgeons feel, however, that thyro-

toxicosis is an indication for surgery and the favorable results obtained by surgical intervention are naturally much enhanced by an early diagnosis.

Iodin.—Undoubtedly iodin has saved many cases of hyperplastic goiter which, without its use, would have been lost. Conversely many patients are given a sense of false security by the temporary benefits derived from its administration, and are influenced to postpone surgical procedures until the prognosis is definitely worse. The previous use of iodin greatly alters the indications for treatment and favors a very grave prognosis. This is particularly true in the severe cases which have been subjected to protracted iodin medication.

Of twenty-eight consecutive cases in our series admitted in crisis or impending crisis, seventeen had repeatedly been subjected to prolonged iodin medication and eleven had received little if any iodin. Of the seventeen that had been subjected to iodin medication, five were in extremis and died within three days of admittance without surgical interference; three died following ligation and one died from influenza two months after a lobectomy. Of the eight who recovered, two have an estimated efficiency of 80 per cent, three of 65 per cent, two of 50 per cent and one of 40 per cent. Of the eleven that had received no iodin previous to admittance, all recovered. The estimated efficiency of seven is over 80 per cent, of three is 70 per cent, and of one is 50 per cent.

Iodin today, outside of its service in endemic goiter and preventive work, finds its principal field of usefulness in the preparation of toxic cases for operation. Patients, who previous to the recognition of the value of iodin would have been considered inoperable owing to severity of symptoms, are today so rapidly improved by means of suitable iodin therapy that they become, in the course of a few days, good operative risks. In the mild cases, with a mortality of less than one-half per cent, the prognosis is not greatly influenced by the use of iodin, but in the very severe ones the judicious use of iodin and surgery may so improve the prognosis that it approaches that of the mild ones.

PROGNOSIS WITH REGARD TO INDIVIDUAL SYMPTOMS

The Heart

It is difficult to evaluate the amount of damage which has been inflicted on the heart in an individual case. It is practically impossible to estimate the degree of toxicity to which the cardiovascular system has been subjected and the period of time over which this toxicity has been operative. Many patients, especially young individuals, seem to effect a complete recovery from damage to the cardiovascular apparatus, while others retain these symptoms in varying degrees.

The incidence of definite but mild heart damage in hyperplastic goiter is variously estimated at from 30 to 50 per cent. In probably five per cent or more the heart damage is sufficiently serious to cause grave disability even after an efficient thyroidectomy has been done. The in-

fluence of a toxic agency operating on the myocardium seems apparent in view of the symptoms of tachycardia, dilatation, hypertrophy, irregularity, fibrillation, and cardiac failure. The degree of cardiac damage seems to increase in direct ratio to the age of the patient and the duration of the toxicity. In our series, over 70 per cent of patients past fifty had developed auricular fibrillation.

The prognosis even in the most pronounced cases of myocarditis associated with hyperplastic goiter is not hopeless. If the patient can be safely brought through an operation, remarkable results may be observed. It may take some time for the diseased or weakened heart muscle to reach its maximal improvement or to return to normal. We have observed definite improvement up to the fourth year following operation.

The prognosis in the postoperative heart condition is dependent, to a certain extent, upon the willingness of the patient to bring his physical activities within the limitations of his heart efficiency. The cardiovascular derangement did not develop in a day and will not disappear in a day. A carefully supervised routine of systematic exercise is necessary if the heart muscle is to be brought back to normal.

Exophthalmos and Nervous Symptoms.—An opinion as to the chances for entire disappearance of exophthalmos and nervous symptoms will have to be based, to a large extent, on the length of time during which these symptoms have been present. The greater their duration and severity, the less is the probability of their complete and permanent disappearance. In many cases the patient, though cured of all other symptoms, retains a very noticeable degree of exophthalmos as a continuous and permanent reminder of the previous condition. Many patients also, apparently otherwise cured, continue to be neurotic and excitable for indefinite periods.

PROGNOSIS UNDER DIFFERENT TYPES OF TREATMENT

Non-Surgical Treatment.—A discussion on the subject of prognosis will not be complete without some remarks on this subject. The internist, the radiologist, and the surgeon each claims best results from his own particular method of treatment.

Kessel, Lieb, and Hyman (120), for instance, find that their system of watchful waiting or "skilful neglect" implies a very favorable prognosis. They speak of a large proportion of their cases as being "economically restored." Economic restoration, however, is not a sufficient index of the degree of permanency of cure.

The internist may feel that the surgeon takes advantage of him, since surgical treatment includes not only a thyroidectomy but a more or less prolonged period of both preoperative and postoperative rest and, in addition, the use of iodin and other indicated medication. The radiologist, in turn, not infrequently thinks that the advantages of x-ray and radium treatment in thyrotoxicosis are ignored by both the internist and the surgeon. The surgeon may believe that a transient improvement from

non-surgical treatment is often mistaken for permanent improvement or cure and that the clinician may not have any means of knowing of a later downward trend of the disease.

Surgical Treatment.—*Timely intervention.* The surgeon frequently sees his patient only after prolonged non-surgical treatment has been tried. The best moment for operation has, in many instances, already passed. Recourse to surgery is too often resorted to only after all other measures have failed. Notwithstanding this, and in spite of the fact that many of the patients present themselves in a serious or even dangerous condition—the surgical mortality, including all cases, is surprisingly low and the results after thyroidectomy often exceed expectations. The surgeon is probably justified in assuming that the greatest factor in a good prognosis is early surgical intervention. This may be true if the timely surgical treatment is followed, over a sufficient period of time, by efficient medical treatment and wise management of the patient.

Risk.—The prognosis, especially with surgical treatment, is to a great extent dependent upon the "risk" as presented by the patient in terms of hazard for a major operation. It is our practice to state the conclusion as to the "risk" presented by the patient in the following terms.

1. *Excellent Risk:*

   Atoxic. No cardiac or visceral damage. No concurrent disease. No symptoms other than the presence of nodes, tumors or degenerations in the thyroid gland.

2. *Good Risk:*

   Atoxic or mildly toxic. No cardiac or visceral damage. No concurrent disease. Little, if any, disturbance of metabolism. Pulse rate below 105. Basal metabolism rate below plus 20.

3. *Fair or Favorable Risk:*

   Mildly toxic, long duration. Cardiac damage compensated, concurrent diseases arrested, metabolism disturbed. Pulse rate and basal metabolism rate only moderately raised.

   Definitely toxic, but of recent appearance and of short duration. Good cardiac efficiency, good elimination and assimilation. Mental symptoms mild.

4. *Poor Risk:*

   Mildly toxic, long duration; visceral damage or concurrent disease; disturbed metabolisms; defective assimilation and elimination; mental symptoms; goiter heart; arhythmia and auricular fibrillation; cardiac inefficiency, tachycardia, marked muscular weakness; basal metabolism and pulse rates moderately raised.

   Acutely toxic, high basal metabolism rate and pulse rate, severe mental symptoms, tachycardia, marked exophthalmos.

5. *Extremely Hazardous Risk:*

   Long duration, severe visceral damage or concurrent disease, goiter heart, muscular weakness, exophthalmos, mental symptoms, etc.

Or extremely high basal metabolism rate and pulse rate, marked mental disturbance, cardiac inefficiency, impending crisis, disturbed assimilation and elimination.

6. *In Crisis or in Extremis (Inoperable)*

SUMMARY

Diffuse Colloid Goiter

Endemic:

Untreated—20% disappear, 80% persist

With treatment—

Instituted within first 3 months, 98% disappear.

Instituted in 3–6 months, 63% disappear, 37% persist.

Instituted in 6–12 months, 42% are satisfactorily reduced in size, 58% persist.

Instituted after 12 months, a satisfactory reduction in size occurs in less than 1%; some reduction in size in 40%. Some glandular hypertrophy remains in 100%.

Sporadic:

Untreated—37% disappear, 63% persist.

With treatment—

Instituted within first 3 months, 98% disappear.

Instituted in 3–6 months; 72% disappear, 28% persist.

Instituted in 6–12 months, 52% are satisfactorily reduced in size and 48% persist.

Instituted after 12 months; same as in endemic.

The prognosis is unfavorably influenced by pregnancy, excessive enlargement, and poor environment.

Nodular Colloid Goiter

Unfavorable prognosis as to cure.

The size may remain stationary but the course is progressive to adenomatous stage. Thyrotoxemia may appear as a complication.

Adenomatous Goiter

Atoxic:

With non-surgical treatment—unfavorable prognosis.

Complications probable; thyrotoxicosis, visceral damage, malignancy.

With timely surgical treatment—excellent prognosis.

Toxic:

With non-surgical treatment—unfavorable prognosis.

With surgical treatment—prognosis is excellent except when influenced by a high operative risk.

Diffuse Hyperplastic Goiter

With non-surgical treatment—good prognosis as to remission, poor prognosis as to cure.

With careful surgical treatment—excellent prognosis.

The prognosis is unfavorably influenced by the fulminating or acute type of disease, crises or concurrent disease. In the Fruste type whether treated or untreated, a considerable period of time is usually required for the occurrence of a marked change in the condition.

Ligneous Thyroiditis

With non-surgical treatment—prognosis unfavorable.

With surgical treatment—prognosis good except that persistent hypothyroidism must be expected as a final result.

Malignancy

Early—no extension to other structures, with complete removal—prognosis good.

Late—surrounding structures involved—prognosis hopeless; with surgical and Roentgen ray treatment, temporary symptom relief may be hoped for.

CHAPTER VIII

INDICATION AND CONTRA-INDICATIONS FOR TREATMENT

GENERAL INDICATIONS FOR TREATMENT

The treatment indicated in any case is governed to a large extent by the objective sought. This may be either relief of symptoms, or improvement in prognosis, or both. Such objectives as the reduction in size of simple colloid goiter, eradication of deformity, relief from pressure or toxic symptoms, and a decrease in the exophthalmos are classed under symptom relief. Prevention and cure of goiter, prevention or reduction of thyrotoxemia, prevention of degenerative or malignant changes, and visceral damage are classed under improved prognosis.

From the standpoint of expected results, treatment may be designated as palliative, expectant, or curative. Palliative, if temporary improvement is looked for; expectant, if permanent improvement is anticipated; and curative, if the probable results will be complete cure. Medical treatment, hygienic measures, physiotherapy, and x-ray, may be expectant, palliative, or curative measures, depending upon the expected results. A permanent cure is not expected from minor operative procedures in most thyroid cases—hence such measures are usually palliative. Major surgical operations are instituted for the most part as curative procedures.

The various forms of non-surgical treatment are often referred to as medical treatment. It is understood that the term surgical treatment includes medical treatment as well.

The decision as to which variety of treatment is indicated rests upon the type of goiter present, its stage of development, and the relative degree of symptom relief or improvement in the prognosis that may be expected under each form of treatment. In some cases, contra-indications to surgical treatment, such as a high degree of risk, modify the indications.

Palliative treatment is indicated for the temporary relief of severe or complicated cases. Insanity, pernicious anemia, advanced tuberculosis, malignancy, Addison's disease, or any other incurable condition is an indication for medical or palliative treatment and a contra-indication for surgery. Such conditions as impending crisis, recent cardiac decompensation, angina pectoris, general edema, renal insufficiency, psychoses, fever, and pregnancy after the fourth month are indications for palliative treatment.

Expectant treatment, unless modified by other factors, is indicated: in cases of hypothyroidism, thyroiditis, simple colloid and atoxic nodular goiters, in the forme fruste or extremely mild cases of Graves' disease,

and in fetal adenoma until the tumor can be outlined on the surface of the gland by palpation. It is generally understood that expectant treatment is always indicated except in the presence of positive indications for surgical or palliative treatment.

Curative treatment is indicated: in early colloid goiter, in nodose goiter, and in all varieties of toxic goiter. Curative treatment by surgical procedures should be instituted only in the presence of positive indications. The indications against operation should receive more attention than those for operation. The danger signals should be heeded and extensive operations should not be undertaken in the face of grave risks, except in cases of dire necessity. When there is any doubt as to the advisability of a major operation, the decision should always be in favor of palliative medical treatment or minor operative procedures. The chief indications for surgical treatment are thyrotoxicosis, deformity, pressure symptoms, the possibility of the development of thyrotoxicosis, degenerations or malignancy, and an unfavorable prognosis without operation.

Simple Colloid Goiter

The treatment of simple colloid goiter is essentially medical. In rare cases surgical interference may be indicated for the relief of pressure symptoms or for cosmetic effect. Defects in speech or in singing, difficulty in swallowing, dyspnea, or evidence of circulatory disturbance in the head or neck, may indicate pressure on the trachea, esophagus, great vessels, recurrent laryngeal, vagus, or sympathetic nerves. The pressure symptoms may be of greater or less severity, making operation, in consequence, more or less urgent.

Nodular Colloid Goiter

This type of goiter, while in the great majority of instances it will eventually come to operation, does not provide an urgent indication for immediate interference. Unless thyrotoxicosis, pressure symptoms, deformity, or other positive indication for surgical treatment is present, operation had best be deferred until adenomas of considerable size are present.

Atoxic Adenoma

Considerable difference of opinion exists as to when an atoxic adenoma ceases to be an exclusively medical problem and becomes a surgical one. Some authorities consider the age of the patient the chief indication for one type of treatment or the other; patients over a certain age should be operated upon; patients under that age should not. Lahey (121) advocates the removal of all adenomas after the age of forty; Coller (122) after the age of twenty-five. Unless one believes that this type of goiter will disappear spontaneously, or can be cured by medical treatment, we see no point in deferring an operation which might have been done at the age of twenty-five to the age of forty.

Are we justified in waiting for the adenomatous goiter to become toxic before we operate? This is in line with the query "should we wait for the appendix to rupture before we operate?" We know that most adenomas will eventually become toxic if the patient lives long enough. Shall we wait for the unfavorable moment when toxicity has already developed and perhaps done visceral damage, or shall we take advantage of the favorable moment while the patient is still in excellent physical condition, and advise the removal of all adenomatous thyroids as a prophylactic measure? It may seem radical to insist that an adenomatous gland is in itself a positive indication for operation; nevertheless the following considerations will indicate that early operation is the safer and more conservative measure.

Intrathoracic prolongations occur in 20 per cent or more of adenomas of the thyroid by the time the patient is sixty years of age; this complication clouds the prognosis and renders the operation more difficult and hazardous. A percentage of thyroid adenomas later develop malignant changes. This fact in itself should have great weight in deciding in favor of early operation. The pressure of the adenoma on the normal areas of gland tissue may cause destruction of adjacent normal thyroid tissue and, if the process is extensive, result in the development of hypothyroidism or myxedema. Even when no subjective symptoms of pressure are noted, there may result certain undesirable pressure effects, such as, flattening of the trachea or paralysis of the vocal cords. Last and most important, operation will forestall the development of thyrotoxicosis and the consequent possibility of serious visceral damage.

Toxic Adenoma

In these cases the adenomatous goiter is usually of long standing and has reached an advanced stage, therefore no hope can be entertained for cure or permanent relief by non-surgical measures. The toxemia may be of recent onset and therefore of short duration—in which case there is probably little if any visceral damage. It may be mild and of a long duration with serious visceral damage. In either case the diagnosis of toxic adenoma furnishes a positive indication for surgical removal, but in some cases the condition of the patient is so grave that a major surgical operation is extremely hazardous. An estimated surgical risk of Class VI or of Class V is a positive contra-indication for major surgical procedures. Other contra-indications for immediate radical operation are recent acute infections, pregnancy after the sixth month, and associated incurable or fatal diseases.

Diffuse Hyperplastic Goiter or Graves' Disease

Numerous statistics may be quoted indicating that large numbers of patients are cured by medical measures or by Roentgen ray treatment and that surgery is indicated only as a last resort. Analysis of these reports, however, will usually reveal that observation of the patients was continued only for a brief period and, in many instances, remission was

mistaken for cure. Some practitioners oppose operative interference in diffuse hyperplastic goiter because of the tendency of the disease toward spontaneous arrest. While we admit the existence of this tendency, we are far from convinced that spontaneous cure ever occurs in a truly hyperplastic gland. The surgeon, impressed by the fact that a large percentage of the patients who present themselves for surgical treatment have waited until the best time for operation is long past, may see no indications for prolonged medical or x-ray therapy in the treatment of this disease.

Speaking from the standpoint of a surgeon, we are inclined to believe that **every definitely established case of hyperplastic goiter is a surgical case** and that operation is indicated as soon as the patient can be properly prepared to undergo a subtotal thyroidectomy with an assurance of success. The urgency of the indications varies with the type of the disease present, and for this reason the indications in each type will be discussed separately.

Larval and Fruste Varieties of Hyperplastic Goiter or Graves' Disease

In saying that medical or expectant treatment is indicated in practically all cases of this variety, we are not retracting our former statement that surgical treatment is indicated in all established cases of hyperplastic goiter. In the fruste variety, the disease is **not established** and the symptom relief and improvement in prognosis to be expected following operation are not sufficient to indicate surgical interference.

The cardiovascular type is the one exception to the rule that fruste or incompletely established hyperplastic goiter is a medical condition. These patients should remain under medical care unless positive indications for surgical interference appear. We have had many cases of other-wise extremely mild or atypical hyperplastic goiter in which we considered operation urgently indicated for the relief of cardiovascular symptoms; operation in these cases is followed by excellent results.

Established Diffuse Hyperplastic Goiter

From the surgeon's point of view, a definite diagnosis of this disease constitutes a positive indication for surgical treatment. In some clinics surgery is not instituted until medical treatment and perhaps x-ray treatment have been tried and found to be ineffectual. The majority of goiter surgeons find this impractical because the average patient cannot pay for extended hospitalization and the prevention of further visceral damage, by the prompt reduction of the thyrotoxicosis, is of utmost importance. In the great majority of cases seen by goiter surgeons, the patient will have had a preliminary course or perhaps many preliminary courses of medical or x-ray treatment before he consults the surgeon. In many instances the surgeon does not see the patient until he is in such a serious condition that operation should not be attempted. A surgical clinic should not be a refuge for last hopes or a clearing station for hopeless cases.

The Acute Type of Diffuse Hyperplastic Goiter

We must distinguish between the case which is truly acute and the chronic cases which remained unrecognized until a psychic trauma or other cause brought on an explosion or crisis. The truly acute case sometimes presents a difficult problem. The prospect of operation on a patient who presents such symptoms as loss of perhaps a third or more of body weight in a period of six or seven weeks, a basal metabolism rate of plus 100, a pulse rate of 160 to 200, intense nervousness and perhaps delirium, is enough to daunt any surgeon. The patient is rapidly going down grade and the surgeon has not much time to lose in deciding whether he will operate or not. He may feel that the extreme degree of risk precludes operative measures. Surgical procedures are instituted in more of these acute cases, however, since the beneficial effects of iodin medication and the decreased hazard of stage operation have been recognized. If it is apparent that there is no hope for the patient without surgery, the surgeon must decide whether there is hope with surgical intervention; if so, he should give the patient the benefit of the doubt.

Thyroiditis

In the acute stage of thyroiditis, the same treatment is indicated as in simple colloid goiter. Iodin and thyroid deficiencies should be corrected. Should suppuration occur, prompt surgical interference is indicated. In ligneous thyroiditis, medical treatment is of no avail. Prompt surgical interference is indicated.

Intrathoracic Goiter

In this condition the indications for the removal of the intrathoracic mass are in proportion to the severity of the symptoms. In most instances alarming respiratory difficulties from pressure upon the trachea or bronchi make prompt symptom relief imperative. Immediate relief from pressure symptoms may be expected the moment the intrathoracic mass is removed from the thoracic cavity.

Tumors

The presence of a benign tumor in the thyroid gland constitutes a positive indication for its removal. Subtotal thyroidectomy is indicated in all good or fair risk cases. In bad risk cases with large tumors in the gland, ligation is of little benefit and stage operation or enucleation of the tumor, to be followed later by subtotal thyroidectomy, is indicated.

Malignant Goiter

Radical surgical treatment is indicated in malignant goiter if the malignancy has not extended beyond the thyroid gland. It may also be indicated in the later stages for the relief of pressure symptoms and as

a means of placing radium or radium emanations deeply in the substance of the gland. Roentgen ray treatment and palliative medical treatment are always indicated.

INDICATIONS FOR OPERATION

The indicated extent of operation is governed by the type of goiter, its stage of development, and the surgical risk presented by the general condition of the patient. In all good or fair risk cases of adenomatous, hyperplastic, and misplaced goiters, one stage subtotal thyroidectomy is the operation of choice. In poor risk cases, however, the safety of the patient demands that major operative procedures be done in multiple stages. The indications for carefully graded operative procedures frequently rest upon the contra-indications for major ones. Therefore the latter will be first discussed.

Contra-Indications and Risk

The most common contra-indication for a major operation is a grave surgical risk. Summarized according to the classes of risks defined in the preceding chapter (*cf.* page 168) the contra-indications are as follows:

I. Excellent Risk.—No contra-indication for subtotal thyroidectomy or any other necessary operation.

II. Good Risk.—No contra-indication for subtotal thyroidectomy or any other necessary operation.

III. Fair or Favorable Risk.—With careful preparation, major surgical operation is not contra-indicated.

IV. Poor Risk.—Major surgical procedures are not indicated except in emergencies until adequate preparation has improved the hazard to class III (p. 168).

V. Extremely Hazardous Risk.—Major surgical operation is contra-indicated until improvement in the condition of the patient raises the risk to class III (p. 168). Injections, ligations or partial lobectomy are indicated.

VI. In Crisis or in Extremis.—Surgery contra-indicated. Palliative, medical, and x-ray treatment is indicated until the risk can be improved.

High Basal Metabolism

Whether a high basal metabolic rate is in itself a contra-indication for surgery is a question on which surgeons are not agreed. In the opinion of the writer the length of time over which the increased metabolism has been present is of more importance than the height of the basal metabolic rate at the time of examination. When it is obvious that the patient is consistently losing even under the best medical treatment, further delay is useless and the surgeon should intervene if in his opinion surgery holds

any hope for the patient. The surgical risk presented by the condition of the patient and not the height of the basal metabolism rate is the paramount consideration.

Crisis

Crisis or impending crisis is always an indication for palliative treatment. The patient in crisis presents a risk of class VI for major operation. Palliative measures, chief of which is the use of iodin, will tide most patients over the crisis. When the condition is improved to the extent that the risk is down to class V or IV, the first step of a carefully graded operation is indicated. In some cases, however, medical treatment will not control the thyrotoxemia, and recourse to palliative minor operative procedures, such as injections or ligations, is indicated.

Cardiac Deficiency

Auricular flutter is always a contra-indication for any operation until the flutter has been eliminated. In the opinion of the author a large percentage of the unexpected deaths that occur during or shortly after operation are due to the presence of auricular flutter.

Auricular fibrillation, however, is not always a contra-indication for thyroid operation. In fact, in the thyrocardiacs the sooner the goiter is removed after the onset of fibrillation, the better the prognosis as to the reestablishment of the normal rhythm. In thyrotoxicosis, a decompensated heart is an indication for removal of the goiter as early as it can be safely done. No amount of medical treatment will improve the condition of the thyrotoxic heart as promptly as the removal of the over-active or toxic thyroid.

Angina pectoris is sometimes mentioned as a distinct contra-indication for operation. If the electrocardiograph tracing shows definite damage to the myocardium and the toxemia is of mild degree, operation is probably contra-indicated. However, many patients have mild symptoms of angina pectoris with negative findings by electrocardiograph tracings and, when the condition is of this type, it is an indication for, rather than against, operation.

Tuberculosis

Although tuberculosis is considered by many a contra-indication for operation, the writer's experience has been that a patient equal to carrying the load of a toxic goiter in addition to tuberculosis is greatly improved after the removal of the goiter. Therefore, tuberculosis should not be considered a contra-indication for operation.

Jaundice

Jaundice if extreme and of long existence is, of course, a contra-indication for any operation. Light or mild degrees of jaundice due to a disturbance of the cholesterol metabolism are often observed and are an indication for and not against operation.

Hypertension

High blood pressure, except that it influences the prognosis as to longevity, is not a contra-indication for operation. Many hypertension patients are made more comfortable by removal of a goiter.

Renal Insufficiency

Renal insufficiency with symptoms of uremia is always a contra-indication for operation until the kidney function has improved. On the other hand, renal insufficiency due to thyrocardiac conditions, is not a contra-indication for operation; in fact, it rarely improves until a goiter operation has been done. Sometimes within a few hours or days following even a unilateral thyroidectomy, the renal function will so improve that the water logged patient has a large output of urine per day and a definite improvement in the general condition results.

Abnormal Mental Conditions

Some confusion exists regarding indications for operation in the case of patients suffering from mental disease either as a complication or as a result of thyrotoxicosis. The indications for or against operation will depend on the existence or non-existence of an etiologic relationship between the abnormal thyroid condition and the abnormal mental state. The more severe the thyrotoxicosis, the greater the probability that it is the cause of the mental disturbance. If no casual relationship can be established, the mental condition is not an indication for operation; if, on the other hand, it is apparent that the mental condition results from, or is aggravated by the thyrotoxicosis, the removal of sufficient gland tissue to definitely lessen the toxemia is indicated. The response to ligation is rarely sufficient to cause satisfactory improvement in the mental condition.

Pregnancy

Pregnancy after the sixth month must be considered a contra-indication for operation. From the first to the fourth month in a toxic goiter case, pregnancy constitutes a positive indication for operation. From the fourth to the sixth month operation is indicated only for the relief of severe conditions.

Age

The age of the patient in itself is neither an indication nor a contra-indication for operation except as it affects the surgical risk. We should consider the age and condition of the adenoma rather than the age of the patient. Other things being equal, the younger the patient, the better the risk. If we consider that an operation will be ultimately unavoidable, we can serve no useful end by deferring intervention.

Foci of Infection

Foci of infection, such as diseased tonsils, teeth, or gall bladder may modify the indications for thyroid surgery. Removal of the foci of in-

fection, before the goiter operation is done, may be indicated. The decision as to which should be done first rests upon the degree of thyrotoxemia, the condition of the heart, and the gravity of the associated condition. If the thyrotoxemia is not extreme and if the heart and other vital organs are in good condition, it may be advisable to eliminate the foci of infection first. However, if the thyrotoxemia is severe, attention to the foci of infection had best be postponed until after the thyroid operation. When an acute self-limited infection is present, operation should be delayed if possible until it has subsided.

INDICATIONS FOR MINOR OPERATIVE PROCEDURES

Contra-indications for a major operation frequently provide positive indications for minor operative procedures as stages of a multiple stage operation. The most useful ones in the order of their magnitude are injection into the gland, ligation of a thyroid artery, and partial or complete lobectomy.

Injections into the Gland

This procedure is indicated, in addition to medical and Roentgen ray treatment, if the condition of the patient makes even primary ligation hazardous.

Ligation of the Thyroid Arteries

This procedure is indicated by an operative hazard of class V (p. 168), that cannot be improved by palliative medical, Roentgen ray, or injection treatment. Ligation is also indicated in severe cases of acute thyrotoxicosis when iodin is not tolerated.

Partial Lobectomy

Partial lobectomy is indicated by the necessity of a prompt reduction in the severity of the thyrotoxicosis in a patient who is a poor risk for a complete lobectomy. This procedure is especially indicated as a palliative procedure in the critical cases which have previously been subjected to ligation. It is frequently indicated, when the patient falls under class V, (p. 168), as the first step in a multiple stage operation.

The operative hazard of partial lobectomy is only slightly greater than that for ligation. The beneficial results obtained by a partial are less than those by a complete lobectomy, but are more than those obtained by the ligation of two thyroid arteries. The ligation of one or both thyroid arteries on the one side may be done in the course of the operation with but little additional hazard.

The limitation of the operative procedure to partial lobectomy may be urgently indicated during the course of operation for lobectomy or subtotal thyroidectomy by the alarming condition of the patient.

Lobectomy

The amount of benefit obtained by any minor operative procedure is usually in direct ratio to its magnitude. Lobectomy, an operation of somewhat greater magnitude and of correspondingly greater benefit than ligation or partial lobectomy, is indicated in unilateral goiters, in cases with a high basal metabolic rate, and in cases with a high surgical risk. The operation can be done in one-fourth the time required for subtotal thyroidectomy; less solution is required to produce the anesthesia; the postoperative ordeal is minimized; such complications as trachitis or obstructive dyspnea are rarely encountered; and the thyrotoxemia is reduced to such an extent that further visceral degeneration is prevented. In case of doubt as to whether lobectomy or subtotal thyroidectomy is indicated, the decision should be in favor of the safer procedure, lobectomy.

Multiple Stage Operation

In critical or severe cases the high degree of surgical risk may make a necessary major operative procedure, such as a subtotal thyroidectomy, extremely dangerous and impractical if executed in one stage. Fortunately extensive thyroid operations may be accomplished in multiple stages, each stage accompanied by only a slight operative hazard. In many instances the preoperative use of iodin, by improving the surgical risk, eliminates the necessity for injections or ligation previous to lobectomy or subtotal thyroidectomy. These procedures are, however, occasionally advisable and, in some cases, essential. For instance, we frequently see thyrotoxic patients who have been treated with iodin to such a degree that we can expect little or no benefit from its administration. In the majority of these cases there is urgent need of prompt, marked reduction in the toxemia. In such a case, subtotal thyroidectomy by several carefully graded stages in the operative procedure may be strongly indicated.

In large goiters of long standing, with a scabbard trachea and considerable softening of the tracheal rings, there is danger of flapping or collapse of the trachea following a complete thyroidectomy. This danger constitutes a strong indication for lobectomy with the other lobe left in place to support the trachea and prevent "flapping" and the tendency to collapse.

The eventual recovery of the severe case of thyrotoxicosis with low resistance is more assured following operation in multiple stages. The heart and circulatory system have not been placed under so great a strain; the postoperative ordeal is lessened. **The change in the metabolic rate has been attained more gradually.**

The severe mental and physical depression, which frequently follows the sudden drop in a high metabolism rate after subtotal thyroidectomy, is not observed after the gradual reduction in metabolism rate which follows two consecutive lobectomies. A reduction of two-thirds to three-fourths of the raised basal metabolism rate may be expected from the

first lobectomy with corresponding improvement in the condition of the patient. After two to four months the other lobe may be removed without fear of inducing a severe depression.

The danger of postoperative thyrotoxicosis following the first lobectomy is sometimes alleged to be a contra-indication. We believe that a careful operation by the technic described in the section on Operative Technic will eliminate this objection. We have never seen acute postoperative thyrotoxicosis follow a lobectomy unless the gland left in situ had been traumatized. We are convinced that if the lobe that is left is not disturbed in any way there is little danger of postoperative thyrotoxicosis.

CHAPTER IX

NON-SURGICAL TREATMENT

The non-surgical treatment is of primary importance in almost every case of goiter. Various medical and x-ray measures may be instituted either as cures in themselves, or as adjuvants of very definite importance in the preoperative and postoperative care of the surgical case. The brilliant results obtained in the surgical treatment of goiter today would not be possible without the aid of the modern methods of medical treatment.

We will consider first the scope of medical treatment in the different types of goiter, reserving for a later section the consideration of the application of Roentgen rays. Many of the measures advocated for treatment are the same as those already discussed in connection with prophylaxis, yet even at the expense of a little repetition, it is deemed advisable to go into some detail concerning the various phases of non-surgical treatment.

ATOXIC GOITER

COLLOID GOITER

Diet

The importance of diet in all goiter conditions, including the early colloid goiter cannot be overemphasized. Since defective diet alone may be the causative factor in early colloid goiter, correction of faulty dietetic habits, without further measures of any kind, may prove curative.

Preliminary Diet

Before outlining to the patient or the family the constituents of the diet in detail, the writer has been in the habit of putting many of the younger patients on a preliminary diet for four or five days of bread and milk, and the child is made to adhere to it strictly for the time stated; after this, other articles of food are gradually added. The efficacy of this preliminary diet when combined with proper medical treatment is seen in a speedy and rather surprising reduction in the size of the gland. This first success establishes confidence, and does much to simplify dietetic regulation in the future.

Meat

Should the patient with early colloid goiter be on a meat or a meat free diet? There is considerable difference of opinion on this point; some advocate a strictly vegetarian diet; others advise a diet containing a very generous meat ration. The proper diet probably lies between these two extremes, or more correctly, will approach one extreme or the other according to the needs of the individual case.

In instances, when a tendency toward hyperthyroidism is noted, a diet largely vegetarian will be indicated. In other cases, for example in that of the undernourished hypothyroid child with a lowered basal metabolism, a diet rich in red meat is almost essential. This type of diet is very effective in the treatment of girls in their teens.

In anemic goitrous children, large amounts of liver—particularly calves' liver—in the diet seems to bring about considerable improvement. The children as a rule will readily take the liver fried or in a stew. For those who cannot take it in the food, a preparation of liver extract may be prescribed. This is not difficult to take and should be a satisfactory substitute.

Vegetables and Fruits

Whether meat is allowed or not, the importance of vegetables of suitable quality and in sufficient quantity must be stressed. The diet in the case of early colloid goiter should include green vegetables and fruits.

Quantity of Food

In regard to the quantity of food, the physician of experience will prescribe according to the special needs of the case in question. For the flabby, overweight child, it is advisable to restrict the total food intake, prohibiting entirely such things as candy, jellies, preserves, and syrups. In the case of the underweight, neurotic child, with some suggestion of autonomic imbalance and possibly a slightly raised metabolic rate, the daily food intake should be approximately 10 per cent more than is required for the normal average child of the same age and height.

The slightly hyperthyroid child, as well as the hyperthyroid adult, requires more food to combat the tendency to wasting. In addition to the loss of weight incident to thyroid hyperfunction, the child must meet the severe metabolic demands of normal growth. A generous diet, largely vegetarian and quantitatively in excess of the diet indicated for the normal youngster of the same age, is indicated for this type of child.

On general principles, coffee, tea, highly spiced food, condiments and alcohol should be prohibited.

Vitamins

The importance of vitamins in goiter diet has been stressed by some authorities. While little experimental investigation has been done on the effect of vitamins in thyroid conditions, experience has shown that a diet correct from the standpoint of vitamin content is of distinct advantage.

Many of the foods that are rich in vitamins have a high mineral content and it is interesting to speculate as to how much of the benefit derived from such foods is due to the minerals and how much to the vitamins. An illustration of this point is afforded by cod liver oil. Goiters recalcitrant in a large degree to routine medical treatment have been found to improve remarkably on the administration of cod liver oil. When the treatment of goiter was largely empirical, the therapeutic value of the oil was attributed to the excellence of the nutritive qualities per se. Now we believe that the results are due in a large measure to the mineral and vitamin content.

Iodin Content

The iodin content of food is quite variable. Patients living near the sea will have easy access to foods rich in iodin. Even those living at considerable distance from the ocean may nowadays, owing to modern refrigeration and transportation, have sea food in sufficient quantity and of good quality. The importance of this fact, in goitrous districts, is not sufficiently realized. A more liberal consumption of such foods as oysters, lobsters, crabs, and other shell fish would be in itself an important curative measure in the treatment of simple colloid goiter. Halibut, mackerel, herring, sardines, sea trout and salmon are also of value in this direction.

In addition to these usual sea foods, we have come, of recent years, to place considerable importance on various preparations of kelp, or seaweed. Many palatable kelp preparations are on the market and contain, not only a good percentage of iodin, but also—which is a matter of some importance—other necessary mineral elements which are present in sea water.

General Mineral Content

In speaking of the mineral content of food or water, we are too apt to limit ourselves entirely to the consideration of iodin. While iodin is of chief importance, other elements such as phosphorus, calcium, sulphur, and iron, are also valuable. Milk, cheese, and eggs contain considerable amounts of calcium and phosphorus and are very important dietary constituents, particularly for the growing organism. Since most of the leafy vegetables contain both calcium and phosphorus, they are important items in a diet formulated with the idea of maintaining the mineral balance.

The writer has repeatedly found—even in well-to-do families—evidence of mineral imbalance, due to the fact that green vegetables were to a large extent omitted from the diet. In such cases, the addition of fresh vegetables to the diet has sufficed to bring about improvement or cure of the milder form of simple colloid goiter.

Hygiene and Living Habits

Considerable importance should be placed on the question of hygiene in the treatment of goiter. A child, particularly, should get as many hours as possible of direct sunlight. Fortunately, many clinics and even some schools now supplement natural with artificial sunlight. Various lamps, both of the carbon arc and mercury vapor type, have been installed in many of our public institutions.

Our modern school building program embraces another feature that may greatly benefit thyroid conditions as well as child health in general; this is the replacement of the ordinary window glass by vitaglass, or some other medium which will not screen out the ultraviolet ray. The actinic ray acting on the children in the school rooms for several hours each day must have an appreciable therapeutic influence, and should prove to be a factor, not only in the prevention of goiter in children, but in the cure of the milder forms of simple colloid goiter.

Habits of living are of considerable importance. To what extent are long hours and overstudy blamable for the persistence of goiter in adolescent girls? To what extent are late hours, late dancing, theaters, sensationalism, emotionalism, erotic novels, "thrillers," responsible? It seems fairly clear that present day life, habits, and customs, make excessive demands on the adolescent female. The thyroid enlargement of puberty is in itself and expression of inadequacy: the gland is unable to meet the exacting demands of the organism at this critical period.

It is difficult to evaluate the influence which exhaustion factors have in modifying the course of goiter. Yet if we add to the excessive energy demands of puberty in the female the further strain of serious dissipation of vital energy, we can hardly escape the conclusion that the personal habits of many young girls of today must exercise an unfavorable influence on the course of simple colloid goiter. The physician should consider it his duty to make definite inquiry into the habits of goiter patients. Medical treatment will be more successful if, at the same time, proper habits of living are instituted. Eight hours in bed should be insisted upon, and, if possible, an hour's rest in the afternoon; the course of studies should, if necessary, be curtailed and simplified. A reasonable amount of healthy recreation in the open air is advisable, but long hours of dancing in stuffy halls should be prohibited.

The tendency to rush through meals should be discouraged. In goiter patients proper absorption and assimilation of food is essential; the required proportion of mineral constituents can only be taken up through the medium of food that is properly digested and assimilated.

The young goiter patient should regulate her life and her habits to a slower tempo voluntarily; she should try to train herself to think, to act, to talk, to live more slowly.

Influence of Climate

It may seem far-fetched to consider the question of climate in the treatment of simple goiter. The writer, however, has often noted rapid improvement and even cure in cases refractory to all treatment at home upon change of residence to another climate. Patients from the Mississippi Valley region, for instance, seem to do well in Southern California. How much of the improvement may be due to the elimination of some unfavorable dietetic or hygienic influence in the home environment, we are in no position to say. Occasionally very good results are obtained by a few weeks residence in a sanitarium. Here again the elimination of unfavorable influences in the home environment may be the deciding factor in the improvement.

Elimination of Foci of Infection

The general treatment of goiter must include a complete survey for foci of infection and the elimination of these foci as far as reasonably possible. Care and judgment are necessary to decide whether the individual procedure contemplated is worth while. We must balance the danger and discomfort of the operation against its possible value and

decide accordingly; we must be on our guard against needless surgery and must not, in our zeal, be led too far afield.

It is well to be on the lookout for history or clinical evidence of such conditions as sinusitis, tonsillitis, adenoids, infections in the posterior nares, dental abscesses, dental caries, pyorrhea, cervical adenitis, otitis media, chronic gall bladder and appendix infections, pyelitis, vaginitis, salpingitis, pelvic peritonitis, pelvic abscess, colitis, ileocolitis, and other gastro-intestinal disorders.

Regulation of Gastro-Intestinal Conditions

Gastro-intestinal conditions are of particular importance. Disturbances of the digestive tract interfere considerably with the processes of absorption and assimilation particularly as regards minerals, and hence have a tendency to disturb the mineral balance. Can pathologic intestinal bacteria fix iodin and other minerals in the intestinal tract so as to render them incapable of absorption and assimilation? Can the action of pathologic intestinal bacteria on the intestinal mucosa, so modify the mucosa as to render it incapable of properly absorbing the mineral elements in the food? Our knowledge of the physiology and pathology of the intestinal tract is not sufficiently advanced to answer either one of these questions. However, we know from experience that chronic infections and disturbances of the alimentary canal play a very definite rôle, both in the causation of goiter, and in modifying unfavorably the course of already existing goiter.

Excretory Functions

Any rational scheme of treatment of simple goiter must include close attention to gastro-intestinal function. The bowels must be regulated and intestinal stasis corrected as far as possible. Lane (123), Bainbridge, and others have emphasized the importance of prevention of intestinal stasis in the treatment of both goiter and hypothyroid conditions. Daily evacuations should be promoted, high colonic flushings given in suitable cases, intestinal antiseptics administered, and in short, every attempt should be made to clear up as quickly as possible chronic infectious disorders of the gastro-intestinal tract.

The writer has for years placed considerable reliance on the use of mercurial preparations in cases of simple goiter. Calomel may be given in small dosage every night over a long period of time, and has been very satisfactory in our hands, particularly for children. Extreme care should be taken not to administer the drug to the point of salivation.

For adults, bichloride of mercury in solution, in dosage of 1/80 to 1/40 grain seems more effective. The warning to discontinue before the point of salivation is reached applies even more strongly in the case of adults on mercurial medication. Some authorities prefer other mercurial preparations to those mentioned. With some the blue mass pill in two to five grain dosage is a favorite and doubtless is quite efficient.

In early colloid goiter cases, we prefer the daily administration of small doses over a considerable period of time; more advanced cases—

especially older patients—respond better to intermittent medication. We frequently employ as a routine method the administration of a mercurial preparation every third or fifth night, followed by a saline or other laxative the next morning.

The improvement following the use of the mercurials cannot be ascribed to their purgative action alone; the improvement noted may be considered as the combined result of the following actions:

(1) Stimulation of the secretory and excretory processes.
(2) Stimulating or adjuvant influence on the various phases of metabolism.
(3) Intestinal antisepsis.

Ipecac and rhubarb seems to have a good effect in some cases not benefited by mercury. The use of such purgatives as cascara, castor oil, mineral oil and salines is not followed by the general systemic improvement consequent on the skilful administration of the mercurial preparations.

Assimilation

Assimilation is often improved more effectively by a correction of hygiene habits, and diet than by medication. Some of the minerals, such as iodin, calcium and sodium, are easily assimilated. More difficulty is experienced in the successful administration of iron, sulphur, phosphorus, manganese, etc. The oral administration of sulphur in a form which will guarantee even a small measure of absorption is a matter of some difficulty. After careful experimentation the writer has come to place considerable reliance on the absorption and assimilation of the sulphur content of ichthyol when administered orally. A capsule containing three minims of a mixture of equal parts of ichthyol and glycerin may be given after each meal and seems to answer the purpose better than any other preparation.

Use of Drugs

Effervescing potassium phosphate supplies potassium and phosphorus in a palatable and assimilable form. Effervescing sodium phosphate is a dependable preparation for the administration of soda and phosphorus, though sodium deficiency is rarely encountered.

Calcium is easily administered in the form of five or ten grain tablets of calcium lactate. The dosage required to correct a nutritional deficiency is not as large as that required in parathyroid deficiency. Twenty to forty grains per day is usually sufficient.

The influence of cod liver oil in providing absorbable iodin, calcium and phosphorus has been referred to. Sunlight as well as cod liver oil is efficient in improving the absorption of calcium and phosphorus from the bowel, and it is due to this fact that sunlight, natural or artificial, has a good influence on goiter.

Many preparations purporting to supply these minerals in an assimilable form have been offered on the market. The manufacturer in each instance claims that all of the mineral elements in his preparation will be assimilated. Reports upon their efficacy are conflicting. It is safer to rely

upon food products known to contain the necessary mineral elements in an assimilable form. Medication by the most reliable preparation procurable may be used as an adjunct to the consumption of leafy vegetables, kelp products, and sea foods in the diet.

The bitter tonics are of some value; dilute hydrochloric acid and pepsin; elixir of iron, quinin and strychnin; nux vomica and such drugs have a limited field of usefulness.

We have, within the last few years, become interested in the effect of the bacterial flora present in the intestine, upon the efficiency of the bowel in the absorption of minerals; theoretically, the lactobacillus acidophilus, if it can be made to thrive in the intestine, will outgrow and displace the pathogenic and objectionable organisms, thus reducing intestinal toxemia. Our results with the lactobacillus acidophilus preparations have not been sufficiently definite to enable us to speak emphatically one way or the other. We have found that either the milk or the chocolate coated block is efficient in controlling certain types of acute gastrointestinal disturbances such as griping and burning diarrhea which are sometimes brought on by mercury.

Intestinal Disinfectants

In addition to the mercurial preparations already mentioned other intestinal disinfectants may be used with profit. McCarrison (124) has successfully treated simple goiter with thymol and other intestinal antiseptics. Some observers have reported good results from the administration of such drugs as bismuth, salol and creosote.

Specific Medication

Some writers seem to assume that the medicinal treatment of simple goiter is summed up in the word "iodin." It is true that iodin is the most important single therapeutic agent at our command; nevertheless many other drugs are of value, and any one of several may be effective in the cure of a specific case even after a thorough trial with iodin has failed.

Quinin and ergot, given empirically, have been favorite drugs for many years. Forchheimer, nearly forty years ago, extolled the therapeutic virtues of quinin hydrobromid and ergot in exophthalmic goiter. His original prescription was

Quinin Hydrobrom.	gr. v.
Ergotin.	gr. i.
In capsule or pill	t.i.d.

This formula has been in extensive use as an empirical remedy up to the present day. No satisfactory explanation has ever been presented of the fact that it apparently is of value in some cases. In our opinion the beneficial effect when observed is from the quinin. When idiosyncrasy is present—found in about one patient in three hundred—sodium salicylate or aspirin may be used as a substitute. The salicylates are also indicated in patients with a rheumatic history.

The patient with a basal metabolic rate below normal, with sallow

muddy complexion, a bloated and puffy look around the eyes, thick tongue, dull mind, and a tendency toward headache and lassitude, who is resistant to all other measures, will sometimes respond promptly to small or moderate doses of neosalvarsan given intravenously at weekly intervals.

Iodin

Some of the facts noted in the chapter on prophylaxis apply equally well to the treatment of simple goiter. The iodin dosage given by Marine in his prophylactic work at Akron was in many instances sufficient to cause considerable reduction in size or even bring about the disappearance of the milder degrees of thyroid enlargement.

Klinger (135), working in the schools in Zurich in a highly endemic area, reports even better results. Of 760 children observed, 90 per cent showed thyroid enlargement at the first examination. The period of observation and treatment was fifteen months. At the end of this time, 643 of the original 760 were reexamined, and goiter was found in only 28.3 per cent. Other preparations of iodin, such as Lugol's solution, the syrup of ferrous iodid or hydriodic acid, may be used instead of sodium iodid and, if properly administered, will be found to be equally efficacious. Iodostarin, in about double the prophylactic dose already discussed, is a favorite with some.

The writer uses for adults a tablet of iodoform, gr. 1/10, Lugol's solution m. 5–10, or sodium iodid gr. ½ almost interchangeably. We administer one of these preparations three times each day, from the first to the fifth, and from the fifteenth to the twentieth of each month. Between the ages of nine and sixteen a tablet containing only 1/50 of a grain of iodoform is given in the same manner. The tablet for children under nine contains 1/100 of a grain.

If the iodin is to prove effective, definite improvement will be noted within a period of two or three months. If no improvement is observed within this time, recourse should be had to other remedies: thyroid extract, thyroxin, or ichthyol.

In cases refractory to the iodin treatment alone, we have frequently secured excellent results by giving the bichloride of mercury and the iodin medication in alternate weeks.

The contra-indications to iodin in simple goiter are idiosyncrasies, sensitization and mercurialization. Idiosyncrasy is very rare indeed, but of sufficient frequency to make it advisable for the first few doses to be small ones. The symptoms of dyspnea, vertigo, slight nausea, coryza, lacrimation and slight salivation appear within a few minutes after the ingestion of even a small dose. Larger doses are followed by alarming dyspnea, urticaria, palpitation of the heart, and a feeling of impending death.

Sensitization to iodin is only encountered after prolonged iodin medication. The symptoms are loss of appetite or a feeling of fullness, catarrhal pharyngitis and laryngitis, and a marked aggravation of the acne which is usually present. If the medication is continued, nausea, vomiting, and aggravation of all the symptoms may occur.

On account of the danger of salivation care should be exercised in the administration of iodin to patients who have been taking some form of mercury over a prolonged period of time.

If, after four or five months thorough treatment with iodin, thyroxin, and the other measures specified, the gland does not show signs of regression, there is little likelihood that it will return to normal.

Iodin Versus Thyroid Extract

A rather popular misconception exists with regard to iodin and thyroid extract in the treatment of simple colloid goiter. It is rather commonly believed that these two medicaments are identical in their therapeutic action, equally efficacious, and practically interchangeable. It is believed that iodin constitutes over 60 per cent of thyroxin, that iodin is the active ingredient of the thyroxin molecule, and that consequently the action of iodin and thyroxin or thyroid extract must be identical. Such is not the case; some goiters refractory to iodin improve or disappear promptly on the administration of thyroid extract and vice versa.

In a general way it may be stated that iodin will be effective in goiters in which an iodin deficiency is the causative factor. In the case of endemic goiter in iodin poor districts, the medicinal iodin supplies or corrects the iodin deficiency in the food or water intake and promotes normal thyroid function; the thyroid enlargement consequently decreases in size or disappears.

In sporadic goiter, including goiter of adolescence or of pregnancy, in goiter free districts, we have a different set of conditions. These cases of sporadic goiter receive as much iodin, in all probability, in their food and water as their neighbors; nevertheless they develop goiter; the neighbors do not. Apparently, there are other factors operative besides a straight iodin deficiency. Experience and observation support this contention.

It is true that in some instances of sporadic goiter, usually those with a basal metabolism rate about normal, the use of iodin is followed by satisfactory results, but in the majority of such cases the basal metabolism rate is below normal and the iodin is ineffective, if not distinctly harmful. Most of these cases, in contrast, are definitely benefited by thyroid extract. In some cases thyroid followed by iodin gives the best results.

These observations indicate that we must individualize carefully in the treatment of simple colloid goiter; we must not treat a case obstinately, without result, for a long period of time with one therapeutic agent to the exclusion of others; we must carefully, patiently and judiciously try first one and then another before we decide that therapeutic treatment is unavailing.

Thyroid Extract

When we prescribe thyroid extract we are prescribing a somewhat dangerous drug. In the case of simple colloid goiter, there is no emergency. In giving thyroid extract it is safe to follow the old precept "make haste slowly." We must gradually go from the smaller to the larger dose while watching the effect of our treatment carefully and make clinical observations at as frequent intervals as possible.

We must be certain of our diagnosis before we administer thyroid extract; we should insist upon a careful and complete physical examination, and repeated basal metabolism tests in order that early or established thyrotoxicosis may be ruled out.

The gland should be carefully examined, previous to the administration of thyroxin, iodin, or thyroid extract, for the existence of possible nodules; the thyroid should be reexamined at intervals for newly formed or developing nodules. If nodular formation is present, iodin or thyroid extract should be given with caution.

Dosage.—The dosage of thyroid will depend on the age of the patient, the possible idiosyncrasies of the individual, the rate of basal metabolism, the size and character of the goiter, the presence or absence of complications, and the quality and freshness of the gland product.

The Quality of the Gland Product.—The quality of the gland product used is a consideration which the practitioner cannot afford to overlook. Preparations which may have lain for months in a supply house or drug store may be inert and no longer of therapeutic value.

Even in fresh preparations, from different houses, one finds that the therapeutic or pharmacologic value varies within very wide limits. Doubtless the raw material from which the extract is made varies greatly from time to time as regards the proportion of potent ingredients. The methods of preparation also vary with the different houses, and possibly with the same houses from time to time. It is of importance that a potent, carefully standardized preparation be secured.

Methods of Administration.—The thyroid preparations are usually given in ascending dosage; commencing with very small doses and gradually increased as the tolerance of the patient is determined.

There is no definite and fixed scheme for the estimation of the size of the dose of thyroid extract. Arbitrary dosage of this substance must be considered inadvisable and illogical. In adults we usually start with the administration of one-half grain of the extract or one grain of the desiccated gland substance twice a day. This dosage is usually continued for a period of about two weeks. After a week's intermission the treatment is resumed, with the dosage adjusted according to the effects noted. We must keep the possibility of cumulative action in mind when administering thyroid, the same as when administering digitalis, and be on our guard against this contingency. For this reason its continuous administration should be avoided. If given intermittently, the effect can be more easily estimated, the danger of accumulative action is minimized and intolerance to or sensitization to the drug delayed. Another advantage of a definite schedule of intermittent administration is that patients are more likely to continue the treatment. The schedule of administration on a monthly basis is more likely to be followed than one based upon alternate weeks. If directed to take the medicine from the first to the fifth and from the fifteenth to the twentieth of each month, the patient is more apt to persevere than if instructed to take it continuously.

In selected cases, when we can definitely rule out the possibility of a preexisting tendency to thyrotoxicosis, we are sometimes justified in

pushing the dosage to the point of physiologic effect and then discontinuing it. It is given in gradually increasing doses until the appearance of such symptoms as mild tachycardia, mild tremor, nervousness, a slightly raised metabolic rate, or transient glycosuria, indicate its discontinuance. An increase in pulse rate, nervous symptoms, and usually tremor, will appear before a rise occurs in the metabolic rate. This method of administration is sometimes successful after no results have been attained by the prolonged administration of small doses. An interval of three to eight weeks should elapse before thyroid medication is resumed. Frequently, iodin will be well tolerated and productive of beneficial results during the interval.

Local Measures

Local measures applied directly to the enlargement in the neck have little value except from the point of view of the psychic effect upon the patient. Ointments soil the clothing and their use cannot be said to rest upon a scientific basis. Their efficacy depends upon their iodin content. There is no means of even approximately estimating the proportion of iodin which is absorbed. If used in conjunction with the internal administration of iodin or thyroid extract, there may be more absorption of iodin than we expect, and undesirable results may follow. The craze for the local application of various types of ointment is, fortunately, on the decline. There can be no scientific reason for this inaccurate method of treatment when we have other means of administration which can be controlled and standardized.

The use of mechanical contrivances devised to exert local pressure on the goiter is also to be deprecated. In the past, adhesive plasters and other such devices have been applied in the hope of reducing the size of the goiter. Such measures are not only useless, but, as they bring about discomfort of various degrees, are objectionable.

SIMPLE COLLOID GOITER AND PREGNANCY

If a simple colloid goiter appears in the early months of pregnancy, it is rather conclusive proof that a condition of mineral deficiency exists. This deficiency should be relieved by special attention to the diet, and by other measures already indicated. The basal metabolism should be carefully estimated at frequent intervals, and if found low, every attempt should be made to bring it up to normal. It must be remembered that in pregnancy the basal metabolic rate is raised approximately 10 per cent at two months, 15 per cent at three months, and 20 per cent after the fourth month. A basal metabolism rate lower than the figures indicated is suggestive of thyroid hypofunction.

NODULAR COLLOID GOITER

In this condition medical treatment holds little promise of cure. The goiter will not disappear, either spontaneously or under medication. The treatment is symptomatic and hygienic along the lines discussed in considering the medical treatment of simple colloid goiter. Mineral de-

ficiencies and thyroid deficiencies should be corrected in an effort to save such portions of gland as are still in colloid state, and prevent as far as possible the development of diffuse fibrosis.

We have found neosalvarsan useful in a certain number of cases of simple colloid goiter. In the diffuse nodular colloid goiters of extreme size with pressure symptoms, neosalvarsan seems to stimulate adenoma formation and to bring about an apparent decrease in the size of the gland. This apparent decrease in size is probably due to improvement in the general systemic condition.

The patient with nodular colloid goiter should be surrounded with every safeguard to prevent infections, local or general. The thyroid condition should be observed closely, both during the course of an infection and afterwards, for the possible onset of toxicity. The onset of toxicity or pressure symptoms will determine the necessity of surgical intervention.

ATOXIC ADENOMA

Medical treatment has only a limited field of usefulness in the case of atoxic adenoma. Care must be taken to prevent infections as far as possible. If infection does set in, the patient should be kept under close supervision both during the course of the infection and afterwards. Careful watch must be maintained for the onset of toxicity; it is only this careful observation that can prevent the serious cardiac damage which may result from even a mild degree of toxicity.

The general health must be kept up to par, foci of infection removed, anemias, and such conditions corrected.

No system of medical or expectant treatment offers any reasonable hope for cure or complete disappearance of the goiter.

FETAL ADENOMA

There is little field for medical treatment in the matter of fetal adenoma. Focal infections should receive prompt and early attention; the patient should be under close supervision during the course of any general systemic infection.

Mineral deficiencies should be looked for and corrected; the general health improved as far as possible, and expectant treatment applied until such time as operation is considered advisable. Operation is, as a rule, indicated as soon as the adenoma has become definitely circumscribed.

INTRATHORACIC GOITER

Intrathoracic goiter is a surgical condition. Medical care is limited to symptomatic treatment.

SYPHILITIC THYROIDITIS

Specific treatment is usually quite effective, if resorted to sufficiently early. It is extremely desirable to institute antiluetic treatment as soon as possible. In the first place, the improvement resultant on such treatment will confirm the clinical diagnosis; in the second place, further

damage to the thyroid structure will be prevented; in the third place, the systemic ravages of the disease will be halted.

In the early case the pain and tenderness in the gland will often disappear within twelve hours after a moderate dose of neosalvarsan; the tenseness and rigidity of the surrounding structures will disappear in two or three days. As the rigidity of the adjacent tissues becomes less marked, there is very definite reduction in the pulse rate, which frequently falls to normal in a few days.

The cases that have escaped observation in the early stages and have remained untreated until symptoms of fully developed diffuse hyperplastic goiter have appeared, should even at this late date have thorough and prolonged antiluetic medication.

Diffuse hyperplastic goiter following untreated syphilitic thyroiditis is frequently accompanied by severe exophthalmos. This exophthalmos is often unilateral and only rarely is improved by thyroidectomy. Even with thorough antisyphilitic treatment in addition to the thyroidectomy, a reduction of more than 40 per cent in the degree of exophthalmos is not to be expected.

MALIGNANCY OF THE THYROID

Unless we include palliative medication under the head of medical treatment, there can of course be no place for medical measures in the treatment of malignancy of the thyroid.

If the capsule of the thyroid is invaded and the surrounding structures involved, it is already too late for surgical intervention, and we must give the patient what help and comfort we may through the media of radium, the x-ray, and palliative medication. The subject will be taken up in more detail in a subsequent section.

NON-SURGICAL TREATMENT OF TOXIC GOITER

All that may be said of the non-surgical treatment of diffuse hyperplastic goiter or Graves' disease is applicable also to the treatment of the thyrotoxicosis in the hyperplastic variety of toxic adenoma. Therefore in order to avoid repetition, the discussion of the non-surgical treatment of Graves' disease will precede that of toxic adenoma.

DIFFUSE HYPERPLASTIC GOITER (GRAVES' DISEASE)

Certain types of Graves' disease, such as the fruste types, the incomplete or mild forms, the cases of autonomic imbalance with little, if any, rise in the metabolic rate, belong exclusively in the domain of the internist. Also cases seen in the very early stages, particularly in young subjects should be given a limited course of medical or expectant treatment before surgery is resorted to.

While it is our contention that surgery is indicated in every well-developed case of Graves' disease, it is not amiss, even in a book on surgery, to consider briefly some of the principles of medical treatment.

The treatment discussed in considerable detail in the section on the treatment of simple goiter is applicable in a large degree to the treatment of Graves' disease. Mineral deficiencies should be corrected; foci of infection eliminated as far as possible; disorders of the gastro-intestinal tract should receive attention; and, every possible effort should be made to improve the processes of assimilation and elimination.

In the experience of the writer the mouth and nasopharynx call for particular attention. If operations are necessary to remove foci of infection, they must be done immediately by an experienced operator.

Rest

From the medical standpoint this is the most important consideration and the most desired objective. It is, unfortunately, also the objective most difficult of attainment. If it were possible in every case to put the patient at absolute rest under ideal conditions, the percentage of cases in which surgical intervention is indicated would be decreased. The rest to be effective must be complete; it must be mental as well as physical; there must be complete rest of body and mind.

The difficulty of securing this ideal, complete rest, under average conditions is one of the reasons why surgical intervention is so often essential. The patient in the severe types should be in bed every minute of the twenty-four hours and relaxed physically as far as possible. After the patient has relaxed physically, we must try to induce him to relax mentally. This is often an impossible task in the home. Even with the best intentions on the part of the family and the patient, the latter is constantly annoyed by visitors, loud talking, petty squabbles, children, financial details, imaginary slights on the part of the relatives or friends, street noises, and a multitude of other disturbances.

Removal to another climate, to an expensive sanitarium, or to the country, may solve the problem for the wealthy patient. In some instances it may get the patient away from a disagreeable and detrimental home environment. On the other hand, since irritability and mental restlessness are of subjective rather than objective origin, and since the patient is irritable because he is ill and thyrotoxic, the change of domicile and environment may exert no noticeable influence. To a great extent the mental reactions and nervousness are a part of the disease and are not to be dismissed by mere change of habitat.

The period of time necessary for the rest cure, if it is to be effective, is another important consideration. Absolute rest, or as near as we can come to absolute rest, must be persisted in for a period of at least six months. If the rest is broken into, the symptoms reappear. This long period of enforced rest is another argument against medical treatment in the average case. The complete disability for at least six months, followed by a longer period of partial disability is, for the family of moderate means, an economic hardship.

Climate

If climate, outside of mere change of environment, can be said to have any influence, a dry moderately cool climate at an elevation of one

thousand to two thousand feet is, in the writer's opinion, the most desirable. The seashore seems to be harmful in many instances.

Diet

Very great differences of opinion exist as to the most suitable diet for patients suffering with Graves' disease. In our experience, individualization is the answer to the diet question. Each healthy individual has different food requirements, different food likes and dislikes. The same is true to even greater extent in individuals suffering with disease, particularly a disease that influences the processes of metabolism.

Any extreme diet is likely to have a deleterious influence on the welfare of the individual suffering with Graves' disease. The so-called starvation cure, for instance, can have very little place in the treatment of a disease characterized by greatly increased metabolism and consequent emaciation. Starvation can only make the condition worse.

Milk Diet

An exclusively milk diet is open to a somewhat similar objection. Superalimentation is essential in the treatment of Graves' disease, if the tendency towards severe wasting is to be checked. Even the normal adult cannot be suitably nourished on an exclusive milk diet. Unless confined to his bed, the patient on milk diet soon becomes nervous, irritable, listless and restless; he may consume four quarts or more of milk daily and still lose weight. It may be advisable at times to make use of a milk diet for a few days, to correct a gastro-intestinal disturbance or for some other reason. To continue the patient on such a diet, for any great length of time, must be considered an error in dietetics and management.

Milk, not as an exclusive diet but in suitable combination with other foods, is one of the best adjuvants in treatment. It should be given generously either by itself or with seltzer water, malted milk, eggnog, milk shakes, milk chocolate, or otherwise modified. The patient should also be encouraged to take milk in the form of ice cream and with breakfast food and puddings.

Mixed Diet

Large quantities of nutritious food of the kind that the patient likes and to which he is accustomed form the most suitable diet. In prescribing diet, we do not take into account sufficiently the factor of racial and personal likes and dislikes. The palates of the Irishman, the Jew, and the Italian have had very different training and will react differently to the various food products. A severe illness does not offer the best occasion for an attempt to modify the dietic likes and dislikes of a lifetime. Patients should not be compelled to eat wholesome food which they do not like, and to forego equally wholesome food which they do like.

The one exception that is indicated is in the matter of meat restriction. While we do not advocate an entirely vegetarian diet, we limit the meat to less than one-fourth the usual intake. A moderate amount of sea food is advisable. Fruits and an abundance of vegetables, particularly of the green varieties, are indicated.

Eggs are frequently well borne and may be used in various ways. They may be taken in the form of eggnogs between meals, and in this way may be of considerable help in bringing the number of calories up to the desired level. If the whole raw egg has a tendency to cause intestinal irritation, the yolks only may be used. If cooked, the eggs should be soft boiled or poached.

Butter is useful, appetizing and should be partaken of generously. The liberal use of butter will also tend to increase the consumption of bread which is a desirable objective. Cream is advisable if the patient can take it; it may be given with the milk in the form of "half and half" or it may be used with breakfast foods, puddings, or cooked fruits. The patient may be able to take a pint or more of pure cream each day in divided portion.

Cod liver oil is also useful in promoting nutrition; even outside of its iodin content, we believe that it has a field of usefulness. It may be given alone or in the form of extract of malt and cod liver oil. For those who find it difficult to take the oil alone, an orange juice sandwich—the oil between two layers of orange juice—may be acceptable and palatable. Olive oil, particularly for Italians and those accustomed to its use, is beneficial. It is useless to try to foist it upon a patient to whom it is distasteful.

Condiments of all kinds and stimulants such as coffee, tea and alcohol, as a general rule, should be prohibited.

Quantity

Forced feeding along practical lines should be the watchword. The method of superalimentation will vary with the individual case. In some instances it may be advisable to supplement the regular meals with extra lunches. The condition of the gastro-intestinal tract will often determine the regimen. During the active stages of the disease the amount of food required to counteract the tendency to wasting is about twice that required by a normal individual of the same age and size; in adults from five thousand to six thousand calories per day.

The process of forced feeding should be carried on under close supervision. If any disturbance of the gastro-intestinal function is noted, such as nausea, vomiting, belching or acidity, a reduction in quantity is indicated. The diet must be carefully scrutinized for any foods that may be particularly troublesome. It may be that one article of food in the diet is causing all of the trouble and, if so, its elimination will have a very beneficial influence on the progress of the patient towards recovery.

A satisfactory and progressive gain in weight is one of the best indications that the patient is receiving proper treatment. As an indication of improvement, it may be said to take precedence over decreased pulse frequency or lessened metabolic rate. For the individual who has lost perhaps a third of his body weight, each additional pound regained means another milestone on the road to recovery.

Other conditions being equal, the patient who is placed on a satisfactory regimen of forced feeding, will at first gain at an extremely rapid

rate. During the first few weeks he may gain as much as two or even three pounds a week. Unfortunately, the improvement does not always last; gastro-intestinal derangement often supervenes. The gain in weight may have occurred during a period of remission, may have raised false hopes of permanent cure to be shattered by disappointment with the onset of an exacerbation and a recurrence of the emaciation. A temporary improvement and gain in weight during an intermission may be a will-o'-the-wisp that leads the patient astray and causes him to postpone surgical intervention until the best moment for intervention has passed.

Medication

There is no specific medication for Graves' disease. Medicinal therapeusis in the established case must be considered purely symptomatic.

Control of Nervous Symptoms

The extreme nervousness, mental excitability and irritability characteristic of Graves' disease are features which are very difficult to control. The list of drugs that have been used in the control of the nervous and mental symptoms, in hyperplastic goiter, includes practically every hypnotic, sedative and narcotic in the pharmacopeia. The writer has found the bromids to be of more value in these cases than any other sedative. They seem to have a favorable effect in reducing the thyrotoxicosis, as well as in relieving the nervous and mental symptoms. If they are not tolerated by the stomach they may be administered by proctoclysis. If skin rashes follow their use, recourse must be had to some of the other sedatives and hypnotics.

The other sedatives most often of value in controlling the severe manifestations are barbital, phenobarbital, hyoscin and sodium amytal. In some cases no other drug seems to control delirium or mild mania as well as acetanilid. It is a powerful cerebral depressant and should be used with great caution and not continued over a long period of time. Other sedative drugs are sometimes used, any one of which may be most effective for the individual case.

Treatment of Cardiovascular Symptoms

The usual remedies effective in heart conditions are to a large degree valueless in Graves' disease.

Digitalis is of no value in controlling the toxic tachycardia or in improving the quality of the pulse in active Graves' disease. Toxic tachycardia is a contra-indication for its use. In long standing cases, auricular fibrillation, auricular flutter, or other conditions associated with arhythmia may demand its use even in the presence of a thyrotoxic tachycardia. For the residual atoxic tachycardia that sometimes persists for varying periods after operation, a course of digitalis is often beneficial.

Quinin in the form of quinidin sulphate or quinin hydrobromid is highly extolled by some. In a few instances we have been convinced that the restoration of the rhythm, in cases of auricular fibrillation, was due to the effect of quinin.

Atropin in small dosage is advised by some; it is said to have some influence in slowing the heart rate. The writer has never been able to see any results from its use for this purpose. In emergency heart conditions arising in the course of Graves' disease, strophanthus is said to be of great value but this has not been our experience. The administration of caffein sodium benzoate by the hypodermic method is a more dependable measure in emergencies.

Treatment of Gastro-Intestinal Symptoms

For the regulation of the bowels the measures recommended in cases of atoxic goiter are applicable in general to Graves' disease.

The diarrhea in cases of Graves' disease may at times be intractable. The first consideration in treating diarrhea is an extremely careful scrutiny of the dietary. The usual astringents are sometimes ineffective. A mercurial laxative in mild dosage followed by bismuth is effective in a good percentage of the cases.

A day's starvation or a day or two of milk diet will occasionally bring about surprisingly happy results in the presence of gastro-intestinal disturbances. The nausea and vomiting of the crisis are best relieved by iodin.

Gastro-intestinal symptoms of nervous origin, particularly if due to vagus irritation, are benefitted by the administration of belladonna or atropin. Diarrhea, nausea, vomiting and abdominal distress, refractory to the usual medicaments, sometimes respond very well to the influence of these drugs.

Endocrine Medication

Extracts and preparations of the other ductless glands have been given a rather exhaustive trial in thyroid disorders. The results reported have not been uniform. Preparations of the pituitary, ovary, testicle, thymus, pancreas, suprarenals, and parathyroids have all been used with varying results. It seems to us that the administration of any glandular product, to be logical, must rest on a definite diagnosis of an associated endocrine disorder in the particular case.

Insulin

There has been some discussion relative to the merits of insulin administration in the medical treatment of Graves' disease. It is claimed that through the administration of insulin the loss of calories, in the form of the intermittent sugar loss, may be prevented. If it fulfilled this function adequately and without danger to the patient, insulin would play a very important rôle in the therapeusis of this disease. In cases with diabetes the control of the diabetes with insulin is urgently indicated. In such cases its use is followed by a rather marked gain in weight. There is not sufficient evidence, however, to establish an especial value in the treatment of the transient glycosuria of Graves' disease.

Treatment by Sera

Up to the present, serotherapy must be characterized as a failure as far as Graves' disease is concerned. Sera prepared from the milk and blood of thyroidectomized animals have been used with doubtful results, judging from reports of different observers. Cytotoxic sera designed to destroy or impair the functioning cells of the thyroid are, in the present state of our knowledge, dangerous and unreliable.

Tonics

Tonics are of doubtful value. Such preparations as elixir of iron, quinin, and strychnin occasionally are beneficial.

Minerals

Most writers give only casual attention to the question of mineral deficiency. The writer, however, considers it of the utmost importance. Sodium phosphate is beneficial; it was recommended originally by Kocher (126). It may be given in twenty to thirty grain doses three times a day. Phosphorus is perhaps best administered in the form of lecithin and may be given in grain or two grain doses three times a day. Sulphur is best administered in the form of ichthyol. The writer has had rather unusual success with ichthyol in the treatment of both atoxic and toxic goiter. Calcium is best prescribed in the form of calcium lactate or calcium gluconate in five to fifteen grain doses three times a day.

Iodin Medication

The use of iodin in connection with thyrotoxic conditions is a two-edged sword; it is both a blessing and a curse. It is a blessing because in recent years, since the work of Plummer in 1923 (127) drew attention to its value in this respect, it has been the best ally of the surgeon. It has simplified preoperative and postoperative care and has materially lessened the surgical mortality incident to Graves' disease. It is a curse because many individuals, having become imbued with the idea that iodin in itself is a curative agent, defer operative intervention until the best moment for surgery is long past.

Effects of Iodin

Iodin exerts a beneficial influence on the local signs or symptoms, such as the exophthalmos and thyroid tumor, and on the general or constitutional symptoms, as evidenced by a reduction in the pulse rate and the basal metabolism. The suddenness of the improvement is at times almost startling; a patient in severe crisis with intractable nausea and vomiting and apparently almost moribund will show results from a large dose of Lugol's solution (30 to 60 minims), or from 20 grains of sodium iodid administered intravenously, within an hour or two; the vomiting will have been completely controlled within twelve to twenty-four hours. It should not be forgotten that such satisfactory results can rarely be extended beyond the fifteenth to the twentieth day.

The effect on the basal metabolism is most noticeable from the sixth

to the eighth day after the iodin therapy has been started. There will be a drop depending to a considerable extent on the iodin dosage; for instance, the basal metabolic rate may show little change on a daily dose of 30 minims of Lugol's solution and may react very favorably to a daily dose of 60 minims. The dose required is usually in proportion to the height of the basal metabolic rate and the rapidity of the pulse; in extreme cases 50, 70 or even 100 minims per day may be required. In crisis or impending crisis, one dose of 100 minims of Lugol's solution by proctoclysis or 24 grains of sodium iodid by the intravenous method may be given. There may be little if any change in the basal metabolic rate for the first few days, although the symptoms during this period may show considerable improvement. Between the sixth and eighth days there is a very definite drop, occasionally to normal in mild cases. In severe cases a drop in the basal metabolic rate of 20 to 40 per cent is usually observed. In our experience the basal metabolic rate is markedly influenced by iodin therapy in proper dosage in about 60 per cent of the mild cases; in about 30 per cent a moderate or slight lowering of the rate is observed and in about 10 per cent little or no change in the metabolic rate is seen. Symptomatic improvement, however, frequently occurs even in the cases in which the metabolism has been apparently unaffected.

If the iodin is continued over a long period it will be found that after the fifteenth day there is a gradual rise of the basal metabolic rate. Finally, after a period which varies from case to case, it may reach a higher level than before.

The sudden withdrawal of the iodin medication is followed after several days by a sharp rise in the basal metabolic rate that may reach the former level; a reinstatement of the iodin medication in the same or increased dosage will not be so effective as before in bringing the rate down.

Iodin in proper dosage has a remarkable effect on the nervous system. The intense nervousness, the psychomotor activity, the twitching, the thrashing around in bed are promptly reduced. The patient is less irritable, more composed and rests easily in bed. It is not unusual to see a delirious or maniacal patient quiet down within a few hours—talking, thinking and acting composedly and rationally—as a result of the administration of iodin.

In the severe intractable vomiting, incident to the crisis, the action of iodin at times seems almost magical. Improvement is noted often in an hour or two following the intravenous administration of 20 to 30 grains of sodium iodid, and complete cessation of vomiting almost invariably occurs within forty-eight hours.

The improvement in the tachycardia is not always in proportion to the improvement in the other symptoms. Frequently, however, it drops from 150 or 160 to 105 or 110. The improvement is most marked on about the eighth to the tenth day. If the iodin medication is continued over several weeks, the pulse rate is frequently raised again to its original rate.

The eye symptoms in some instances show remarkable improve-

ment. The stare becomes less noticeable. The protrusion of the eyeballs often remains stationary or even retrogresses. The thyroid becomes tense and slightly larger and harder. Occasionally slight pressure symptoms such as dyspnea or dysphagia due to the enlargement are noticed.

Dosage and Method of Administration

Lugol's solution—the compound tincture of iodin—owing to the fact that it is soluble in water, is the preparation most commonly used. It is by no means the only effective one. We may use iodoform tablets, sodium iodid, potassium iodid, syrup of ferrous iodid, or tincture of iodin. The dosage and methods of administration of other iodin preparations are generally stated in terms of Lugol's solution.

The dosage varies with the case. In the average case it is usually safe to start with 5 minims of Lugol's solution two or three times a day. If the basal metabolism and pulse rate are high, proportionately more should be given. In crisis, up to 100 minims a day may be given until the thyrotoxicosis is brought under control. Then the dose should be reduced.

Some writers report unsatisfactory results from the rectal administration of iodin. In our experience, the administration of a dilute solution of Lugol's by proctoclysis has proved effective and the method is less liable to danger of overdosage than oral administration. From clinical observations we are certain that the absorption of iodin from the rectum is dependent to a great extent upon the systemic demands. When these have been met, absorption is very slow, if it occurs at all, and overdosage by this method can produce little or no harmful effect.

Results of Iodin Medication

1. The symptoms in the ordinary case show improvement. The nervousness, the tachycardia and the gastro-intestinal symptoms are favorably influenced.
2. The patient gains in weight.
3. The basal metabolism is greatly reduced in the majority of cases.
4. It brings the patient out of crisis.
5. Local findings incident to Graves' disease are favorably influenced, the progress of the exophthalmos is frequently halted, the thyroid becomes less vascular and its colloid content is increased.

Contra-indications to the Use of Iodin

Sensitization or intolerance to iodin from repeated or prolonged medication is the most frequent contra-indication. It is a common observation that after repeated or prolonged periods of iodin medication the beneficial effect of the drug is lost and the symptoms are aggravated rather than diminished by its use. If a history of iodin medication is procured, great care should be exercised in the institution of iodin therapy.

Tracheal compression whether due to large thyroid tumor or other cause, likewise the presence of active tuberculosis are usually considered contra-indications. In each case the advantages to be derived from iodin

medication should be weighed against the possible dangers and the decision should be made accordingly.

Iodin medication in the treatment of thyrotoxic cases preparatory to operation and for postoperative conditions will be discussed in later sections.

TOXIC ADENOMA

This subject may be briefly disposed of since the treatment of the adenomatous condition and the treatment of the thyrotoxemia have been discussed in previous sections. There is no expectant non-surgical treatment for toxic adenoma. The only treatment that holds expectation of cure is surgical treatment. Preventive measures will be effective in reducing the incidence of goiter in general and consequently in lessening the occurrence of adenoma and toxic adenoma.

After toxicity has developed in an adenomatous goiter non-surgical treatment cannot be curative; it must be considered merely palliative, directed at the amelioration of the symptoms, either preparatory to or in lieu of operation.

The palliative treatment differs in some important respects according to whether the cardiovascular symptoms, the symptoms of thyrotoxicosis, or the symptoms from absorption of the products of degeneration dominate the clinical picture.

Cardiovascular Group

The palliative treatment of the cases in the cardiovascular group consists almost entirely of measures directed toward relief from symptoms of cardiac embarrassment. A permanent improvement in the real condition of the cardiovascular apparatus cannot be expected from either non-surgical or surgical treatment alone. Not only timely surgical intervention but judicious non-surgical treatment, both preoperative and postoperative, is of especial importance in these cases.

The treatment must be symptomatic. Medical treatment as indicated by the symptoms present should be instituted. In these cases the severity of the cardiovascular symptoms and the mildness of the thyrotoxicosis increases the relative importance of measures for relief from cardiac embarrassment. In many cases digitalis is of more value than iodin. In some cases of long standing the cautious administration of thyroid will be indicated by symptoms of myxedema. Favorable progress in the treatment of a case is evidenced by the amelioration of symptoms rather than by basal metabolism determinations.

The disappearance of edema, improvement in the regularity and quality of the pulse, improvement in mental and nervous states, and a gain in weight, are of good prognostic import. Rigid adherence, for a considerable time, to a strict schedule of living should be insisted upon This schedule should provide for a least eight hours of sleep at night and two hours of sleep in the middle of the day and should definitely limit the amount of exercise allowed. Otherwise the treatment does not differ from that indicated in similar cardiovascular conditions from other causes.

Anaphylactic Group

The treatment of patients in this group is usually limited to treatment preparatory to operation, yet, in a few cases, surgical interference is contra-indicated, as by advanced pregnancy or by some co-existing fatal disease, and treatment with special efforts at desensitization is advisable. In cases of this type many of the symptoms are due to the fact that the patient has become sensitized to foreign proteins; the remedy, as in hay fever and certain types of asthma, lies in desensitization.

It will be found on careful observation that many of the patients suffering with adenomatous goiter resemble asthma cases in that they show sensitization to certain food stuffs. The removal of the objectionable article of food from the dietary may have a very beneficial effect in the individual case. In other cases desensitization by the injection of various foreign proteins as typhoid vaccine, horse serum, diphtheria antitoxin or sterile milk is indicated.

The care and thoroughness with which the process of desensitization is undertaken will have much to do with the results observed. The initial dose, given subcutaneously with a finely graduated syringe, should be small—half a minim usually—and doubled every third day until the first reaction occurs. Upon the appearance of symptoms of a mild reaction the dosage should be decreased to about four-fifths of the dose that produced the reaction. This subreaction dose should at three day intervals again be carefully increased until reaction is again noted. The procedure is repeated and each time the tolerance for foreign protein is raised. As a rule the tolerance is practically doubled by each such procedure. Finally the patient becomes desensitized and large doses cause no reaction. At this stage many of the symptoms clear up and much subjective and objective improvement is noted.

This process of desensitization is especially valuable when the type of toxic adenoma to which it may be applied is noted as a complication of the later months of pregnancy. It is very satisfying to note the improvement consequent to desensitization. The procedure if successful will take the patient through her pregnancy and carry her along until such time as she may be safely operated upon. After the degenerated thyroid is removed and the absorption of degenerated products is checked, no special treatment is required.

The author is convinced that the improvement recorded by some authorities after the use of sera of various kinds is sometimes due to the fact that the use of the sera with its foreign protein content has brought about desensitization. The good results obtained in some instances cannot be scientifically ascribed to a direct specific effect on the thyroid tissue or the thyroid hormone.

Hyperplastic Group

The general principles already outlined in the treatment of Graves' disease apply equally well to the cases of toxic adenoma in this group and need not be repeated here. The preoperative and postoperative treatment will be discussed in chapters on those subjects.

Mixed Group

The treatment of the patients in this group must necessarily be individualized. The treatment described for the cardiovascular group, for the anaphylactic group, or for the hyperplastic group will be indicated according to the preponderance of cardiovascular, anaphylactic, or thyrotoxic symptoms present.

ROENTGEN RAY TREATMENT OF GOITER

It is not our purpose to enter into a comprehensive account of the roentgen ray treatment of goiter. Even a review of the voluminous literature on this subject is unnecessary and perhaps out of place in a book that is intended primarily to present the opinions and conclusions formed from experience in a surgical clinic. We will limit ourselves therefore to a brief discussion of the results of our own experience with roentgen ray treatment, as compared with the methods and results which have been reported by others.

Technic

The technic of roentgen treatment seems to differ considerably with various operators. Some prefer large dosage at infrequent intervals and others favor moderate dosage at frequent intervals. Some roentgenologists advise small doses on alternate days for three weeks, then a free interval of three weeks and a repetition of this routine of treatment and free interval until three or more such courses are completed. Those who place importance on the influence of the thymus, advocate a simultaneous application of the rays over the upper part of the sternum.

Reported Results

Numerous reports of results have been published quoting roentgen ray "cures" in 65 to 75 per cent of a series of cases and improvement in 10 to 20 per cent more. While these figures can be accepted only with reservations, it is only fair to state that the reports presented by many competent roentgenologists furnish statistical evidence of results in the treatment of toxic goiter that compare favorably with the best results obtained by surgical treatment.

It is difficult or impossible from the consideration of statistics alone to draw definite and incontrovertible conclusions concerning the efficacy of roentgen ray treatment. In our experience about 20 per cent of the patients that we see have had more or less prolonged roentgen ray treatment previous to coming under our observation. About 50 per cent of these patients state that although they were improved, and were classed as cured for perhaps one or two years following the x-ray treatment, that they have not been entirely well since the onset of the disease. The other 50 per cent report no results from the treatment.

Roentgen Ray Versus Surgical Treatment

The claims put forward in favor of roentgen ray treatment include the following points:

(A) There is no deforming scar.

While there is no scar as the result of x-ray or radium treatment, there is not infrequently considerable pigmentation of the skin and even formation of telangiectases or keloid. These manifestations may be months or even years in making their appearance. These skin affections may of course be avoided by skilful operators; nevertheless, they are not infrequently seen as a result of treatment. We have seen a number of cases in which the x-ray burn and subsequent scar caused much more deformity than would result from the most poorly managed skin incision. Lack of success or even unfortunate results by inexperienced or unskilful operators is no indictment against the proper use of the roentgen ray. However, we are convinced that roentgen ray treatment of goiter as a curative measure had best be left to those who are exceptionally proficient in its use.



FIG. 22.—Scars from Roentgen Ray Burns.

(B) There is no mortality.

Under this heading the x-ray specialist reminds us that even in our best clinics, surgical mortality runs in the neighborhood of 0.5 to 2 per cent. He intimates furthermore, that if all surgeons doing goiter work were included the mortality would be much larger.

Even though we are compelled to admit that the mortality as computed for all goiter operations throughout the country is very much too high, it must be acknowledged that lack of success in inexperienced hands is no more an indictment of surgical treatment than unfortunate results from x-ray treatment in inexperienced hands are an indictment of x-ray treatment. Moreover, it would be of interest to know how many of the fatal cases which are charged up to the surgeon were first subjected to prolonged x-ray or radium treatments by operators of various degrees of proficiency.

(C) It is stated that the thymus, which may at times not be readily accessible to surgical attack, can be treated efficiently by the x-ray.

In answer to this we may say that the efficacy of thymus radiation is open to question, but in the cases that cannot be adequately dealt with surgically, the results are encouraging enough to justify roentgen ray treatment.

(D) It is also stated in favor of the x-ray that no period of hospitalization is necessary, that the patient can attend to his or her occupation or housework and that the treatment is not associated with pain or discomfort.

The strength of this fourth point of argument may be questioned. In view of the psychology of the thyrotoxic individual, the long period of waiting which roentgen treatment necessitates is more likely to be a disadvantage than an advantage. The expense will probably be just as great in the end, and the patient undergoing treatment for toxic goiter is often mentally if not physically incapable of steady occupation or sustained effort. One may gain from surgery in a few weeks all the benefits which are supposed to result from a six months' course in roentgen ray treatment.



FIG. 23A.—Scars from Roentgen Ray Burns.

(E) The radiologist believes that he can through the medium of the selective action of radium or x-rays, check or modify the secretion from harmful cells without injury to the normal thyroid tissue.

This might be true if we could gauge the dosage for every case, under all conditions, with infinite accuracy. This is obviously impossible. Indeed, the surgeon's knife in the open wound can exercise a much finer degree of discrimination as regards normal or diseased tissue than can the roentgen ray in its present state of development.

(F) It is alleged that if the roentgen ray is given a thorough trial and fails, there is still time for surgical intervention.

We cannot agree with Means (128) and some other writers who claim that the difficulty and risk of thyroidectomy are decreased by preliminary x-ray work. We have found, on the contrary, that preliminary roentgen ray treatment, by causing delay, tends to make the operation both more difficult and more dangerous.

Radium

In the last few years radium treatments have been used in the severe cases with increasing frequency. No excitement need be provoked by this method of treatment, hence it is especially indicated in the case of the extremely nervous or the critically ill patient.

In the reports of the results following radium treatment, an improvement in the nervous and other constitutional symptoms is usually mentioned, but statements as to a noted reduction in size of the gland are not often seen. Radium treatment possesses an advantage in that it may be given in accurate dosage—an average dose being 20 milligrams applied for a period of twenty-four hours or in other words 480 milligram hours.

In our experience the radiation is equally effective whether produced by radium or by an x-ray machine. The advantage of radium treatment —that the patient is not disturbed by the noise and manipulation incident

to the exposure to x-ray—is offset in great measure by the commonly observed fact that unpleasant skin changes are more likely to result from radium treatment than from x-ray treatment.

Conclusions in Regard to X-ray Treatment

Eighteen years ago, as the result of our experience with x-ray treatment, we reported the following conclusions:



FIG. 23B.—Scars from Roentgen Ray Burns.

(A) X-ray treatment is contraindicated in the cases of goiters with normal or reduced thyroid function and in the case of large goiters producing pressure symptoms.

(B) X-ray treatment should not be used as a curative measure but for improvement of the symptoms of thyrotoxicosis.

We became convinced that exposure of the thyroid to a massive dose of x-ray is, in the majority of cases, followed by a marked reduction in the degree of thyrotoxicosis with consequent improvement in the constitutional symptoms.

We were not successful in reducing the thyrotoxicosis by the use of small or fractional doses. It seemed to us, that, following small doses, the normal secretion from areas of normal thyroid tissue was decreased, while the qualitatively changed secretion from abnormal gland areas was relatively increased. In an effort to produce curative results we treated 190 cases of thyrotoxicosis with x-ray, and 10 cases with radium, during the years of 1917 and 1918. From careful observation of the results in these cases we formed the following conclusions:

(a) Fractional doses of radiation will often stimulate the secretion from the gland and aggravate the toxic condition.

(b) Insufficient doses will sometimes check the normal secretion from the areas of normal tissue present in the thyroid, without checking the toxic secretion from the changed or abnormal areas in the gland.

(c) All thyroid secretion can be definitely and positively checked for a period of two or three weeks by massive dosage of radiation. The condition of the toxic patient can be confidently expected to improve for a period of from two to four weeks following a massive dose.

(d) The second massive x-ray treatment is about one-half as effective as the first one.

(e) The third x-ray treatment is ineffective in the majority of cases.

Six years afterward, in 1925, the results of a review of these cases were reported as follows:

"In the six years that have elapsed since that series of cases were treated, 162 of the 200 have been operated without a mortality; 7 are apparently well without operation; 12 are invalids from goiter; 9 have died without operation; and the other 10 have been lost track of." (129)

X-ray treatment continued to be the most dependable non-surgical measure for reduction in the degree of thyrotoxicosis until 1923 when Plummer announced his discovery of the effect of iodin in the control of thyrotoxicosis. Since that time the use of iodin has in a great measure supplanted x-ray treatment in the control of thyrotoxicosis. It is possible that in some cases, in addition to the administration of iodin, x-ray treatments should be used.

We are of the opinion that the conclusions formulated in 1918 are correct and that roentgen ray treatment has a field in the treatment of thyrotoxic conditions.

X-ray and Radium Treatment of Colloid Goiter

It is generally understood that x-ray and radium are useless or even contra-indicated in the case of simple colloid goiter. Nevertheless, in the early stages of colloid goiter, it has seemed to us that we have secured good results from the use of fractional or small doses of x-ray or radium. As the patients were under routine medical treatment it was difficult to determine how much of the improvement was due to the medical treatment and how much to the roentgen ray.

It is perhaps safer and more scientific to reserve the x-ray for refractory cases of toxic goiter that do not respond to therapeutic measures discussed.

X-ray and Intrathoracic Goiter

X-ray therapy has been advocated for intrathoracic goiter, in the expectation that it might cause regression or diminution in size in the intrathoracic prolongation. In our experience with this type of goiter, the x-ray has harmed oftener than it has helped.

Roentgen Ray Treatment of Malignancy

The roentgen ray is useful and advisable in the treatment of cases of malignancy which have progressed too far for operation, and in the postoperative treatment of patients who have been subjected to thyroidectomy for malignancy. It is true that beneficial results are in most cases limited to a period of months or weeks but in these cases attainment of a measure of relief for even a few weeks is a great boon. In cases of potential or suspected malignancy x-ray should not be used until the diagnosis is confirmed. Inefficient dosage is harmful rather than helpful, and maximum dosage should not be used without positive indications.

CHAPTER X

ANESTHESIA IN THYROID OPERATION

FACTORS IN CHOICE OF ANESTHESIA AND THE SKILL OF ITS ADMINISTRATION

The selection of the most favorable anesthetic is of vital importance in thyroid surgery. No other factor has more influence upon the hazard of operation. In the wise choice of anesthesia there are three variable factors to be considered: the surgeon, the anesthetist, and the patient. Each one of these factors will mark indications, contra-indications, and limitations for modes of anesthesia.

Surgeon

The surgeon may quite possibly be temperamentally unfitted to do his best work under local anesthesia. He may not have the delicacy of touch that is necessary for handling the tissues under local anesthesia without discomfort to the patient. The surgeon may be antagonistic and unsympathetic, and hence not qualified to reassure and control the apprehensive patient. The sensitive surgeon may be disturbed by knowing that the patient is a watcher at the operating table and may feel impelled to be overly cautious and unduly dilatory. Under such conditions local anesthesia may constitute such a handicap to his work that general anesthesia is indicated.

Anesthetist

The anesthetist who is chosen for goiter operations faces a very delicate responsibility. It is of utmost importance that he induce anesthesia without excitement, sense of suffocation, or vomiting and that he maintain it at a depth that is within the margin of safety but deep enough for the surgeon to do his work expeditiously. This is not all that is expected of the anesthetist. He must also be able to recognize promptly any unfavorable symptoms or changes in the condition of the patient. In no other type of operation is the anesthetist compelled to face, day after day, such grave risks and sudden catastrophes as in goiter surgery.

Furthermore, there must be a definite spirit of cooperation and understanding between the surgeon and the anesthetist. The surgeon should see that he has available the services of an anesthetist upon whom he can rely. The anesthetist will frequently develop a form of second sight or mental telepathy which enables him to anticipate, to an extraordinary degree, the wishes and movements of the surgeon. With prolonged association between the surgeon and the anesthetist a certain sense of security is developed. Each knows that any untoward complications which may appear during an operation will be swiftly and adequately met.

Patient

The patient himself is perhaps the most variable factor because of differences in temperament, local conditions, and the degree of thyrotoxicosis and visceral damage sustained.

Temperament.—The temperament of some patients is such that they may safely and comfortably be subjected to the ordeal of local anesthesia. Other patients, temperamentally fearful and apprehensive, suffer agonies of mind which must be recognized as having an even worse influence on the condition of the patient than would general anesthesia. It has been said repeatedly that the patient's confidence must be gained for the successful administration of a local anesthetic. This is sometimes easier said than done; indeed, in some cases it cannot be done and resort to general anesthesia is necessary.

Local Condition.—The size and position of the tumor mass should be considered in determining the type of anesthesia indicated. Tumors situated in the thorax or those that exert sufficient pressure to cause tracheal deformation or that are accompanied by myocardial change, chronic bronchitis or other congestive symptoms, present strong contra-indications for general anesthesia. In tumors of comparatively small size, with little or no respiratory obstruction, the surgeon may very well feel that from the standpoint of the local condition, general anesthesia offers the best prospect for a speedy, comfortable, and safe operation.

Toxicity and Visceral Damage.—In some cases the thyrotoxicosis may be of such a degree and accompanied by such visceral change as to absolutely contra-indicate general anesthesia. There are exceptions however. Very young patients with severely toxic goiters may be absolutely intractable under local anesthesia and general anesthesia must be resorted to. Thorough consideration of the patient, taking into account his physical as well as his mental condition, should operate against fixed and unalterable dogmatism in prescribing only one type of anesthesia for all patients, presenting all types of goiter. One should suit the anesthetic to the patient rather than try to suit the patient to the anesthetic.

TYPES OF ANESTHESIA

If all anesthetists were highly skilled, we would, perhaps, be compelled to agree with the statements emanating from one of the large goiter clinics to the effect that nitrous oxid oxygen anesthesia is the anesthetic method of choice for all goiter operations; that the more serious the risk presented by the physical condition of the patient, the greater the necessity for using gas anesthesia. If we were all as skilful in the use of local anesthesia and in the control of the patient as Hertzler (130), we might agree with the operators who contend that general anesthesia presents an unjustifiable extra hazard and that all thyroid operations may be more safely and successfully done under local anesthesia.

General Anesthesia

The main advantages of general anesthesia are: ease of administration, the complete control of the patient by the anesthetist, an anesthetic

state to which the surgeon is accustomed for operation and conformity to the usual routine of the operation room. In the opinion of many surgeons, these advantages make a general anesthetic the one of choice in cases of atoxic goiter with little or no visceral change.

There are, however, drawbacks and disadvantages connected with general anesthesia that should not be ignored. In the case of a patient with obstructive dyspnea or whose cardiovascular system has been ravaged by thyrotoxicosis, the danger of cardiac or respiratory collapse is very real. A period of excitation under general anesthesia, especially if the patient coughs and struggles, is not without danger. A very deep anesthesia is not required for thyroid surgery, but even light anesthesia may in some cases accelerate the pulse, disturb the respiration, and increase the danger of postoperative complications.

Local Anesthesia

Local anesthesia is safer than general anesthesia. By its use postoperative vomiting, bronchitis, and pulmonary complications are avoided. Most important, the danger of injury to the recurrent laryngeal nerve is lessened. Should the surgeon desire to assure himself that the voice is unimpaired, the patient may be encouraged to talk at any time during the operation.

Local anesthesia possesses certain disadvantages which cannot be overcome in all instances. Some patients will not submit to operation under a local anesthetic no matter how successfully the surgeon has gained the patient's confidence in other respects. Other patients, even though they agree to operation under local anesthesia, are not temperamentally qualified to carry out their determination. All surgeons are not able to administer a local anesthetic in such a way as to give the greatest comfort and the greatest security to their patients.

Mixed Anesthesia

Mixed anesthesia, or anesthesia by a combination or sequence of agents each one of which contributes to the anesthesia, has been in general use for several decades, although from the theoretic standpoint it has been widely condemned as a pernicious form of polypharmacy. By the use of a combination of drugs not only can complete anesthesia be induced during the short period of time required for the operation but a condition of euphoria can be maintained during the pre- and postoperative periods. Resorts to preliminary medication is so general that in discussions on anesthesia, comments are more often heard upon its non-use than upon its use. The most popular mixed anesthesia is nitrous oxid oxygen analgesia, reinforced by local anesthesia, and preceded by preliminary medication with such drugs as barbital, sodium amytal, and morphine.

ANESTHETIC AGENTS

Chloroform

Chloroform has a very restricted field of usefulness in the present day practice of goiter surgery. It was in general use in the early days of

thyroid surgery and many untoward accidents resulted from its use. The heart in the thyrotoxic patient is unusually susceptible to its influence and its use in thyroid surgery is especially dangerous. Chloroform in light dosage has been advocated by some surgeons during the removal of large intrathoracic goiters, on the grounds that the lung congestion set up by the pressure on the trachea and vessels acts in the nature of a contra-indication to ether or gas oxygen anesthesia. Should the surgeon for any reason decide to use chloroform, he should be particularly careful if adrenalin has been used in a solution for local anesthesia. The combination of chloroform and adrenalin is particularly dangerous.

Ether

Ether still has its field of usefulness—a field of usefulness considerably reduced from that of former days. The disadvantages of ether given by the open method are so well understood that comment is unnecessary. It is in common use as an adjuvant to nitrous oxide oxygen. When used in this way its disadvantages are not so apparent.

Small or moderate doses of ether administered by the rectal method seems to be especially useful in intrathoracic goiter and cases with difficulty of respiration. Ether rectal anesthesia is accompanied by no irritation of the upper air passages and rarely by postoperative nausea and vomiting. Properly given, it induces anesthesia with no sense of suffocation or period of excitement and does not influence the pulse or blood pressure. The anesthesia is of uniform depth and may be stopped at any time by removing the residue from the rectum or colon.

Nitrous Oxid Oxygen

Nitrous oxid gas with oxygen has come to be recognized in this country as the most valuable agent in the production of mixed anesthesia for goiter operations. In former years its use met with severe objections from many goiter surgeons. It was alleged that it was difficult to administer, that its effects were transient, that the muscular relaxation was imperfect, and that very special skill was demanded on the part of the anesthetist to produce anesthesia without cyanosis. These objections are well founded when applied to the use of nitrous oxid oxygen alone. Some adjuvant, such as adequate preliminary medication or the addition of ether to the mixture, is necessary for the maintenance of complete anesthesia without cyanosis or anoxemia. When properly reinforced, however, it is so satisfactory that the use of nitrous oxid gas and oxygen, in combination with sodium amytal, morphin and hyoscin, or local anesthesia, has come into general use in the majority of the goiter clinics. The wide range of the stage of analgesia and the fact that it precedes the stage of excitement makes nitrous oxid oxygen an ideal agent for the production of this form of anesthesia.

Ethylene

Ethylene is more potent and produces a greater degree of relaxation than nitrous oxid. It will induce relaxation, in practically every case, without exhaustion or cyanosis. Deep anesthesia may be more rapidly

produced with ethylene oxygen than with any other known safe anesthetic and recovery from its effects is correspondingly rapid.

One of its greatest advantages is the rapid disappearance of the anesthesia. If grave symptoms occur or a sudden complication develops during the course of an operation, there is urgent indication for the discontinuance of the anesthetic. The effects of ethylene will usually disappear within two minutes after its administration has been stopped. Fifteen minutes or more are necessary for the effect of an ether anesthetic to disappear and in the meantime irreparable damage may have occurred. Many observers claim that the blood pressure and the pulse are influenced less by ethylene oxygen than by any other anesthetic.

The advantages of ethylene as an anesthetic may be summed up as follows: Deep anesthesia without cyanosis, headaches, or other untoward symptoms; good relaxation without preliminary medication; ease and rapidity of administration; and, prompt recovery from its effects.

The greatest disadvantage of ethylene is the ever present danger of explosion. It has been asserted that to make ethylene anesthesia free from danger it is only necessary to keep flames and electric sparks out of the operating room during the progess of an operation, but some distressing accidents have occurred in spite of great precautions. A minor disadvantage is that to some people the odor is rather offensive. It has been likened to garlic and in some instances the odor, without other injurious effects, may remain for several hours.

Ethylene has a definite effect on the color of the blood, which is a valid objection to its use because it masks cyanosis to such a degree that serious conditions may go unnoted. The fact that ethylene colors the blood pink has also given rise to a belief that it increases hemorrhage, but this is probably an erroneous impression due to the appearance of venous hemorrhage and oozing, which, under ethylene, looks like arterial bleeding. In other words, from the point of view of its clinical importance, the cyanosis is over emphasized in the cases of nitrous oxid and under emphasized in the case of ethylene.

It is our experience that there is a slightly greater tendency to nausea following ethylene oxygen anesthesia than there is following nitrous oxid oxygen anesthesia. This may be due to the fact that slight degrees of cyanosis are not so readily observed under ethylene as under nitrous oxid anesthesia and consequently mild degrees of anoxemia are overlooked.

The margin between full consciousness and full anesthesia, under ethylene, is so narrow that a state of analgesia is difficult to maintain. The patient is not so rational, while in the analgesic state produced by ethylene, as in that produced by nitrous oxid. For these reasons we think that for deep anesthesia, ethylene is superior to nitrous oxid, but for analgesia, nitrous oxid is far better than ethylene.

As regards after-effects, there is small choice between ethylene oxygen and nitrous oxid oxygen anesthesia. The patient recovers from the effects of either one very rapidly. The time required for recovery does not bear a definite ratio to the length of the anesthesia or the amount of the

anesthetic administered, as the gases are quickly eliminated by the lungs. The patients awake rapidly, apparently to full consciousness, and may answer questions rationally within a period of two minutes.

Carbon Dioxid

Before leaving the subject of gas anesthetics a word should be said concerning carbon dioxid. Carbon dioxid as a respiratory stimulant has its place in conjunction with general anesthesia especially for thyroid surgery. In certain instances the addition of carbon dioxid in a weak concentration to the respired gases has a definite tendency to quiet overtense patients. It may be used in combination with oxygen and ether, nitrous oxid or ethylene. When so used, it apparently increases the rate of absorption of oxygen as well as of the particular gas that produces anesthesia.

Properly given carbon dioxid tends to eliminate or minimize breath holding, struggling and cyanosis during the stage of excitement. By stimulating respiration, it shortens the period of induction and prevents cyanosis. Considerable caution must be exercised in its use, as strong concentrations are inadvisable or even dangerous. The danger signs are labored or rapid respiration, convulsive abdominal movements, and congested face. This gas should always be used with oxygen and in concentration of not greater than 10 per cent.

Morphin

Morphin is an anesthetic only in the sense that it contributes to the effect of other anesthetic agents. Its use is restricted to preliminary medication for which purpose it is widely used. It has the disadvantage of often producing nausea and vomiting.

Morphin and Hyoscin

Hyoscin has no place in anesthesia except when used with morphin. The combination of morphin and hyoscin, when used in proper dosage, produces ideal anesthesia. The exact dose required cannot be stipulated as the effect varies widely with different patients. The same dose may have little effect upon one patient and produce a dangerous degree of anesthesia upon another. The high incidence of delayed elimination, prolonged stupor, retarded respiration and other untoward effects, necessitates extreme caution in its administration. In moderate dosage, this combination is a valuable agent for preliminary medication. It rarely produces nausea or vomiting.

Barbital

Barbital cannot be used with safety for complete anesthesia but for the control of mental states previous to operation it is of value. Given on the night before and repeated on the morning of the operation, it produces a condition of euphoria that lasts for several hours. The intensity and duration of its effect is not constant, varying with different patients over a wide range. Idiosyncrasies to it are not uncommon.

Phenobarbital

Phenobarbital is used in the same way as barbital and its action is quite similar. It is more constant in effect than barbital and, while it does not produce as pleasant a dream state, it is not so likely to produce delirium or hallucinations.

Pernocton

Pernocton is a German preparation which has been used quite extensively in Germany since 1926. It is given intravenously and has the advantage of rapid effect. If injected very slowly, the effect can be watched and by noting the early symptoms the required amount for anesthesia can be determined with a fair degree of accuracy. We used it in 100 cases in 1927 and 1928 with successful anesthesia in seventy-two. In twenty-eight cases the dose given was not sufficient for complete anesthesia and a small amount of nitrous oxid oxygen was required as an adjuvant. It would be an ideal agent for anesthesia if the required dosage could be accurately estimated.

Sodium Amytal

Sodium amytal was first presented as an agent for complete anesthesia and administered intravenously in the same manner as pernocton. So far as we can determine it is similar to pernocton in effect. Here again, if we could always accurately estimate the dose required, would be an ideal agent for anesthesia. Experience has demonstrated that this is very difficult to do. Owing to the danger of excessive dosage we have discontinued its use, except by oral administration as an adjuvant to other anesthetics. It is more constant in its action than barbital or phenobarbital and is one of the best agents available for the production of euphoria preliminary to operation. It has the advantage of being slowly eliminated, some sedative effect being evident for a period of from twelve to twenty-four hours. In the presence of hepatic insufficiency, barbital, phenobarbital and sodium amytal are all very slowly eliminated, and should be given with great caution to patients who are jaundiced or have other evidence of hepatic insufficiency.

Procain

Procain (Novocain) is the most widely used and perhaps the best and safest drug for local anesthesia. It is only one-fortieth as toxic as cocain and does not produce the localized edema that follows the infiltration with a solution containing some of the other drugs. Caution is necessary in the case of patients who have been digitalized, since the toxic effects of digitalis and of procain are quite similar, and each increases the effect of the other.

TECHNIC OF ANESTHESIA

The preparation of the patient for the operation has been discussed in the chapter on Preoperative Management. It is of the utmost importance, particularly with patients suffering from hyperplastic goiter, that the most favorable physical and mental condition for operation should

be secured. In toxic cases the maximum beneficial effects of iodin should have been obtained. The patient should, from the effect of the preliminary medication, be in a condition of euphoria and free from apprehension and nervousness. Should the condition of the patient indicate that a sufficient degree of euphoria has not been obtained, one-eighth, one-sixth or even one-fourth grain of morphin either with or without hyoscin may be administered hypodermically.

Many patients, whose condition strongly contra-indicates a general anesthesia, strenuously object to the thought of local anesthesia. Such a patient may be told truthfully that he will be attended while in the operating room by an expert anesthetist who will protect him from pain and discomfort and will be ready to administer a gas anesthetic as soon as the needed preparations for operation have been completed. Such an assertion will greatly relieve the patient's mind and assure a much better mental state for operation.

The mental control of the patient while in the operating room is in the hands of the anesthetist. It is his duty, by counsel and encouragement, to allay the patient's fears and obtain his cooperation. Usually this will not be difficult if the patient has been subjected to a similar routine on previous mornings and has been convinced that he can rely upon the anesthetist to protect him from discomfort.

Should the patient become fearful during the course of the operation, the anesthetist will perhaps inform him that more medicine has been used in the hypodermic than was used on previous mornings, that the treatment he has received will prevent all pain and therefore the surgeon may quite well proceed with further steps in the preparation for operation. He may explain that it is best for the patient that the duration of the anesthesia be limited as much as possible and enlist the cooperation of the patient to that end. He may even feel justified in reassuring the patient during the operation by some such statement as "It takes some time for the surgeon to get ready to operate and you must not be impatient." In the majority of cases the operation can be completed under local anesthesia before the patient is aware of the fact that the operation has begun. If the patient becomes restless or uncomfortable, the administration of nitrous oxid oxygen to the point of analgesia is indicated.

Administration of General Anesthetics

Ether.—Ether may be administered by the open method, in combination with nitrous oxid oxygen or ethylene oxygen gas, or by the rectal method. When administered by the open method through a thin mask the elimination of carbon dioxid from the lungs is stimulated, the normal ratio of carbon dioxid to oxygen in the residual air in the lungs is disturbed with consequent respiratory inefficiency. The excessive elimination of carbon dioxid may to a considerable degree be prevented by using a large, well-fitting, thickly covered mask that will retain a portion of the air exhaled during a respiration. Enough carbon dioxid is retained in the exhaled air under the mask to have considerable effect, when reinhaled, in stimulating the respiratory center.

When ether is administered in combination with nitrous oxid oxygen or ethylene oxygen gas, it is usually used only as an adjuvant to the other gases. The ether vapor is usually not added to the mixture until the patient is anesthetized and its use is discontinued at some little time before the end of the anesthesia.

When ether is used by the rectal method the estimated amount in solution with olive oil is slowly injected into the rectum fifteen or twenty minutes after a hypodermic has been given of morphin, or morphin and hyoscin, and thirty minutes before the patient is to go to the operating room.

The maximum dose is one fluid ounce of ether per twenty pounds of body weight. Forty per cent of the maximum dose is given by using one ounce, per twenty pounds of body weight, of a 40 per cent mixture of ether in olive oil. This small dose does not produce complete anesthesia but is a very satisfactory adjuvant for gas oxygen anesthesia or for local anesthesia. This mixture rarely causes irritation and is rarely expelled. We have never found it necessary to remove the residue during or after operation when this dose was given.

Nitrous Oxid Oxygen.—Nitrous oxid oxygen is best administered under low positive pressure. It is important that the apparatus for its administration be such that dangerously high pressures can not be obtained and that the flow of the different gases can be automatically controlled. A mechanically perfect apparatus with a well-fitting mask is a requisite for the maintenance of the correct degree of positive pressure necessary for smooth even administration.

Success in the administration of nitrous oxid oxygen anesthesia depends upon an accurate estimation of the amount of oxygen required. The respiratory apparatus of the thyrotoxic patient is already severely taxed in properly oxygenating the blood. With even a slightly diminished supply of oxygen the patient will show lividity of varying degrees. Cyanosis of any serious degree is a danger signal. When the skin is cyanotic, it must be remembered that the oxygen supply of the internal organs is also deficient. With cyanosis we not infrequently have venous engorgement of the head and neck, particularly the tongue. This may cause some interference with the respiratory function. Safety requires that anoxemia be prevented at all times. Nitrous oxid imparts a blue tint to the blood and, in light complexioned patients, to the skin. The experienced anesthetist will not mistake this effect for cyanosis.

The analgesic stage in the administration of nitrous oxid oxygen precedes the stage of excitement. In this, the ideal stage of anesthesia for thyroid surgery, consciousness is not lost. The patient is still rational and can respond to suggestions from the anesthetist, can cough and even answer questions when aroused. The reflexes are slow; the question or suggestion may have to be repeated before the patient responds and the response may be delayed for half a minute or more. In some instances the hearing is acute and noises, such as those from the handling of instruments or basins or the moving of tables, may sound terrifying to the patient. Fright and struggling may not be recognized as the effect of

such noises on account of the delayed response. The actual pain is obtunded more than the sensations of choking or of difficulty in breathing. In some instances the patient is insensible to the actual pain of the operative procedure but is terrorized by the exaggerated sensation of palpitation of the heart.

The analgesic stage should be induced slowly and on the appearance of any evidence of the onset of the stage of excitement, such as fright, discomfort, struggling or delirium the mask should be removed, the patient reassured and his cooperation secured before the administration is resumed. Usually the difficulties encountered are less each time the administration is resumed and in the second or third attempt a satisfactory analgesic state is obtained.

A short period of anesthesia widens the range of the stage of analgesia and narrows the stage of excitement. In some rare instances it is necessary, before a state of analgesia can be maintained, to induce anesthesia for a short time. The transition, from anesthesia to a satisfactory state of analgesia, usually occurs without marked evidence of the stage of excitement, unless the patient is disturbed by noise of some kind.

Ethylene Oxygen.—Ethylene is given in the same manner as nitrous oxid oxygen. As it imparts a pink tint to the blood and skin even in the presence of cyanosis of moderate degree, it is important that symptoms of anoxemia be carefully watched for. One may change from nitrous oxid to ethylene if nitrous oxid will not, with safety, hold the patient in the degree of anesthesia desired. (We have never found it necessary to so do.)

It is a dangerous practice, in view of the danger of explosion, to administer ethylene through a bag containing nitrous oxid. If only one apparatus is available, the mask should be removed from the patient's face for a moment, the bag quickly emptied by compression and washed with oxygen or carbon dioxid gas before ethylene is admitted to the bag. Every precaution should be observed so that sparks and open flame do not come near the apparatus.

Technic of Local Anesthesia

Local anesthesia may be obtained by simple infiltration of the tissues in advance of the operative procedure, by blocking nerves of the cervical plexus, or by a combination of nerve block and infiltration. One-half or 1 per cent solutions are effective for infiltration anesthesia. A concentration of 1 per cent is necessary for blocking large nerve trunks unless the solution is injected within the sheath. Not more than 100 cubic centimeters of a 0.5 per cent or 60 cubic centimeters of a 1.0 per cent solution should be used.

The addition of adrenalin to the solution delays the absorption of the procain but prolongs its effect. From the standpoint of the prevention of toxic effects, slow absorption is of advantage. This advantage, however, is offset by the fact that less solution escapes from the wound during the operation and more procain is absorbed. In some cases a dangerous rise in blood pressure and pulse rate follows the absorption of adrenalin. The fact that some persons are hypersensitive to adrenalin

should not be ignored. The reaction of the patient to adrenalin should be tested by the Goetsch method before operation if the use of adrenalin is contemplated.

Infiltration Method.—The steps in the infiltration method are as follows:

(1) The whole area of the skin flap is infiltrated subcutaneously.
(2) After the skin flap is raised and before the fascia has been opened, the prethyroid muscles are infiltrated.
(3) After the prethyroid muscles have been separated down to the anterior surface of the gland, the prethyroid space is infiltrated.

Infiltration of the area of the skin flap is begun by the subcutaneous injection of 3 to 5 cubic centimeters of 0.5 per cent solution of procain over the manubrium sterni at a point just below the suprasternal notch. The infiltrated subcutaneous area is extended upward by inserting a long needle through the anesthetized area and injecting the solution as it is passed upward in various directions. Twenty to 30 cubic centimeters of the solution is required for the infiltration in most cases, but as the flap is raised immediately on the completion of the injection, a large part of the solution escapes through the wound and is not absorbed.

After the skin flap is raised, the prethyroid muscles and overlying fasciae near the median line are infiltrated and five to ten cubic centimeters of the solution are deposited under the prethyroid muscles in the perithyroid space, between them and the surface of the gland. Prompt separation of the prethyroid muscles and exposure of the anterior surface of the gland permits the escape of the greater part of the solution.

After the anterior surface of the gland is exposed, the infiltration is extended in advance of the operative procedure throughout the perithyroid space. All actual pain may be prevented by this method, but it does not abolish the sense of dragging and pressure caused by manipulations in the deep parts of the wound.

A skilful operator may inject the prethyroid muscles and the perithyroid space before the incision is made. The injection of the perithyroid space around the upper pole is of most importance as the majority of the nerves to the gland are found in this location. Infiltration of this area blocks the nerves of sensation of the entire gland except in the region of the lower pole. Great care should be exercised that none of the solution is injected directly into a blood vessel.

The sudden introduction of large quantities of solution into the blood stream may be followed by pallor, extreme restlessness, tachypnea, rapid pulse rate, lowered blood pressure, a feeling of impending death and, in severe cases, nausea and vomiting followed by syncope.

The appearance of pallor, restlessness or tachypnea during the injection of the solution is an indication for the lowering of the head and prompt stimulation. The nervous symptoms may be controlled and the other symptoms masked, by morphin or a general anesthetic but these measures will have little effect upon the lowered blood pressure and tachycardia. The most reliable remedy for this condition is caffein sodium benzoate. The inhalation of 5 to 8 per cent of carbon dioxid in oxygen

is almost as effective. In some cases the addition of carbon dioxid to the anesthetic mixture produces prompt relief.

The administration of adrenalin is usually followed by a rise in the blood pressure but may result in aggravation of the other symptoms. The unfavorable reaction to adrenalin, especially in those who are hypersensitive to it, can be largely prevented by the simultaneous injection of pituitary extract. The effect of the adrenalin in raising blood pressure is greatly increased by the pituitary extract, therefore smaller doses of adrenalin are required if pituitary is also given. The rise in blood pressure from adrenalin alone is preceded by a rise in the pulse rate. The rise in blood pressure when pituitary is given at the same time as adrenalin, is rarely accompanied by an increase in pulse rate, in fact, in most cases a reduction in pulse rate occurs coincident with a rise in blood pressure.

Cervical Plexus Block.—The nerves of the cervical plexus may be blocked by the injection of a 1.0 per cent solution of procain in front of the transverse processes of the second, third, and fourth cervical vertebrae. The superficial landmark usually used is a point at the junction of the upper and middle thirds of a line drawn from the anterior border of the mastoid process to the sternoclavicular joint. No superficial landmark is entirely reliable as the relations of the deeper structures change with variations in the positions of the head and neck. The location of the posterior border of the sternomastoid muscle must be taken into consideration.

In thin subjects the location of the transverse processes may be determined by palpation and the procedure presents little difficulties. The needle is thrust in until it strikes the tip of the transverse process of the third cervical vertebra. It is then slightly withdrawn and passed in front of the process and 5 to 10 cubic centimeters of a 1.0 per cent solution of procain is injected. By slightly withdrawing the needle and then thrusting it upward and downward injections are also made in front of the transverse processes of the second and of the fourth cervical vertebrae. The same procedure is carried out on the other side. If the solution has been accurately deposited on both sides there is a complete block of the nerves of the cervical plexus with anesthesia of the majority of the superficial and deep tissues in about ten minutes. The nerve supply to the sternomastoid and the platysma muscle is not interfered with, and sensation at the upper pole of the gland is not abolished.

Superficial Cervical Nerve Block.—The superficial cervical nerves may be blocked at the point where they exit from behind the middle of the posterior border of the sternomastoid muscle. With a fine needle (27 gage) a few drops of a 0.5 per cent solution of procain is placed in the skin, at a point in the midline just below the suprasternal fossae. Through the white area of skin thus formed, the point of a six-inch, 22 gage needle is introduced just beneath the skin and passed upward, over the lateral border of the suprasternal notch, and over the sternomastoid muscle to the point at the middle of its posterior border where the superficial nerves of the cervical plexus emerge from behind it. Injection of a 1.0 per cent solution of procain as the needle is slowly advanced

prevents pain or discomfort. The infiltration should extend upward for at least an inch above the point at which the course of the external jugular vein crosses the posterior border of the sternomastoid muscle. Infiltration of the superficial and deep cervical fascia down to the muscle, over an area of about one and one-half inches in diameter, blocks the superficial branches of the cervical plexus on that side. The needle is withdrawn until its point is just beneath the skin and reintroduced on the opposite side and the injection made in the same manner. Blocking the superficial nerves of the cervical plexus on both sides results in complete anesthesia of all the superficial structures.

Nerve Block and Infiltration.—The combination method consists of nerve block anesthesia for the superficial structures, and infiltration anesthesia for the deep ones. The superficial structures in the field of operation are anesthetized by blocking the cervical nerves by either of the methods already described. A needle is then inserted to the mesial side of the upper pole and the perithyroid space in the region of the upper pole is infiltrated with a 0.5 per cent solution of procain. The prethyroid muscles and the fascia over the region between the upper pole and the larynx are infiltrated as the needle is withdrawn. This injection produces anesthesia of the anterior portion of the upper three-fourths of the gland, the prethyroid muscles and the deep fascia, but not of the deeper structures. This anesthesia is entirely satisfactory for the exposure of the gland but in the majority of cases does not prevent pain and discomfort from operative procedures near the posterior surface of the gland. To make the anesthesia complete in all the structures involved and to render the operation entirely painless, the posterior portion of the gland with adjacent structures must be anesthetized. This is easily done after the anterior surface of the gland is exposed. The prethyroid muscles on one side are retracted laterally and the prethyroid plane of cleavage is developed until the anterior surface of the postthyroid fascia, over the postthyroid space, is exposed. A needle is introduced through the thin prethyroid fascia into the postthyroid space and a 0.5 per cent solution of procain is injected until the space is distended. By the same procedure the postthyroid space on the other side is infiltrated. Infiltration of both postthyroid spaces produces anesthesia of the deeper portions of the gland and of the pretracheal fascia. Thus complete anesthesia is obtained of all the structures involved in the operative procedures.

Mixed Anesthesia

Mixed anesthesia is the anesthesia of choice in our clinic in the majority of cases. The routine of administration varies with the method employed. In mild cases, the administration of the anesthetic is the same as for any other operation in which complete relaxation is not required. In severe cases, if the operation is to be done under general anesthesia, the administration of nitrous oxid oxygen is begun in the same manner as on previous mornings but is continued until anesthesia is induced. For local anesthesia, the first injection is made with the same routine as

that of previous mornings and the subsequent steps in producing the anesthesia are effected with extreme care.

If the combination of local anesthesia and nitrous oxid oxygen analgesia is to be used, one of two methods may be employed: General analgesia may be induced first and the local anesthetic solution introduced afterward, or local anesthesia may be effected first and analgesia induced after the gland is exposed or upon the appearance of restlessness or discomfort. When mixed anesthesia is used in our clinic, the latter method is preferred. The local anesthesia prevents painful stimuli and the nitrous oxid oxygen analgesia makes the patient comfortable.

The conditions for operation that we consider necessary for an ideal anesthesia and their sequence are as follows:

Surgical Risk of I, II, or III (p. 168).

A condition of euphoria when the patient enters the operation room.

Induction of nitrous oxid oxygen analgesia at any time that the patient is nervous or uncomfortable.

Introduction of local anesthesia by cervical plexus block and infiltration of the perithyroid space in the region of the upper role.

Exposure of the gland, development of the prethyroid plane of cleavage on each side until the prethyroid fasciae are exposed and infiltration of both postthyroid spaces.

This sequence of anesthetic measures, when properly performed, minimizes the ordeal of operation to the greatest possible degree compatible with safety. The technical difficulties encountered are not great and the anesthesia produced is ideal for all operations on the thyroid gland.

CHAPTER XI

SURGICAL ANATOMY

Exact anatomic knowledge is the basis of technic for any surgical operation; it is especially desirable for those undertaking the responsibilities of thyroid surgery.

The thyroid surgeon should have the descriptive and topographic anatomy, and the relationship of important structures of the region in which he is interested, so definitely in mind that he can clearly visualize them through the overlying tissues. He should be able to picture the deeper structures in relation to the surface landmarks. Furthermore, his "anatomic vision" should be sufficiently clear to enable him to place or localize important structures **irrespective of the position in which the head and neck may lie.**

Knowledge of the exact location of the deep structures is greatly facilitated by thorough knowledge of the triangles of the neck, the different layers of the fascia, and the planes of cleavage. If one has a correct and thorough knowledge of the contents of the cervical triangles and of the planes of cleavage, he can hardly under any circumstances become seriously confused. The triangles of the neck are well marked. Their boundaries are clearly defined by landmarks that appear successively as the approach is made in the operative procedure. Although the triangles change their shape and position with every movement of the head and neck, the different structures remain in the same position relative to the landmarks or boundaries of their respective triangles.

Confusion is more likely to arise from failure to identify different planes or different layers of structures. This confusion is obviated if the surgeon has taken the pains to acquaint himself thoroughly with the distribution of the fascial sheaths, and with the location of the planes of cleavage which is dependent upon the fascial distribution.

The importance of the fascial layers and the planes of cleavage cannot be overestimated. In the early days of goiter surgery this consideration was disregarded. The goiter was removed with a nonchalant disregard for the finer nuances of topographic anatomy. As a consequence, the operation was accompanied by more difficulties and trauma than it would have been if the planes of cleavage had been carefully followed.

A thyroidectomy performed according to a technic which takes cognizance of definitely constituted planes of cleavage is attended with less effort on the part of the surgeon and is much less likely to result in complications.

Knowledge of these interfascial spaces or planes of cleavage is of great importance from another angle: It enables the surgeon engaged in goiter work to appreciate the irregularities in size, shape, and position

of the various structures concerned. The irregularities in location may be due to different positions of the head and neck; there are also irregularities in location, size, shape, and relationship, due to anomalies and disease. Pathologic conditions of the thyroid may appreciably change the relationship of surrounding structures. Similar conditions may so displace some of the parathyroids that they are endangered by a thy-

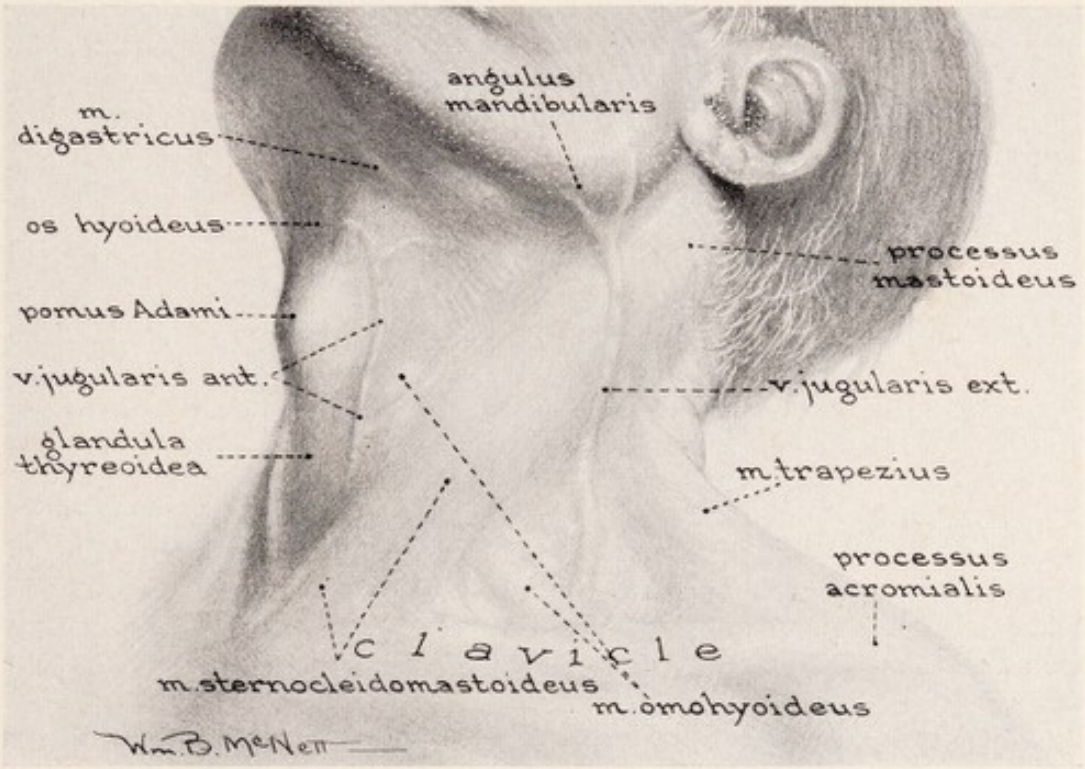


FIG. 24.—Superficial Landmarks of the Anterior Cervical Region.

roidectomy performed according to the usual technic. It sometimes happens that parathyroids in an apparently abnormal location are removed during operation and, when discovered afterwards in the specimen, are classified as aberrant parathyroids when, in reality, they are parathyroids whose position in relation to the thyroid has been changed by a growth in the posterior part of the lateral lobe.

The detailed consideration of the surgical anatomy of the thyroid region begins with structure and relationships from before, backward, and proceeds to a more detailed account of the fascial sheaths and planes of cleavage, since these are of major importance to those interested in goiter surgery.

SURFACE LANDMARKS

The anterior cervical region is bounded above by the lower border of the mandible, below, by the upper border of the sternum and the inner two-thirds of the upper borders of the clavicles, and laterally, by the anterior margin of the trapezius muscle on each side. This anterior

cervical region is bisected by the mesial plane. Each lateral region is divided by the sternocleidomastoid muscle, into an anterior and a posterior triangle.

Landmarks Near the Midline

From above downward we note as landmarks near the midline, first, the symphysis of the lower jaw. Downward from the symphysis about two fingerbreadths is the slight prominence of the hyoid bone. The horns or cornua of the hyoid bone project backward and upward on either side, and may be palpated by placing a finger on one side and the thumb on the other, in the region between the symphysis and the prominence of the thyroid cartilage. Below the hyoid bone, and between the hyoid and the thyroid cartilage, can be felt a depression over the thyrohyoid membrane.

Next, the prominence of the thyroid cartilage or the pomum adami may be seen or palpated. The upper margin of the thyroid cartilage is on a plane with the disk between the bodies of the third and fourth cervical vertebrae. The prominence can usually be seen without difficulty in thin subjects and in adult males. In women with fat necks however and in children it frequently cannot be determined by inspection; but even in these cases it can be definitely palpated.

The V-shaped notch on the upper border of the thyroid cartilage is plainly felt, as well as the expanding ala or wing on either side. A fingerbreadth or so below the promum adami the thick, rounded surface of the cricoid cartilage may be felt. The bulge of the cricoid cartilage can be seen in thin people, and can be felt by careful palpation in almost all cases.

Just below the lower border of the thyroid cartilage, in the midline, the exploring finger sinks into a depression. The floor of this depression is the cricothyroid membrane connecting the thyroid cartilage above to the cricoid below.

On either side of the cricoid and at some distance laterally the palpating fingers will encounter a bony prominence which is the anterior tubercle of the transverse process of the sixth cervical vertebra. This bony prominence, an important landmark for the procedure of local anesthesia, is called the carotid tubercle or the tubercle of Chassaignac. The anterior surface of the cricoid cartilage corresponds to the level at which the carotid sheath is crossed by the anterior belly of the omohyoid muscle.

Below the cricoid cartilage the isthmus of the thyroid gland, the surface anatomy of which varies greatly in different subjects, can in some instances be palpated. Extending out from the isthmus the lateral lobes of the thyroid are felt. The lateral lobe may be felt on each side, extending down to about the fifth tracheal ring, on the normal person. If a pyramidal lobe is present it may be defined by palpation in its extension upward from the isthmus.

Below the isthmus, in the normal individual, the tracheal rings are palpable, sinking more deeply and becoming more indistinct as the root of

the neck is reached. In young children the thymus may be felt, extending upward on the trachea for some distance above the manubrium.

At the base of the neck, where the upper border of the sternum, the sternoclavicular articulations, and the clavicle form the lower boundary of the anterior cervical region, a depression or fossa is noted in the midline, lying just above the upper border of the manubrium sterni. This depression lies between the sternal heads of the sternocleidomastoid muscles and is called the jugular fossa or suprasternal notch.

Landmarks of the Lateral Regions

The landmarks of the lateral regions that are prominent superficially are: the inferior border of the mandible, the anterior margin of the trapezius, the superior border of the clavicle, and the oblique ridge of the sternomastoid muscle. The sternomastoid muscle, extending in a diagonal direction upward and backward, from the sternoclavicular articulation to the mastoid process, is one of the chief landmarks of the neck. To bring out the muscle on one side in bold relief, the head is turned so as to direct the face toward the opposite shoulder. The sternomastoid is thus seen as a thick, more or less rounded ridge, which divides the lateral surface of the neck into two areas called the anterior and posterior cervical triangles.

Immediately above the inner end of the clavicle, between the two heads of origin of the muscle, lies a small triangular space beneath which, at some distance, run the carotid artery and the internal jugular vein. A line drawn from the angle of the inferior maxilla to the center of the clavicle, and crossing the sternomastoid a little below the junction of the upper and middle thirds, indicates with sufficient accuracy the course of the external jugular vein.

Beneath the inner margin of the sternomastoid muscle, just below the level of the upper border of the thyroid cartilage, the pulsation of the common carotid artery can be felt. The course of the common carotid, as it lies beneath the anterior border of the muscle, may be indicated roughly by a line drawn from the sternoclavicular articulation to a point approximately midway between the angle of the inferior maxilla and the tip of the mastoid process. The middle of the posterior border of the sternomastoid muscle is a landmark indicating the point of exit of the superficial branches of the cervical plexus from behind the muscle. Blocking the nerves at this point produces anesthesia of the superficial structures of the anterior cervical region. The course of the external jugular vein can usually be seen, crossing the posterior border of the muscle just below this point.

The outline of the posterior belly of the omohyoid muscle can usually be defined by sight or by palpation as it crosses the posterior triangle. In thin people the course of the anterior jugular vein may be seen as it passes down the neck between the median line and the anterior border of the sternomastoid, to about the junction of the middle and lower thirds of the prethyroid muscles.

TRIANGLES OF THE NECK

First, each lateral cervical region, quadrilateral in shape, is divided by the oblique ridge of the sternomastoid muscle into two triangles. From the median line outward to the oblique ridge of the sternomastoid on either side lies a triangular space called the anterior cervical triangle. The region on each side, from the oblique ridge of the sternomastoid out-

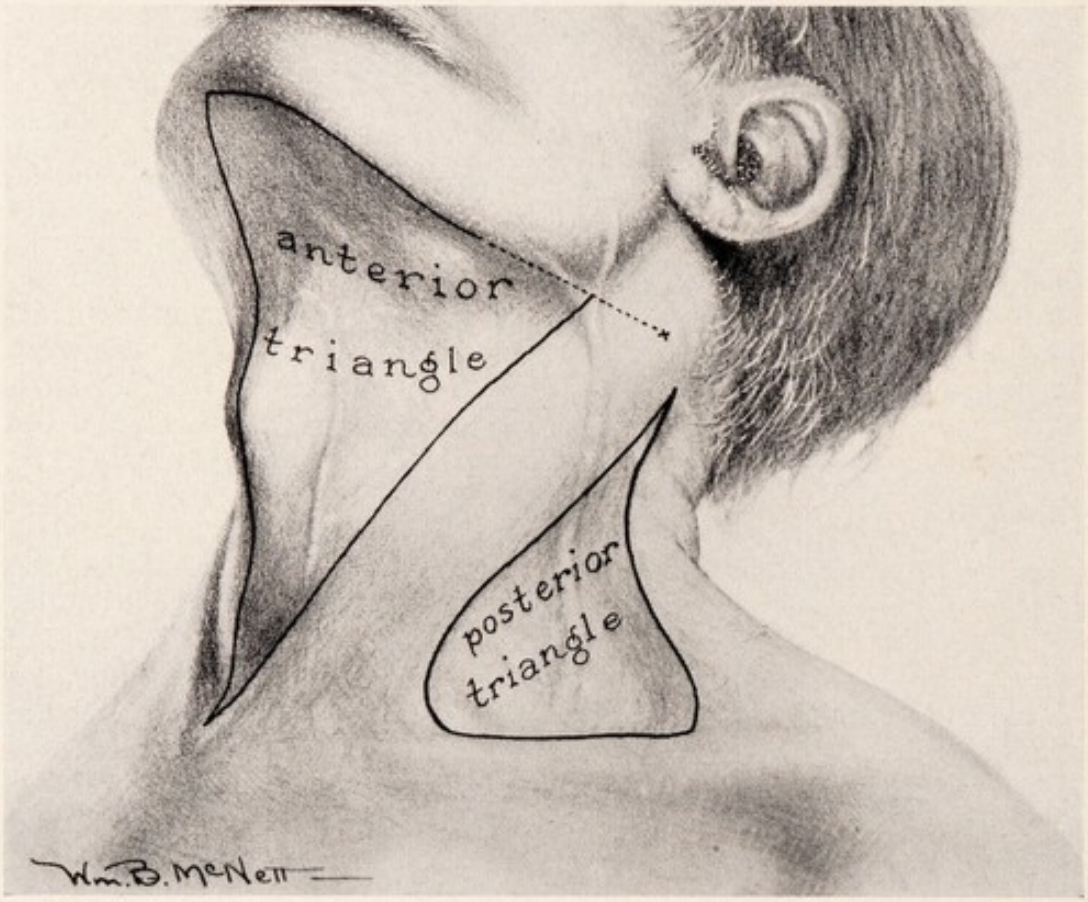


Fig. 25.—Major Cervical Triangles.

ward to the anterior margin of the trapezius, is called the posterior cervical triangle. These triangles are important, mainly, because they are the superficial landmarks for the smaller triangles located in the deeper planes of the neck.

The entire region is covered by a layer of structures: the skin, a layer of fat and connective tissue, and the superficial fascia and platysma muscle. The only important vascular structure in this layer is the external jugular vein. Its course has already been described. The superficial branches of the cervical plexus of nerves supply all the structures except the platysma muscle.

Anterior Cervical Triangle

The anterior triangle, with its apex downward, is bounded: behind, by the oblique ridge near the anterior margin of the sternomastoid muscle;

above, by a line along the lower border of the mandible and continued backward to the mastoid process; and in front, by the median line of the neck. Its apex is at the sternum.

After removal of the layer of skin, fat, superficial fascia, and the platysma muscle, down to the deep cervical fascia, the deeper structures in the area of the anterior triangle can be seen to be divided into three smaller triangles by the digastric muscle and the anterior belly of the

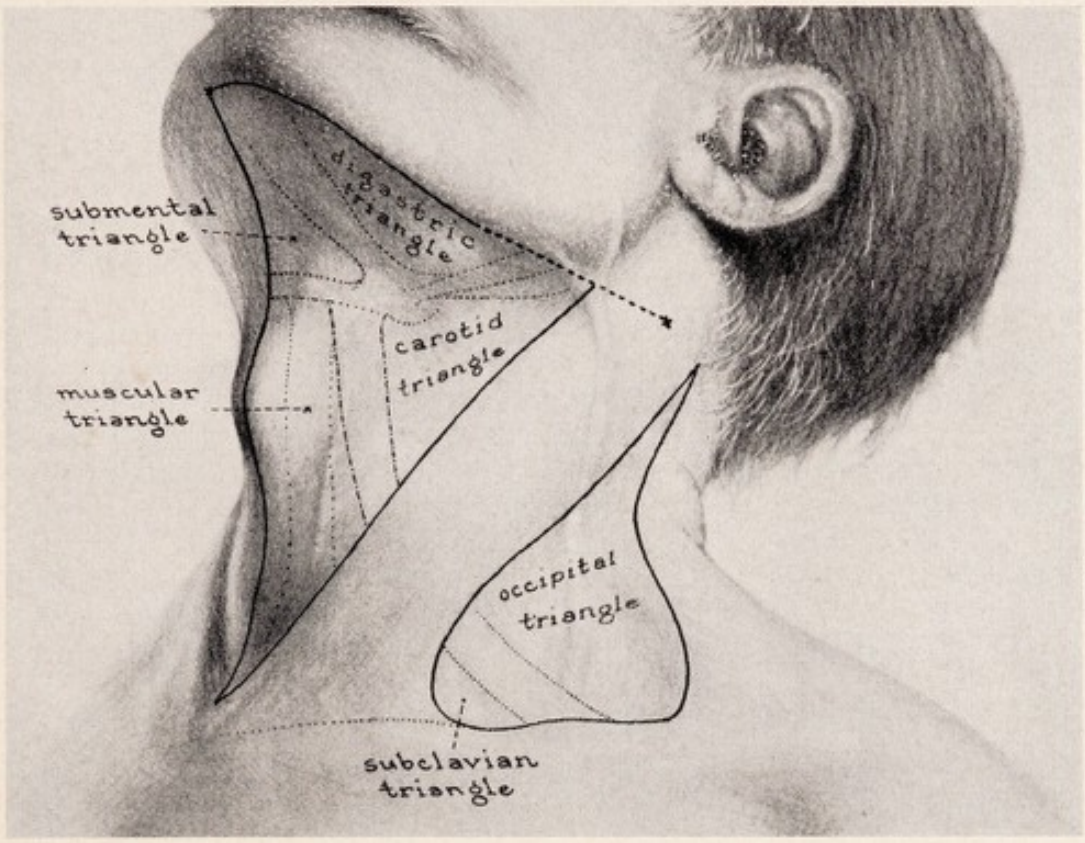


FIG. 26.—Minor Triangles of the Neck.

omohyoid. These triangles deep to the superficial fascia, include the greater portion of the prethyroid muscles and the anterior jugular veins. These smaller triangles into which the anterior superficial triangle is divided are, naming them from below upward:

(1) The inferior carotid or muscular triangle
(2) The superior carotid or arterial triangle
(3) The submaxillary triangle.

Each **inferior carotid** or muscular triangle is bounded: in front by the median line, behind and below by the anterior border of the sternomastoid, behind and above by the anterior belly of the omohyoid. Its base is at the median line; its apex at the point at which the sternomastoid crosses the omohyoid muscle.

Close to the apex of the triangle the sternohyoid and sternothyroid muscles, together with the anterior margin of the sternomastoid in this

location, overlie the lower part of the common carotid. Deep to the prethyroid muscles the parathyroid and thyroid glands are situated, lying upon the trachea.

Behind the trachea but with a slight inclination toward the left, at the base of the neck, is the esophagus. Anterior to its lateral border, and near the esophago-tracheal groove, lies the cervical portion of the recurrent nerve. The course of the inferior thyroid artery, after it emerges from behind the carotid sheath, is in this triangle. The floor of the muscular triangle is formed by the longus colli and scalenus anterior muscles and between these two the vertebral artery and vein are located.

The **superior carotid** or arterial triangle represents the most important region of the neck as far as thyroid surgery is concerned. The superior carotid triangle is in the form of an isosceles triangle with a broad base formed by the anterior border of the sternomastoid muscle in its upper three-quarters. The apex pointing toward the symphysis is represented by the central tendon of the digastric. The triangle is bounded above by the posterior belly of the digastric; below by the anterior belly of the omohyoid. The triangle is covered by the skin, superficial fascia, platysma, and deep fascia. The floor is formed by portions of the thyrohyoid, the hyoglossus, and the middle and inferior constrictor muscles of the pharynx. An important landmark for the location of structures in this triangle is the great cornu of the hyoid bone, which may be felt in front of the anterior border of the sternomastoid muscle.

The approach to the trunk of the superior thyroid artery, for the purpose of ligation, is made in this triangle. The lower angle, formed by the junction of the anterior border of the sternomastoid and the posterior border of the anterior belly of the omohyoid, is the most important landmark for the location of this artery.

The superior carotid triangle contains the upper portion of the common carotid artery. Opposite the upper border of the thyroid cartilage, the common carotid bifurcates to form the external and internal carotid. The origins of the superior thyroid, the lingual, the fascial, and the occipital arteries (all are branches of the external carotid) are also found in this space.

The veins found in the superior carotid triangle are the internal jugular, the superior thyroid, the lingual, and the fascial. The nerves met with are the descendens hypoglossi, the vagus nerve (within the carotid sheath and lying between the artery and the vein), the cervical trunk of the sympathetic (behind the carotid sheath), the spinal accessory, and the superior laryngeal nerve and its branches. The superior portion of the larynx and the lower part of the pharynx are also located in this triangle.

The **submaxillary triangle** is not of special interest to the goiter surgeon. It is bounded above by the lower border of the mandible and an imaginary line continued outward to the tip of the mastoid process. Below, it is bounded by the posterior belly of the digastric muscle, and mesially by the midline. Its floor is formed by the mylohyoid and hyoglossus muscles and by the anterior belly of the digastric muscle.

Posterior Cervical Triangle

The posterior triangle with the apex upward is bounded: behind, by the anterior margin of the trapezius; in front, by the oblique ridge of the sternomastoid; and below, by the middle third of the upper border of the clavicle. This triangle is divided into two unequal portions by the posterior belly of the omohyoid, which crosses this space about an inch above the clavicle. The space above the omohyoid is known as the occipital triangle; the space below the omohyoid constitutes the subclavian triangle.

The **occipital triangle** is the larger of the two posterior triangles. Its apex points upward and the triangle is bounded: below, by the posterior belly of the omohyoid; in front, by the oblique ridge of the sternomastoid muscle; and behind, by the anterior margin of the trapezius. Its floor is formed by the following muscles: splenius capitis, levator scapulae, and the middle and posterior scaleni muscles. It is covered by the skin, the superficial and deep fascia and in the lower part by the platysma muscle.

In the occipital triangle are found the spinal accessory nerve, the superficial branches of the cervical plexus (which emerge from behind the posterior edge of the sternomastoid muscle), and the branches of the cervical plexus to the levator scapulae and trapezius muscle. A portion of the occipital artery is found as it emerges from behind the sternomastoid. The external jugular vein may be seen through the superficial cervical fascia. A chain of lymphatic glands runs along the posterior border of the sternomastoid.

The approach to the cervical plexus in nerve blocking operations is made through this triangle. The approach to the inferior thyroid artery, for purposes of ligation, is usually made through the inferior mesial angle formed by the junction of the sternomastoid and posterior belly of the omohyoid.

The inferior or **subclavian triangle** is much the smaller of the two. Its base, directed toward the midline of the neck, is formed by the posterior border of the lower portion (about one-sixth) of the sternomastoid muscle. It is bounded: below, by the clavicle; and above, by the posterior belly of the omohyoid muscle. The triangle is covered by the skin, and the superficial and deep fascia. The size of the triangle varies with the level above the clavicle at which the omohyoid crosses the posterior triangle, and with the extent of the attachments of the sternocleidomastoid and trapezius muscles to the clavicle. The depth of the triangle varies with the position of the shoulders.

ANTERIOR CERVICAL MUSCLES

Ordinarily the distribution of the fascia is considered before the muscles, organs, and vascular structures are discussed. In this book, however, owing to the fact that we wish particularly to emphasize the fascial distribution and the planes of cleavage, we will leave consideration of the fasciae for a later section of the chapter.

On incising the skin we come to a layer of fat and areolar tissue that varies much in thickness in the different regions of the neck. The skin is intimately attached, by fascia through the fatty layer, to the superficial fascia and moves with it.

Platysma Muscle

Beneath the fatty layer we come to the superficial fascia in which the platysma muscle is embedded. The platysma takes origin from the superficial fascia covering the clavicular parts of the pectoralis major, and the deltoid muscles. It is inserted, in part, in the upper aspect of the inferior maxilla. Most of the fibers, however, pass on and are inserted into the skin and subcutaneous tissue of the lower part of the face, particularly in the region about the angle of the mouth. The muscle extends from its origin as a thin sheet which covers nearly all of the lower two-thirds of the posterior triangle, and the lateral portion of the anterior triangle. The superficial fascia covers both the anterior and posterior surfaces of the platysma, and in addition sends numerous laminae between the bundles of muscle fibers, thus connecting the anterior and posterior layers of fascia.

In the upper portion, below the symphysis, the inner fibers of the platysma decussate across the middle line with those of the opposite side. The fibers, in general, run in a diagonal direction from below upward and forward. The muscle, consequently, in its lower portion is placed laterally so that the platysma muscles near the root of the neck do not meet in the midline. Usually, in goiter operations employing the customary collar incision, unless the incision is of extreme length and carried laterally beyond the sternomastoid, the fibers of the platysma are not encountered.

The fibers in the inferior portion are rather thin and delicate; in the superior portion, the muscle is heavy and well-developed. In ligation of the trunk of the superior thyroid artery, the surgeon should keep this fact in mind lest he be confused by the unexpected thickness of the muscle at this point.

Relations.—The platysma is separated from the skin by the anterior layer of the superficial fascia, a layer of fat and the subcutaneous fascia. Its internal surface is in contact with the deep fascia covering the subclavian, the superior carotid, and the submaxillary triangles and the inferior portion of the occipital triangle.

Nerve Supply.—The platysma is supplied chiefly by the inframaxillary branch of the seventh or facial nerve; it also receives some superficial branches of the cervical plexus.

Sternocleidomastoid Muscle

The sternocleidomastoid muscle, which divides the anterolateral surface of the neck into the anterior and posterior superficial cervical triangles, is a large, thick muscle which passes, obliquely from below upwards and backwards, across the neck from its sternoclavicular origin to its insertion into the outer surface of the mastoid process, and into the superior curved line of the occipital bone.

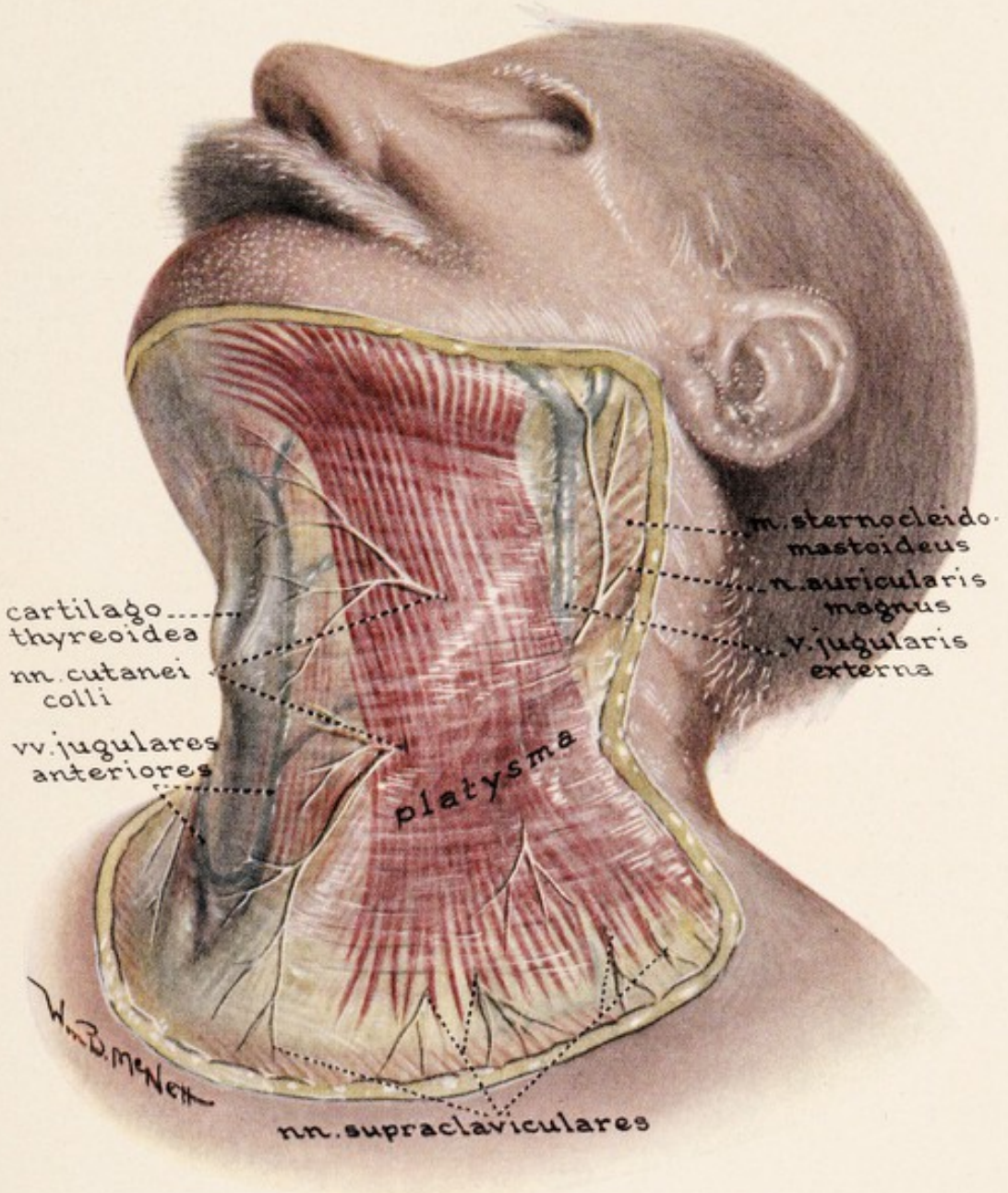


FIG. 27.—Anterior Cervical Region with Superficial Fascia Exposed.

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It originates by two heads, the sternal and the clavicular. These heads are separated at their origin by a triangular, cellular interval extending upward about one and one-half or two inches, and above this are united to form a thick, somewhat rounded muscle.

Relations.—The sternomastoid is separated from the skin by the superficial layer of the deep cervical fascia, the superficial fascia, and over a large portion of its extent by the platysma muscle. Between the platysma and the sternomastoid are located the external jugular vein, the superficial branches of the cervical plexus, and some superficial cervical glands.

Deep to the sternomastoid are, from below upward, the sternoclavicular articulation, the first and second parts of the subclavian artery, the phrenic nerve as it lies upon the scalenus anterior muscle, the sternohyoid, the sternothyroid, the omohyoid and scalenus anticus muscles and above, the posterior belly of the digastric.

In its lower portion, it is in deep relation to the transverse colli and transverse scapular arteries, and the lower transverse portion of the anterior jugular vein. Above this level it covers the scalenus posterior and the levator scapulae muscles, the cervical plexus and the hypoglossus and accessory nerves. The anterior portion of the muscle, forms the posterior boundary of the anterior triangle of the neck, and covers the carotid sheath and its contents up to the level of the upper portion of the thyroid cartilage. Above this point, which marks the bifurcation of the common carotid, it covers the internal and external carotid arteries for a short distance.

Nerve Supply.—The sternomastoid receives its nerve supply from the accessory and the deep branches of the cervical plexus.

Blood Supply.—Its blood supply is derived from: the sternomastoid branch of the superior thyroid artery, which enters the deep surface of the muscle at the level of the upper border of the cricoid cartilage; the small sternomastoid branch of the occipital, which enters the muscle at the level of the angle of the mandible; and the fine branch from the transverse scapular artery, which enters the muscle a short distance above the clavicle. The surgical importance of the sternomastoid lies in the fact that it covers most of the important blood vessels and nerves of the anterior cervical region.

Sternohyoid Muscle

The sternohyoid, a narrow, ribbonlike muscle, is anterior or superficial to the other prethyroid muscles. It rises from the superior and lateral part of the posterior surface of the manubrium sterni, and from the posterior surface of the inner extremity of the clavicle. It passes upward and a little inward, and is inserted into the lower portion of the body of the hyoid bone. Below, it is separated from its fellow of the opposite side by a considerable interval. As they ascend, the sternohyoid muscles on each side converge slightly as far as the level of the cricoid cartilage, where they commence to diverge a little. The free interval left by the divergence of the sternohyoids, close to their origin, is partly filled in by the sternothyroid muscles as they leave the thorax.

Relations.—At its origin, the sternohyoid lies immediately posterior to the sternum, the sternoclavicular articulation, and the sternal head of the sternomastoid muscle. Above the sternum, the anterior surface of the sternohyoid, a part of which forms the floor of Burns' space, is covered by the superficial fascia and the superficial layers of the deep cervical fascia. The internal surface of the sternohyoid is in contact with: the sternothyroid, the cricothyroid and the thyrohyoid muscles; the superior thyroid vessels; part of the lateral lobe of the thyroid gland; and, with the cricothyroid and thyrohyoid membranes.

The **nerve supply** is derived from the ansa hypoglossi. Its **blood supply** is from the muscular branches of the superior thyroid artery.

Sternothyroid Muscle

The sternothyroid, in the upper part of its course, is situated beneath the sternohyoid. It arises from the posterior surface of the manubrium (at its upper median part, below the origin of the sternohyoid) and from the deep surface of the cartilage of the first rib. It is inserted into the outer surface of the ala of the thyroid cartilage along the oblique line.

Relations.—In the lower third of its course it is in rather close contact with its fellow of the opposite side, occupying to a large extent the space left by the divergence of the sternohyoid muscles. The middle portion of the floor of Burns' space is formed by the anterior surface of these muscles. Inside the thorax, the posterior surface of the sternothyroid is in contact, on the right side with the innominate artery, and on the left side, with the left common carotid artery and the left innominate vein. In the neck, its posterior surface is in contact with the carotid sheath, the thyroid vessels, the isthmus and part of the lateral lobe of the thyroid gland. The inferior thyroid veins run downward under cover of its median border.

The **nerve supply** is derived from the ansa hypoglossi. Its **blood supply** is from the muscular branches of the superior thyroid artery.

The surgical importance of these prethyroid muscles lies in the fact that the usual approach to the thyroid gland is made between them. For thyroidectomy, separation is effected in the median line and the relations to each other of the muscles on each side are not disturbed. In a lobectomy the approach is sometimes made by splitting the muscle fibers and sometimes by separating the omohyoid from the sternohyoid and sternothyroid muscles.

Thyrohyoid Muscle

The thyrohyoid is an upward continuation of the sternothyroid. It arises from the oblique line on the external surface of the ala of the thyroid cartilage, proceeds upward as a small quadrilateral band, and is inserted into the inferior border of the body of the hyoid bone.

Relations.—Its anterior surface is in contact with the sternohyoid muscle toward the median line, and with the omohyoid more laterally. At its origin, its posterior surface is in contact with the thyroid cartilage

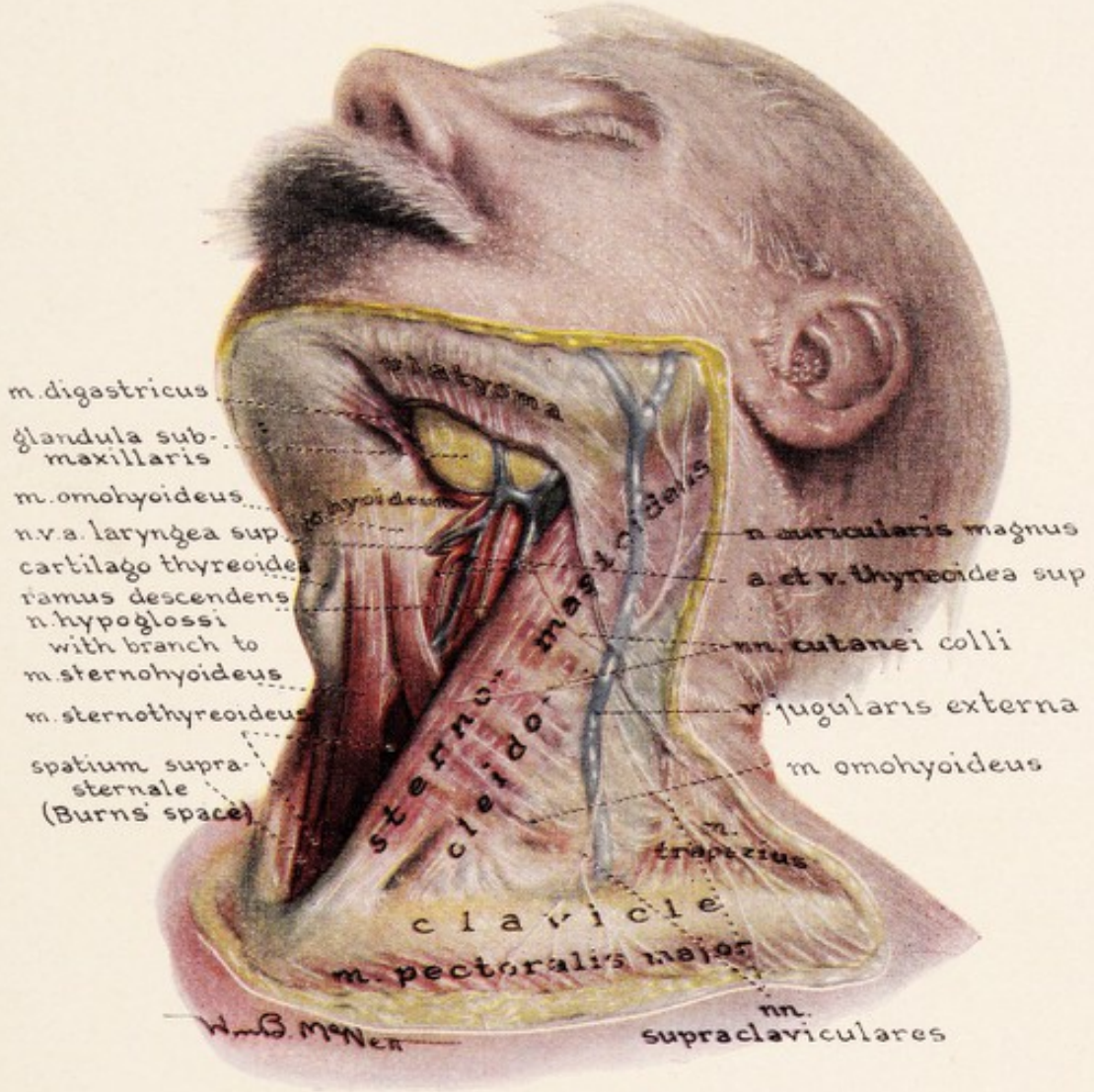


Fig. 28.—Superficial Anatomical Structures Immediately Beneath Superficial and Deep Cervical Fascia.

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and above with the thyrohyoid membrane and the superior laryngeal vessels and nerve.

The **nerve supply** of the thyrohyoid is derived from the thyrohyoid branch of the hypoglossal. Its **blood supply** is from the cricoid branches of the superior thyroid artery.

Omohyoid Muscle

The omohyoid muscle consists of two bellies—the anterior and the posterior—and a central tendon. The posterior belly arises from the upper border of the scapula and from the suprascapular ligament. It runs diagonally and slightly upward across the posterior cervical triangle and crosses beneath the sternomastoid muscle. At this point the fibers coalesce to form the central tendon.

The central tendon passes through an opening in the carotid lamina of the deep cervical fascia. It is thus anchored in a fixed position in relation to the sheaths of the sternomastoid and of the carotid vessels. The central tendon expands again to form the anterior belly and, forming an obtuse angle with the posterior belly, passes almost directly upward, close to the external border of the sternohyoid, and is inserted into the lower border of the body of the hyoid bone, external to the insertion of the sternohyoid.

The **nerve supply** of both bellies is derived from the ansa hypoglossi. The **blood supply** of the posterior belly is derived from the transverse colli and the transverse scapular arteries. The blood supply of the anterior belly is from the muscular branches of the superior thyroid artery.

CONTENTS OF THE VISCERAL COMPARTMENT

The thyroid and parathyroid glands, the larynx, trachea, pharynx, and esophagus are situated in a fascial compartment in front of the cervical vertebrae. They are loosely bound together and suspended from the skull by various muscles and reflexions of the deep cervical fasciae. Posteriorly they are suspended by folds of the buccopharyngeal and prevertebral laminae of the deep cervical fascia and by the median raphe, in which the constrictor muscles, the pharyngeal fasciae, and the pharyngeal aponeuroses terminate. Anteriorly, the larynx is attached to the hyoid bone, by the thyrohyoid membrane and ligaments and the thyrohyoid muscle. The hyoid bone, in turn, is supported by the suprahyoid muscles and ligaments.

The pretracheal fascia crosses the visceral compartment from side to side, anterior to the esophagus and trachea. The anterior layers divide to form a complete investment for the thyroid and parathyroid glands. From its posterior layers one thin lamina extends between the trachea and esophagus and another blends with the buccopharyngeal fascia to form the fascial investment of the pharynx and esophagus.

These organs, the relative position of which are maintained by the pretracheal fascia, normally move *en masse* in two directions only, upward and downward. They are elevated by the constrictor and suprahyoid muscles, and depressed by the prethyroid muscles.

Pharynx

The pharynx is a conical musculomembranous tube, about twelve centimeters in length, and extends from the base of the skull to the level of the lower border of the cricoid cartilage, where it becomes continuous with the esophagus. It is narrow anteroposteriorly and wide transversely. At its widest point, opposite the interval between the hyoid bone and the thyroid cartilage, it is about two inches in diameter. At its narrowest point—its junction with the esophagus—it is about three quarters of an inch in diameter. Its muscular coat is composed of the superior, middle, and inferior constrictor muscles. Beneath the lower border of the inferior constrictor muscle, just behind the cricothyroid joint, the intralaryngeal branch of the recurrent nerve and the inferior laryngeal artery pass obliquely upward and inward, and pierce the thyrohyoid membrane to enter the larynx.

The course of the internal laryngeal branch of the superior laryngeal nerve and the superior laryngeal artery is superficial to the lower border of the middle constrictor, and passes under the overlapping superior border of the inferior constrictor muscle. The pharyngeal plexus of nerves lies upon the middle constrictor muscle.

Esophagus

The esophagus begins at the lower, narrow end of the pharynx, behind the lower border of the cricoid cartilage. It passes downward, behind the trachea, and terminates at the cardiac opening of the stomach. When at rest it is flattened anteroposteriorly, and is wider than the trachea. When distended anteroposteriorly, its transverse diameter is shortened and it is no wider than the trachea. At its beginning, the esophagus lies immediately posterior to the trachea, but in the lower part of the neck it inclines to the left side. Its muscular layer is continuous with the inferior constrictor muscle of the pharynx. The buccopharyngeal fascia, after forming an aponeurotic investment of the constrictor muscles of the pharynx, continues downward and, with some fibers from the pretracheal fascia, forms a delicate fibrous investment of the muscular layer of the esophagus. The recurrent laryngeal nerves ascend in the pretracheal fascia, on the anterior surfaces of its lateral borders. When the esophagus is collapsed anteroposteriorly these nerves lie near the trachea. When the esophagus is distended anteroposteriorly they are at some distance from the trachea.

Larynx

The larynx is a hollow membrano cartilaginous organ situated in front of the lower portion of the pharynx. The cartilaginous framework of fifteen cartilages maintains its shape, furnishes attachments for its muscles, and contains the vocal cords and the intrinsic muscles of the larynx. Variations in speech and in the size of the air aperture through the larynx occur with changes in relative position of these cartilages as well as with changes in position of the larynx as a whole. Its lining of mucous membrane is continuous with the mucosa of the pharynx above, and with that of the trachea below.

The larynx is suspended from the hyoid bone by the thyrohyoid membrane, the thyrohyoid ligaments, and the thyrohyoid muscles. The thyrohyoid membrane is a thin layer of elastic fascia which extends from the upper border of the thyroid cartilage to the posterior border of the hyoid bone. In its central and lateral portions are thickened areas that are called middle and lateral thyrohyoid ligaments.

The thyroid cartilage forms the greater part of the anterior and lateral walls of the larynx. It is composed of two wings, or alae, that meet in the midline and form the rigid pomum adami. These alae are irregular in contour and each one is formed with a superior and an inferior tubercle, or cornu. The superior are longer than the inferior and extend upward and backward and are attached to the greater cornua of the hyoid bone by the thyrohyoid ligaments.

Cricoid Cartilage

The cricoid cartilage is signet ring in shape, broader behind than in front, and completely encircles the lower portion of the cavity of the larynx. The thyroid cartilage overlaps the anterolateral surfaces of the cricoid like a shield, the inferior cornu of the thyroid cartilage on each side forming a joint with the cricoid cartilage, at the cricothyroid articulation. The cricoid cartilage gives origin to the crico-arytenoid muscle and ligaments. On its anterior surface is situated the cricothyroid articulation; the crico-arytenoid articulations are on each side.

Hyoid Bone

The hyoid bone is suspended from the skull by the suprahyoid muscles and ligaments. It furnishes support to the pharynx anteriorly and prevents collapse of its cavity. It is connected to the larynx by the thyrohyoid membrane, ligaments and muscles.

Trachea

The trachea is the continuation of the larynx, below the cricoid cartilage. In the male, it is four and one-half to five inches in length and about three-eighths of an inch in width. In the female, it is slightly smaller. It is composed of sixteen to twenty horseshoe-shaped cartilaginous rings, connected by fibro-elastic membrane. The ends of the horseshoe-shaped cartilages are posterior, and are connected by the fibro-elastic membrane which, on the posterior wall, is in intimate relation with the wall of the esophagus. When the head and neck are in the normal position seven or eight of these rings, extending over a distance of two or two and one-half inches, are suprasternal. With full extension of the head and neck, especially during swallowing, the trachea is elevated until nine or ten rings are above the sternum. In the cervical region the trachea lies in front of the esophagus and is surrounded on its anterior and lateral surfaces by the thyroid gland.

Thyroid Gland

The thyroid gland is suspended within the pretracheal fascia; over the front and sides of the upper three or four tracheal cartilages, and on

each side over the lower portion of the larynx. It varies greatly in size in different individuals, and is relatively larger in infancy and childhood than in adult life. It consists of a lateral lobe on each side, an isthmus, and occasionally a pyramidal lobe. The junction of each lateral lobe with the isthmus is usually marked by a depression on the anterior surface. The isthmus is absent in about one in four hundred cases; in about 10 per cent of cases it is so small that it may be ignored in operative procedures. In about one case in one thousand the gland is unilateral, either with both lobes situated on one side of the trachea or with the lobes closely joined together, one of them lying in front of the trachea. In these cases the superior and inferior thyroid arteries and the middle thyroid vein will be found crossing the trachea.

The **lateral lobes** are somewhat the shape of the folded wings of a bird. The upper poles, corresponding to the tips of the wings, extend upward on either side of the larynx, between the layers of the pretracheal fascia. Each upper pole rests upon the inferior constrictor muscle of the pharynx and the vascular stalk joins it at the tip (or inferior to the tip), near the mesial border of the deep surface.

In early life the vascular stalk, composed of the superior thyroid artery and veins, is situated at the tip of the upper pole. As the gland enlarges, the upper pole ascends by rotation around the vascular stalk as an axis. When there is considerable enlargement of the gland at the upper pole, the vascular stalk will be found on the mesial side of the upper pole inferior to its tip.

Below the upper poles, the lateral lobes are separated from the trachea and esophagus by the pretracheal fascia. In the region of the esophagotracheal notch on each side, this fascia forms the thyroid pedicle from which the interlobular septa extend into the lateral lobe. This region has been called the "danger zone," since immediately behind it lie the middle thyroid artery and the recurrent nerve.

The **isthmus** extends across the anterior surface of the trachea, and connects the mesial borders of the lateral lobes. It is subject to much variation in size and position and fits closely over the anterior segment of one, two, or three of the upper tracheal rings. It is separated from the trachea by the pretracheal fascia, between the layers of which is a definite plane of cleavage. Along its upper border, there is a branch of the superior thyroid artery known as the artery of the isthmus.

In some cases a middle or **pyramidal lobe,** usually in the form of a long pyramid, extends upward from the upper border of the isthmus. Occasionally it reaches as high as the hyoid bone. The pyramidal lobe is frequently attached to the hyoid bone by a fibrous band which sometimes contains muscular fibers. These fibers when present constitute the levator glandulae thyroideae muscle.

The normal gland in early life is quite regular in contour. Its superficial surface, convex and peritoneal-like, is directed forward and outward. The middle thyroid and inferior thyroid veins are the only structures that join the gland on its superficial surface (except the prethyroid fascia, which blends with the superficial surface of the lateral lobe, at the

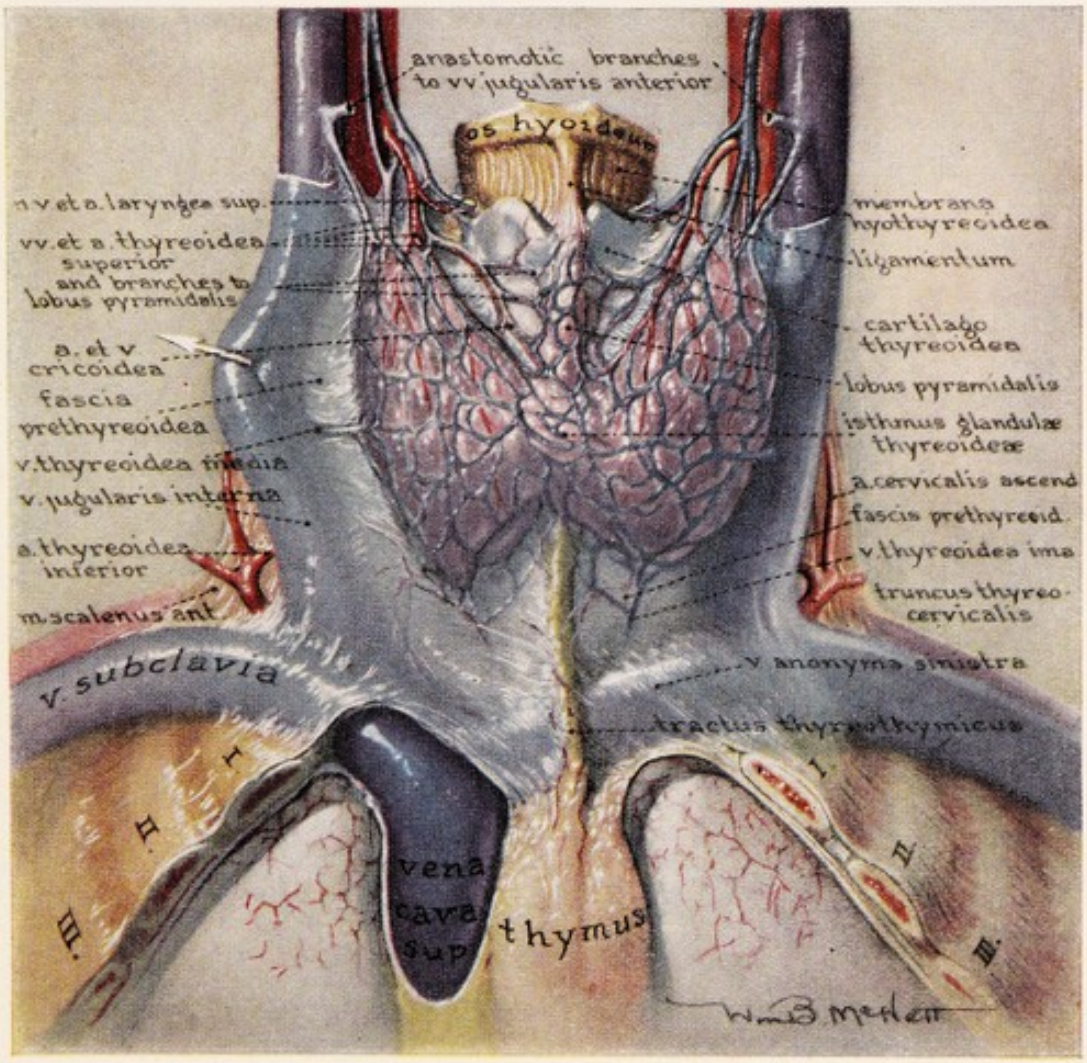


Fig. 29.—Thyroid Gland: Vascular Structures Prethyroid Fascia.

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junction of its middle and outer thirds). The outer third of the superficial surface of the lateral lobe faces laterally, is situated in the postthyroid space, and is covered by the prethyroid fascia.

Behind the isthmus, and between the mesial margins of the thyroid pedicles, the central portion of the deep surface of the isthmus is concave, and follows the curve of the tracheal cartilages. Over this area the superficial layer of the pretracheal fascia is firmly adherent to the gland surface. The deep surface of the lateral lobe, near the upper pole, faces inward and backward, is concave, and follows the outline of the larynx. Below the level of the lower border of the thyroid cartilage, the deep surface of the lateral lobe is irregular, and conforms somewhat to the outline of the lateral surface of the trachea and the anterior surface of the lateral border of the esophagus. Its mesial three-fourths is firmly blended with the superficial surface of the thyroid pedicle. Lateral to the thyroid pedicle, in the postthyroid space, is situated a narrow area of the deep surface covered with loose areolar tissue.

The anterior border of the upper pole is thin and from the apex follows the contour of the larynx and trachea in an inferior and mesial direction to the isthmus. The posterior border is thick and regular in outline. In the enlarged glands occurring in later life, a depression or sulcus on the lateral surface and posterior border of the lateral lobe is frequently observed extending posteriorly from the origin of the middle thyroid vein. In the cadaver, when the tissues are hardened, this sulcus is not obvious, but in the living subject it is quite distinct upon rotation of the lateral lobe anteriorly.

VASCULAR STRUCTURES OF THE NECK

Carotid Sheath

Contents

The carotid sheath, as will be described in detail later, is derived from the deep cervical fascia. The sheath contains an outer, inner, and a posterior compartment, separated from each other by thin fibrous septa. The inner compartment contains the common carotid artery, and in some instances, the descendens hypoglossi nerve. The outer compartment contains the internal jugular vein. The posterior compartment contains the vagus nerve. The relations of the vessels to each other are as follows: the internal jugular vein is lateral to the common carotid artery and on the same plane; the vagus nerve lies between the artery and vein and on a plane that is posterior to both; the right internal jugular vein in the lower part of the neck diverges slightly from the common carotid artery. In the small interval so fashioned, the right vagus nerve is seen before it passes over the first part of the right subclavian artery. The direction of the carotid sheath is upward and outward, in a slightly diagonal direction, from the sternoclavicular articulation to a point midway between the angle of the lower jaw and the mastoid process. As the carotid sheaths rise above the sternoclavicular articulations they are situated rather close together, with the trachea between. As they rise

higher in the neck they tend to diverge owing to the projection of the larynx, pharynx and thyroid into the interval between them.

Relations

In the lower part of the neck, below the central tendon of the omohyoid, the carotid sheath is deeply situated and is covered from outside inward by the skin, superficial fascia, superficial layers of the deep cervical fascia, the sternomastoid, sternohyoid and sternothyroid muscles. The lower transverse portion of the anterior jugular vein is situated behind the sternomastoid muscle and in front of the carotid sheath; the vein is separated, however, from the sheath by the interposition of the sternohyoid and sternothyroid muscles.

The central tendon of the omohyoid muscle, passing through an opening in the carotid lamina of the deep cervical fascia, crosses the sheath in an oblique direction at varying levels above the clavicle. Above the central tendon the sheath lies in the superior carotid triangle. In this location, the carotid sheath is much nearer the surface, being covered only by the skin, superficial fascia, platysma, deep fascia, and the anterior margin of the sternomastoid. The descendens hypoglossi nerve is found, as a rule, on the anterior surface of the sheath; it may, however, be within the sheath.

The carotid sheath lies in front of the longus colli and the longus capitis muscles, the ganglionated trunk of the sympathetic nerve and the prevertebral fascia. The lower part of the sheath is in front of the inferior thyroid artery and the recurrent laryngeal nerve. Mesial to the sheath are the pharynx, larynx, trachea, recurrent laryngeal nerve, inferior thyroid artery and thyroid gland.

Arteries

Common Carotid Arteries

The right common carotid artery arises behind the sternoclavicular joint as a terminal branch of the innominate artery. The left common carotid artery springs from the arch of the aorta, in the superior mediastinum, and ascends back of the left sternoclavicular joint to the cervical region. From the level of the sternoclavicular joint, the course of each artery is in an upward, backward and slightly lateral direction to its termination at its bifurcation into the internal and external carotid arteries. Usually, the only branches of the common carotid artery are the terminal ones. Occasionally, when the bifurcation of the common carotid is situated at a higher level than usual, the ascending pharyngeal, or the superior thyroid artery, arises from the common carotid instead of from the external carotid.

The common carotid artery lies within its compartment in the carotid sheath, the relations of which have been given. As it lies in the sheath its anterior surface is crossed from within outward by the sternomastoid branch of the superior thyroid artery. It is crossed, just below the level of the cricoid cartilage, by the middle thyroid vein or veins. The superior thyroid vein crosses the common carotid artery close to the level of the

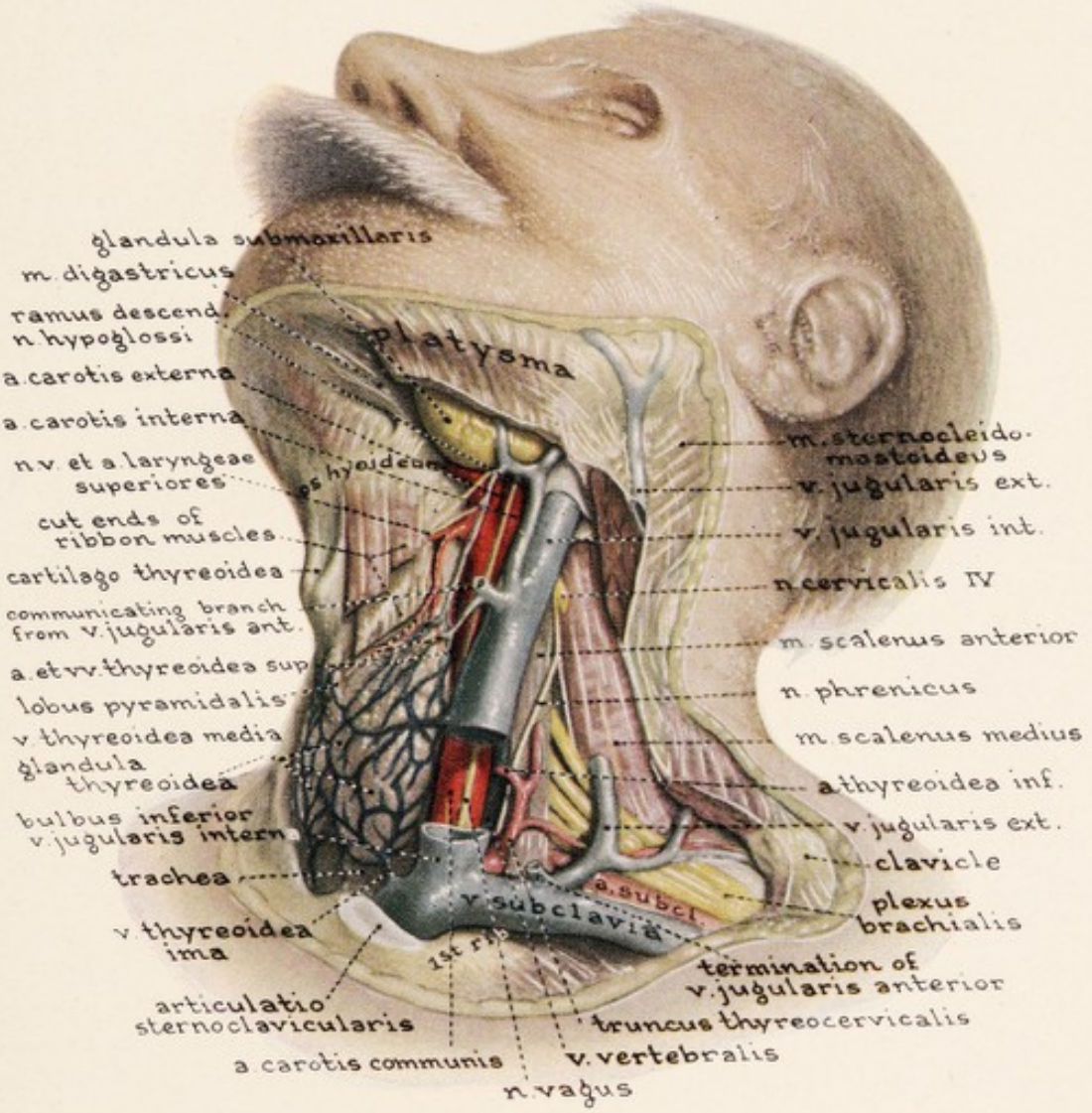


FIG. 30.—Deep Anatomical Structures Anterior Cervical Regions. (Fascia, platysma; and sternomastoid muscle removed)

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upper border of the thyroid cartilage. On the right side, the artery, near its origin, is crossed posteriorly by the recurrent nerve (as it passes in an upward and inward direction to reach the medial side). On the left side, the recurrent nerve crosses (behind) to the median side of the artery in the mediastinum. Posterior to its bifurcation lies the glomus caroticum, a small gland the function of which is not known. It is of surgical importance because in some instances malignancy arising from it is encountered.

External and Internal Carotid Arteries

The bifurcation of the common carotid into the external and internal carotids, which takes place in the superior carotid triangle at the level of the upper border of the thyroid cartilage, has already been mentioned. It will be necessary to consider merely such relations and branches of these vessels as may be of interest to the thyroid surgeon.

The external carotid, in the superior carotid triangle, lies somewhat anterior and mesial to the internal carotid. It passes upward and slightly forward. After it leaves the carotid triangle it passes backward. In the triangle it gives off three branches: the superior thyroid and the lingual from its anterior surface, the occipital from its posterior surface.

In the carotid triangle it is situated beneath the skin, superficial fascia, platysma, deep fascia, anterior border of the sternomastoid, hypoglossal nerve, the lingual and facial veins, and the internal carotid artery. Mesial to the artery are the hyoid bone, the pharynx, and the superior laryngeal nerve.

Superior Thyroid Artery

The superior thyroid is the first branch of the external carotid artery. It is given off from the anterior aspect of the vessel (just above the origin of the external carotid at the bifurcation of the common carotid). In this location it is situated just below the great tip of the cornu of the hyoid bone. At its origin it lies in the carotid triangle and is covered by the skin, the fascia and the platysma.

The superior thyroid follows a curving course: first a very short distance upward and inward and then downward and forward, and leaves the triangle beneath the omohyoid. It continues downward behind the omohyoid, sternohyoid, and sternothyroid muscles, to the tip of the upper pole of the lateral lobe; it divides into branches that enter the gland and anastomose with each other and with branches of the inferior thyroid, and, in the region of the isthmus, with branches from its fellow of the opposite side.

The branches of the superior thyroid are the infrahyoid, sternomastoid, superior laryngeal, cricothyroid, glandular and muscular arteries. The sternomastoid branch passes over the upper part of the carotid sheath, in a direction obliquely downward and outward, and enters the sternomastoid muscle on its posterior surface. The superior laryngeal branch, in company with the internal laryngeal nerve, passes beneath the thyrohyoid muscle, pierces the thyrohyoid membrane, and is distributed to the interior of the larynx and trachea. The cricothyroid

artery courses horizontally inward upon the surface of the cricothyroid membrane to anastomose with its fellow of the opposite side and form the cricothyroid arch.

Inferior Thyroid Artery

The inferior thyroid artery passes upward, from the thyrocervical trunk, behind the lateral border of the carotid sheath and along the anterior surface of the scalenus anterior muscle. It passes in front of the vertebral artery, the phrenic nerve, and the longus colli muscle. It turns medially, near the level of the cricoid cartilage, passes behind the carotid sheath and sympathetic nerve, and appears on the mesial side of the carotid sheath behind the pretracheal fascia, approximately at the level of the middle thyroid vein. After giving off the parathyroid branch, the inferior thyroid artery proceeds inward and slightly downward, between the deeper layers of the pretracheal fascia, posterior to the lateral lobe. It divides into two or more branches that enter the lateral lobe of the thyroid on its inner and posterior surfaces.

From these branches is derived the major portion of the blood supply for the lower half of the thyroid gland, the cervical portion of the esophagus, and the tracheal rings. Within the gland, the branches freely anastomose with each other and with branches from the superior thyroid, and, in the region of the isthmus, with branches from its fellow of the opposite side. The inferior thyroid artery gives rise to the following branches: the parathyroid, esophageal, tracheal, inferior laryngeal, ascending cervical, and muscular.

Parathyroid Artery

After the inferior thyroid emerges from behind the carotid vessels it gives off a branch to the parathyroid glands. This branch runs between the layers of the pretracheal fascia in a mesial and downward direction, behind the posterior margin of the lateral lobe, to a point below the level of the lower border of the isthmus. After giving off a branch to each of one or more parathyroid glands, situated below the lower pole, it curves upward and ascends in the pedicle of the thyroid, terminating in a communicating branch with the posterior branch of the superior thyroid artery. In its ascending course it supplies each parathyroid gland in the pedicle of the thyroid with a fine branch.

The inferior thyroid artery is in relation posteriorly with the vertebral artery, the phrenic nerve, the scalenus anterior and the longus colli muscles, and the esophagus. It is in relation anteriorly with the carotid sheath and the ganglionated cord of the sympathetic nerve. It passes anterior or posterior to the recurrent nerve; on the left side the thoracic duct passes in front of the vessel.

Thyroidea Ima Artery

The thyroidea ima artery, which is present only in some instances, is derived from the innominate artery or from the arch of the aorta. The vessel ascends, in front of the trachea near the median line, to the isthmus of the thyroid which it supplies. It varies in size and in its relative position

and in some cases it apparently compensates for the absence of one or the other of the inferior thyroid arteries.

VEINS

Superficial Veins

The principal superficial veins in the anterior cervical region are the facial, the anterior jugular, and the external jugular veins. The *common*

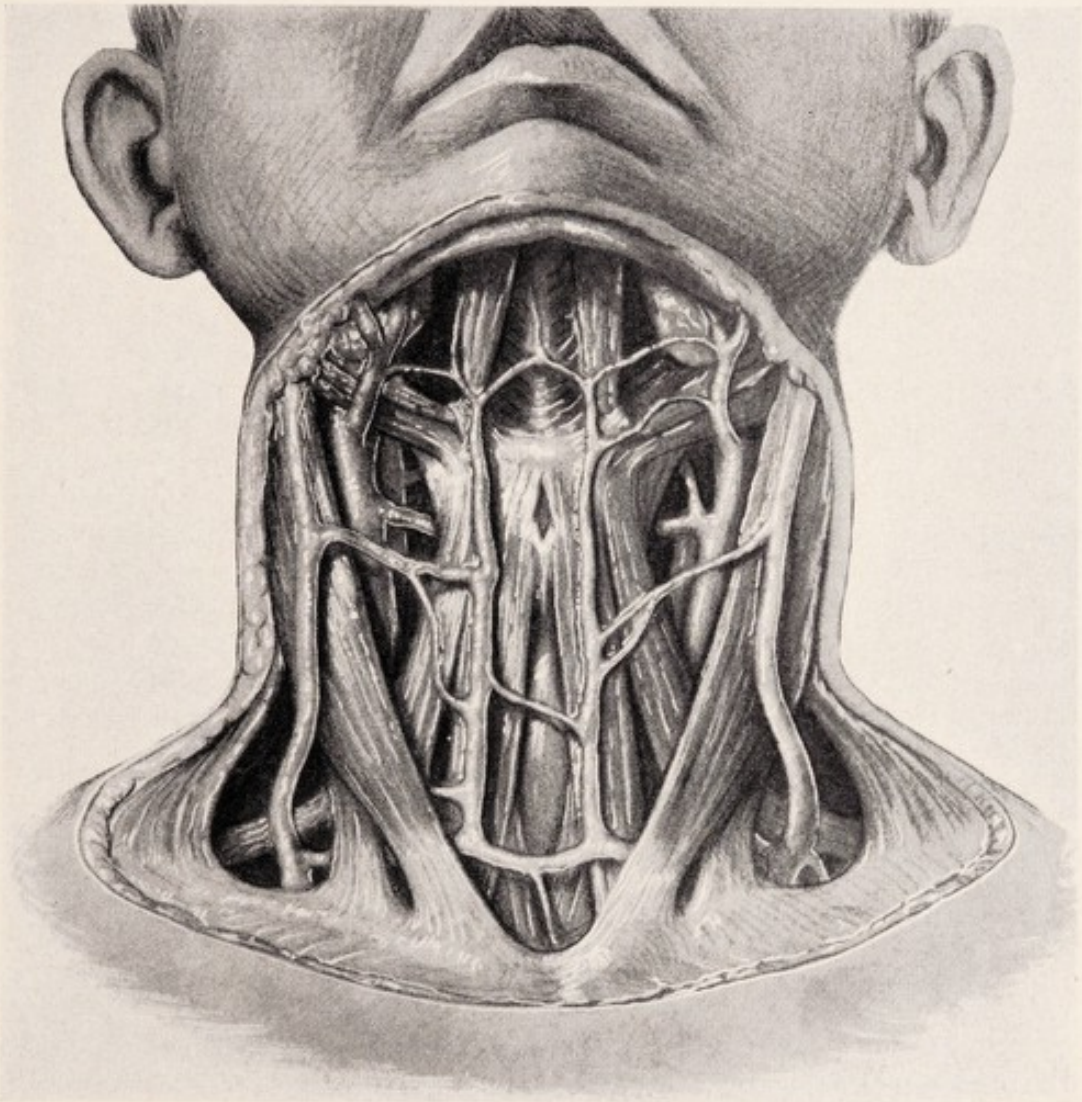


FIG. 31.—Superficial Veins of the Neck.

facial vein, formed by union of the *anterior* and *posterior facial veins*, empties into the internal jugular just below the level of the hyoid bone.

The **anterior jugular vein** (on either side) is formed in the digastric region by the union of superficial veins. It descends vertically, near the median line, between the superficial and deep fascia to the point where it penetrates the superficial layer of the deep fascia and enters Burns' space. In Burns' space it descends vertically for a short distance and, after

giving off the anastomosing branch with its fellow of the opposite side, it turns laterally and, passing behind the tendon of the sternocleidomastoid muscle, empties into the subclavian vein. In some cases, it joins with the external jugular vein just before it empties into the subclavian.

A communicating branch between the external jugular vein and the superior portion of the anterior jugular vein is present, in the majority of cases, at the level of the isthmus of the thyroid gland. In 90 per cent of cases the inferior curving portions of the anterior jugular veins lie on either side of Burns' space separated by an interval containing fat and areolar tissue, through which runs the connecting anastomosing branch. In 10 per cent of cases the anterior jugulars show some anastomosing branches above Burns' space. It has been noted that when an anastomosing branch above the space is present, the anastomosing branch which crosses the space itself is as a rule quite small, and in some instances is absent. Furthermore, when the anastomosing branch above Burns' space is present the anterior jugular veins are more apt to be joined near their termination, the single vein occupying an anomalous position.

The **external jugular vein** has its origin on the surface of the sternomastoid muscle behind the angle of the jaw. It is formed by the union of a branch from the posterior fascial vein with the posterior auricular. Its course is downward and backward, between the superficial and deep fasciae, to the middle of the posterior margin of the sternomastoid muscle, where it enters the posterior triangle. In the posterior triangle it passes downward, parallel to the border of the sternomastoid, and superficial to the posterior belly of the omohyoid, after which, curving mesially behind the clavicular head of the sternomastoid, it pierces the deep fascia and enters the subclavian vein. Sometimes it joins with the anterior jugular before it enters the subclavian.

Deep Veins

The principal deep veins of the anterior cervical region are the internal jugular and the thyroid veins.

The **internal jugular vein,** a continuation of the intracranial lateral sinus, descends vertically, first accompanying the internal and then the common carotid artery. It lies lateral to these vessels, slightly overlapping their anterior surfaces. It terminates behind the medial end of the clavicle where it unites with the subclavian of the same side to form the innominate vein. The relations, in so far as they interest us, have already been given in discussing the relations of the carotid sheath.

Thyroid Veins.—The tributaries of the internal jugular vein in which we are particularly interested are the superior and middle thyroid veins.

The **superior thyroid veins** are formed by the union of small tributaries from the plexus of veins on the surface of the gland with small veins from the substance of the upper and middle parts of the lateral lobes. One or more veins on each side ascend in the vascular stalk, between the prethyroid and pretracheal fascia, from their origin near the upper pole, outward and upward to the superior margin of the visceral



Fig. 32.—Thyroid Veins.

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space behind the omohyoid muscle. After receiving the superior laryngeal and cricoid veins, they leave the visceral compartment and, continuing in an upward and outward direction, enter the superior carotid triangle, cross the anterior surface of the carotid artery, and terminate in the internal jugular vein. Near their termination they are occasionally joined by the pharyngeal or lingual vein.

The **middle thyroid veins** arise in the same manner as the superior veins but from the middle portion of the gland. The vein on each side,

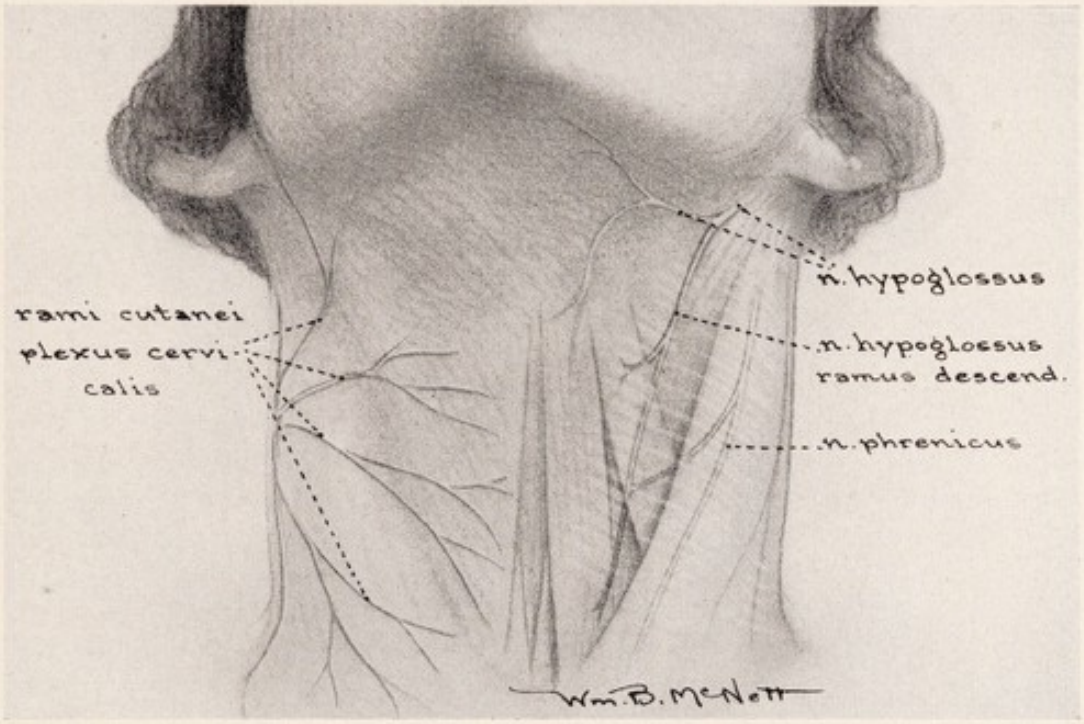


FIG. 33.—Superficial Nerves of the Neck.

from its origin on the anterior surface of the lateral lobe, follows a transverse course outward and empties into the lower part of the internal jugular. The middle thyroid veins lie within and are completely invested by the prethyroid fascia.

The **inferior thyroid veins** originate from a plexus of veins, on the lower portion of the anterior surface of the gland, pass downward in front of the trachea and empty into the innominate veins. Occasionally, instead of two, there is only one vein and infrequently there are three or even four such veins.

The **parathyroid veins** accompany the arteries for a short distance from the parathyroid glands, after which they join the thyroid veins.

NERVES

The superficial nerves with which the thyroid surgeon is concerned are the superficial branches of the cervical plexus, the muscular branches from the ansa hypoglossi, the inframaxillary branch of the facial nerve,

and the superficial branches of the accessory nerve. The deep nerves in the ventral region are branches of the vagus, the hypoglossal or the accessory nerve.

Cervical Plexus

The superficial branches of the cervical plexus emerge from behind the middle of the posterior edge of the sternomastoid muscle. The posterior and greater auricular nerves pass upward over the lateral border of the sternomastoid and supply the superficial structures over the upper part of the posterior triangle, the mastoid area and the occipital region. The cutaneous colli is distributed to the superficial fasciae and skin over the middle cervical region. The descending cervical branches descend under cover of the superficial fasciae to the clavicular region. In their descending course the nerves give off fine branches to the superficial fascia and to the skin. In the clavicular region the branches perforate the superficial fascia and divide into recurrent and infraclavicular branches. The recurrent ones pass upward superficial to the fascia and are distributed to the skin in the supraclavicular region. The infraclavicular branches are distributed to the skin below the clavicle. The superficial fascia in the entire anterior cervical region derives its nerve supply from this plexus.

Hypoglossal Nerve

The hypoglossal or twelfth cranial nerve emerges from the cranium through the anterior condyloid foramen. After it leaves the foramen it lies under cover of the internal carotid artery and internal jugular vein. It is intimately connected with the vagus nerve. It descends downward and a little forward to a level corresponding with the angle of the jaw. At this point it passes forward between the carotid artery and internal jugular vein. It continues on the anterior surface of these vessels and becomes practically superficial below the digastric muscle. At this point the nerve curves around the occipital artery crossing the external carotid and its lingual branches from above downward and outward. It next curves forward and upward above the hyoid bone to the suprahyoid muscle and tongue.

Branches

The only branches in which we are interested are the thyrohyoid and the descendens hypoglossi. The **thyrohyoid** is briefly disposed of. It is a small branch arising from the hypoglossal near the posterior border of the hyoglossus muscle and distributed to the thyrohyoid muscle.

The **descendens hypoglossi** is given off just as the main stem of the hypoglossal nerve curves round the occipital artery. It is a slender, long filament which descends somewhat obliquely across the carotid sheath. It generally lies upon, though it may lie within, the sheath and as a rule is in line with the direction of the common carotid artery. About the center of the neck it is joined by a filament which represents the union of the communicating branches from the second and third cervical nerves.

The **ansa hypoglossi** is a loop formed by the descendens hypoglossi after it has been joined by communicating branches from the second and

third cervical and the vagus nerves. This loop lies posterior and mesial to the carotid sheath at the level of the greater cornu of the hyoid bone. Muscular branches from the ansa hypoglossi supply the prethyroid muscles and a filament joins the laryngeal plexus.

Inframaxillary Branch of the Facial Nerve

From its origin at the bifurcation of the facial nerve, just below the lower border of the maxilla, this branch descends within the superficial fascia and is distributed to the cervical portion of the platysma muscle.

Accessory Nerve

The accessory or eleventh cranial nerve emerges through the jugular foramen enclosed in the same sheath of dura mater as the vagus. The accessory nerve consists of two parts, the bulbar and the spinal. The bulbar or accessory part passes over the surface of the interior ganglion of the vagus, is adherent to it, and is distributed in the form of fibers to the pharyngeal and superior laryngeal branches of the vagus. Some filaments are continued, through the trunk of the vagus, below the ganglion and are distributed with the cardiac and recurrent laryngeal branches of this nerve.

From the bulbar fibers of the accessory are thought to be derived the motor nerves of the palatal muscles (with the exception of the tensor palati), the motor nerves of the constrictor muscles of the pharynx, and the motor nerves of the intrinsic muscles of the pharynx. It is from this nerve that the vagus receives its cardio-inhibitory fibers.

The spinal part of the accessory nerve passes downward and a little backward, sometimes behind and sometimes in front of the internal jugular vein, and pierces the deep surface of the sternomastoid muscle. This muscle is supplied by branches from this nerve and a branch of the second cervical nerve. Leaving the sternomastoid, it crosses the occipital triangle obliquely and terminates in the deep surface of the trapezius. In the occipital triangle it joins with branches from the second and third and beneath the trapezius with branches from the third and fourth cervical nerves.

Vagus Nerve

The vagus or tenth cranial nerve is composed of both motor and sensory (efferent and afferent) fibers. We are concerned mainly with its relations and the distribution of its branches in the neck. The nerve emerges from the skull through the middle compartment of the jugular foramen. As it passes through the foramen it is accompanied by the spinal accessory nerve. These two nerves are contained in a sheath of the dura mater, a septum separating them from the glossopharyngeal nerve which lies in front.

In the neck the nerve pursues a vertical course downward, lying at first between the internal jugular vein and the internal carotid artery. In this situation—above the bifurcation of the common carotid—the glossopharyngeal nerve lies in front of the vagus and the accessory nerve lies behind it. Below the bifurcation of the common carotid, the vagus

lies in its own compartment of the carotid sheath between the common carotid and the internal jugular vein and on a plane posterior to both of these vessels.

Disregarding the origin, ganglion and course of the nerve in its upper part, and the course and distribution of the nerve in the thorax, and considering only the cervical portion, we find that the important branches of the vagus given off in the neck are:

(1) The pharyngeal
(2) The superior laryngeal
(3) The recurrent laryngeal

Pharyngeal Branch

The pharyngeal branch is the principal motor nerve of the pharynx. It originates from the upper portion of the trunk ganglion of the vagus. It passes from its origin downward and forward over the internal carotid artery and combines, with branches of the glossopharyngeal and the superior cervical ganglion of the sympathetic, to form the pharyngeal plexus.

Superior Laryngeal Nerve

The superior laryngeal nerve passes downward and forward from the middle of the ganglion nodosum of the vagus, where it originates. It passes behind the internal carotid artery at which position it divides into two branches, the internal and external laryngeal nerves.

The **internal laryngeal** nerve, principally sensory in character, passes forward with the superior laryngeal branch of the superior thyroid artery, to the thyrohyoid membrane. It pierces this membrane beneath the posterior border of the thyrohyoid muscle and reaches the interior of the larynx, serving as sensory nerve for the mucous membrane of the epiglottis and of the larynx. The surgical importance of this nerve lies in the fact that if it is injured, sensation in the mucous membrane of the larynx is lost.

The **external laryngeal** nerve, the smaller of the two branches of the superior laryngeal, descends along the side of the larynx and beneath the sternothyroid muscle to supply the cricothyroid.

Recurrent Nerve

The inferior laryngeal or recurrent nerve may be considered, from the standpoint of the surgeon, the most important nerve structure in the neck. This nerve is the main motor nerve of the larynx. Injury or section of this nerve will cause hoarseness or aphonia and inspiratory dyspnea, depending on the degree of injury. The origin and relations of the nerve in the lower part of its course are different on the two sides.

The **right recurrent nerve** arises in the thorax from the vagus as the latter nerve crosses the subclavian artery. It bends around the lower border of the subclavian from before backward and then turns upward and inward behind the origin of the common carotid, enters the cervical region and ascends in the pretracheal fascia. The first part of its ascending

course follows a superior and posterior direction. The nerve gradually assumes a more posterior position as regards the trachea, crossing the lateral border of the trachea obliquely backward to reach the anterior surface of the lateral border of the esophagus a short distance above the subclavian artery. It ascends, in the pretracheal fascia on the esophagus, quite close to the esophagotracheal groove to the level of the lower border of the thyroid gland. Continuing upward in the thyroid pedicle it grad-

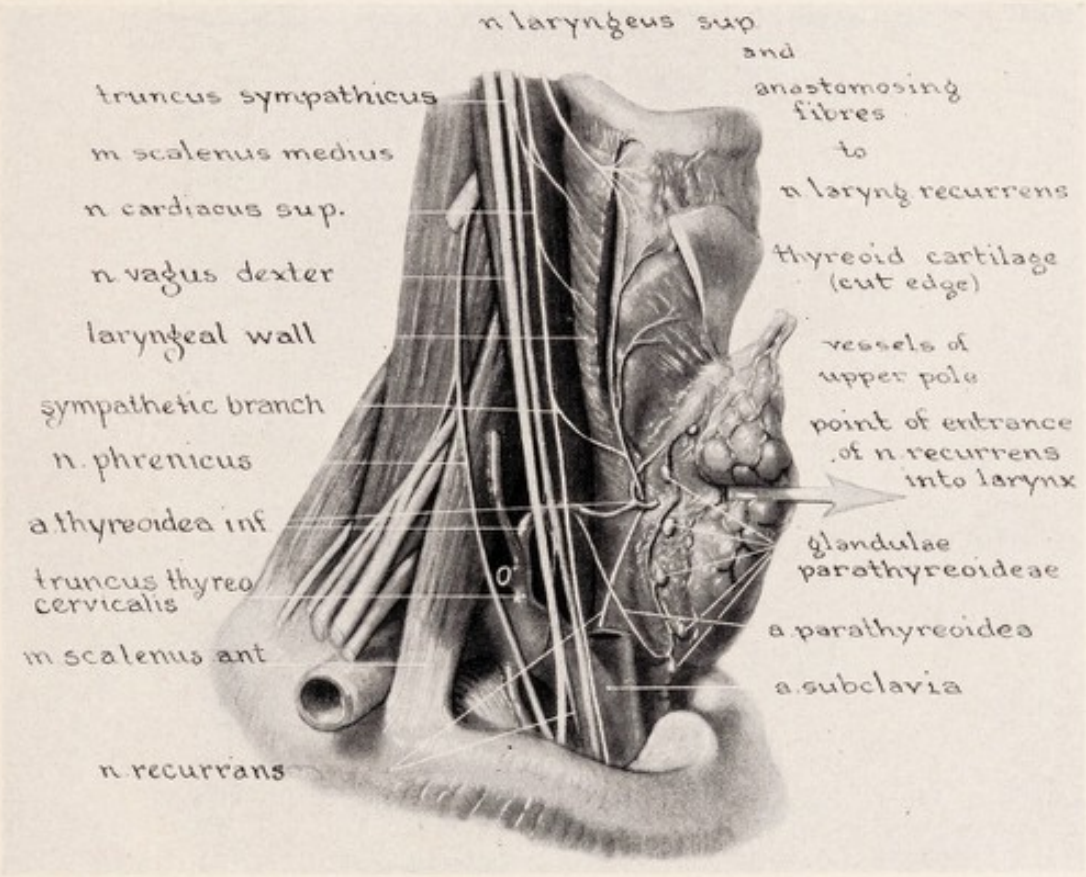


FIG. 34.—Relation, Inferior Thyroid Artery, Recurrent Nerve.

ually assumes a more mesial position and in the region of the cricoid cartilage lies in the esophagotracheal groove. In its ascending course in the thyroid pedicle the nerve crosses the inferior thyroid artery or its branches at the level of the upper tracheal ring. It passes posterior to the trunk or all of the branches in about 24 per cent of the cases, and anterior to all the branches in about 40 per cent. In the other 36 per cent of cases the nerve passes between the branches. Leaving the thyroid pedicle the nerve ascends on the lateral aspect of the cricoid cartilage and, passing behind the lower edge of the inferior constrictor muscle and the cricothyroid articulation, pierces the thyrohyoid membrane and enters the larynx. Inside the larynx, with the help of its fellow of the opposite side, it supplies all of the laryngeal muscles except the cricothyroid and the interarytenoid.

The **left recurrent nerve** is given off by the vagus in front of the arch of the aorta and on a level with the lower border of the arch. The nerve then winds backward within the arch near the point of attachment of the ductus arteriosus and then courses upward and in a slightly mesial

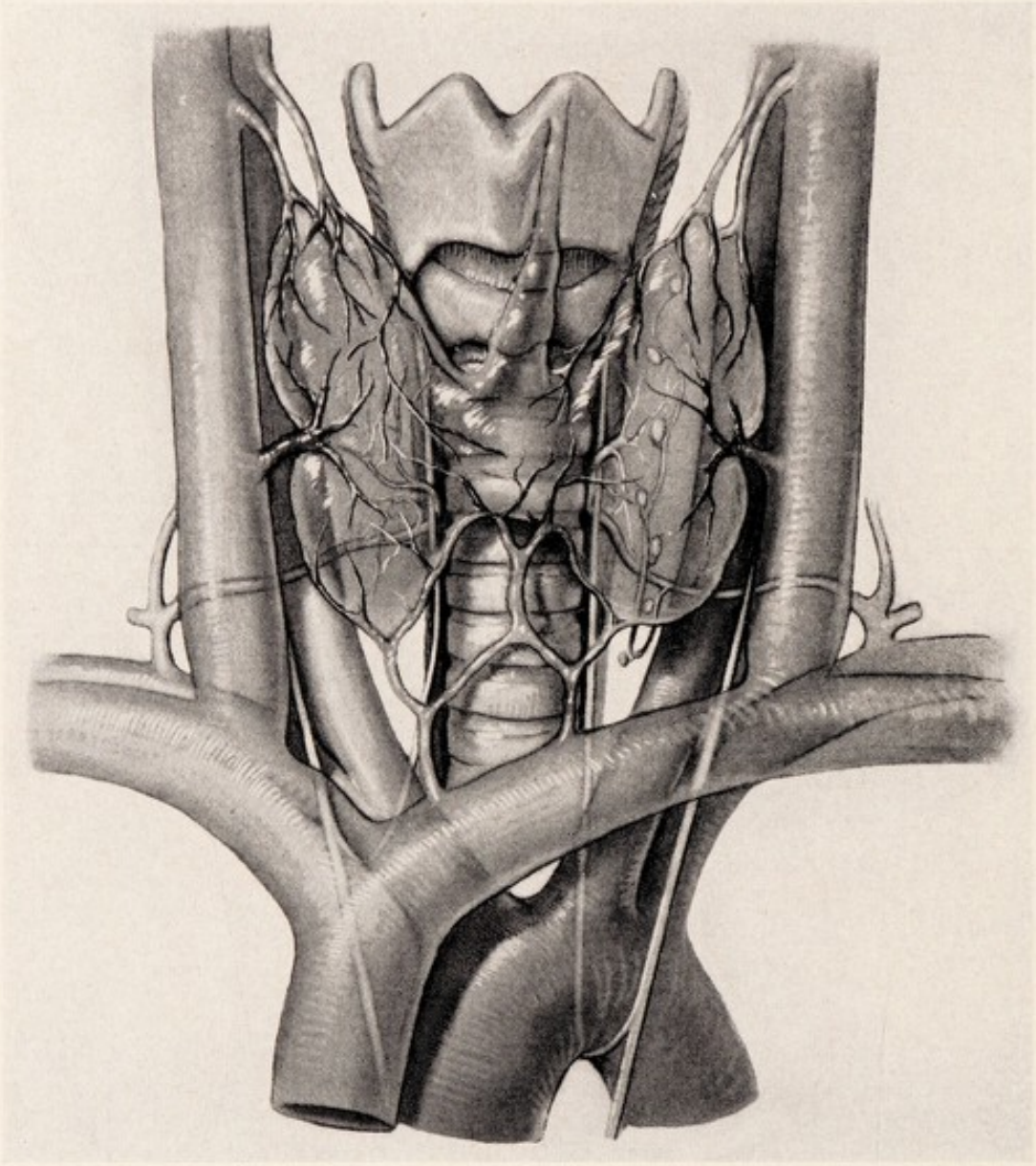


Fig. 35.—Recurrent Nerve.

direction between the layers of the pretracheal fascia. As the esophagus is situated to the left of the midline in the lower part of the neck the recurrent laryngeal nerve on the left side passes over the lateral border of the esophagus at a lower level and at a greater distance from the trachea than does the nerve on the right. The nerve ascends in the pretracheal fascia, on the anterior surface of the extreme lateral edge of the

esophagus, to the cervical region. Its course in the cervical region is the same as that of the right.

Branches of the Recurrent Laryngeal Nerve.—As they ascend, the recurrent laryngeal nerves give off communicating twigs to the inferior cervical ganglia of the sympathetic, tracheal and esophageal branches; cardiac branches to the deep cardiac plexus; and muscular twigs to the inferior constrictor. The muscular branches supplying the intrinsic

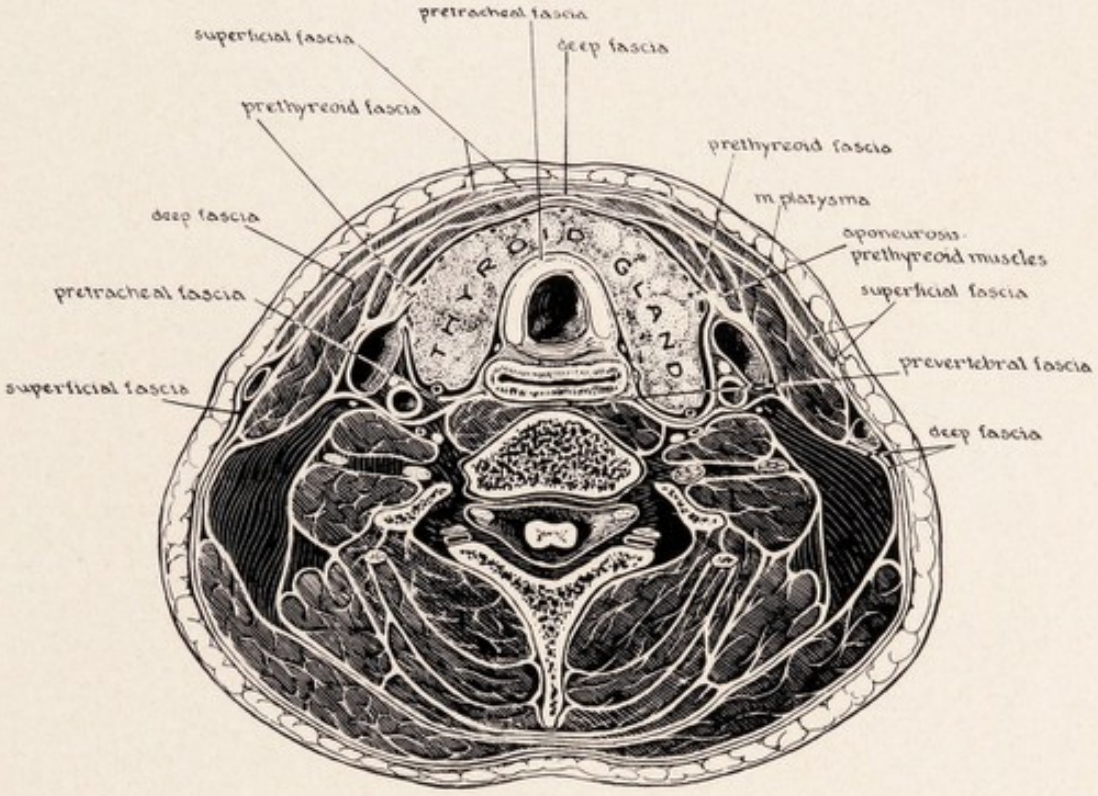


FIG. 36.—Transverse Section—Level of the Isthmus.

muscles of the larynx are given off within the larynx. In the majority of instances, one or more of the direct branches of the inferior thyroid artery lie deep to the recurrent nerve in its ascending course in the thyroid pedicle. Consequently, the recurrent nerve is endangered if the branches of the inferior thyroid artery are ligated near the esophagotracheal groove. Ligation of the structures at the lower pole likewise endangers the recurrent nerve.

CERVICAL FASCIAE

The most extensive, and perhaps the most important, structures in the neck from the standpoint of surgical anatomy are the cervical fasciae. There are two distinct fasciae—the superficial and the deep. The superficial fascia completely envelops the entire cervical region. The deep fascia invests all the important structures of the neck with the exception

of the skin, platysma, superficial fascia, and external jugular vein, and divides the neck into different compartments, the contents of which are uniformly constant.

Superficial Cervical Fascia

Beneath the skin and the fatty layer, which varies in thickness in the different regions of the neck, is located the superficial fascia. This fascia is continuous with the superficial fascia of the pectoral region below and with the superficial fascia of the head above. The skin is connected intimately with the superficial fascia by fibers which pierce the subcutaneous fatty layer.

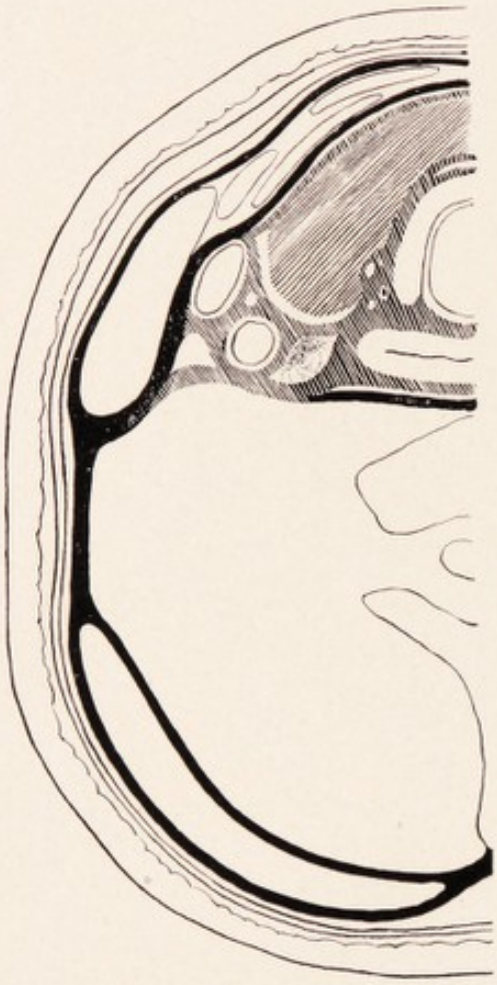


Fig. 37.—Perimuscular Layers of Deep Cervical Fascia.

The superficial fascia completely invests the neck. From the ligamentum nuchae posteriorly it spreads around the neck covering the posterior triangle, the sternocleidomastoid muscle, and the anterior triangle, eventually becoming continuous in the midline with the layer of superficial fascia from the opposite side. As the superficial fascia comes around to the anterolateral portion of the neck, it invests the fibers of the platysma with an anterior and a posterior layer. The main trunks of the cervical plexus of nerves lie beneath it upon the deep fascia, but the terminal branches are distributed within the layers of the superficial fascia. The external jugular vein throughout a large portion of its course is situated just beneath this fascia.

Deep Cervical Fascia

Of much more importance to the surgeon than the superficial fascia is the deep cervical fascia. The deep cervical fascia and its various processes or laminae separate the various structures of the neck into different compartments. It is a strong, fibrous fascia varying in consistency and thickness in its different laminae. It has its origin, in common with the superficial fascia, at the ligamentum nuchae and the spinal process the seventh cervical vertebra. Its superficial layer, which completely envelops the entire cervical region passes forward from its origin and invests first the trapezius muscle, sending laminae both anterior and posterior to this structure. At the anterior border of the trapezius the

two investing laminae unite and proceed forward as one layer, from the trapezius across the posterior triangle of the neck to the posterior border of the sternomastoid muscle. At this point again it splits into two laminae that enclose the sternomastoid muscle in a sheath, one lamina passing behind and the other in front of the muscle. Along the upper four-fifths of the anterior border of the sternomastoid muscle these two layers blend and form a rather dense fascia that in the midline becomes continuous with the fascia from the other side. Along the lower fifth of the anterior border of the sternomastoid muscle these layers of the deep cervical fascia do not unite but proceed to the midline with an interval between them called Burns' space.

In the anterior cervical region, external to the heads of the sternocleidomastoid, the superficial layers of the deep cervical fascia are attached below, as one layer, to the superior border of the clavicle. From the clavicular head of the sternomastoid to the median line, the superficial lamina is attached to the anterior, and the deeper lamina to the posterior margin of the upper border of the clavicle and the manubrium sterni. The fascia is attached above to the mastoid process of the temporal bone, to the zygomatic arch and the lower border of the mandible. We thus have the superficial layers of deep cervical fasciae completely surrounding the neck and splitting into two laminae to enclose the trapezius and the sternomastoid muscles and Burns' space. Externally the superficial layer of the deep fascia is in contact with the superficial fascia and some of its fibers blend loosely with the latter.

The deep processes or laminae are derived from the inner surface of the superficial layers of the deep fascia which surrounds the neck. Named in order from behind they are:

(1) The prevertebral lamina
(2) The buccopharyngeal lamina
(3) The carotid lamina
(4) The muscular lamina

A rough summary of the arrangement of the deep processes may give the reader a general idea of its wide distribution and make the detailed explanation more readily understood.

The first deep process to be given off is the prevertebral lamina which crosses in front of the spinal muscles and forms the anterior wall of the vertebral compartment.

The next process is the buccopharyngeal lamina given off just a little anteriorly to the prevertebral lamina and investing the pharynx and esophagus.

The next process anteriorly is the carotid lamina which forms the carotid sheath. From the carotid sheath in turn is given off the pretracheal lamina, the process which invests the trachea anteriorly and the thyroid gland both anteriorly and posteriorly.

The most anterior process of the deep fascia is that which we term the muscular lamina, from which are derived the aponeuroses that invest the prethyroid muscles. With this summary in mind we shall consider the laminae in detail.

Prevertebral Lamina

This, the most posterior process, is given off from the inner surface of the superficial layers behind the posterior border of the sternocleidomastoid muscle. It passes mesially over the scaleni muscles and the body of the vertebrae and behind the pharynx and esophagus. In midline, it joins with its fellow of the opposite side. At its origin, it blends with the carotid sheath and above is attached to the base of the skull. Below, it passes over the longus colli muscle into the posterior mediastinum. This fascia is the posterior boundary of the part of the neck in which we are interested.

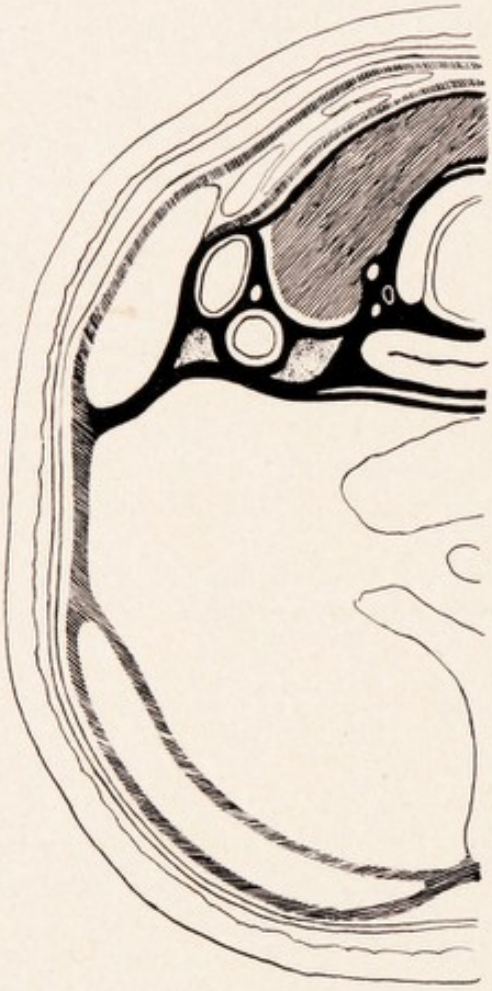


FIG. 38.—Carotid Lamina and Its Sub-Division.

Buccopharyngeal Lamina

The buccopharyngeal lamina is situated slightly anterior to the prevertebral process of the deep fascia. It is a thin, elastic lamina which laterally blends with the prevertebral lamina and the posterior border of the carotid sheath and then passes mesially to the region of the esophagus and pharynx, where it joins with some fibers derived from the pretracheal fascia to form the fascial investment of the pharynx.

Carotid Lamina

This lamina is given off from the inner surface of the sheath of the sternomastoid muscle. It forms the carotid sheath, investing in separate compartments the common carotid artery, the internal jugular vein, the vagus nerve, and, in some instances, the descendens hypoglossi nerve. The carotid sheath, at its posterior border, blends with the prevertebral and buccopharyngeal fasciae. Having formed the carotid sheath the carotid lamina extends mesially as the pretracheal fascia.

Pretracheal Fascia

Leaving the carotid sheath along the mesial surface as one layer of fascia, the pretracheal fascia soon splits into two layers, the prethyroid layer and the pretracheal layer proper, each of which will be considered separately.

The **prethyroid fascia,** the thin anterior lamina of the pretracheal fascia, extends mesially, anterior to the lateral border of the lobe of the thyroid. It is attached to the gland over an irregular line along the junction of the middle and posterior thirds of the superficial surface of the lateral lobe. Above the upper pole of the thyroid, this fascia extends inward, anterior to the vascular stalk. On the surface of the upper pole, the prethyroid fascia is very thin and almost indistinguishable on the external side, but above the pole where it forms the covering of the vascular stalk, it again becomes quite strong. Toward the midline, mesial to the upper pole and the vascular stalk, it blends intimately with the pretracheal fascia proper, to the margin of the pyramidal lobe, where it again divides from the pretracheal fascia, extends over the anterior surface of the pyramidal lobe, and blends with the layer of the prethyroid fascia from the opposite side.

Below the thyroid the prethyroid fascia is attached to the gland on a line extending around the lower pole and across the inferior margin of the isthmus. It covers anteriorly, the inferior thyroid veins and accompanying lymphatic vessels, the recurrent loop of the parathyroid artery, one or more parathyroid glands, the trachea and the thyrothymus tract. Lateral to the thyroid gland, it is separated from the surface of the thyroid and from the superficial surface of the pretracheal fascia proper by an interval, filled with loose connective tissue, that we have termed "the postthyroid space." This triangular space extends along the posterior lateral border of each lateral lobe and the vascular stalk, from the tip of the lower pole to the bifurcation of the superior thyroid artery. The sides of the triangle are represented by the prethyroid fascia, the pretracheal fascia and the surface of the thyroid gland.

Superficially, the prethyroid fascia is in contact with the prethyroid muscles. The aponeurosis upon the posterior surface of the prethyroid muscles is attached to the superficial surface of this prethyroid fascia by loose, areolar tissue. A definite plane of cleavage is found on the entire superficial surface of the prethyroid fascia that is continuous with the plane of cleavage on the anterior surface of the capsule of the thyroid gland. This is the prethyroid plane of cleavage to be described later.

Pretracheal Fascia Proper.—After giving off the prethyroid lamina the pretracheal fascia proper extends mesially to the posterolateral border of the thyroid. Passing behind the posterolateral border its fibers converge and form the pedicle of the gland in the irregular interval between the deep surface of the lateral lobe, the lateral border of the esophagus, and the trachea. In this interval—that might be called the thyroesophagotracheal space—the fibers of the different layers decussate and are so firmly blended with the fibrous origin of the interlobular septae of the gland that no definite plane of cleavage can be demonstrated. Some fibers from its posterior layers blend with the buccopharyngeal fascia and invest the pharynx, the esophagus, the larynx, and the trachea. From the pedicle of the gland the fascia extends mesially over the trachea and larynx and becomes continuous with the fascia from the other side. Anterior to the pedicle of the gland the fascia separates into layers connected

by areolar tissue. Immediately behind the isthmus, and the pyramidal lobe when present, a definite plane of cleavage may be demonstrated between the layer of fascia closely adherent to the posterior surface of the isthmus and pyramidal lobe, and the layer of fascia covering the trachea.

The upper margin of the isthmus of the gland is firmly anchored to the trachea by the prethyroid and pretracheal fasciae. This is the shortest

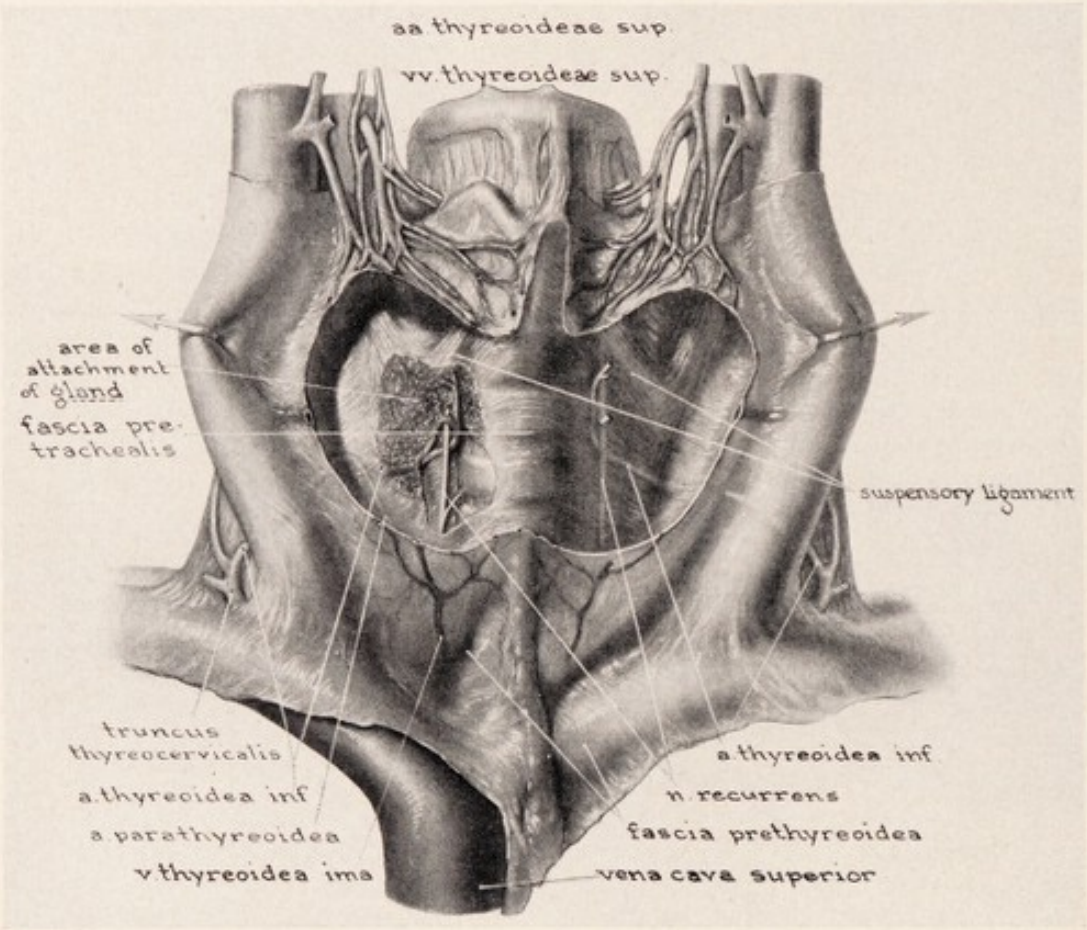


FIG. 39.—Schematic Illustration—Pretracheal Fascia.

and least elastic attachment of the gland to the trachea. When a pyramidal lobe is present this short attachment follows its lateral margins to its tip. Along the inferior margins of the isthmus and lower poles the gland is loosely attached to the trachea. The postisthmial plane of cleavage, extending downward for some distance below the isthmus, contributes to the mobility of the gland on the trachea. The pretracheal fascia binds the thyroid pedicle, on the deep surface of each lateral lobe, to the trachea, larynx, pharynx and esophagus and maintains its position relative to the carotid sheath. The prethyroid fascia controls anterior rotation of the lateral lobes. The elasticity of these fasciae provides for the necessary movements of the viscera, in coughing, in swallowing, and in flexion, extension and rotation of the head and neck.

Structures within the Pretracheal Fasciae.—The thyroid and parathyroid glands, the superior thyroid arteries and veins, the parathyroid arteries, the inferior thyroid veins, and the thyrothymus tract, lie between the prethyroid and the pretracheal layers of the pretracheal fascia. They are invested on their superficial surfaces by the prethyroid fascia and on their deep surfaces by the pretracheal fascia. The only structure of surgical importance in the prethyroid fascia is the middle thyroid vein.

The superior thyroid vessels are situated in the vascular stalk between the prethyroid fascia and the pretracheal fascia. The inferior thyroid artery, as it emerges from behind the carotid sheath, penetrates the thin posterior layers of the pretracheal fascia and passes mesially (in the thin, elastic, posterior layers of this fascia) parallel with the fascia fibers until it reaches the pedicle of the gland, where it usually divides into two or more branches. After some fine branches to the cosphagus and trachea have been given off, the main branches pass through the pedicle of the gland, to the origin of the interlobular septae, and in company with some fascia fibers continue through the interlobular septae into the substance of the gland. The course of one or more of the main branches lies deep to the recurrent laryngeal nerve.

Parathyroid glands found above or below the thyroid are situated between the pretracheal and prethyroid fasciae. The parathyroid artery in its descending portion, from its origin to its inferior curvature near the tip of the lower pole, lies between the layers of the pretracheal fascia.

The recurrent laryngeal nerve ascends between the layers of the pretracheal fascia, on the anterior surface of the lateral border of the esophagus, to the pedicle of the gland.

Suspensory Ligaments

As the fibers converge on each side of the pedicle of the gland they form strong fascial bands or ligaments, two in the pretracheal and one in the prethyroid fascia. The thicker of the pretracheal ligaments is called the **suspensory ligament.** Some of the fibers that constitute the suspensory ligament pass downward from the hyoid bone, some from the thyroid cartilage and some from the perilaryngeal fascia. The fibers converge as they descend over the lateral portion of the anterior surface of the larynx and form a strong band of fascia that passes behind the junction of the anterior border of the lateral lobe and the upper border of the isthmus and terminates in the dense pedicle of the gland.

Another fold in the pretracheal fascia that might logically be called a suspensory ligament is situated on each side, lateral to the gland. It is composed of the fascial fibers that extend mesially, from the inch and a quarter of the carotid sheath immediately above the level of the isthmus, and converge behind the posterior border of the lateral lobe to form a flat ligament that terminates in the pedicle of the gland at the level of the cricoid cartilage. We have termed it the **"lateral suspensory ligament."**

In the prethyroid fascia a definite fold encloses the middle thyroid vein and anchors the anterior surface of the gland to the carotid sheath. We have called this fold the **"prethyroid ligament."**

The thyroid pedicle on each side is supported mesially and superiorly by the suspensory ligament, and laterally and superiorly by the lateral suspensory ligament. The anterior rotation of the lateral lobe is limited by the prethyroid ligament.

Muscular Lamina

This, the most anterior lamina, arises as two or three layers of thin elastic fascia from the inner surface of the superficial layers of the deep fascia anterior to the origin of the carotid lamina. The layers join the aponeurosis of the prethyroid muscles to form a fascial investment that binds these muscles loosely together. The deep surface of this lamina forms a roof for the prethyroid plane of cleavage and is separated from the thyroid gland by a layer of loose connective tissue. Its superficial surface is loosely attached to the deep surface of the superficial layers of the deep cervical fascia by connective tissue.

COMPARTMENTS OF THE NECK

We have referred to the fact that the distribution of the deep fascia divides the neck into compartments. The distinct ones are the vertebral, the visceral, the vascular, the sternomastoid, and the suprasternal compartment or space of Burns'. De Quervain describes in addition the "small thyroid muscle compartment" (131). We do not find that this is really a definite compartment in the same sense that the other five are. The prethyroid muscles are invested by this reflexion of the deep cervical fascia that provides aponeuroses for each muscle but forms no definite compartment.

Vertebral Compartment

The vertebral compartment lies between the prevertebral layer of the deep fascia and attachment of the fascia to the ligamentum nuchae behind. It contains the vertebrae, spinal cord, and the pre- and post-vertebral muscles.

Visceral Compartment

This is the division or compartment of the neck in which we are more interested. It contains the viscera of the neck, the larynx, the trachea, the esophagus, the thyroid, and parathyroid glands, as well as arteries and veins. It is bounded in front by the thin aponeurosis covering the posterior surface of the prethyroid muscles, behind by the prevertebral fascia, and on each side by the fascia of the carotid sheath.

Vascular Compartment

The vascular compartment comprises the structures in the carotid sheath.

Sternomastoid Compartment

The sternomastoid compartment, containing the sternomastoid muscle, is formed by the two processes of the deep cervical fascia which surround and enclose the sternocleidomastoid muscle.

Burns' Space

The suprasternal or Burns' space is a small compartment situated between two fascia layers just above the superior border of the sternum. The anterior wall is formed by the superficial layer of the deep cervical fascia. The floor or posterior wall of Burns' space is composed of the layer of the deep fascia which, after forming the sheath on the posterior surface of the sternomastoid, extends mesially over the sternohyoid and sternothyroid muscles. Inferiorly it is attached along the posterior border of the upper surface of the manubrium sterni. Between the sternal heads

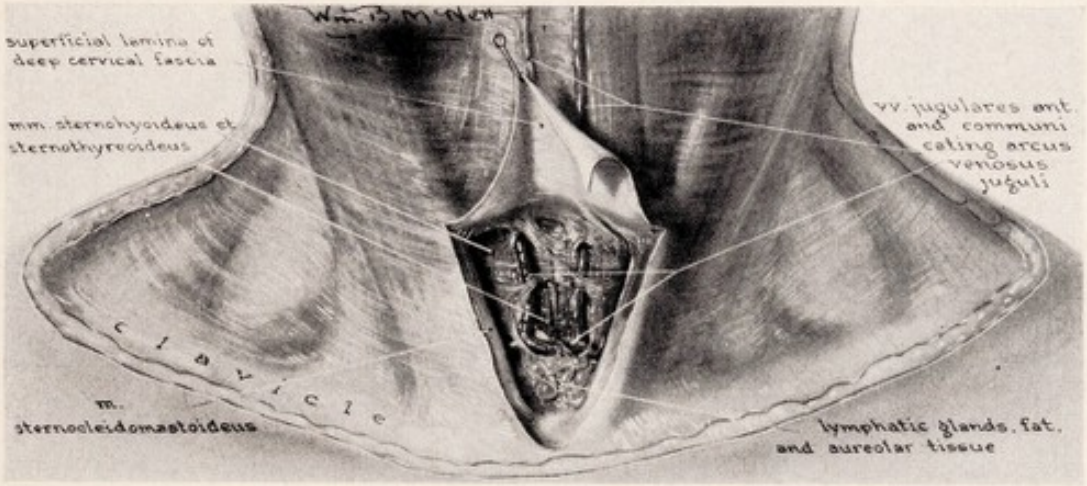


FIG. 40.—Anatomical Structures in Burns' Space.

of the sternomastoid muscles, these two layers are separated by an interval, the depth of which corresponds to the thickness of the sternal heads of the sternomastoid. Just above the sternum, in the sternal notch, the space is deeper than laterally. It is somewhat triangular in shape and lies immediately above the upper border of the sternum.

Burns' space contains the inferior curving portions of the anterior jugular veins, their anastomosing branches, some lymphatic glands, fat and areolar tissue, and the sternal heads of the sternocleidomastoid muscles.

From an operative point of view the posterior wall of Burns' space is of the utmost importance. The development of scar tissue in this region may result in angulation of the trachea, or in fixation to the sternum of either the trachea or deeper structures, with consequent severe respiratory disturbance. It is imperative that great care be exercised in closing the posterior wall if it is incised or separated during operative procedure. For the same reasons, drainage through Burns' space should be avoided.

The cervical compartments are clearly defined as to their boundaries, their contents, and the relationship of the structures contained in them. Anomalies in the location of these structures are rare.

PLANES OF CLEAVAGE

The planes of cleavage dependent on the distribution of the fascia processes are of great importance from the standpoint of operative technic. The following planes of cleavage will be described:

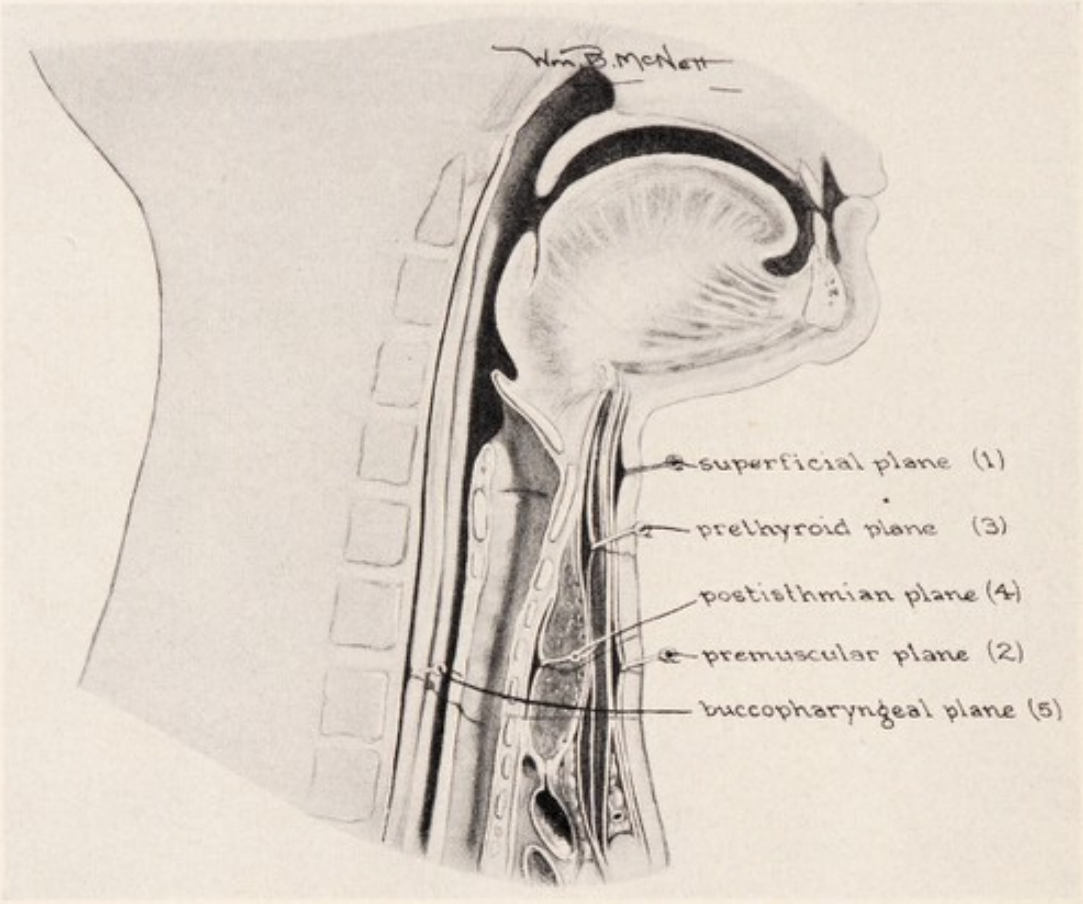


FIG. 41.—Longitudinal Section Showing Planes of Cleavage.

(1) The superficial plane.
(2) The premuscular plane.
(3) The prethyroid plane.
(4) The postthyroid plane.
(5) The postisthmial plane.
(6) The retropharyngeal plane.

Superficial Plane

The superficial plane of cleavage is situated between the superficial layers of the superficial fascia covering the entire cervical region. Therefore this plane of cleavage may be followed over a wide extent. The only blood vessels of any size encountered in developing this plane of cleavage are the rather unimportant terminal branches of the sternomastoid artery that emerge from the anterior border of the sternomastoid muscle at the level of the isthmus, perforate the superficial layer of the deep fascia and

the superficial fascia, and are distributed to the subcutaneous fascia and the skin in this region. In developing the plane, no fibers of the platysma muscle are encountered since the plane lies superficial to it.

Its importance from the surgical standpoint rests on the fact that in the majority of operations for goiter this plane of cleavage is utilized in the raising of the superficial flaps. When the incision is made in the

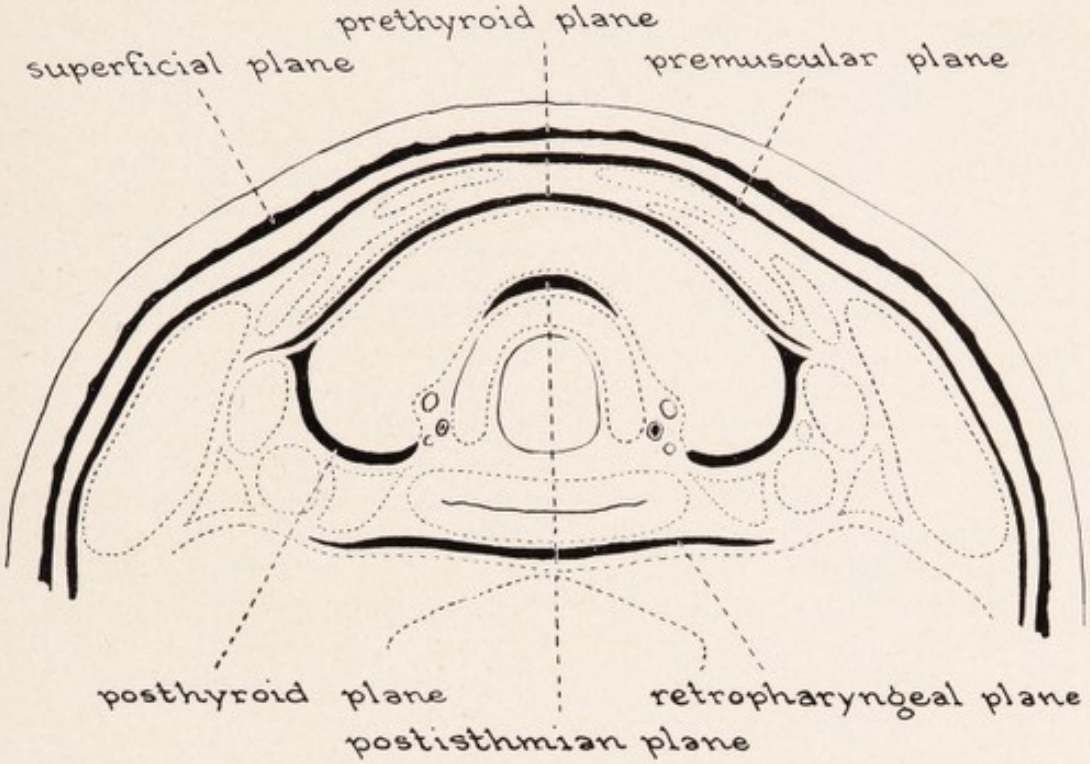


FIG. 42.—Schema of Planes of Cleavage.

usual manner this plane is readily recognized. The flaps may be pushed upward and downward on this plane exposing the fascia over the deeper structures of the entire neck as far as may be necessary.

As the flaps are reflected over this superficial plane of cleavage, the external surface of the sternohyoid, and a small portion of the sternothyroid, omohyoid, and sternomastoid muscles—all covered by the superficial fascia and the superficial layer of the deep cervical fascia—will be exposed. If the flap is raised to the level of the hyoid bone, the promontory of the thyroid cartilage and the structures in the superior carotid triangle will come into view. Showing through the fascia in this plane of cleavage may be seen the anterior jugular veins, the outline of the muscles, and the boundaries and landmarks of the anterior cervical triangles. The division of the anterior cervical triangle into three triangles by the anterior belly of the omohyoid and the posterior belly of the digastric will now be apparent.

If the superficial plane of cleavage is developed laterally, the anterior margin of the trapezius muscle and the landmarks of the deeper struc-

tures of the posterior triangle will be exposed. The division of the posterior triangle into two triangles by the posterior belly of the omohyoid muscle may be seen.

Premuscular Plane of Cleavage

The premuscular plane of cleavage lies over the prethyroid muscles and beneath the superficial fascia and the superficial layers of the deep fascia. In raising the flaps this plane of cleavage may be followed upward to the hyoid bone, laterally to the median borders of the sternomastoid muscles, and downward to the upper border of the sternum. In the lateral and superior regions, the superficial fascia invests the fibers of the platysma muscle, but in the region of the usual incision for thyroidectomy no platysma fibers are found near the midline. No important blood vessels or nerves are encountered in this plane of cleavage, but the anterior jugular veins in the greater part of their descending course lie between the superficial fascia and the deep fascia. Hence, if the premuscular plane of cleavage is utilized in raising the flap, the anterior veins are encountered in making the incision through the fasciae and must be severed between ligatures. The incision through the fascia layer is limited on each side by the median border of the sternomastoid muscle unless the muscle is cut or the line of incision is carried upward along its border. Since the sternomastoid muscles diverge in their upward course, it follows that the higher the level chosen for incision through the fascia, the larger the incision may be.

The planes of cleavage next to be discussed, the prethyroid and postthyroid planes, are of particular importance to the surgeon owing to the fact that familiarity with them greatly facilitates the mobilization of the thyroid.

Prethyroid Plane of Cleavage

Separation of the prethyroid muscles in the middle line exposes the prethyroid plane of cleavage on the anterior surface of the thyroid gland. Its floor is the anterior surface of the capsule of the thyroid gland and the anterior surface of the prethyroid fasciae. Its roof is the posterior surface of the aponeurosis that invests the prethyroid muscles. In the midline, the prethyroid plane of cleavage extends downward over the anterior surfaces of the thyroid gland, the lower border of the isthmus, the inferior thyroid veins, the thyrothymus tract and the thyroidea ima when present. In the midline, it will be found to continue downward into the mediastinum—deep to the prethyroid muscles at their origin and anterior to the capsule of the thymus gland—to the anterior superior surface of the pericardium. This plane of cleavage extends upward in the middle line over the pyramidal lobe to its tip. In front of the larynx, it extends laterally on each side to the inner borders of the sternothyroid and thyrohyoid muscles. At the level of the isthmus, it extends from the midline laterally on each side beneath the prethyroid muscles and over the anterior surface of the isthmus, the mesial two-thirds of the superficial surface of the lateral lobe and over the entire superficial surface of the prethyroid fascia to its lateral limits along the inner border of the carotid sheath.

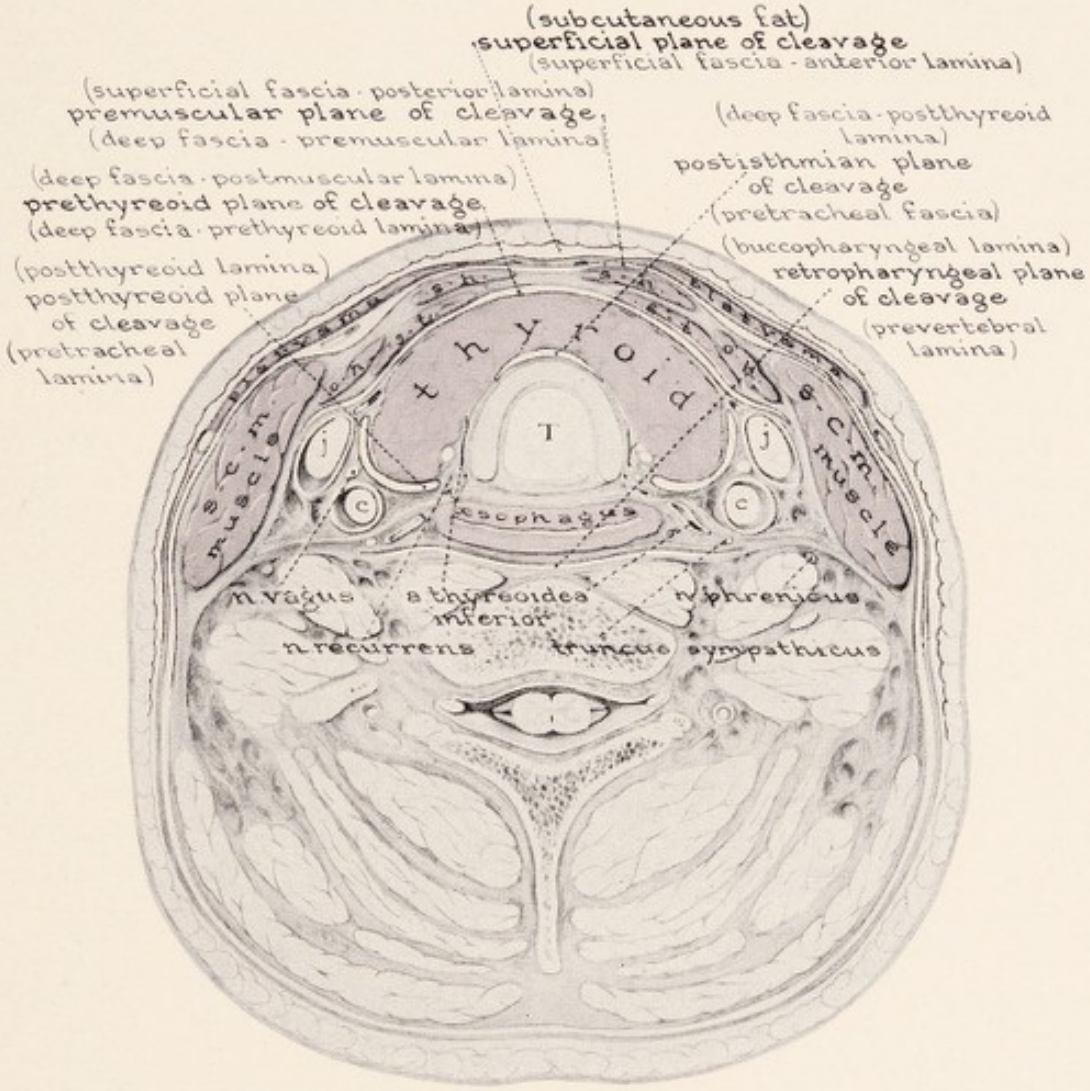


FIG. 43.—Transverse Section, Level of the Isthmus, Planes of Cleavage.

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The superior limit of the prethyroid plane on each side is an irregular line extending from the midline at the upper border of the isthmus or pyramidal lobe over the thyroid cartilage in an outward and downward direction and curving around the inner and lower borders of the insertion of the sternothyroid muscles into the thyroid cartilage. The line continues in an upward and outward direction behind the omohyoid muscle and parallel with the anterior branch of the superior thyroid artery to the anterior surface of the vascular stalk above the upper pole, and curving downward to the mesial border of the carotid sheath. The anterior surface of the plane is seen as the aponeurosis upon the posterior surface of the sternohyoid, the sternothyroid, and the anterior belly of the omohyoid muscles.

The prethyroid plane of cleavage is of surgical importance, not only from the standpoint of facilitating operative procedure, but also because it affords a tract through which pus in the visceral compartment may burrow into the mediastinum.

Postthyroid Plane of Cleavage

In the description of the prethyroid fascia reference was made to the postthyroid space situated between the prethyroid and pretracheal fasciae immediately lateral to the posterolateral border of each lateral lobe. The anterior or superficial wall of this postthyroid space is formed by the prethyroid layer of the pretracheal fascia as already explained. The posterior wall is formed by the pretracheal fascia proper. The other side of the triangular space is represented by an area of gland surface extending anteroposteriorly from a point near the junction of the middle and posterior thirds of the anterolateral surface of the lateral lobe around the posterior border of the lateral lobe to the lateral margin of the thyroid pedicle on the deep surface of the lateral lobe. On this area of gland surface which forms one side of the postthyroid space is a definite plane of cleavage that we have called the postthyroid plane of cleavage. It may be well to note that the prethyroid and postthyroid planes of cleavage are separated merely by the thin prethyroid fascia. This fact is fundamental. It will readily be seen that separation of this thin layer of prethyroid fascia from the lateral lobe will make the prethyroid and the postthyroid planes of cleavage continuous.

The prethyroid fascia, that is, the layer of pretracheal fascia connecting the carotid sheath with the anterolateral surface of the lateral lobe, limits anterior rotation and is the greatest obstacle to mobilization of the gland. Separation of this connection greatly facilitates anterior rotation and dislocation of the lateral lobe. It also mobilizes and frees the superior pole and the vascular stalk and exposes the lateral margin of the thyroid pedicle. As the lateral margin of the thyroid pedicle is also the lateral margin of what has been termed the "danger zone," development of this plane of cleavage is of importance from the standpoint of identifying the lateral margin of the danger zone and thus safeguarding the recurrent laryngeal nerve in this location. Separation of the prethyroid fascia from the lateral lobe of the gland offers no difficulty since

the only structure in this fascia requiring special attention is the middle thyroid vein. After this vein is cut and ligated the prethyroid fascia can be readily stripped from the gland and the posterior plane of cleavage is thus exposed with impunity.

Postisthmial Plane of Cleavage

In the thyroid pedicle in the region of the esophagotracheal notch, there is no plane of cleavage between the thyroid gland, the trachea, and the esophagus. But on the anterior segment of the surface of the trachea, the pretracheal fascia consists of two or more loosely connected layers, between which a distinct plane of cleavage exists that we have called the postisthmial plane of cleavage. It extends upward behind the pyramidal lobe to its tip, downward behind the isthmus to a point below its inferior border, laterally on each side to the margin of the thyroid pedicle. Development of this plane of cleavage separates the isthmus from the trachea, leaving a layer of pretracheal fascia on the trachea and one on the deep surface of the isthmus. Recognition of the lateral margin of this plane of cleavage identifies the mesial margin of the thyroid pedicle.

Retropharyngeal Plane of Cleavage

Between the buccopharyngeal and the prevertebral layers of fascia there is an interval called the retropharyngeal space which is filled with loose connective tissue. This space extends as a definite plane of cleavage above to the base of the skull and is continuous below with the posterior mediastinum. It is bounded laterally by the blending of the carotid lamina, posterior to the carotid sheath, with the buccopharyngeal and prevertebral lamina. This space when considered in relation to thyroid surgery, may well be called the retropharyngeal plane of cleavage.

CHAPTER XII

INSTRUMENTS AND LIGATURES

Instruments

Even the most able operator finds his work greatly facilitated by well-chosen instruments. The more delicate the task, the more refined and reliable must be the tool with which to do it. Anatomic considerations, the delicate quality of the work, and the responsibility entailed, demand that the goiter surgeon be especially painstaking in his selection of instruments.

The splendid armentarium of instruments gradually built up by Kocher, Halsted, and the other pioneers in goiter surgery, offers the surgeon of today a wide choice in the selection of his instruments.

The number of instruments required will depend upon the technic followed. The operator who ligates the blood vessels before he cuts them, as is common practice in Europe, or ties as he goes, will not need as many instruments as the operator who cuts between clamps and ties later.

Knives and Scissors

It is not necessary to discuss the choice of the scalpel, but the selection of scissors is of some importance. Narrow, slender blades facilitate dissection in some situations but no advantage is served by sharp points. The danger of accidental injury to such structures as the trachea, the esophagus, and the internal jugular vein, is in great measure avoided by the use of blunt pointed scissors.

Tissue Forceps

Thin walled veins, especially those on the surface of the gland, are easily torn with toothed tissue forceps or with forceps that do not hold the grasped tissues securely. The tissue forceps with round serrated tips called Russian Tissue Forceps, not only hold the grasped tissues securely but may also be used to catch a bleeding point or a needle after it has been passed through the tissues.

Artery Forceps

Light, slender, dependable artery forceps, without teeth, should be selected for thyroid surgery. The use of stiff or toothed forceps increases the danger of crushing or tearing delicate structures, and heavy forceps may drag upon structures connected with the trachea and cause its collapse.

The presence of a number of large forceps in the wound may seriously interfere with the succeeding steps of the operation. In our experience forceps that have slender flexible blades with cross serrations and no teeth are the most satisfactory.

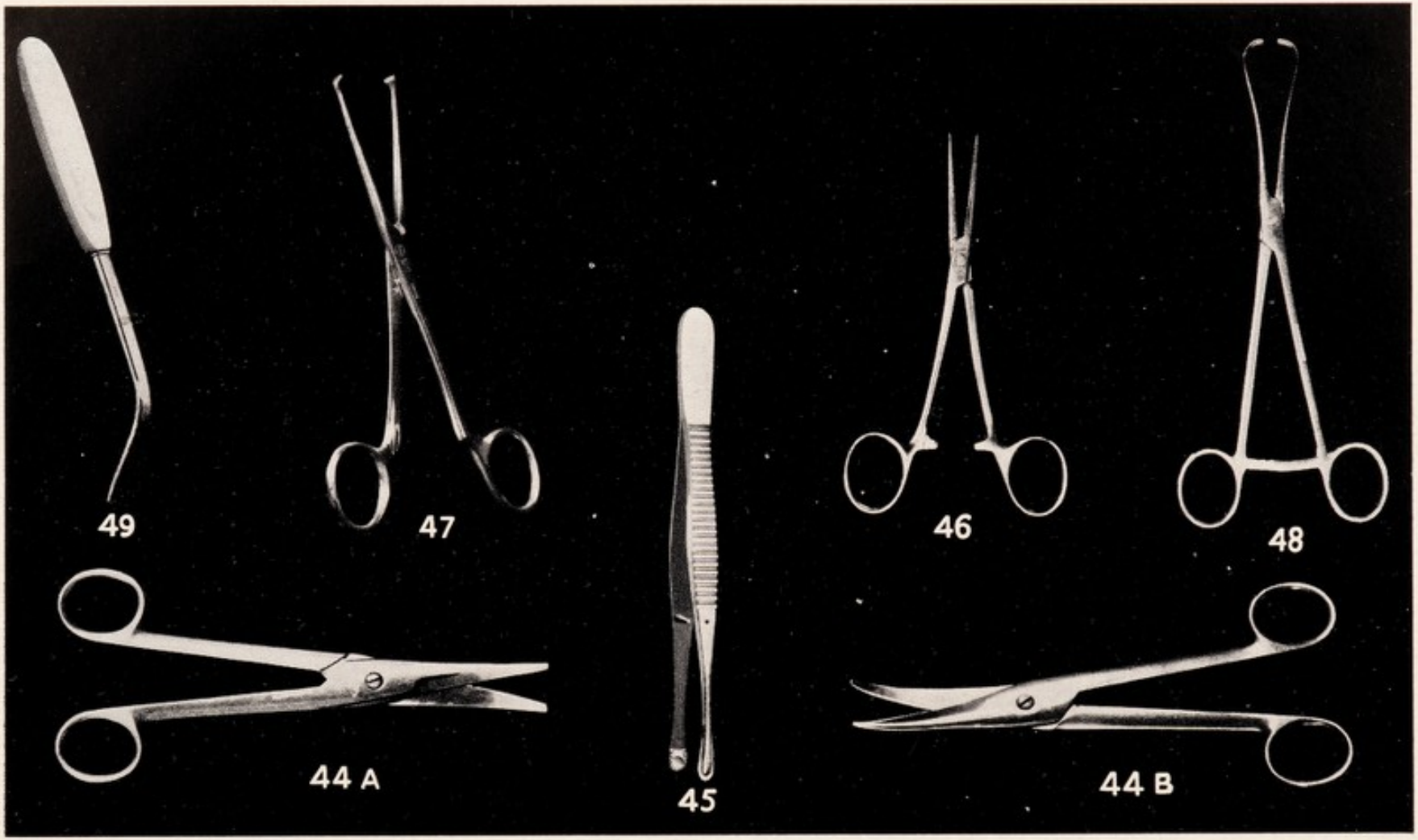


Fig. 44. A. and B.—Scissors.
Fig. 45.—Russian Tissue Forceps.
Fig. 46.—Artery Forceps.
Fig. 47.—Allis' Forceps.
Fig. 48.—Goiter Forceps.
Fig. 49.—Flap Dissector.

Allis' Forceps

Structures other than blood vessels should be caught by Allis' forceps. The fine teeth of the Allis' instrument do not crush the tissues grasped, as do the jaws of artery forceps.

Goiter Forceps

Hemostatic forceps are not satisfactory for catching blood vessels upon the surface of the gland or for grasping gland tissue, since they easily cut through the friable tissue. In 1914 the author devised a goiter forceps that holds gland tissue firmly. The form of the three-pronged blades leaves considerable space between them near the tip. A considerable portion of gland tissue may be grasped with this forceps and, as it has five notches upon the ratchet handle, it may be closed just enough to compress the grasped gland tissue lightly between the blades. A surprising amount of traction may be exerted without causing the forceps to tear out, and all bleeding points within its grasp are controlled.

Flap Dissector

The raising of the flaps may be greatly facilitated by the use of a flat point dissector to push the flaps upward and downward from the line of the skin incision. The one illustrated is shaped somewhat like a periosteal elevator with a serrated edge.

Retractors

In 1922 the writer devised a selfretaining retractor for the flaps, which is used with very satisfactory results. The retractors, which are paired, are made of heavy spring wire. When in place they accurately fit the contour of the neck on each side. This unique feature is an advantage, in that the retractors do not obtrude themselves in the least. It will be noted that the upper arm of the instrument in place is shorter than the lower arm; this inequality in the arms raises the ring or angle of the instrument upward and outward above the clavicle so that it is out of the way. The elasticity of the springs serves to adjust the retractor, automatically, to an incision of any size, and makes possible the retraction of the superficial flaps without dangerous tension. By the use of this instrument the operator is enabled to dispense with one assistant.

For adequate exposure of the deep structures, careful hand retraction of the muscles laterally is essential. The danger of injury to deeper structures, especially veins, by the tip of a hook-shaped retractor may be avoided by using a retractor with a right angle straight blade.

The usual retractor presents a difficulty in the upward and outward retraction for exposure of the upper pole, since its long straight handle must be held close to the head of the patient, and against the drapes which protect the field of operation. Both the retractor and the assistant using it seem to be always in the way. To obviate this annoyance we adapted a retractor to the space by bending the handle till it formed a right angle with the shank. In position the middle section lies evenly and firmly

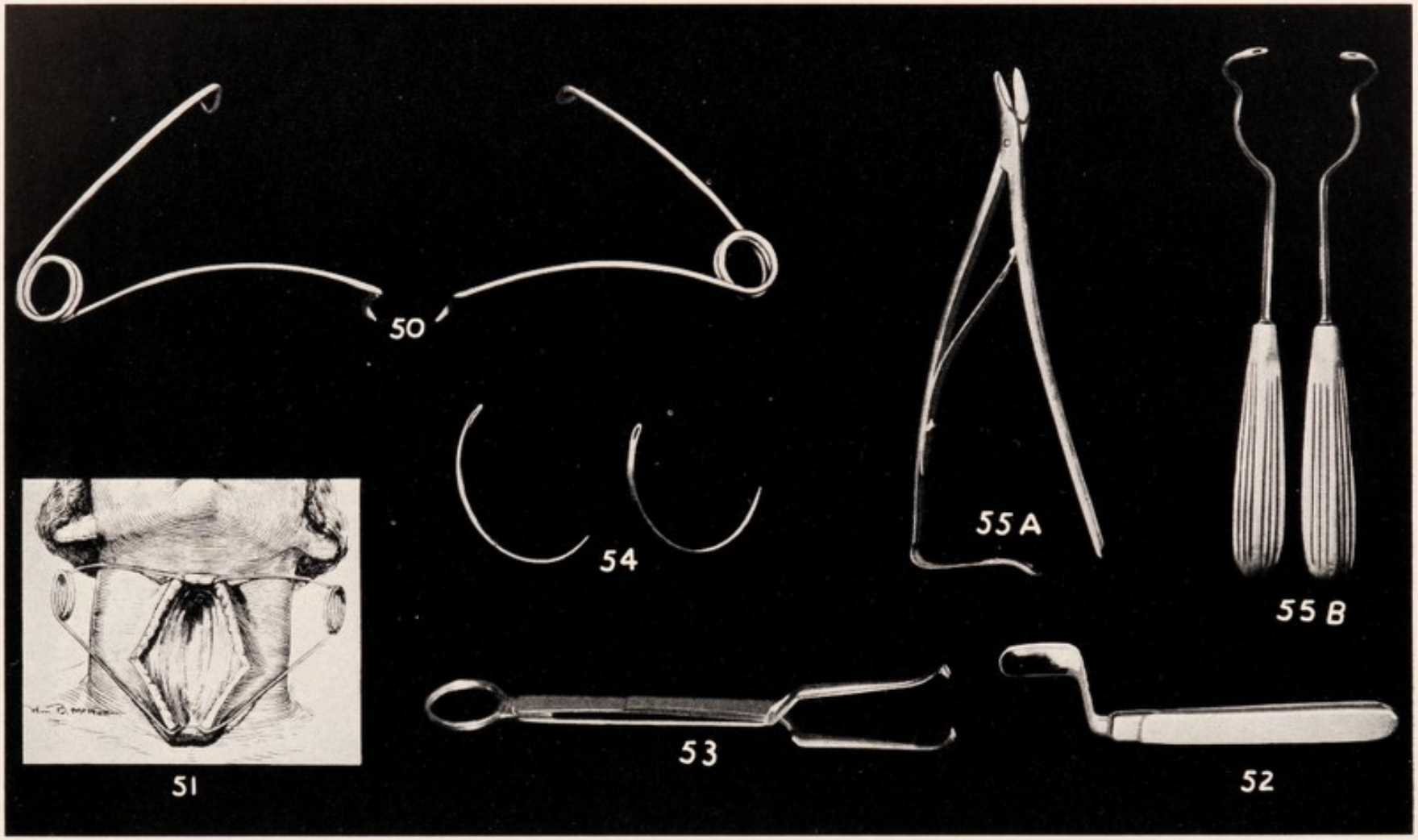


Fig. 50.—Self-Retaining Retractor.
Fig. 51.—Self-Retaining Retractor in Place.
Fig. 52.—Right Angle Retractor.
Fig. 53.—Towel Clip.
Fig. 54.—Needles.
Fig. 55A.—Needle Holder.
Fig. 55B.—Vascular Stalk Ligature Carrier.

against the neck and the handle is directed outward at right angles. The hand of the assistant has better control of the tissues and at the same time remains out of the surgeon's way.

Towel Clips

After the self-retaining retractors are in place, a towel is drawn under the retractor (on each side) and the middle of one edge of the towel is fastened to the skin edge, close to the upper prong of the self-retaining retractor by the towel clip illustrated. The angle of curvature near the tips permits the clip to fall downward and rest easily against the neck. The towels are brought together at the lower angle of the incision and fastened with the usual towel clip. The loose section of the towel, above the towel clips anteriorly, is turned back and covers the self-retaining retractors and the towel clips.

Needles

The selection of proper needles is of the utmost importance. Unnecessary trauma is inflicted by the use of needles with a cutting edge, of too large a caliber or of insufficient curve. Increased difficulties are encountered in some situations where the space is limited if an attempt is made to use a needle that is too long. However, the needle should be of sufficient length to pass through the tissues, without undue compression of the parts included in its grasp. Fine, round point, flat shank, full curve needles in three-fourth, one and one-fourth, and one and three-fourth inch lengths are the ones most often selected.

Needle Holder

In some situations, especially in the region of the upper pole, the ease with which a needle may be accurately passed through the tissues is dependant upon the angle at which it is held in the needle holder. The holder shown in the illustration is light and slender and holds the needle securely in any one of four positions.

Ligature Carrier

In some cases the inaccessible position of the vascular stalk makes it extremely difficult to pass a ligature around it by means of a needle in a holder. The danger of puncturing a blood vessel or of injuring a nerve, with the sharp point of a needle, is a real one. The procedure is simplified and the danger of injury to all structures in the region is minimized by the use of a properly designed ligature carrier. Those in general use are not designed to fit the peculiar form of the space available. The ligature carrier devised by us follows the peculiar form of the space around the upper pole and enables the operator to pass the ligature around the vascular stalk with ease and safety.

The passage of a ligature around the trunk of the inferior thyroid artery is easily and expeditiously accomplished by means of the standard ligature carrier with a single full curve at the tip.

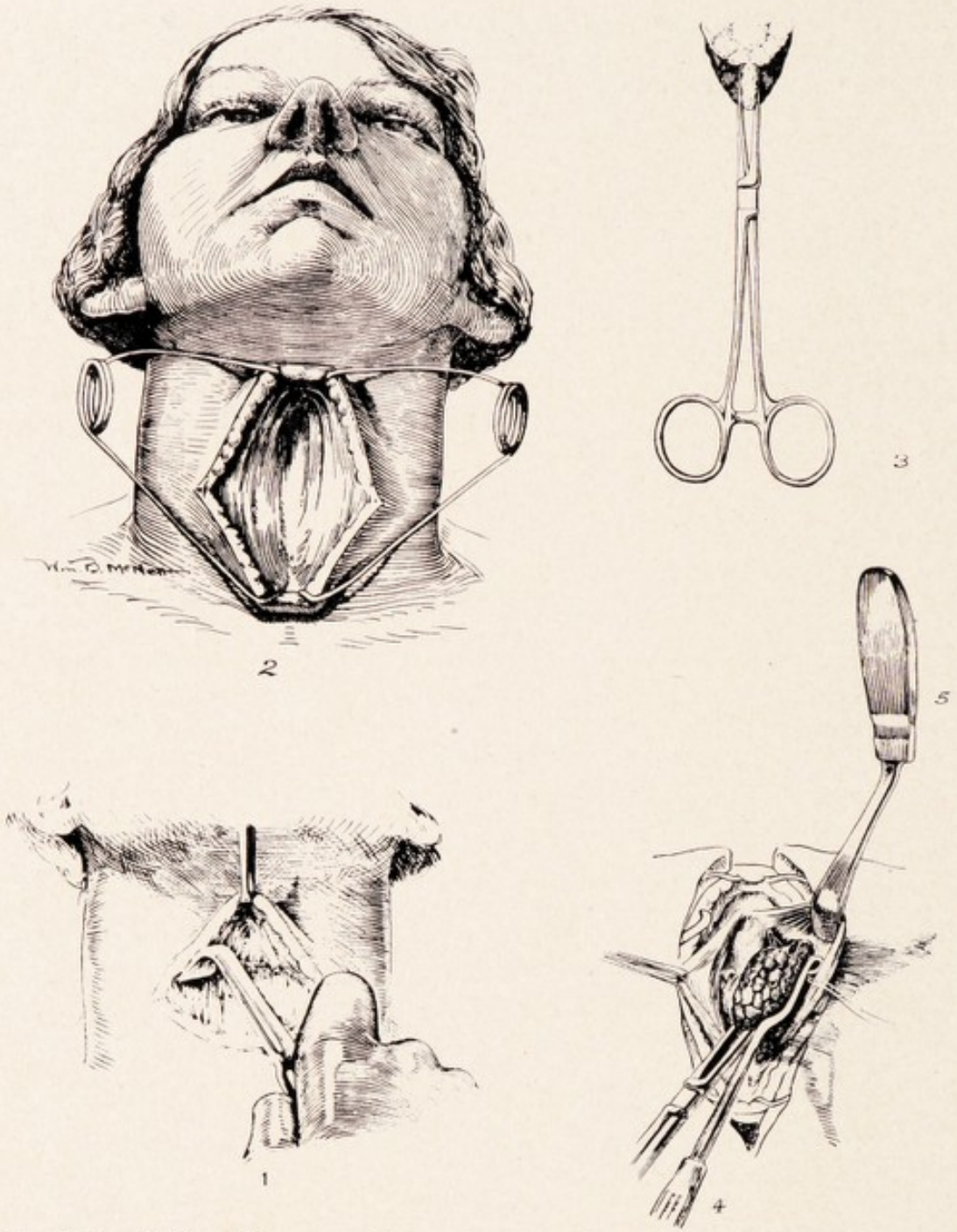


FIG. 56.—(1) Flap Dissector; (2) Self-Retaining Retractors; (3) Goiter Forceps; (4) Upper Pole Ligature Carrier; (5) Right Angle Retractor.

Ligatures

The pioneers in thyroid surgery recognized the high incidence of late infections, knots under the skin, and prolonged drainage following the use of non-absorbable sutures, but the dangers of secondary hemorrhage and of infection from the catgut available at that time prompted them to use heavy, strong ligatures of silk or linen. For a long time the idea was

prevalent that the danger of secondary hemorrhage could be avoided only by using silk or linen for the ligation of the thyroid arteries. Extended observations have shown, however, that secondary hemorrhage is usually caused by the knot giving way or the ligature slipping off the blood vessel, and that it is rarely, if ever, due to the premature absorption of the ligature.

In our first one thousand thyroid operations, silk or No. 2 chromic catgut ligatures, tied with reef knots, were used routinely for the ligation of all large blood vessels. Secondary hemorrhage of sufficient severity to demand the reopening of the wound occurred in nineteen cases. Upon reopening the wound it was found that hemorrhage was caused by the slipping of the ligature off the blood vessel in eleven cases; by giving way of the knot in five cases; by a retracted inferior thyroid vein, that had not been tied at the time of operation, in one case, and by oozing from all cut surfaces in the other two cases. In no case was it due to absorption of the ligature. The high incidence of prolonged drainage and late complications, from the presence of silk and unabsorbed heavy chromic catgut sutures, prompted us to use finer and more easily absorbable sutures until we adopted sutures of No. 1 plain catgut for the ligation of the chief blood vessels and of No. 0 or 00 plain catgut for all other buried sutures. An extra precaution usually observed is the ligation of the vascular stalk at the upper pole with two strands of No. 1 catgut tied separately. By tying these fine absorbable sutures with triple knots and placing them with extreme care, the incidence of prolonged drainage and postoperative hemorrhage has been almost entirely eliminated.

In our last three thousand thyroid operations, recognizable secondary hemorrhage occurred in only three cases. The hemorrhage occurred from a single blood vessel—a retracted inferior thyroid vein that had not been ligated at the time of operation—in only one of these three cases. In the other two, the hemorrhage was due to oozing from all cut surfaces. Oozing from the finer blood vessels, especially those situated immediately under the skin flap and along the edges of the skin incision, can be effectively and more expeditiously closed with electrocoagulation than by ligation. The use of electrocoagulation for this purpose obviates placing many sutures, and by reducing the amount of catgut buried promotes the healing of the wound.

In our clinic, No. 1 plain catgut is used for the ligation of the vascular stalks, the middle thyroid veins and the inferior thyroid arteries; No. 0 plain catgut for the ligation of the inferior thyroid veins and the thyroidea ima artery; and No. 00 plain catgut for the ligation of small blood vessels and for the coaptation of the prethyroid muscles and edges of the cervical fascia. For the closure of the skin incision no sutures are required as skin clips are used exclusively.

CHAPTER XIII

PREOPERATIVE TREATMENT

Previous to a goiter operation a patient should spend at least two nights in the hospital. Rest is valuable even in the simple cases. In addition to the beneficial effect on the physical and mental condition of the patient, the rest will have considerable influence in promoting better relaxation of the muscles of the neck which in turn will, to some extent, facilitate the operative procedure.

Physical and Laboratory Examination

Thorough physical and laboratory examination is necessary to determine the condition of the kidneys and the cardiovascular system and to discover the presence of such possible complications as pulmonary conditions, hemophilia, or acute infections. The teeth, tonsils, and nasal sinuses should be carefully examined for infections.

Valuable information may be secured in thyrotoxic cases by the estimation, at regular intervals, of the basal metabolic rate. Even in cases of atoxic goiter one or more such estimations should be made in order that the information acquired may be available in the future. Fluoroscopic examination of the chest should be done routinely so as to discover in advance the presence of thoracic prolongations, tracheal deviation of marked degree, or aortic aneurism. The vocal chords should be examined **in every instance** to rule out the possibility of an already existing paresis or paralysis.

The coagulation time should be determined and, if prolonged, the coagulability of the blood should be increased before the operation is attempted. The oral administration of 20 grains of calcium lactate or calcium gluconate every four hours for three or four days, followed by the intramuscular injection of hemostatic serum on the night before operation will, in most cases, reduce the coagulation time to nearly normal. If it does not, resort should be had to transfusion of whole blood.

Cathartics should not be given on the night preceding the operation. When indicated, they should be administered at least twenty-four hours before operation so that the patient may recover from their effects before being taken to the operating room.

Care of the Skin

Generally, insufficient attention is given, preoperatively, to the skin in the operative field. The surgeon may be inclined to use heroic antisepsis measures in the presence of mild, superficial skin infections such as pustular acne or follicular infections. In our experience, strong antiseptics and vigorous measures are apt to change the mild, subacute infection into an active, virulent one. It is essential to avoid irritation as far as possible;

neither violent scrubbing nor the application of irritating antiseptics should be permitted. When pustules are present, they were opened after the adjacent skin had been treated with iodin or similar antiseptic. While the lesions are open and discharging pus, a wet dressing, saturated with any of the non-irritating but efficient antiseptics, is applied continuously. For cases of this kind the standard solution used by us for many years is a saturated solution of boric acid. Care should be taken that the solution is completely saturated, otherwise the applications will soften and thicken the skin until it has the appearance of a washerwoman's hand. A saturated solution of magnesium sulphate has also been satisfactorily used. Solutions of mercurochrome are sometimes employed but they are objectionable due to the fact that they cause intense discoloration of the skin. Superficial infections will sometimes yield to x-ray treatment when antiseptics seem to aggravate them. Prompt opening of all pustules followed by the continuous application of autogenous bacteriophage is a dependable treatment. The operation should, when possible, be postponed until all open pustules in the field of operation have healed.

On the morning of operation the field is cleansed thoroughly with soap and water, then washed with alcohol. A sterile dressing is applied and allowed to remain in place until the patient reaches the operating room.

ATOXIC GOITER CASES

Little need be said concerning the preoperative care and management of atoxic cases; the same amount of care must be exercised as in preparation for any other major operation. Since no thyrotoxemia is present, iodin medication is not indicated.

TOXIC ADENOMA CASES

The details of preoperative management vary somewhat in the different types of toxic adenoma. We will consider the types separately.

Cardiovascular Type

The condition of the heart, as determined by physical examination and electrocardiograph studies, is the ruling consideration in cases of this kind. Arhythmias and auricular fibrillation are found as a rule. In many instances decompensation of varying degrees is noted. Such factors as high blood pressure and vascular degeneration must be taken into consideration in outlining the preoperative treatment.

Rest and Diet

It will be seen at once that the preoperative care of this condition must include certain special features. In some severe cases several weeks may be profitably employed in preparing the patient for operation. Complete rest, in bed in a hospital, and a carefully arranged diet consisting largely of vegetables, should be insisted upon. If the basal metabolic rate is high, the diet should include large amounts of carbohydrates.

Medication

Digitalis is of the utmost value if arhythmias or auricular fibrillation are present, or if the heart has decompensated. Strophanthus and caffein are often useful. In addition to the drugs already mentioned, theobromin sodiosalicylate or novasurol may be indicated if edema is present.

If there is serious impairment of the kidney function, great caution must be exercised in the administration of large doses of novasurol. Small doses of the salines are permissible but should not be used to the point of exhaustion. Since, in many of these patients, the gland is almost completely destroyed (either by degenerative processes or by the atrophic changes of the final stages of hyperplastic evolution) hypothyroidism of varying degree is not infrequent. This necessitates the cautious administration of thyroid extract. Small doses of iodin are indicated by iodin deficiency and large doses by thyrotoxemia.

Anaphylactic Type

For patients with this type of adenoma the amount of protein in the diet should be greatly reduced. During the preoperative period in the hospital, every attempt should be made to determine whether the patient is sensitized to any particular foods. If any of these foods are found they must be rigorously avoided. Anaphylactic type patients, as a rule, should have five days or a week of hospital care before operation. Stimulation of the assimilative and excretory functions should be promoted as far as possible and rest in bed insisted upon.

Great care should be exercised in administering bromids, iodin, and other drugs. Patients with this type of adenoma are often extremely sensitive to certain drugs as well as to certain foods.

Hyperplastic Type

Control of thyrotoxicosis.—The proper use of iodin, in the preoperative care of a patient with this type of adenoma, will be productive of markedly beneficial results. The improper use may result in serious damage. The importance of iodin medication is in direct proportion to the severity of the thyrotoxemia. The improvement following the use of iodin is often definite and prompt: the pulse rate and basal metabolism drop, the appetite increases, the emotional and mental condition is bettered, the restlessness decreases, and the patient experiences a feeling of well-being. In rare cases the administration of even small doses is followed by alarming symptoms and we must depend mainly upon symptomatic treatment. Empirical treatment with such drugs as quinin, sodium salicylate, ergot, mercury, and ichthyol may be of assistance.

No drug, except iodin, is so dependable in the control of the thyrotoxicosis as quinin, when given in sufficient dosage. The administration of 10 to 20 grains of quinin every four hours will, in most cases, reduce the pulse rate twenty beats per minute, and lower the basal metabolic rate 15 per cent within thirty-six hours. The general condition of the patient is more improved than is indicated by the reduction in the pulse and metabolic rates. In some cases sodium salicylate in the same dosage is effectual.

Sedatives

After the iodin treatment has been instituted, it is only in occasional instances that sedatives are necessary. If the indication arises, the most satisfactory sedatives are the bromids, given in 10 to 20 grain doses, four times daily. More potent sedatives should be given only when absolutely necessary.

Symptomatic Treatment

The control of nausea and vomiting is of extreme importance. In some severe cases, the vomiting is aggravated by the ingestion of small portions of food but is controlled by the ingestion of large portions. Diarrhea indicates the elimination of vegetables from the diet and the administration of such remedies as bismuth and opium. For stomach irritability, which is not infrequent, bismuth, the alkalis, and cerium oxalate are often beneficial. Serious nervous symptoms must be controlled even though resort to large doses of morphin is necessary.

One or more degrees of fever requires the elimination of the excess heat by hydrotherapy. If ice bags applied to the head and the precordial area do not reduce the temperature sufficiently, cold sponging, ice packs, and even cold immersion baths must be resorted to. The oral temperature is not a reliable index of the body heat.

The remedies usually prescribed for cardiac disorders are often ineffectual in the control of the toxic tachycardia. Improvement in the cardiac condition will be dependent upon the control of the thyrotoxicosis. In selected cases a reduction of the pulse rate may be obtained in the course of a few days by means of roentgen ray treatment.

Mixed Type

In this group the symptoms of true thyrotoxicosis and the symptoms of anaphylactic toxemia are both present simultaneously. In consequence the features of the proper preoperative management vary greatly with the individual case. Arhythmia and other heart conditions may be present and digitalis of use. Iodin must be used with great caution and carefully controlled. Mercury is useful in some instances; it stimulates the excretory functions and reduces the toxemia.

DIFFUSE HYPERPLASTIC GOITER

The preoperative management of diffuse hyperplastic goiter is of paramount importance. Owing to the marked degree of nervous instability, the acute sensitiveness and the emotional imbalance characteristic produced by the disease—especial safeguards must be thrown about patients suffering from this disease before they may be safely submitted to operation.

Psychic Management

It may seem odd to place this consideration first. Those who have had experience in the preoperative management of this disease must be convinced of the very great importance of the psychic element in the preoperative treatment. Our first effort should be to make the patient com-

fortable in the hospital environment: sources of excitement and confusion should, as far as possible, be eliminated. A private room is almost a necessity: it is as difficult to manage a case of hyperplastic goiter in a crowded ward as in the home. Visitors should be few and should not remain long. The clinical and laboratory examinations should be carried out with an effort to disturb the patient as little as possible. The severely ill patient should be allowed to rest and become accustomed to the new environment before extensive examinations are undertaken.

Every goiter surgeon has his own method of influencing the mental attitude and reaction of the patient. It is usually not advisable for a nervous patient to know the exact time set for operation. To keep him in ignorance of this many subterfuges are adopted.

Some surgeons go so far as to do the operation in the patient's room. This practice has both advantages and disadvantages. One can, of course, "steal up" on the patient more easily in this manner; however, the difficulty of obtaining perfect asepsis in the patient's room more than counterbalances this advantage. It is true that the operative procedures, with proper preparation, can be carried out with a very small percentage of postoperative infections but this is a severe strain on the energies and resourcefulness of the hospital staff, and the objectives sought can be gained just as effectively in other ways.

It is not the changing from one room to another that is disturbing; it is the fright occasioned by the patient's knowledge that he is leaving a comfortable haven for the unknown dangers of the operating room. In order to protect nervous patients from the consequences of such knowledge we frequently make use of the following procedure.

During the days preceding operation the patient is taken to the operating room two or three times on the pretext that he is to have a basal metabolism test; before he leaves his room he is given a hypodermic injection of sterile water. The operating room is effectively camouflaged so that the patient will have no idea where he is; no instruments are in sight, the patient is in a corner of the room walled off by a screen. The anesthetist is present to make the "metabolism test." He talks reassuringly to the patient for a few minutes, manipulates some apparatus, places the mask and gives the patient a few whiffs of oxygen and gas. The same routine is carried out on the day of operation except that morphin or other narcotic is given in the hypodermic injection and the administration of gas is continued until anesthesia is induced.

Doctors, nurses, and other patients familiar with the procedure, offer a problem. In the case of these excitable patients who know too much, their knowledge may be turned against them. Instead of the expected sterile water such a patient may be given a narcotic and operated upon without preliminary skirmishing on the occasion when the gas mask is put on for the first time. One such patient, a physician, had to be kept in bed for several weeks before operation. He looked forward anxiously and fearfully to the preliminary routine which he was certain would occupy a few days or a week preceding the ordeal of operation. He took his "first hypo" and "first" inhalation gracefully and without much trepidation and

thought that he had a week to worry. He was agreeably surprised on awakening to find that the dreaded ordeal was over.

Hospital Observation

A careful history should be taken, the occurrence of crises noted, and any facts, which might serve to indicate the present stage of the disease, analyzed. The history in a particular case may indicate whether the patient is approaching crisis, is on the upward trend after a crisis, or is in a quiescent period between crises. Inquiries should be made with respect to previous treatment or medication, particularly with iodin. The heart should be carefully examined with the aid of fluoroscopic observations and electrocardiographic tracings. The kidney condition should be carefully investigated, the blood chemistry determined, all indicated tests employed, and a complete physical examination made giving careful attention to the possibility of the presence of associated disease.

Basal metabolism readings should be repeatedly and consistently taken under as ideal conditions as possible. The metabolic rate in itself should not be featured as the main consideration nor should it determine the moment for surgical intervention; the time during which increased metabolism has been present is of as much importance as the height of the reading at the time of examination. Also, a high rate which is falling is of better import than a moderate rate which is climbing. The basal metabolic rate is of great importance and value only when considered in conjunction with the pulse rate, blood and pulse pressure, heart sounds, electrocardiograph tracing, digestive disturbances, loss or gain in weight, insomnia, nervousness, and other features of the clinical picture.

Rest

Preoperative rest is an essential. The rest should be mental as well as physical. Complete rest in bed is advisable for the average case. Occasionally, for a very fretful patient, more may be gained by allowing him an hour or two each day in an easy chair. For the average case requiring "heart rest," seven days will suffice as far as the heart is concerned. Everything that rest can do for the heart will be done within this time.

Nursing Care

The surgeon will do well to choose nurses with the proper temperament to care for thyrotoxic patients facing operation. A good nurse will have a remarkable influence in the control of nervous and mental states. Individualization is essential; practically every patient presents a different problem. The nurse should be discreet and observant, study the idiosyncrasies, likes and dislikes of her patient; learn to anticipate wants, calm fears, and augment confidence. These patients often are unduly suspicious, have harmless little obsessions and peculiar mental quirks which should as far as possible be humored. Nothing is to be gained by arguing with the patient.

The nurse should always accompany the patient to the operating room for "basal metabolism readings" on the mornings previous to opera-

tion so that nothing out of the ordinary will be remarked when her presence is noted on the morning of operation. The special nurse should either be in attendance for some days previous to the operation or should not appear until the patient returns from the operating room. Even though the patient is informed in advance of the time set for the operation, the change in routine just before operation is very disturbing.

Diet

The dietary considerations are an important part of the preoperative treatment; the food must be abundant—over three thousand calories a day—it must be palatable and well prepared, and consist largely of carbohydrates. Milk and lactose drinks may be given between meals if it is thought advisable to increase the caloric intake above the level represented by the food taken at the regular meal times. It is sometimes well to give an ounce of glucose every four hours for twenty-four hours or more previous to operation.

Occasionally delirious or semidelirious patients refuse food and the introduction of concentrated foods into the stomach by the nasal or stomach tube must be resorted to. In urgent cases glucose solution may be administered intravenously. Fluids should be forced and the patient—unless dropsy or other contra-indication exists—compelled to take from 2500 to 3000 cubic centimeters of fluids in every twenty-four hours. If fluids and foods are not retained by the stomach and cannot be successfully administered by proctoclysis, at least 2000 cubic centimeters of fluids should be given daily by hypodermoclysis or intravenously. Stimulants such as tea, coffee, of alcohol are prohibited unless positive indications for their use are present.

Medication

Sedatives.—The use of sedatives for the prevention of insomnia and the control of nervous symptoms is frequently necessary. Sodium bromid is the drug of choice in these conditions since in addition to its sedative effect and freedom from deleterious action it seems to have a favorable influence upon the thyrotoxemia. It may be administered in 15 to 30 grain doses orally or in 30 to 60 grain doses by proctoclysis every six to twelve hours. A large single dose once or twice a day is sometimes more effective than smaller doses at shorter intervals.

Should the sedative effect of bromids be insufficient, such drugs as barbital, phenobarbital, and amidopyrene may also be given. The last two named seem to be less likely to produce hallucinations than barbital, when given over a period of several days.

For preoperative medication, the more powerful drug, sodium amytal, is more dependable in effect and has a wider range of safety than any of the other drugs just mentioned. Occasionally the administration of codein, as an adjuvant to other sedatives, is indicated.

Morphin should be used only for urgent indications and at the time of operation. Opium administered orally in the form of Dover's powder is usually dependable for the control of nervous states. If morphin must

be used, it may be used in combination with hyoscin. The hyoscin increases the sedative effect of the morphin and is especially valuable in the presence of delirium or psychoses. In acute toxic delirium quinin has a sedative effect by reducing the fever, the tachycardia, and other manifestations of thyrotoxemia. Favorable effects are observed only when large doses are given. Its use is purely empirical.

Stimulants.—The heart in thyrotoxic patients is already overstimulated and cardiac stimulants are, as a rule, contra-indicated. Digitalis is no exception. It does not control toxic tachycardia and its use adds another toxic product to the blood stream. The danger of poisoning following the administration of procain is increased by the digitalization of the patient. In toxic cases, digitalis should be reserved for definite indications, such as heart conditions accompanied by arhythmia or fibrillation.

Iodin.—Iodin is the most valuable drug at our command in the preparation of thyrotoxic patients for operation. Its proper preoperative administration is followed by a reduction in degree of the thyrotoxemia, a decrease in the severity of the symptoms, and a reduction in the incidence of postoperative thyrotoxicosis. It is best administered in the form of Lugol's solution, the preparation in general use. If the patient has not been overtreated with iodin, ten to twenty drops of Lugol's solution may be given three times a day. Some patients tolerate iodoform—1/10 to 1/5 grain in tablet form—better than Lugol's solution. In the presence of digestive disturbances, iodin may not be borne well by mouth but in almost all cases it is tolerated when given by proctoclysis.

When the patient cannot take iodin by mouth, some physicians advise the application of iodin to the skin of the abdomen. The administration of Lugol's solution in saline solution by hypodermoclysis is a dependable method but in our opinion it is better practice in severe cases, when immediate effect is desired, to give sodium iodid, in solution, intravenously. This may be given in doses of 20 to 30 grains every six hours until such symptoms as vomiting, diarrhea, and intense restlessness have subsided. Especially in critical cases, the injection of an alcoholic solution of iodin directly into the gland is productive of better and more rapid results than any other method. Care should be taken that the patient's tolerance for the drug is not exceeded. Such symptoms as flushed face, slightly raised pulse rate, nervousness, loss of appetite, pruritus, urticaria, and excessive salivation are indications for a reduction in the dose.

It is difficult to give general indications for the use of iodin in the individual case; there are however certain types of cases which may be considered:

The patient who has not had iodin.—This patient is placed on Lugol's solution or iodoform tablets and operated on between the seventh and tenth day according to indications.

The patient who has had iodin.—It may be that the optimum moment for operation has passed; conditions may still, however, be sufficiently favorable for operation, and perhaps nothing is to be gained by waiting. In such cases operation is indicated as soon after admission to the hospital as circumstances will permit. In other cases the

conditions are unfavorable and the operation must be delayed until the surgical risk is improved.

The patient who has been overtreated.—The patient may have developed an intolerance from prolonged iodin medication. In some cases the intolerance will disappear following such measures as the reduction of the temperature by hydrotherapy or the intravenous administration of glucose. The intolerance, however, may be due to the oral method of administration rather than to the drug itself, in which case it should be given intravenously or by proctoclysis.

Previous excessive administration, especially if the tolerance point has been reached repeatedly, may have developed an intolerance to the drug itself. If iodin is used at all in such cases, it should be only after an interval of two weeks or more has elapsed since it was last taken. Even then extreme caution should be observed in its use. The favorable results obtained in the untreated case by its preoperative use cannot be expected in cases that have been iodized—therefore it is advisable to rely upon other measures: prolonged rest in bed, quinin and mercury medication, roentgen ray treatments and, when necessary, injections into the gland or ligations for the control of the thyrotoxicosis.

Moment for Operation

It is important that the operation be performed as soon as the maximum degree of improvement in the condition of the patient has been obtained, as the beneficial effects of the preoperative treatment may be of short duration. This favorable moment for operation may in atoxic cases be reached in two or three days and in thyrotoxic cases—depending upon the patient's response to iodin therapy—in from six to fourteen days. It is often inadvisable in thyrotoxic cases to wait for the basal metabolic rate to drop to normal or even approximately to normal. When the clinical findings indicate that the maximum improvement has been reached, operative procedures should be instituted even though the abnormal rate has not been reduced by more than one-half or two-thirds. The presence of complications, however, may provide positive indication for many days or even weeks of preparatory treatment.

From the standpoint of the prevention of postoperative thyrotoxicosis, the operation should be so timed that it occurs on the day before the maximum effect of iodin therapy is reached. This is usually reached on the ninth to the fifteenth day, thus indicating the eighth to the fourteenth as the day for operation.

Preoperative Medication

If the patient is apprehensive and inclined to insomnia the night before operation, a moderate dose of barbital (gr. 5) or of phenobarbital (gr. $1\frac{1}{2}$) will induce sleep and in addition have some sedative effect throughout the next forenoon. The dose may be repeated on the morning of the operation as soon as the patient awakens and another dose may be given one and one-half hours or more before the time set for the opera-

tion. In many cases the three doses of one of these sedatives will induce a condition of euphoria.

Sodium amytal in 3 grain doses may be used instead of the barbital or phenobarbital. It seems to create a deeper state of amnesia and euphoria than either of the other drugs. If three such doses are given on the morning of the operation—the first when the patient awakens, the second three hours before operation, and the third one hour before—the patient, in 70 per cent of the cases, will be in a state of amnesia when he enters the operation room and will require little, if any, additional anesthesia. When hepatic insufficiency is present, the elimination of these drugs is delayed—therefore great caution should be observed in their use when there is a history of jaundice or other hepatic disorder. If these drugs are contraindicated in the doses specified, or if further sedative effect is required, 1/6 or1/4 grain of morphin, with or without hyoscin, may be given hypodermically one hour before operation.

Standardized Preoperative Treatment

The complete standardization of the preoperative treatment is impossible. Standardization along general lines, however, is feasible and facilitates the institution of proper hospital care and the evaluation of the results.

CHAPTER XIV

OPERATIVE TECHNIC

The literature on operative technic is so voluminous that no attempt will be made to present all the operative procedures that have been described. The discussion of this subject will be limited to the methods used by the author. Such points as he considers distinctive or in some way different from the usual operations will be considered in more detail than the standard procedures.

PREPARATION OF THE PATIENT

Posture

The position of the patient on the table is of importance. A table, with an adjustable head rest, that may be tilted so as to place the patient in the reverse Trendelenburg position is a convenience for the operator but is not a necessary requirement. A flat table or even a bed may be used if a firm cushion or pillow is placed under the shoulders in such a manner that the head is extended to a rather extreme degree. Some operators like to use a sand pillow between the shoulders at the base of the neck but a pillow that extends outward and supports the shoulders adds to the comfort of the patient. The extension of the head should be sufficient to bring the neck well forward, but should not be of such degree as to cause discomfort. Straps and cuffs should be adjusted in such a way as to support the arms as well as to keep the patient in the proper position during the operation.

Preparation of the Field

Every operator has his own method of preparation and draping. In our clinic the neck is first washed carefully with ether to remove all oily substances and then the field is washed with alcohol. Pustules or superficial infections if present are painted with iodin. This preparation suffices in most instances. If further precaution is deemed necessary, the entire field of operation is painted with a solution of iodin or of 5 per cent picric acid in alcohol.

It is imperative to shield the field of operation from possible contamination by secretions from the mouth or nose of the patient or anesthetist. A wire frame ten or twelve inches in height, suitably draped, and placed between the face and neck, thoroughly protects the field.

Draping

The routine method used in our clinic is:

First, a sterile drape sheet is so placed that it covers the patient and table from the lower margin of the sterilized field downward to the level of the hips.

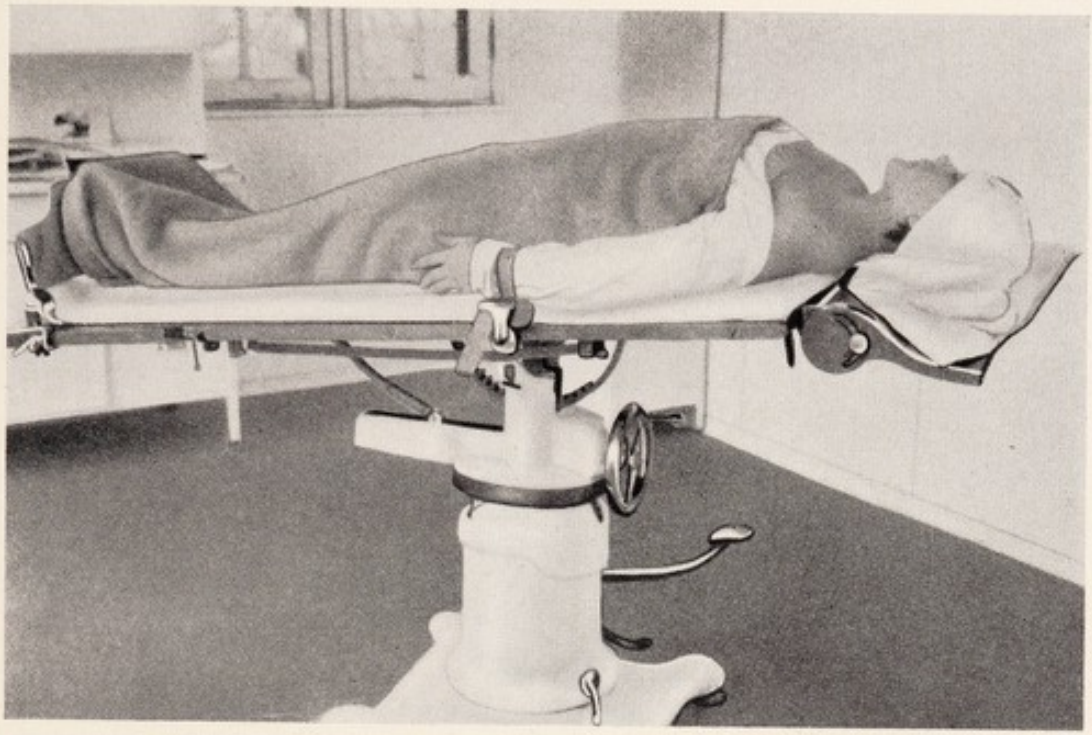


FIG. 57

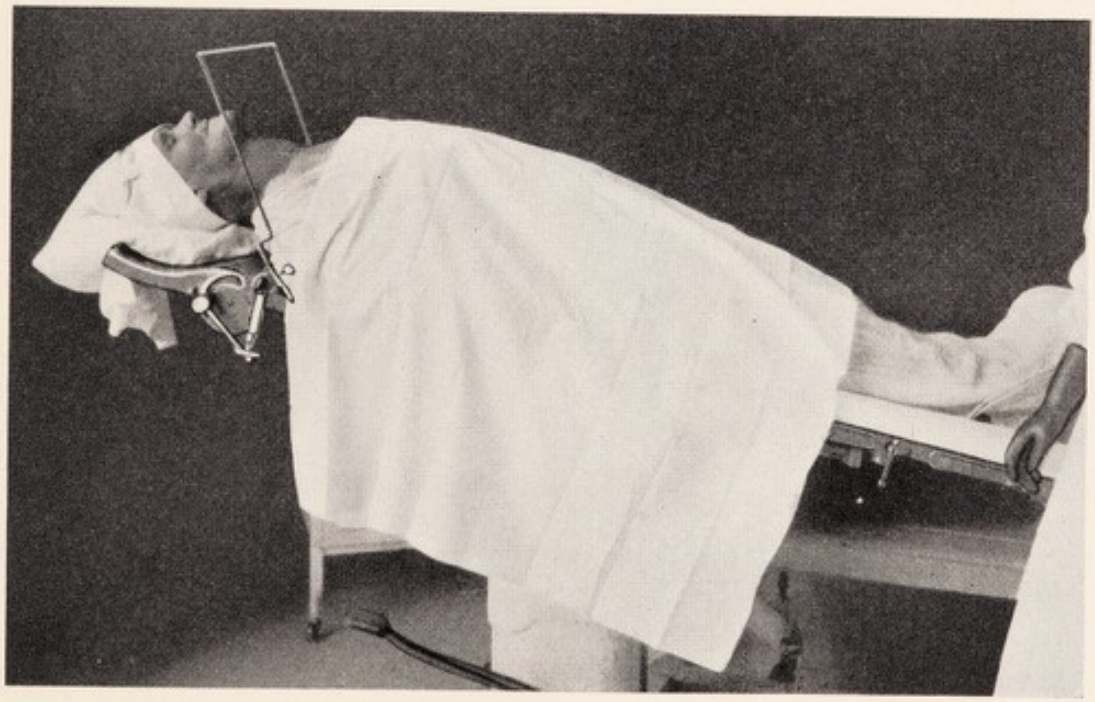


FIG. 58

Second, a goiter sheet—a small sterile sheet with two strings attached at the apex of a U-shaped opening—is applied as follows: The sheet, folded transversely across the middle, is placed with the fold upward on the drape sheet over the chest. The strings are carried up behind the ears and tied over the top of the patient's head, thus holding the center of the

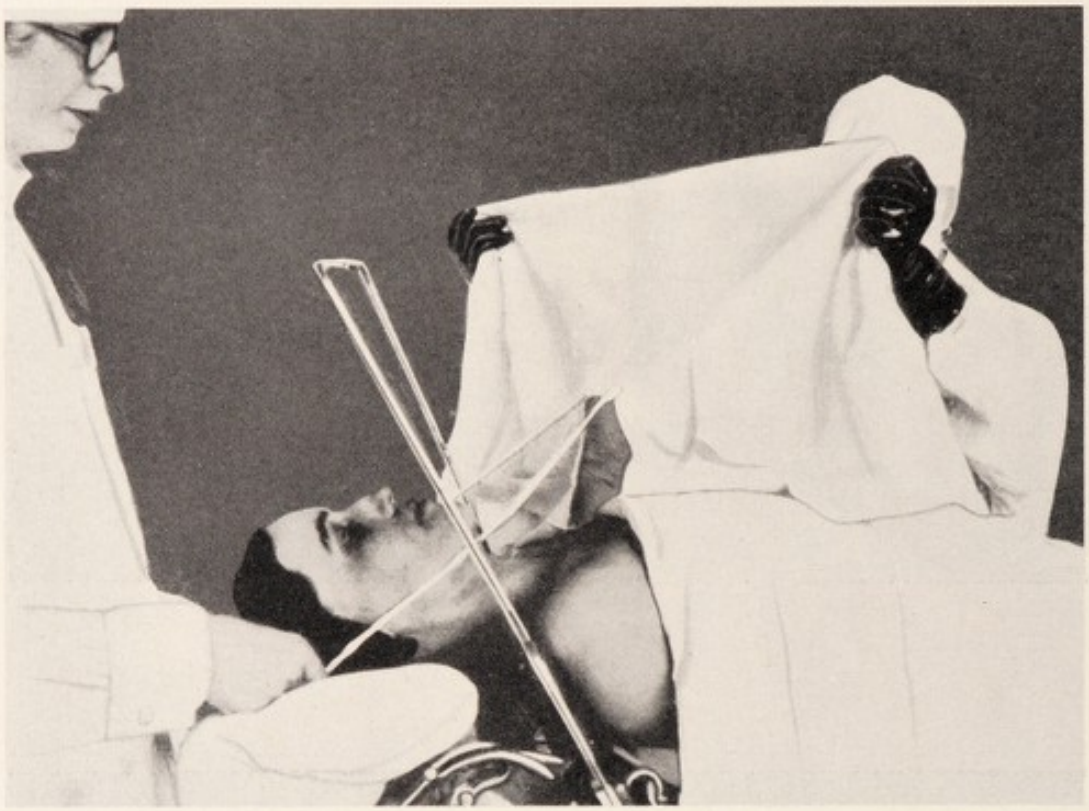


FIG. 59

sheet in a snug position under the chin. The upper end of the goiter sheet is fastened over the top of the wire frame with towel clips. The flaps of the lower divided portion extend downward over the first drape sheet, covering the regions at the sides of the neck, but leaving the entire operative field exposed by the U-shaped opening.

Third, after the instrument table has been adjusted over the thighs, a full sized sheet is spread from the lower edge of the operative field downward over the patient, the instrument table, and the lower end of the operating table.

Fourth, a common laparotomy sheet is spread over the patient and the table in such a manner that the usual sized aperture falls over the field of operation. The short end is carried up over the wire frame and under the chin of the patient, thus giving an added protection from the mouth of the patient and the anesthetist. The longer end of the sheet is thrown downwards and covers the entire patient. The sides of the aperture in the laparotomy sheet are pressed backward, exposing the side of the neck, while the upper and lower borders of the aperture are held in con-

tact with the skin above and below the field of operation by means of a roll of gauze on each side, the end of the roll being tucked in between the side of the neck and the side of the opening in the sheet. The gauze also catches any blood that may escape from the incision on either side and prevents it from running down the patient's back.

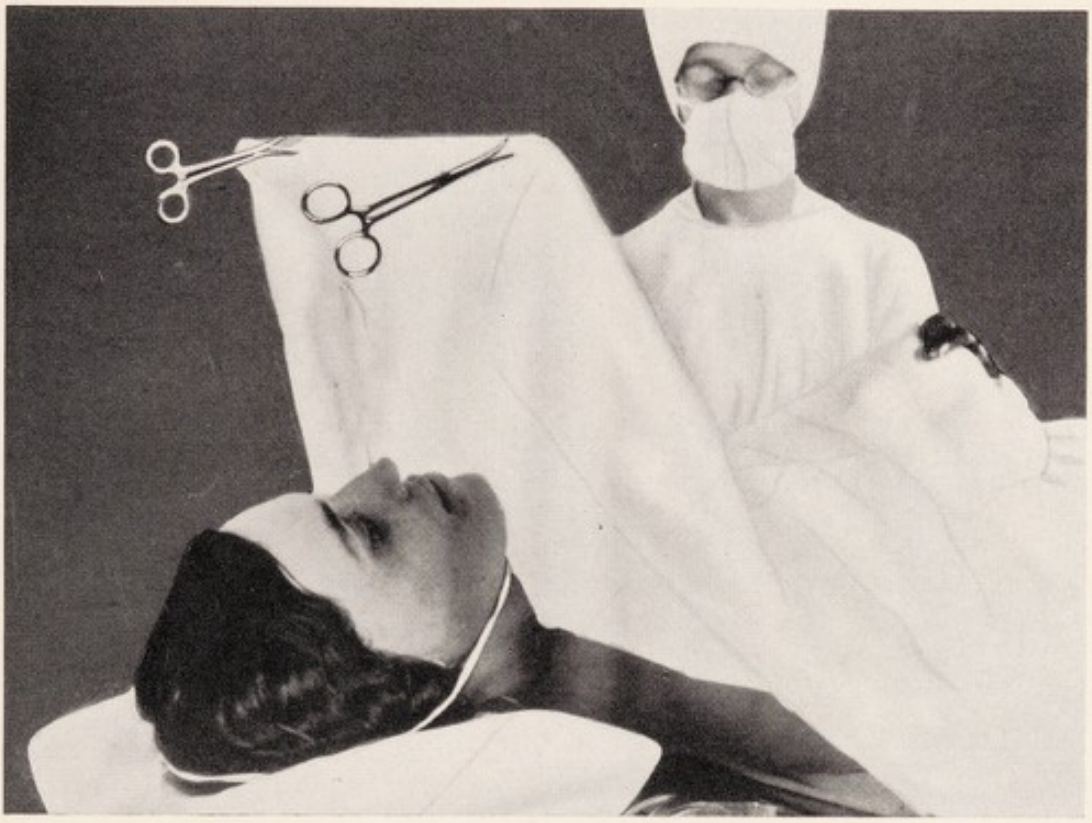


FIG. 60

MINOR OPERATIVE PROCEDURES

Minor operative procedures preliminary to subtotal thyroidectomy may be necessary: (a) In case of patients who have been repeatedly and injudiciously iodized, thus losing the beneficial preoperative effect of iodin. (b) In case of patients received in an advanced stage or in extreme thyrotoxicosis.

The procedures usually employed are injections into the gland or ligation of one or more thryoid arteries.

Injections into the Gland

Several years ago the injection of boiling water into the gland was extensively advocated. If enough water, at boiling temperature, is introduced into the gland an inflammatory reaction occurs that checks the secretion from the infiltrated portion for about two weeks. The difficulties attending the procedure are considerable and we have discontinued the use of this method. It is much easier and equally effective to infiltrate

the gland with a 1 or 2 per cent solution of quinin urea hydrochlorid. With patients who have an idiosyncrasy to quinin, some other solution may be used.

The preparation earliest used for gland injecton, a 5 per cent solution of carbolic acid, is still a favorite with some physicians. Repeated injections are required for marked effect and in some cases they are not tolerated. Cases of long standing do not seem to tolerate this solution as well as recent ones. Should no contra-indication to the administration of iodin be present, a 10 per cent solution of tincture of iodin or a 5 per cent solu-



FIG. 61

tion of sodium iodid may be used with about the same effect. The injection of absolute alcohol into the gland is attended by the same degree of improvement as the injection of boiling water.

It should be stated that if injections into the gland are used at all, they must be used with considerable caution. Only the areas of the gland which are to be later removed should be injected as an effective infiltration is certain to damage the gland structure.

Ligation of the Arteries

Ligation of one or more of the thyroid arteries, a popular procedure in the early years of thyroid surgery, has—as the sole method of treatment—been generally abandoned. In recent years it has been recognized that under most circumstances the benefit resulting from ligation is not sufficient to justify its use. Exception may be made in the case of extremely ill patients and in the multiple stage operation, where ligation still has its place. A reduction of 15 to 25 per cent of the abnormal increase in the pulse and basal metabolism rates with a corresponding improvement in the patient's general condition may be expected from the ligation of one thyroid artery.

Ligation is occasionally indicated as the first operative procedure in a multiple stage operation of the severely ill patient, especially when the goiter is a vascular one. With proper preparation, however, it is usually possible to do a lobectomy with only slightly greater strain on the physical resources of the patient than is occasioned by a ligation.

Superior Thyroid Artery

Ligation of the superior thyroid artery, although not so effective in the relief of symptoms as ligation of the inferior, has been generally ac-



FIG. 62

cepted as the operation of choice when ligation is indicated. The superior thyroid artery may be ligated in either of two locations: first, as a single artery or trunk near its origin in the superior carotid triangle; or second, at a point near the upper pole of the gland, distal to its division into three or more branches. Ligation at the latter point is usually called a polar ligation.

Ligation of the Trunk.—The approach to the artery is made by a transverse or slightly oblique incision over the lower angle of the superior carotid triangle at the level of the superior border of the thyroid cartilage (Fig. 63). The skin incision about one inch long exposing the superficial plane of cleavage can be made in any direction, but for cosmetic reasons it is best to make it parallel to the folds of the skin. The platysma and superficial fascia may be divided down to the premuscular plane of cleavage in line with the incision (Fig. 64), or the skin flaps may be raised upward and downward along the superficial plane of cleavage, and the fascia and muscle divided in the direction of the fibers of the platysma.

Retraction of the flaps, including the platysma, the superficial fascia, and the skin, exposes the thin layer of the deep fascia covering the lower

portion of the carotid triangle (Fig. 65). The landmarks of the inferior angle of the carotid triangle, the anterior margin of the sternomastoid muscle, and the lateral border of the omohyoid near where the muscle disappears under the sternomastoid, may be seen through the fascia.

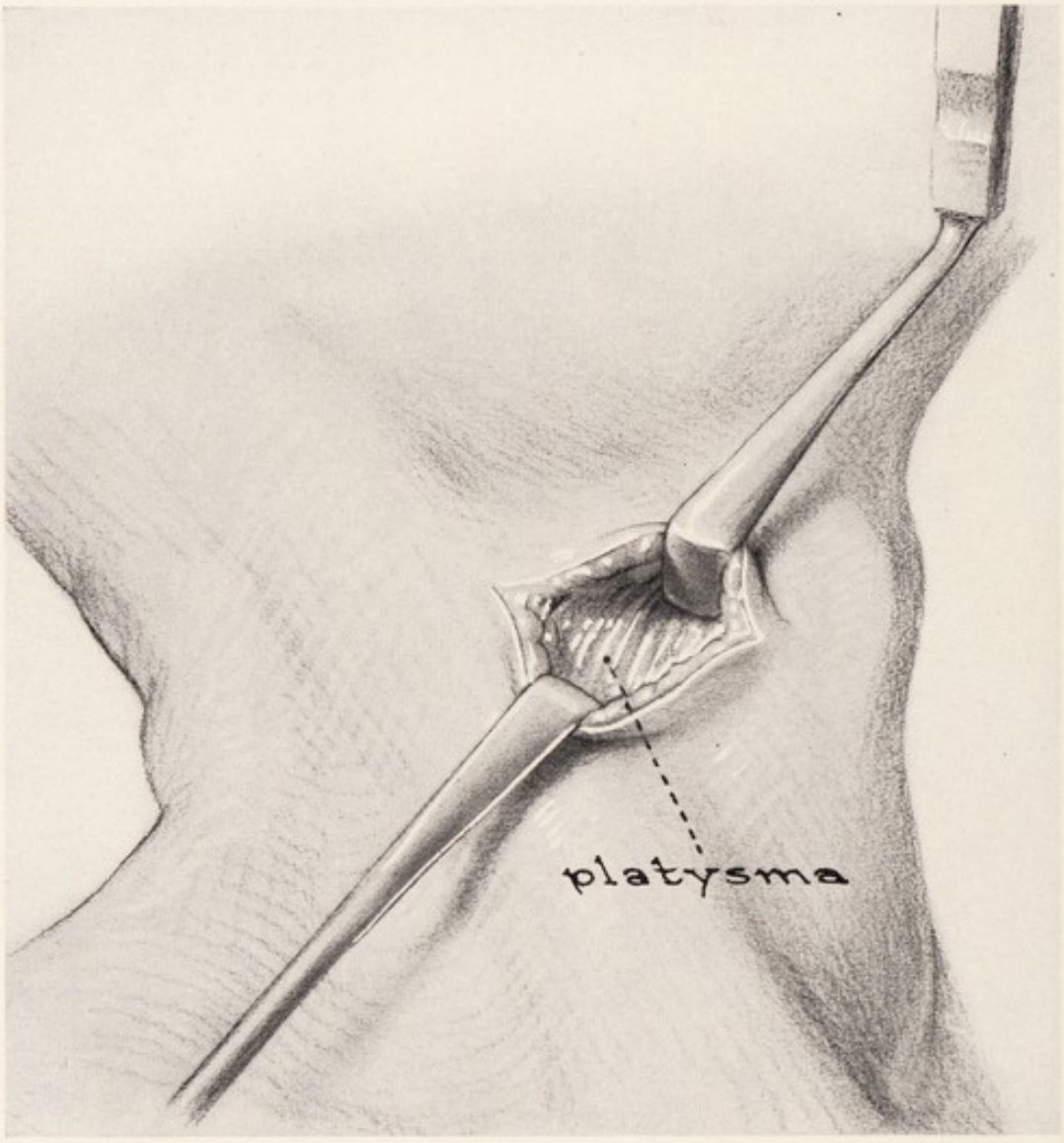


Fig. 63

These landmarks should be clearly identified before any attempt is made to penetrate the layer of fascia covering the triangle in order to isolate the artery. Division of the fascia covering the lower portion of the carotid triangle exposes the artery lying on the superficial surface of the middle constrictor muscle near the lateral border of the omohyoid. The only difficulty likely to be encountered is in differentiating the artery from the veins that frequently lie superficial to it.

On account of their irregularity more veins than anticipated may be found just beneath the thin fascia. The superior thyroid vein—or veins—

in its upward course usually crosses this triangle superficial to the superior thyroid artery. Sometimes a communicating branch between the superior thyroid and the anterior jugular veins ascends parallel to the lateral border of the omohyoid muscle. In a few instances we have found the superior thyroid veins ascending across this area to join the facial vein. In one instance the superior thyroid vein, the communicating branch between the facial and external jugular vein, and a communicating branch

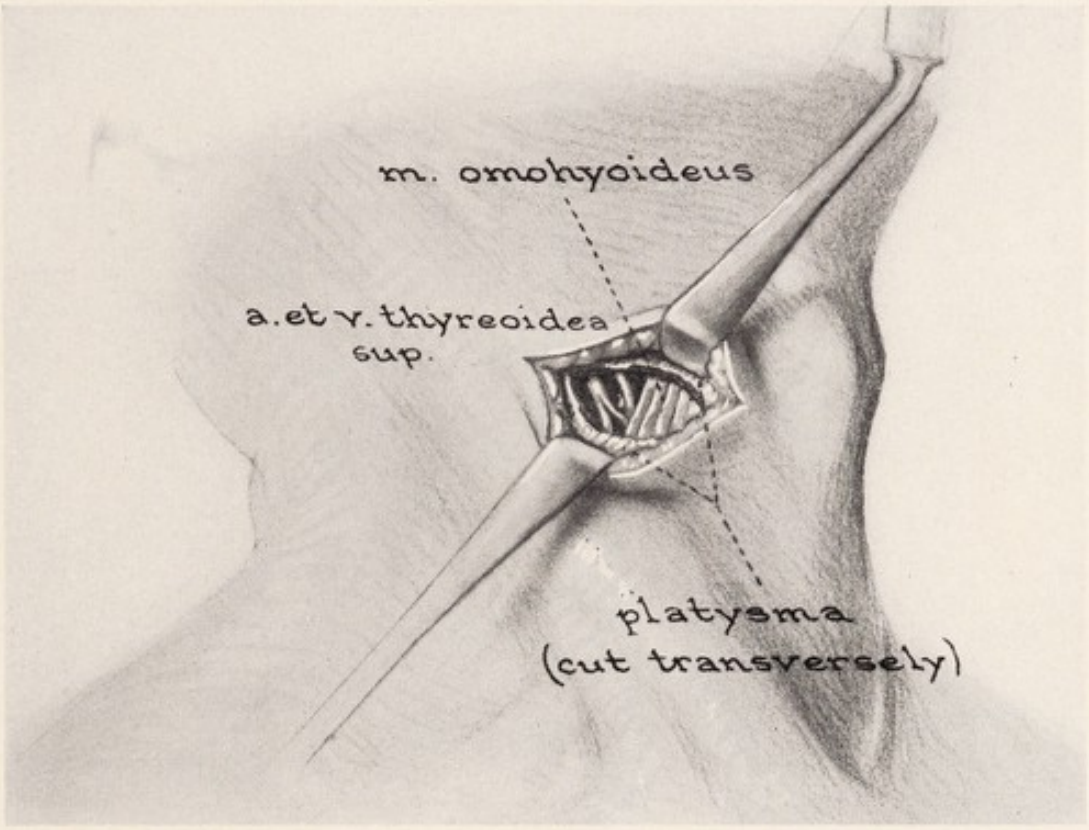


FIG. 64.—Ligation Superior Thyroid Artery above the Omohyoid.

from the anterior jugular vein joined in this area and formed a large trunk that emptied into the internal jugular vein.

It would be an easy matter to recognize the artery through the fascia by its pulsations were it not for the fact that in the living subject, especially under local anesthesia, the pulsation of the artery is sometimes indistinguishable. To add to the difficulty, a definite pulsation is sometimes transmitted to a vein that crosses the carotid artery, and may readily be mistaken for the pulsation of the superior thyroid artery. Even when the artery can be actually touched with the finger, it may be difficult to recognize it by palpation. The arteries in the neck are more elastic than those found in the abdomen, limbs, and some other parts of the body, and the difference in the thickness of the walls of the arteries and veins is not so apparent. If the position of the head and neck is changed or if the patient can be induced to hold her breath as long as possible, the pulsation in the

artery may become apparent. For identification of the artery, reliance should be placed upon accurate dissection guided by the anatomic landmarks rather than by palpation.

If the artery is not readily found, the veins should be isolated and drawn aside. If the approach to the artery is obscured by the veins, those

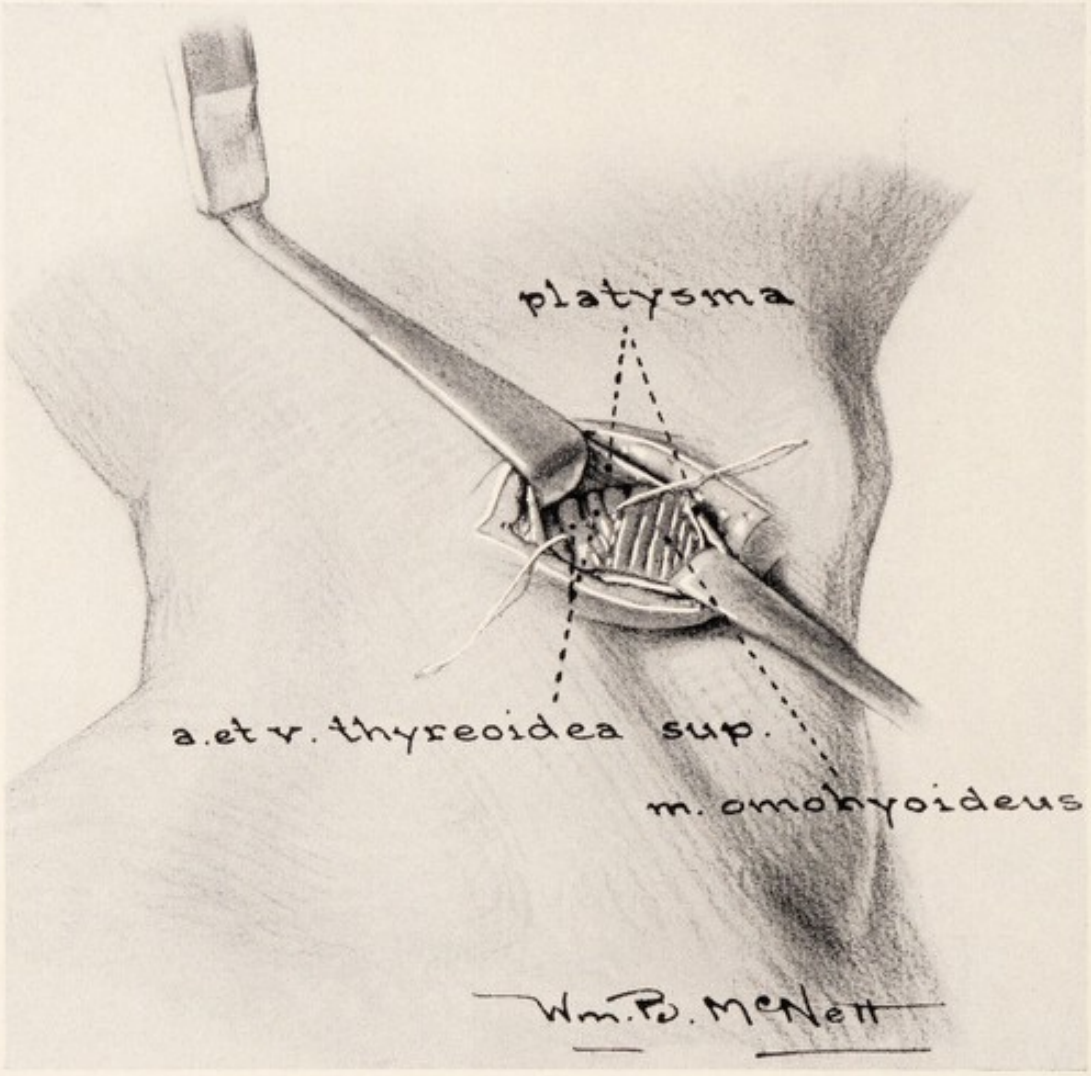


Fig. 65

ascending from under the omohyoid at the extreme lower angle may be isolated and cut between ligatures. Retraction of the ends of the veins and the omohyoid in a mesial and inferior direction usually exposes the artery near the lower angle of the triangle. When the upper pole of the lobe on that side is enlarged and occupies a superior position, the artery is likely to be found under cover of the omohyoid. If the larynx has been misplaced by the enlargement of the thyroid on the other side, the superior thyroid artery may be found beneath the anterior border of the sternomastoid lying parallel to and upon the carotid artery. If it is not readily located, the sternomastoid branch should be looked for under cover of the edge of that muscle and followed to the superior thyroid artery.

The artery, having been isolated, may be ligated just above the inferior angle of the carotid triangle and distal to the branch of the sternomastoid or near its origin. For ligation in continuity, a silk or linen ligature is more dependable than catgut. For ligature of the cut ends, a strand of No. 0 or No. 1 catgut is sufficient.

The only important structures endangered are the nerves. The descendens hypoglossi nerve crosses behind the artery near the point where the sternomastoid branch is given off. The superior laryngeal nerve lies superior and deep in relation to the artery. The danger of injury to the nerves may be obviated by passing the ligature close to the artery and from above downward. Isolation of the artery by careful dissection accomplishes the same purpose and also provides a favorable preparation for cutting the artery between ligatures if desired.

The closure of the wound should be accomplished with as few buried sutures as possible. If the fibers of the platysma have been divided transversely, two or three fine catgut sutures may be required to approximate them, but, if they have been divided parallel to their direction, no suture is necessary. In fact, with a short incision, approximation of the edges of the superficial flap by skin clips may be all that is required for satisfactory closure.

Polar Ligation.—It has been a common observation that ligation of the glandular branches of the superior thyroid artery at the upper pole is a much more effective procedure than ligation of the trunk. In a polar ligation, some or all of the superior thyroid veins as well as the branches of the artery on that side are included in the ligature. This disturbance of the blood supply to a larger area may be a factor in producing the favorable results. It has been observed that the relation of the beneficial results derived to the amount of trauma produced is quite constant. The more intense the reaction of the gland to the trauma, the greater the effect. Proof of this is afforded by the fact that artificial trauma produced by injection into the exposed portion of the gland of absolute alcohol, carbolic acid solution, or some other irritating agent will increase the manifest improvement in symptoms.

The level at which the incision is made for approach to the superior pole will depend somewhat upon the height of the pole. Usually the incision is made near the level of the lower border of the thyroid cartilage. The skin incision should be parallel with the skin folds, preferably within a fold if one is present. An incision about one and one-half inches long is made down to the superficial plane of cleavage, from a point three-fourths of an inch from the median line obliquely outward and upward across the median border of the sternomastoid muscle. Separation of the flaps along the superficial plane of cleavage upward and downward exposes the superficial fascia between the anterior border of the sternomastoid and the thyroid cartilage. The fibers of the platysma muscle may be seen through the fascia over the outer portion of this area. An incision parallel with the anterior margin of the sternomastoid muscle through the superficial fascia, the platysma and the layers of the deep fascia down to the premuscular plane of cleavage exposes the mesial border of the omohyoid and the lateral border of the sternohyoid muscles.

Retraction of the skin flaps upward and downward, and of the omohyoid and sternomastoid muscles laterally, and the sternohyoid mesially, exposes the sternothyroid muscle covering the upper pole. Division of the sternothyroid muscle in the direction of its fibers exposes the upper pole. A ligature may be passed by a curved blunt pointed ligature carrier around the vascular stalk, including all the branches of the superior

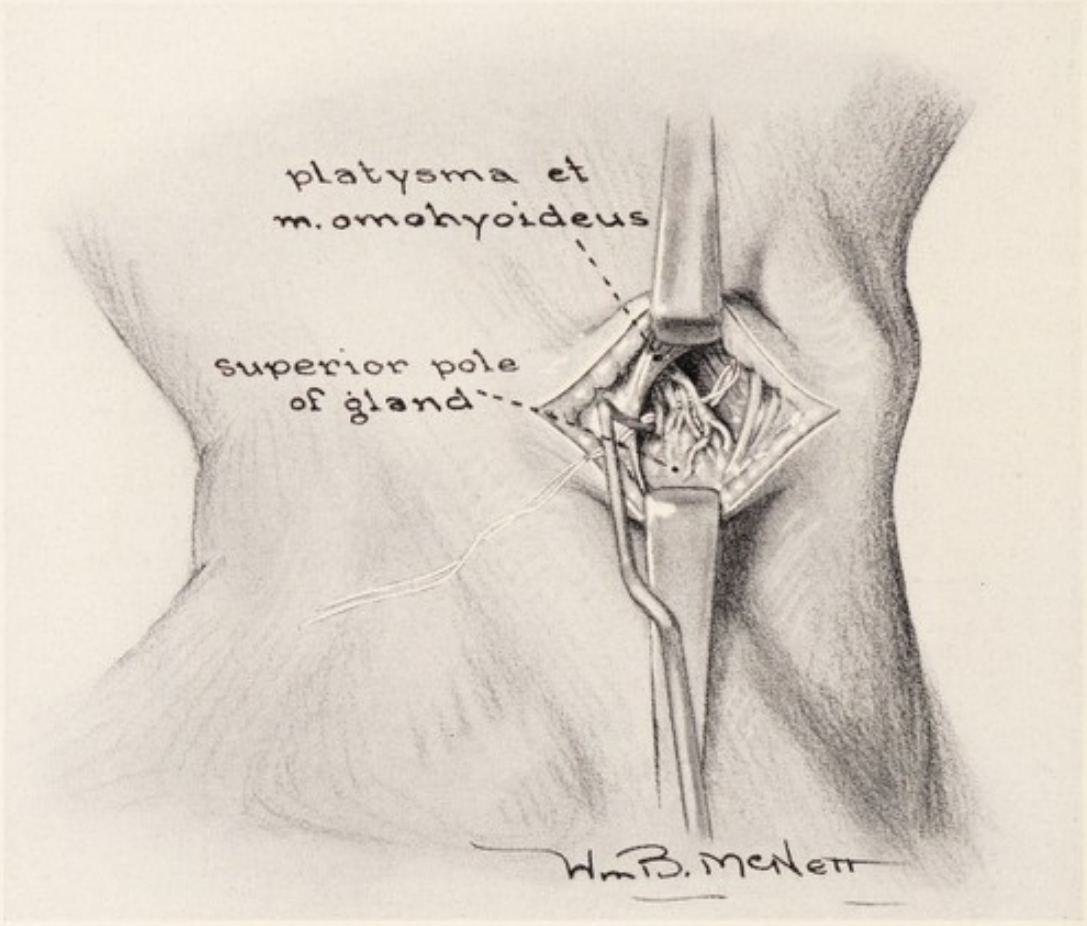


Fig. 66.—Ligation of the Superior Vascular Stalk below the Omohyoid Muscle. (Arteries & Veins.)

thyroid arteries and the superior thyroid veins, and tied. Care should be taken to include the dorsal branch in the ligature. If only the anterior and external branches are ligated, the amelioration of symptoms obtained will be slight. This ligature should be sufficiently resistant to remain intact for at least three weeks unless further operative procedures are contemplated within that time.

The technic will vary under certain conditions. In the normal gland, the vessels enter the upper pole at the tip or superior point. In the enlarged gland, the apex or superior point of the upper pole may be at a higher level than the point of the division of the artery into its glandular branches. This is especially true if the upper pole has undergone excessive

hypertrophy and ascended by rotating around the vascular stalk. This leaves the vascular stalk at the median border of the pole instead of the superior tip. In some instances the excessive enlargement of the gland raises the relative position of the upper pole to such an extent that the superior tip is located above the omohyoid in the carotid triangle, and the vascular stalk joins the gland in a location that is apparently slightly

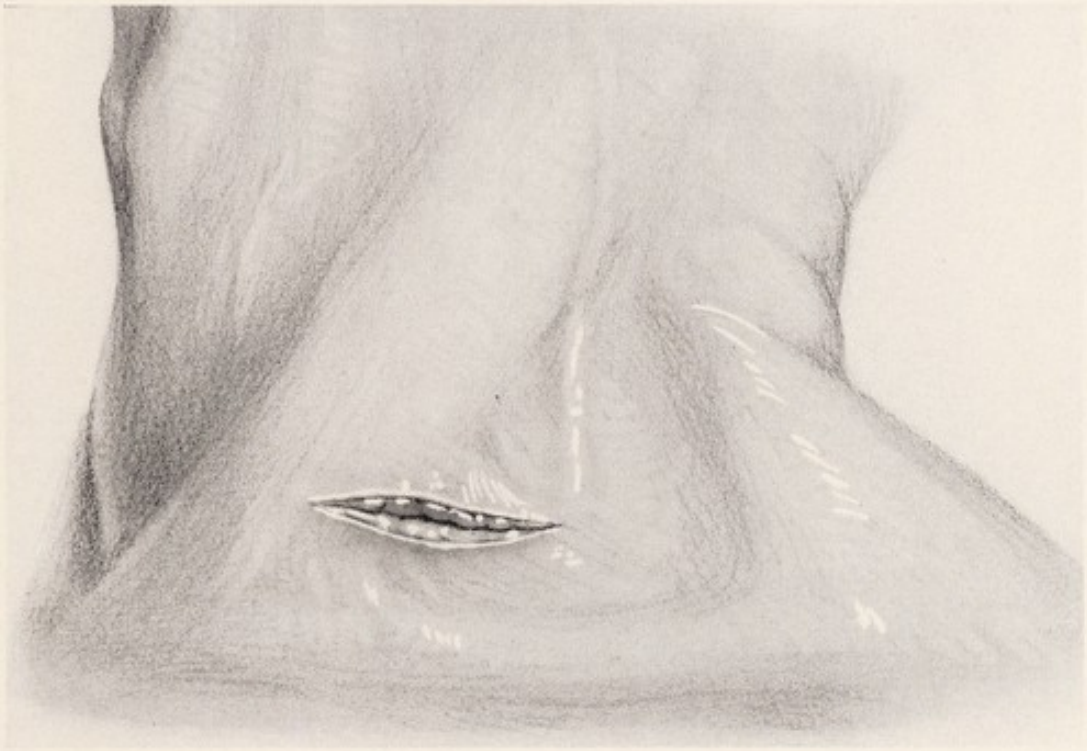


FIG. 67.—Location of Incision for Ligation of the Trunk of the Inferior Thyroid Artery.

above the upper border of the isthmus. In such a case ligation of the trunk above the omohyoid is the operation of choice.

If the upper pole is not too large and the superior tip is not located at too high a level, the vascular stalk may be ligated in the following manner: The upper pole is exposed and, by blunt dissection, an opening is made in the prethyroid fascia between the upper pole and the thyroid cartilage. Care should be taken that this opening is mesial to the anterior glandular branch of the superior thyroid artery. Another opening is made in the prethyroid fascia on the lateral border of the lobe at a point opposite the first one. A finger passed around the lateral surface of the gland enters the postthyroid plane of cleavage through the opening in the prethyroid fascia and passing posterior to the lobe approaches the anterior opening. A ligature carrier with a large arc is passed through the anterior opening, and guided by the finger, passes around the lobe and emerges lateral to the lobe. Thus a ligature is passed around the upper pole at a level slightly higher than the upper border of the isthmus. The outer or

lateral strand of the ligature can usually be swept up over the tip of the pole by the finger with surprising ease. With the tying of the ligature all structures entering the upper pole are gathered together in one pedicle on its mesial side.

With careful technic no hemorrhage is encountered and the only structures requiring suture are the fasciae. The skin may be closed with clips.

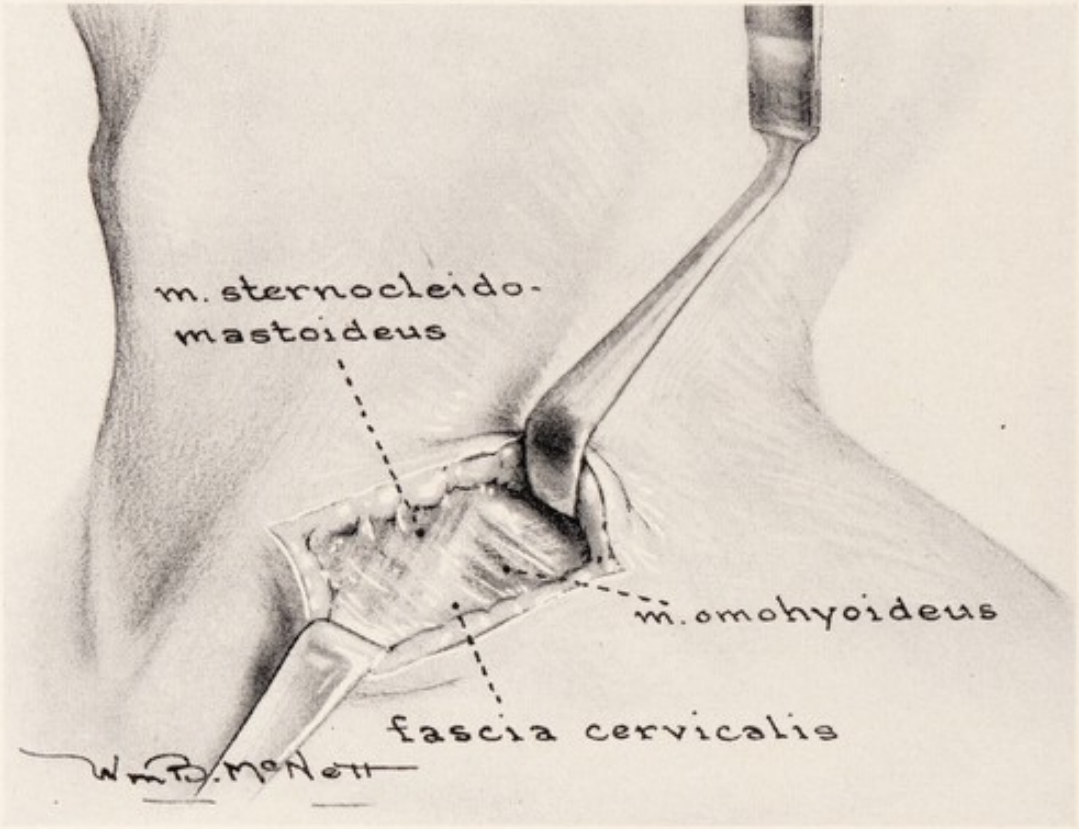


FIG. 68.—Ligation Inferior Thyroid Artery. Exposure Superficial Cervical Fascia over Region of the External Border of the Sternocleidomastoid Muscle.

The Inferior Thyroid Artery

The inferior thyroid artery may be ligated in the following locations:

(1) In its ascending portion.
(2) At its superior curvature.
(3) In its transverse portion.
(4) In its descending portion.

Ligation of the Ascending Portion.—The approach to the ascending portion of the inferior thyroid artery is by a transverse incision about one and one-half inches long, crossing the lateral border of the sternomastoid muscle, about one inch above the clavicle. The incision is made parallel with the folds of the skin down to the superficial plane of cleavage.

The flaps of skin and subcutaneous fascia are raised over the lateral border of the sternomastoid from about half an inch above the clavicle

to about two inches above the clavicle. Incision through the superficial and deep fascia along the lateral border of the sternomastoid exposes the inferior border of the tendon of the omohyoid where it emerges from behind the sternomastoid and the lateral surfaces of the sternomastoid muscle and the carotid sheath.

The direction of approach after the edge of the sternomastoid has been exposed is transverse or straight in toward the esophagus through

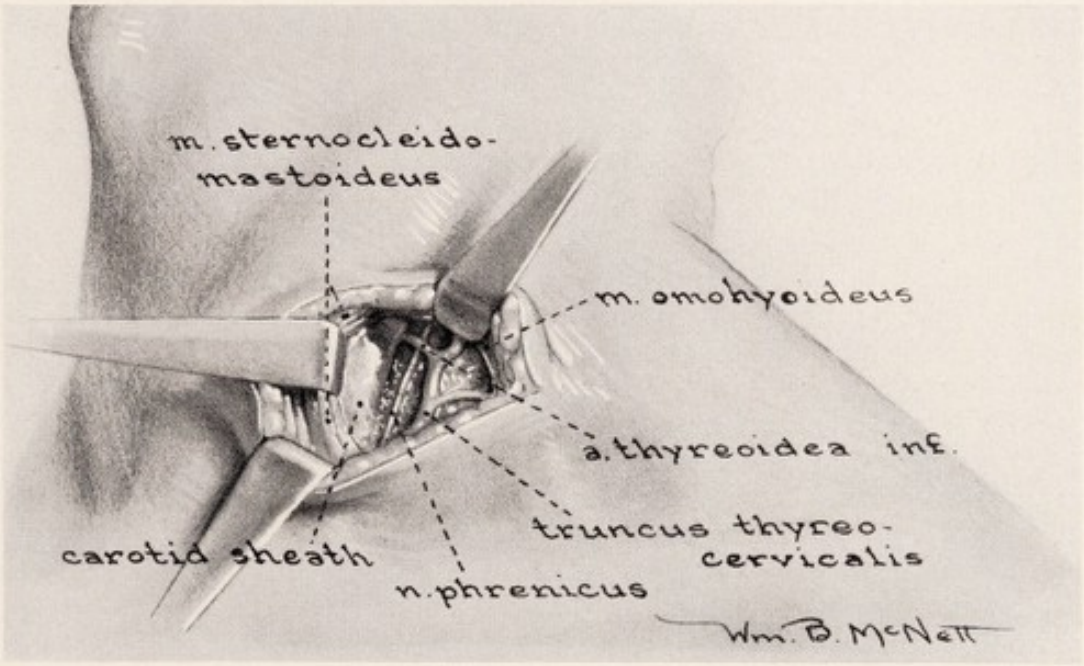


FIG. 69.—Schema Prethyroid Fascia, Middle Thyroid Vein, Postthyroid Plane of Cleavage.

the area of loose connective tissue that passes lateral to, and behind, the sternomastoid muscle and the carotid sheath. Blunt dissection through this area of areolar tissue and retraction, anteriorly and mesially, of the carotid sheath and its vessels together with the sternomastoid muscle, will expose the inferior thyroid artery or the thyreocervical trunk.

These vessels lie at a level, inferior to that of the central tendon of the omohyoid, directly posterior to the internal jugular vein, and on the mesial side of the scalenus antious muscle. If the inferior thyroid first comes to view and difficulty is experienced in positively identifying it, it can be exposed inferiorly to its origin. The mesial branch of the thyreocervical trunk coursing in an almost vertical direction is the inferior thyroid artery. It lies in front of and mesial to the vertebral artery.

Unnecessary traumation of deep structures should be avoided; therefore, ligation in continuity is advisable. This artery is easily severed by a fine ligature if tied too tightly. For this reason two ligatures one-half inch apart tied lightly are safer than one tied tightly. Care should be taken to avoid the phrenic nerve and on the left side the thoracic duct.

Ligation at the Superior Curvature.—The approach to the superior curvature of the inferior thyroid may be made in the same manner described for the approach to the ascending portion but must be made at a level above or superior to the tendon of the omohyoid. The posterior belly of the omohyoid is retracted mesially together with the sternomastoid and the carotid sheath.

The landmarks for the approach in this superior position are the external border of the sternomastoid, superior border of the tendinous omohyoid and, deep to them, the carotid sheath. By following the cellular space posteriorly around the carotid sheath, the curving arch of the inferior thyroid artery is exposed, just below the level of the carotid tubercle. The dissection should be carried on, posterior to the carotid sheath, with extreme caution as the sympathetic nerve with its inferior ganglion lies immediately behind the carotid sheath and between it and the inferior thyroid artery. Injury to the accessory should also be avoided.

In some cases, the ascending cervical artery is given off from the inferior thyroid artery instead of from the thyreocervical trunk. In this case, the inferior thyroid artery bifurcates near its superior point and the ascending cervical artery proceeds in a vertical direction while the inferior thyroid bends inward and disappears under the carotid sheath. Should the approach be made too high, the operator might ligate the ascending cervical artery, mistaking it for the ascending portion of the inferior thyroid artery. If, after making this superior approach, the operator does not find the curving portion of the inferior thyroid, he should extend his dissection along the external surface of the carotid sheath downward rather than upward.

Ligation of the Transverse Portion.—The approach to the artery may be made anterior to the sternomastoid muscle according to the method described by de Quervain. Through the usual collar incision for thyroidectomy the dissection is carried in a backward direction—mesial to the sternomastoid muscle, the carotid sheath, and the omohyoid muscle, and external to the sternohyoid and sternothyroid muscles—until the pretracheal fascia lateral to the thyroid gland and mesial to the carotid sheath is encountered.

Retraction of the thyroid gland mesially and the carotid sheath laterally, places the pretracheal fascia under tension. The pretracheal fascia should be opened by blunt dissection, exposing the transverse portion of the inferior thyroid artery lying just beneath it. The artery should be ligated as far from the carotid sheath as possible, in the endeavor to make the ligation distal to the origin of the parathyroid artery. In this procedure retractors similar to those described by de Quervain are required for adequate exposure.

Ligation in the Descending Portion.—In the operation for the removal of a very vascular goiter, ligation of the descending portion of the inferior thyroid artery is at times advisable as a preliminary procedure. After the thyroid gland has been exposed, the prethyroid muscles, sternomastoid muscle, and carotid sheath are retracted outward exposing the superficial surface of the prethyroid fascia.

The middle thyroid vein is ligated and cut. The prethyroid fascia is separated from the gland, exposing the postthyroid plane of cleavage. Having obtained free access through the postthyroid plane of cleavage, the carotid sheath and overlying muscles are retracted outward and the thyroid gland retracted inward, thus stretching the pretracheal fascia. Usually, the pulsations of the artery can be seen or palpated through the pretracheal fascia on the floor of the postthyroid plane of cleavage. If the artery can be identified through the fascia by sight or palpation, a ligature may be passed under it and the ligation be made without dividing the pretracheal fascia.

If the artery is not easily identified by sight or palpation, division of the pretracheal fascia for a short distance usually exposes it and the pulsations may then be plainly seen. In some cases the pulsations of the exposed artery appear to be quite forcible but are still not evident on palpation. A careful choice of retractors will facilitate ligation of the artery in this location.

TECHNIC OF THYROIDECTOMY

Incision and Scar

The incision, from the surgeon's point of view, must be adequate to give proper approach; from the patient's standpoint, it must be so placed and managed that it will cause no undesirable postoperative results, either functionally or aesthetically. In other words, it must be symmetrical, suitably placed, properly shaped, and of sufficient length.

It is well to think in terms of location of the scar, rather than location of the incision. The terms are not synonymous: the difference between them, as every surgeon knows, may be just the difference between a good and a poor cosmetic result. To the surgeon who wishes to please his patient, a good cosmetic result is of paramount importance. A disfiguring scar may be the cause of more dissatisfaction than serious residual symptoms.

Position

If the incision is placed without regard to the posture of the patient and heedless of the size and shape of the tumor, the resulting scar cannot be symmetrical. In the upright position, particularly in women of middle life with heavy pendulous breasts, the weight of the breasts is considerable and has a tendency to pull the skin of the neck downward. When the patient is on the operating table with the head thrown back, the chin (and with it the skin of the neck) is considerably raised. In the prone position, the effect of the pull of the breasts on the skin and fascia of the neck is neutralized.

It is obvious that the incision which is in the proper location when the head is extended and the patient is in the prone position, will be much too low when the patient is up and about with the head in the normal position and with traction from the breasts tending to pull the scar downwards. The scar from such an incision will eventually cross the inner ends of the clavicles. It will be unsightly in the extreme and will

be difficult to cover with a string of beads. The incision, of course, may be made too high, in which case the resulting scar will be equally unsightly and unsatisfactory.

In the operating room, before making the incision, the surgeon should try to visualize the scar as it will look in two weeks, and in making the incision allow for every influence that may modify its location. We should take into consideration the age and weight of the patient, the



FIG. 70.—Location of Incision, Marked.

length of the neck, the size of the breasts, the size and form of the tumor mass, the position on the table, and the degree of extension of the head. Our objective should be to place the incision so that the resultant scar will fall in the notch of the neck about a thumb's breadth above the inner ends of the clavicles.

What method is to be followed to assure accuracy in placing the incision? For the experienced surgeon fixed methods for mapping out an incision which will result in a correctly placed scar are usually superfluous, yet there are a number of expedients which have proved useful and are worth knowing.

One of the obvious ways is to map out the incision with the help of a string of beads; the line may be marked with ink or if the surgeon wishes a more permanent visualization, the outline of the incision may be traced with the help of a sharp needle. It is better to follow one of the natural folds of the skin which are usually found if carefully looked for. The majority of patients have a small fine fold or crease across the neck at exactly the right level. If, before the chin is extended, this fold is

marked out by a temporary discoloration, it will be a serviceable guide in locating the incision properly.

The location of the incision may be marked previous to operation. The patient sitting with the head thrown forward to accentuate the folds in the skin, the neck above the clavicles is lightly painted with a staining solution—iodin, potassium permangate, picric acid, or mercurochrome. If the skin is permitted to dry while the patient is in the sitting position, permanent white lines will be left at the site of the natural folds. Mercurochrome probably gives a more distinct line than any of the other agents mentioned but clips or stitches on a skin surface painted with mercurochrome sometimes produce points of discoloration. These give an effect similar to tattooing and are very difficult to remove.

One important point to remember: if the goiter is large the incision must be made at a correspondingly high level. With a goiter of considerable size, the skin is drawn upward from below and not pulled downward from above. Then the tumor is removed, a large area of redundant skin is released and, if the incision has not been placed with this in mind, the scar will be low and conspicuous.

Symmetry

A scar, even if it is located at the proper level, will be unsightly if it is not symmetrical; it must be of equal length and have an equal curve or incline on each side. Kocher's incision "en cravate" is an ideal symmetrical incision, both sides are even and the curve follows the outlines of the neck. In the small goiter of even contour, no special precautions need be taken to insure the symmetry of the scar.

With the irregular or unilateral goiter the matter is otherwise. The incision in this type of case must be higher over the tumor mass than elsewhere. Similarly, if one side of the gland is larger than the other, the incision should be slightly higher on that side to allow for a greater sinking of the scar after the removal of the tumor mass. In the usual case the incision should be made perpendicular to the skin surface in the natural transverse fold of the skin of the neck or paralleling it in a slightly curved line.

We sometimes use the following technic: The skin is stretched laterally by traction of each angle of the proposed incision; this traction raises the skin near the midline to a higher level and throws it into fine small transverse folds. The incision may be carried straight across from one end to the other parallel to these folds. Because the traction has kept the center at a higher level, as soon as the traction is released, the skin reverts to its normal relationships and the incision assumes the desired, slightly curved, outline.

Particularly with goiters in which one side is larger than the other, it is sometimes rather difficult to so locate the incision that both arms of the scar will be of equal length. If one lobe of the goiter is considerably larger than the other, especially if the enlargement extends across the midline, the trachea is displaced to the opposite side. With the trachea and larynx, the superficial tissues are also displaced, and the skin on the

larger side is stretched. An incision, in consequence, which looks perfectly symmetrical at the time it is made, will be found to leave an asymmetrical scar. As the pressure is removed, the trachea and overlying structures assume their normal relationships, and the scar will be shorter on the side toward which the trachea had been displaced than on the other.

To obviate this undesirable result, the writer frequently resorts to

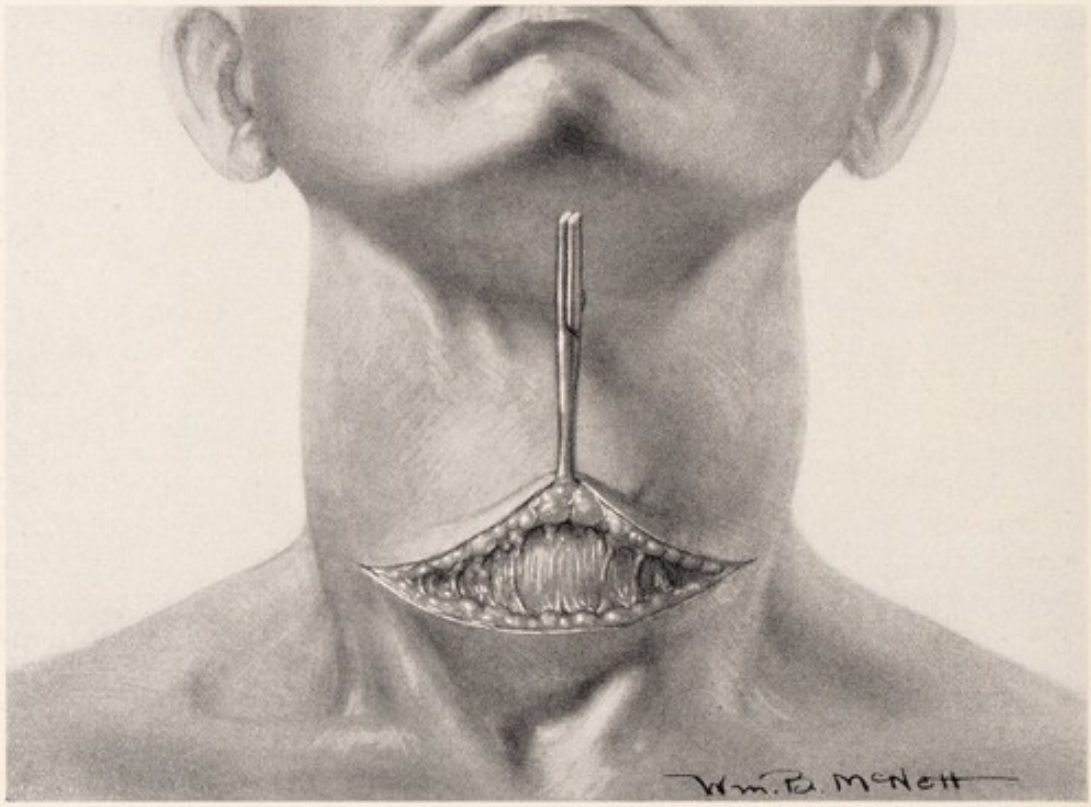


FIG. 71.—Incision Down to Superficial Plane of Cleavage.

the following maneuver: A short incision is first made across the midline; the upper and lower borders of the incision are next grasped with Allis' forceps; the lower forceps is placed first, on the skin edge of the lower flap directly over the trachea. The other forceps is placed on the skin edge of the upper flap just opposite, in line with the thyroid cartilage. Traction is now made outward, away from the muscles of the neck, and the skin is placed on tension. The forceps are approximated, and it is immediately apparent whether or not they are in the correct median position. If they are correctly placed, the incision may be extended laterally to the same distance on each side.

Incision Superficial Structures

With the forceps in place as described and lifting the tissues that should be included in the superficial flap away from the muscles of the neck, the incision is made through the skin and subcutaneous fat down to the superficial plane of cleavage. This superficial plane is identified

and developed outward beyond the outer angles of the incision for an inch or more. This mobilization of the skin permits the opening to be lengthened perpendicularly by displacement of the outer angles of the incision inward toward the midline.

Raising or freeing of the flaps is the next step. The upper flap may be wiped or pushed upward to about the level of the upper border of the

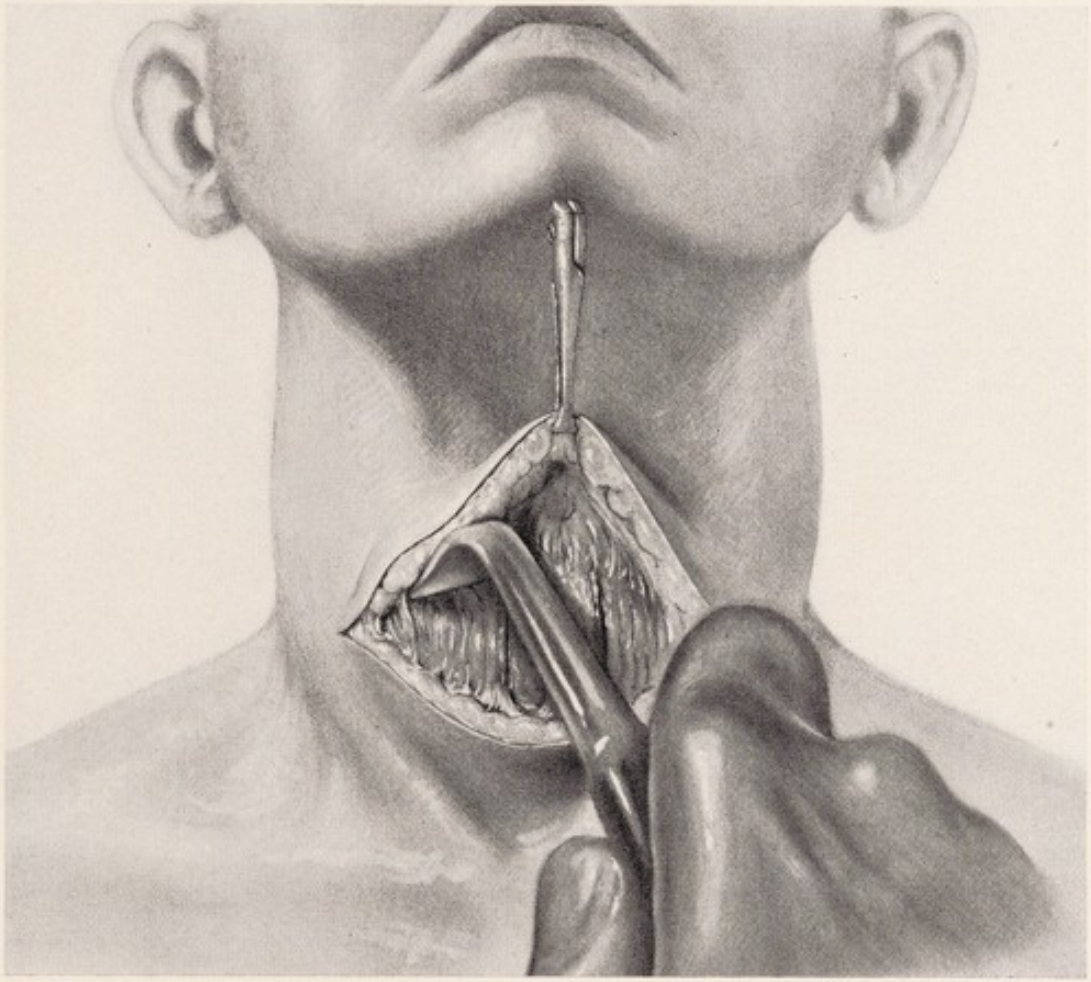


FIG. 72.—Raising Flap Following Superficial Plane of Cleavage.

thyroid cartilage. This is done easily by gauze dissection. One hand holds the flap with a piece of gauze and exerts traction outward, while the other hand—also using a piece of gauze—pushes the flap upward. Thus the flap is literally wiped upward off the deeper structures. Sometimes for this purpose a flap dissector is of value and one may be used to facilitate the procedure of "stripping up" the flap. During this stage of the operation, if the plane of cleavage is followed, few if any bleeding points require ligation. Should there be definite oozing at any point, it should be carefully controlled; the bleeding vessels should be meticulously ligated or closed by electro-coagulation.

After the upper flap has been raised and the field made dry, the lower

flap may be retracted downward in the midline and released along the superficial plane of cleavage down to the level of the upper border of the sternum. The lower flap is not freed laterally beyond the inner border of the sternomastoid muscles.

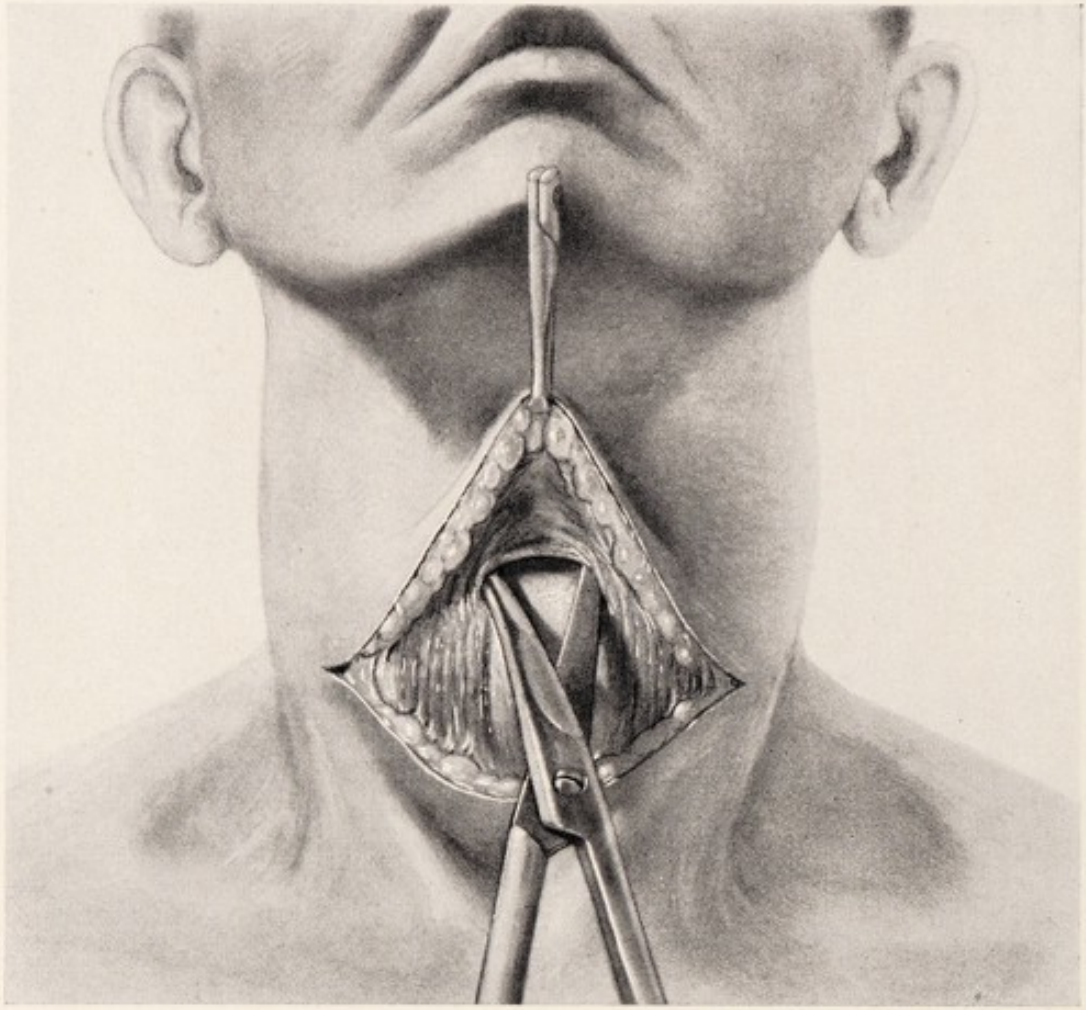


Fig. 73.—Opening Superficial and Deep Cervical Fascia.

Incision Cervical Fascia

The flaps are retracted upward and downward until the fascia is put on a stretch; in this tense cervical fascia an opening is made, by blunt dissection, in the midline just below the promontory of the thyroid cartilage. Another opening is made through the fascia layers constituting the roof of Burns' space.

Self-retaining retractors are then placed in such a manner as to retract the flaps upward and downward. We have found the self-retaining retractor devised by us of great service at this stage of the operation.

Towels are draped around these retractors to cover all exposed skin surfaces and the handles of the towel forceps. (See illustration, Towel Clips p. 76.)

An incision through the cervical fascia in the midline connects the two openings in the fascia—the one at the upper angle of the wound, the other at the lower angle just above the sternal notch.

Separation Prethyroid Structures

After the opening of the cervical fascia, the next step is the ligation of the anterior jugular veins. This should be done at a low level to dis-

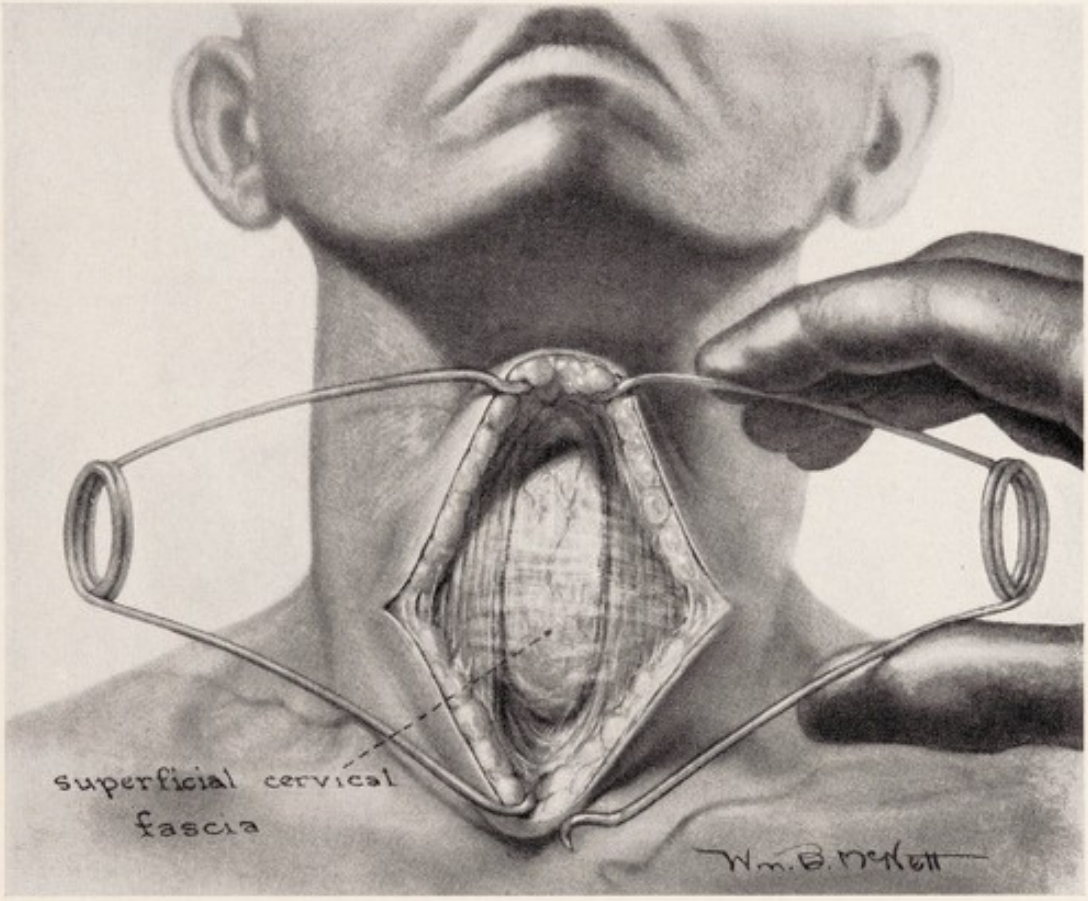


FIG. 74.—Insertion Spring Retractor.

count the danger of embolism. The prethyroid muscles are then separated by sharp dissection from a point just below the promontory of the thyroid cartilage down as far as the upper border of Burns' space. If necessary, the incision may be extended through the posterior wall of Burns' space down to the sternum.

It is well to note that in the majority of cases the anastomosing branch between the anterior jugular veins crosses Burns' space. This may be cut and ligated if so required. In some cases the anterior jugular veins in the lower part of their course descend as one large vein that not infrequently occupies an anomalous position. If the branch descends on one side, in the usual location of one of these veins, it may present no additional problem. Sometimes, however, it crosses from one side to the other



FIG. 75.—Draping around Spring Retractor.

at the upper border of, or even within, Burns' space. In such a case it is usually necessary to cut the vein between ligatures. **Extreme caution** should be exercised as this connecting vein may be very large and tortuous. There is danger both of excessive hemorrhage and of admitting air into the circulation.

Muscle Cutting versus Muscle Splitting.—For years we have avoided cutting the muscles transversely, therein differing from the many opera-

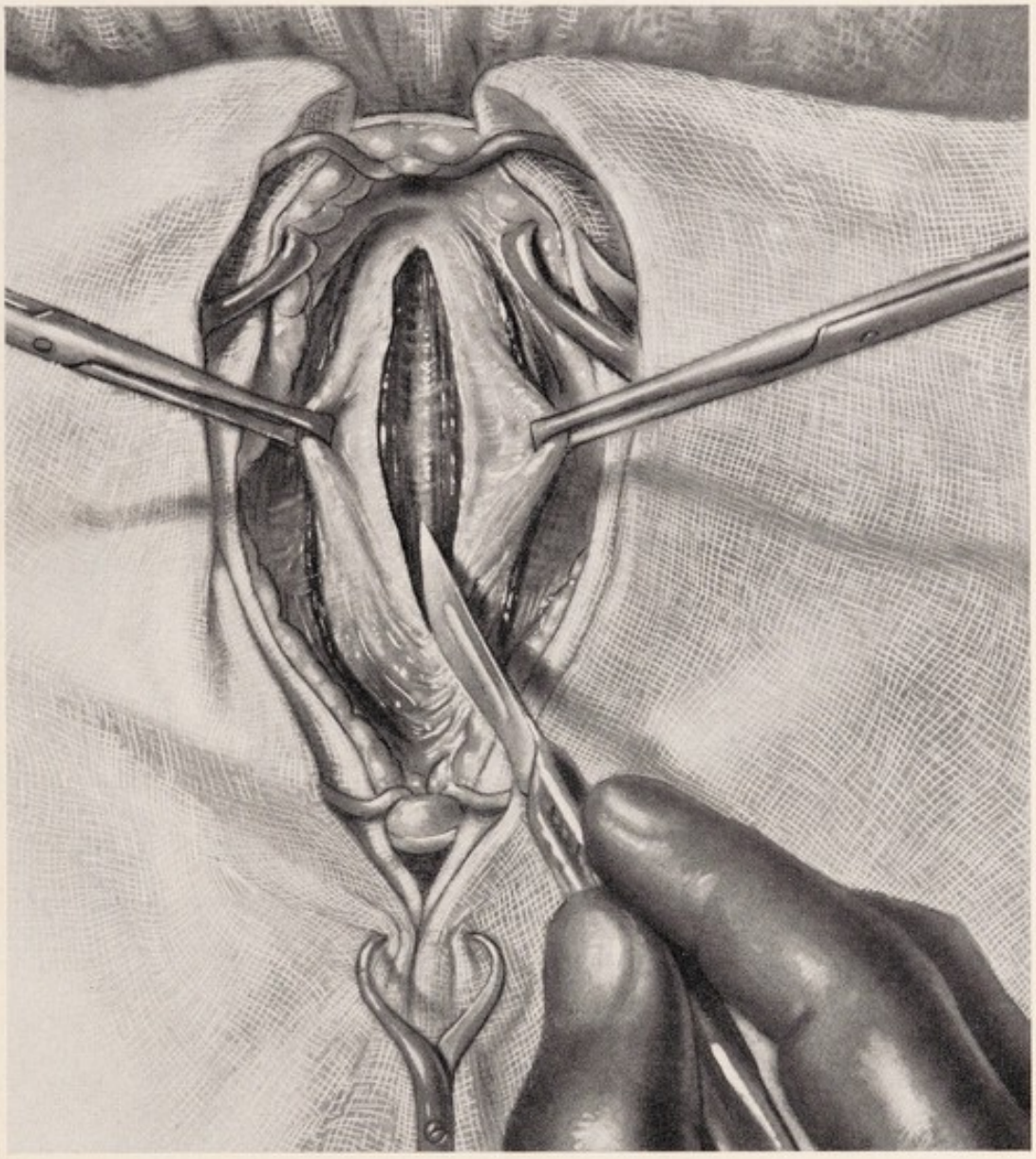


FIG. 76.—Incision Midline to Prethyroid of Cleavage.

tors who still prefer to cut the muscles to gain proper approach to the gland. This latter procedure perhaps makes the operation easier for the surgeon who has not accustomed himself to other methods, but it involves the risk that, in case infection develops, the muscles may not unite and the skin flap may be left as the sole covering over the larynx and trachea.

The operation which dispenses with transverse section of the muscles has many advantages. The shock is not so great, the muscles are uninjured, convalescence is shortened, discomfort is lessened, and, in our belief, mortality is lowered. We are convinced that dispensing with transverse section of the muscles has simplified rather than complicated the operation for us. We feel that many patients who are good surgical risks

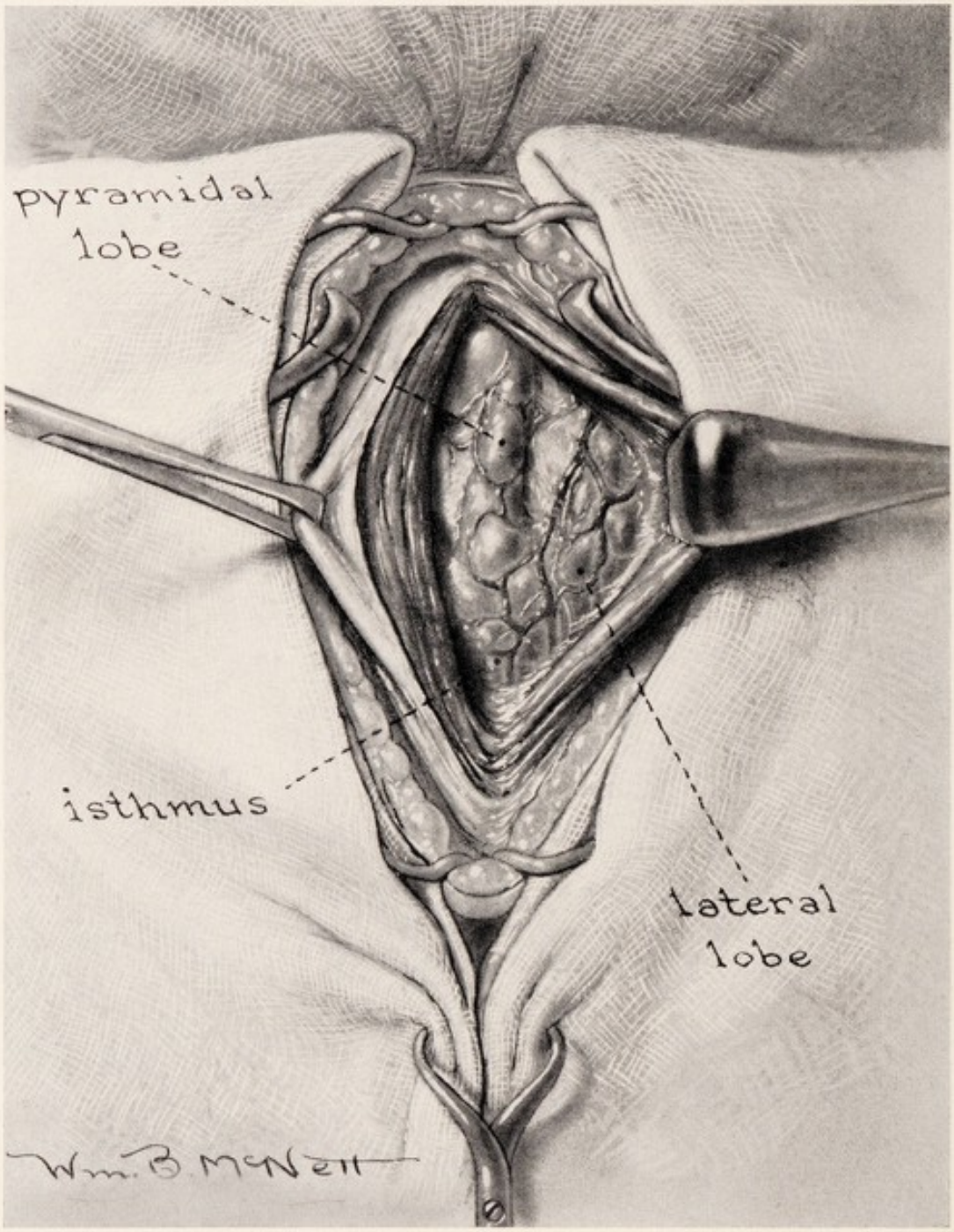


Fig. 77.—Exposure Area of Prethyroid Plane of Cleavage.

for operation done without cutting the muscles are poor surgical risks for the type of operation in which muscles are clamped and cut. For these reasons the prethyroid muscles instead of being cut transversely are separated by retractors held in the hands of an assistant.

Exposure of the Gland

After all of the muscles and fascia from the sternum to the promontory of the thyroid cartilage (except the elastic wall of Burns' space)

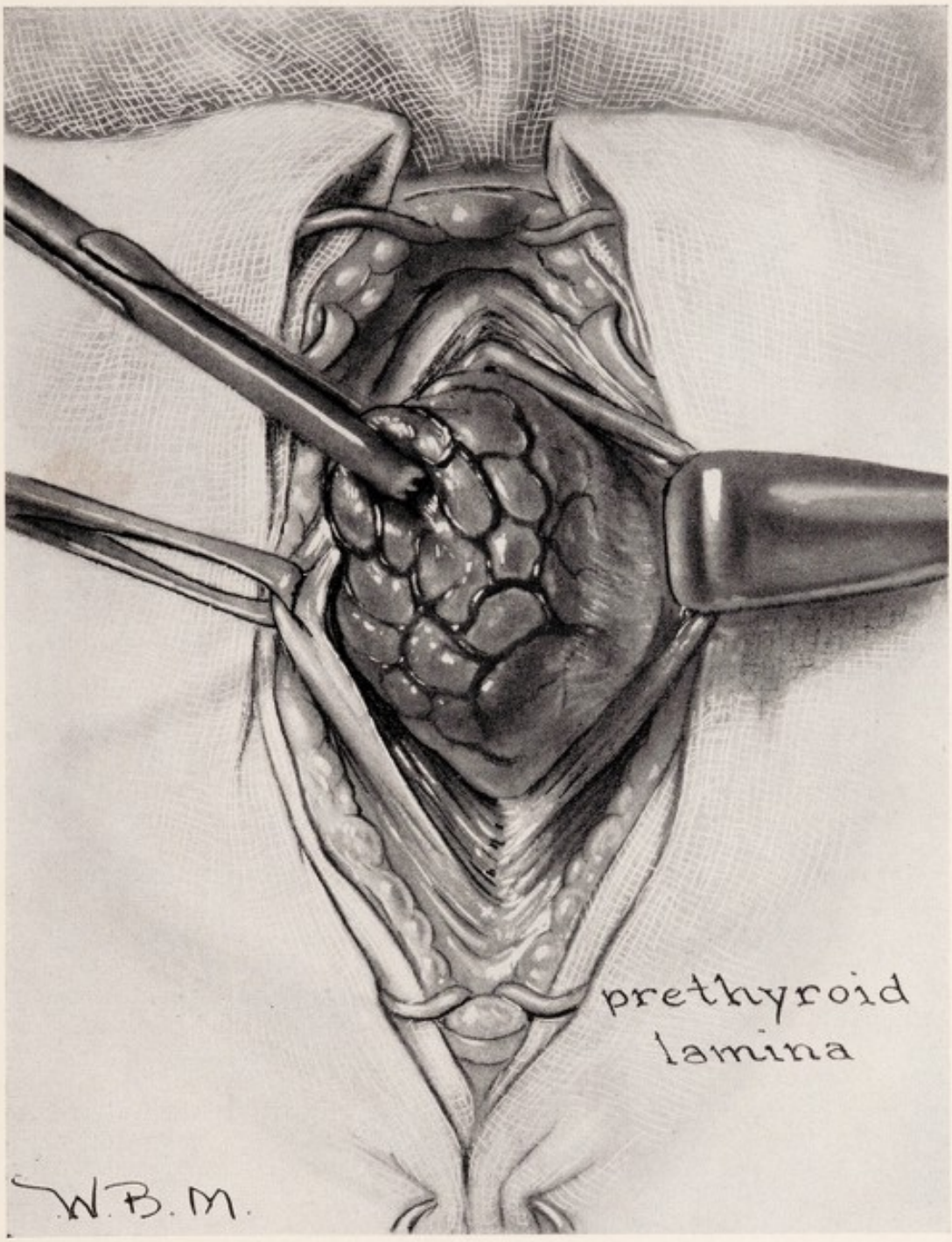


Fig. 78.—Traction on Lateral Lobe Exposing Prethyroid Lamina of the Pretracheal Fascia.

have been separated, the prethyroid plane of cleavage is in the floor of the incision.

This plane—indicated by the anterior surfaces of the thyroid cartilage, the pyramidal lobe and the isthmus of the gland—is followed outward and backward to the carotid sheath, thus freeing the anterior

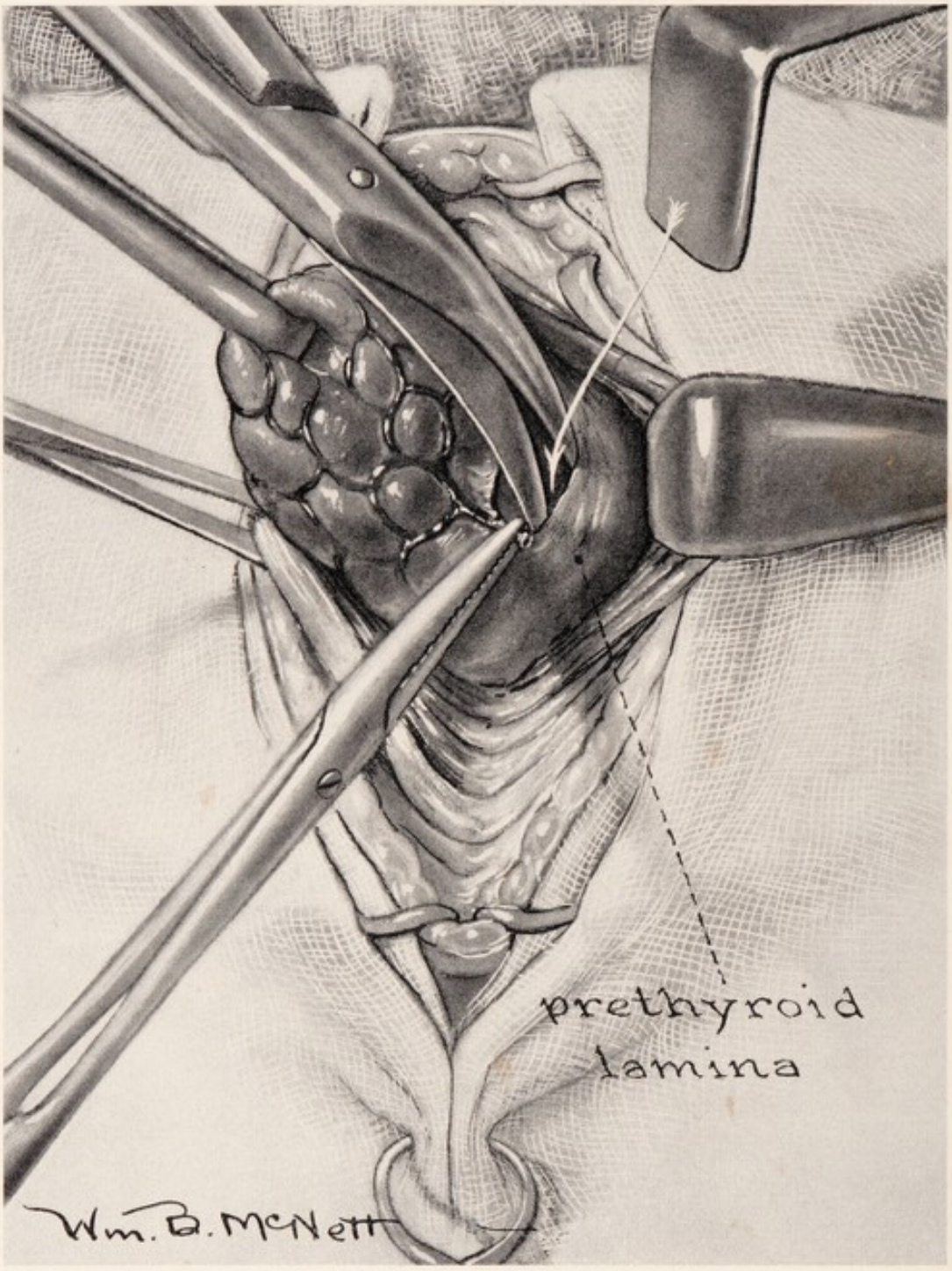


Fig. 79.—Separation of the Prethyroid Fascia from Lateral Surface of Lateral Lobe. Middle Thyroid Vein Cut and Tied.

surfaces of the thyroid gland and prethyroid fascia. The retraction of the muscles also exposes the thyroid cartilage and the pyramidal lobe when present.

Mobilization

Freeing the mobilization of the gland is the next objective. The *first step* towards this is accomplished by severing all structures connecting the pyramidal lobe (if present) and the upper border of the isthmus to the larynx or trachea.

The *second step* is separation of the structures connecting the inner borders of the superior poles of the gland to the perilaryngeal fascia. Slight traction on a forceps attached to the freed pyramidal lobe, or isthmus, as the case may be, puts the attachments (between the inferior portion of the inner borders of the upper poles and the larynx) on a stretch; the dissection is continued outward and upward along the inner border of each upper pole almost to the tip. The blood vessels in these pretracheal and prethyroid fascia attachments, should be severed between forceps and the bleeding points in the pretracheal fascia on the surface of the larynx and trachea ligated.

The *third step* in mobilization of the gland is section of the suspensory ligaments. Slight traction on the forceps attached to the upper border of the isthmus of the gland will now lift the gland away from the perilaryngeal structures and place the suspensory ligament on each side under tension. The stretched suspensory ligaments can then be severed and any vessels in the proximal ends ligated. When this is accomplished, the shortest attachments of the thyroid to the larynx and trachea have been severed and the gland is, to a great extent, mobilized. It may be moved without traction upon the trachea or larynx from half an inch to an inch upward or downward.

For complete mobilization there remains the *fourth step*, or freeing the posterior border of the lateral lobes. This is accomplished by following the prethyroid plane of cleavage, usually called the capsule of the gland, outward until the prethyroid fascia has been reached. Retraction of the muscles on one side outward with a single narrow retractor exposes the anterior surfaces of the lateral lobe and the prethyroid fascia. The gland should be grasped by traction forceps just anterior to the point of attachment of the prethyroid fascia, and the lateral lobe rotated anteriorly, thus placing the prethyroid fascia on a stretch. For this purpose we have found that the goiter forceps described on page 267 is most useful.

By blunt dissection through the prethyroid fascia just external to the area of its attachment to the gland an opening is made which permits the operator to pass a finger through the prethyroid fascia into the posterior plane of cleavage. The prethyroid fascia is stripped from its attachment to the gland by either sharp or blunt dissection upward and downward except at the point where the middle thyroid vein runs within it. This vein should be severed between ligatures. This dissection of the prethyroid fascia from both lobes of the gland leaves the posterior planes of cleavage continuous with the anterior, releases the external attachments of the gland to the carotid sheath and, except for the thyroid pedicle, completes the mobilization of the gland. The short attachments at the upper border of the isthmus and the inner borders of the upper poles,

the suspensory ligaments and the prethyroid fascia all having been severed, the gland may now be moved, flexed, or rotated upon the pedicles of the lateral lobes without torsion, twisting, or pressure upon the trachea or larynx.

Goiter Obstetrics

Goiter obstetrics, a term used by the author in 1914 (132) before the Illinois State Medical Society and again in 1916 before the Tri-State Medical Association, suggests in plain language the marked similarity in mechanics of the delivery of the lobe and the delivery of a vertex presentation in obstetrics. Let us conceive of the upper pole of each lobe as representing the vertex, the lower pole the chin, the superior angle of the opening between the muscles representing the pubic arch, and the lower angle the perineum. As in delivery of the head, the mechanical maneuvers necessary for delivery of the lobe, according to the author's method, are flexion, rotation, and extension. In the case of both vertex and lobe, these manipulations enable delivery to be accomplished with greater ease and through a smaller opening than would otherwise be possible.

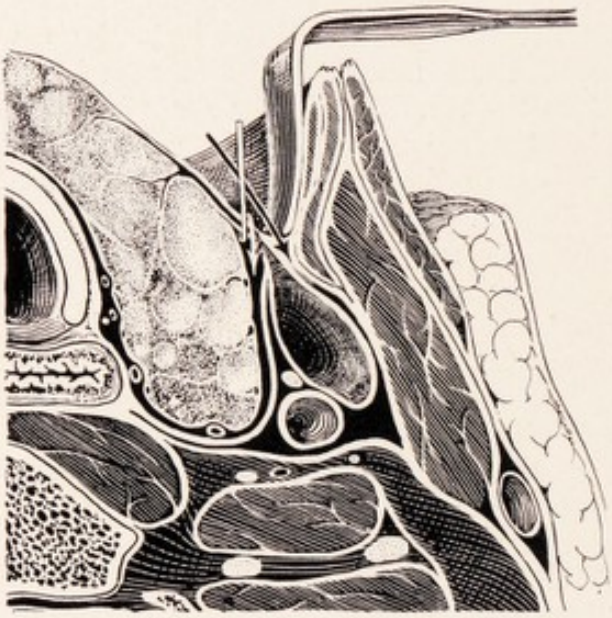


FIG. 80

It is, of course, possible to deliver the gland by simple lateral rotation and that method is still preferred by some surgeons. Delivery by lateral rotation, however, necessitates an opening sufficiently large to permit the passage of the lobe in its greatest diameter and presupposes a transverse cutting of the thyroid muscles. By the obstetric method the gland is delivered through an opening barely large enough to permit its passage in the smallest or transverse diameter—an opening approximately one-third the size necessary for delivery according to the other technic.

Delivery of the Upper Pole

We usually deliver the upper pole first. The question may arise as to whether it is better to ligate the blood vessels *en masse*, or to cut them between clamps. There can be little doubt but that ligation of the vessels of the upper pole before they are cut is the safer procedure. When they are cut between clamps there is danger that the forceps may cut through the vessel walls and there is the additional danger that the blood vessels may be released as they are about to be tied later on.

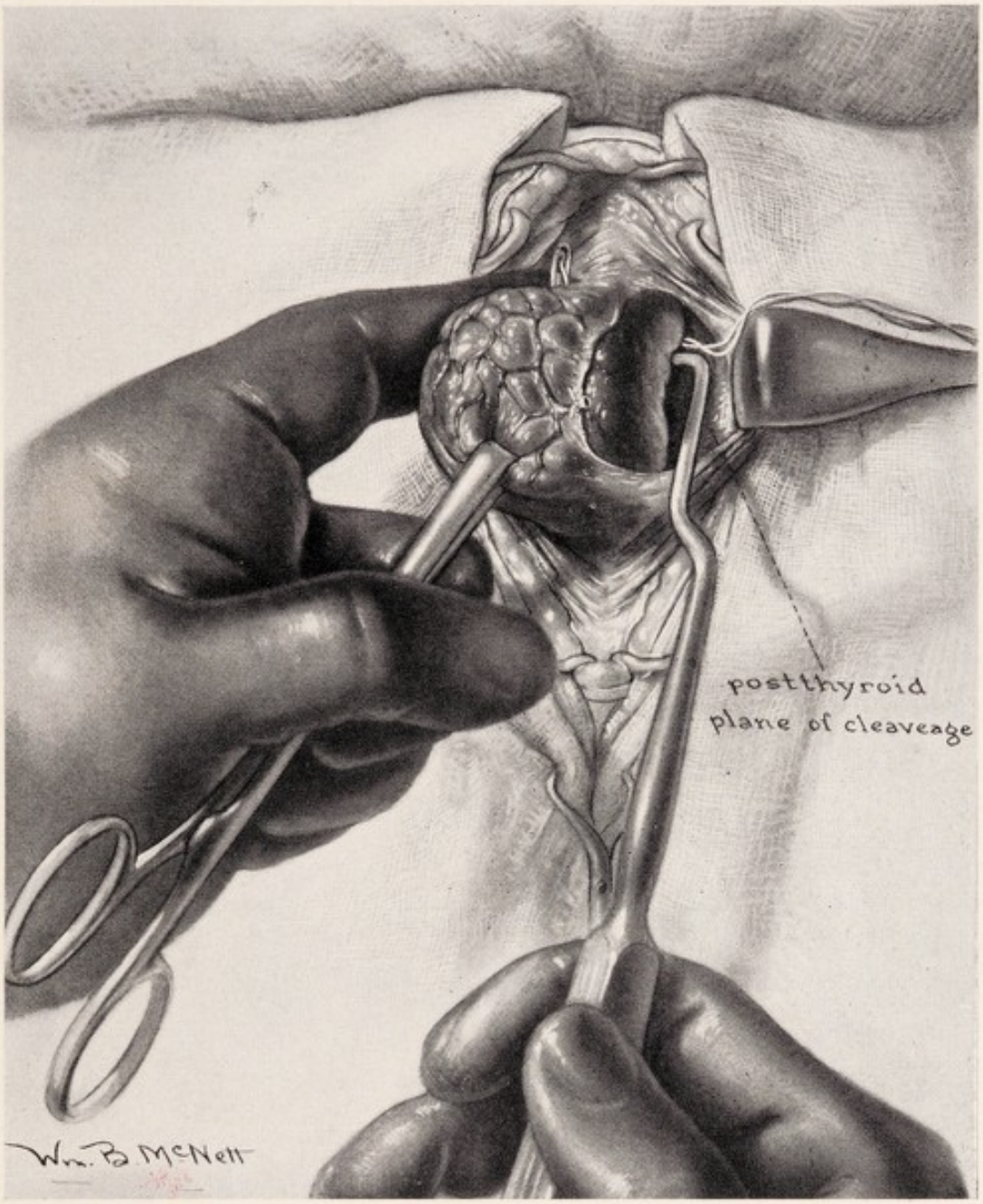


FIG. 81.—Postthyroid Plane of Cleavage Opened. Lobe Rotated Mesially and Ligature Passed Under Superior Vascular Stalk.

In order to ligate the vessels the pole is first exposed upward and outward by retraction of the muscles and flap. The lateral surface of the gland at the upper pole is grasped with forceps, and anterior rotation of the upper pole brings the superior vessels into view. Since the space around the upper pole, in which the ligature carrier must be introduced, is irregular and somewhat small, we have found the ligature carrier described on page 269 to be of very great assistance in carrying the ligature around the pole. The double curve enables one to pass the ligatures around the structures without interference by the overlying muscles.

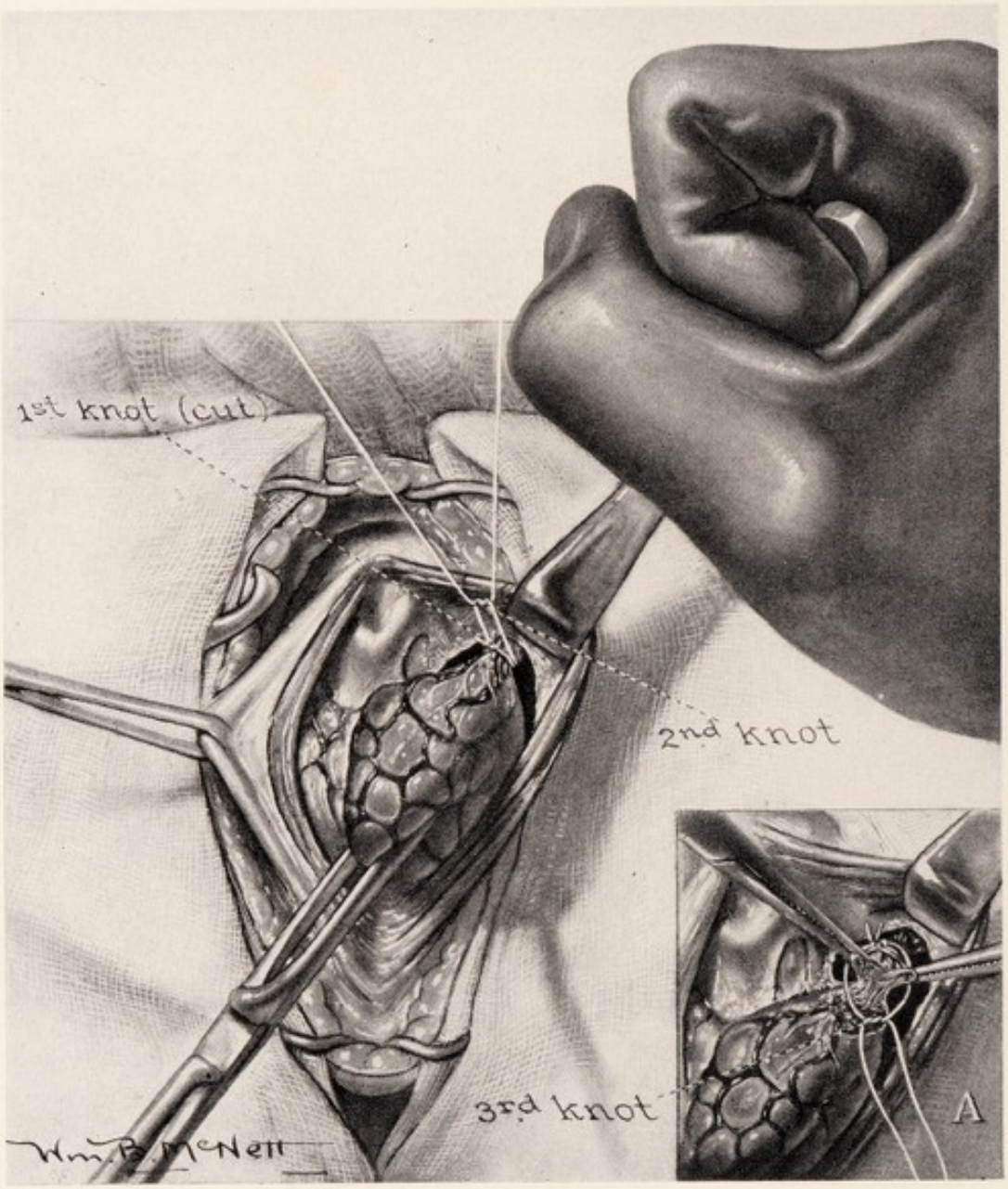


FIG. 82.—Double Ligation Superior Vascular Stalk (No. 1 Plain Cat Gut).

The vascular pedicle above the upper pole is ligated by two strands of No. 1 plain catgut, tied separately, and severed. The ligature at the upper pole includes the superior thyroid veins and may include all of the branches of the superior thyroid artery. It is probably a wiser proceeding to pass the ligature anterior to the dorsal branch and sever only the anterior and external branches. If the dorsal branch is retained, the operator can be assured of adequate blood supply to the portions of gland permitted to remain.

Flexion, Rotation, Extension, Progress.—Maneuvers borrowed from obstetrics are utilized as the operation proceeds. Flexion of the lobe upon

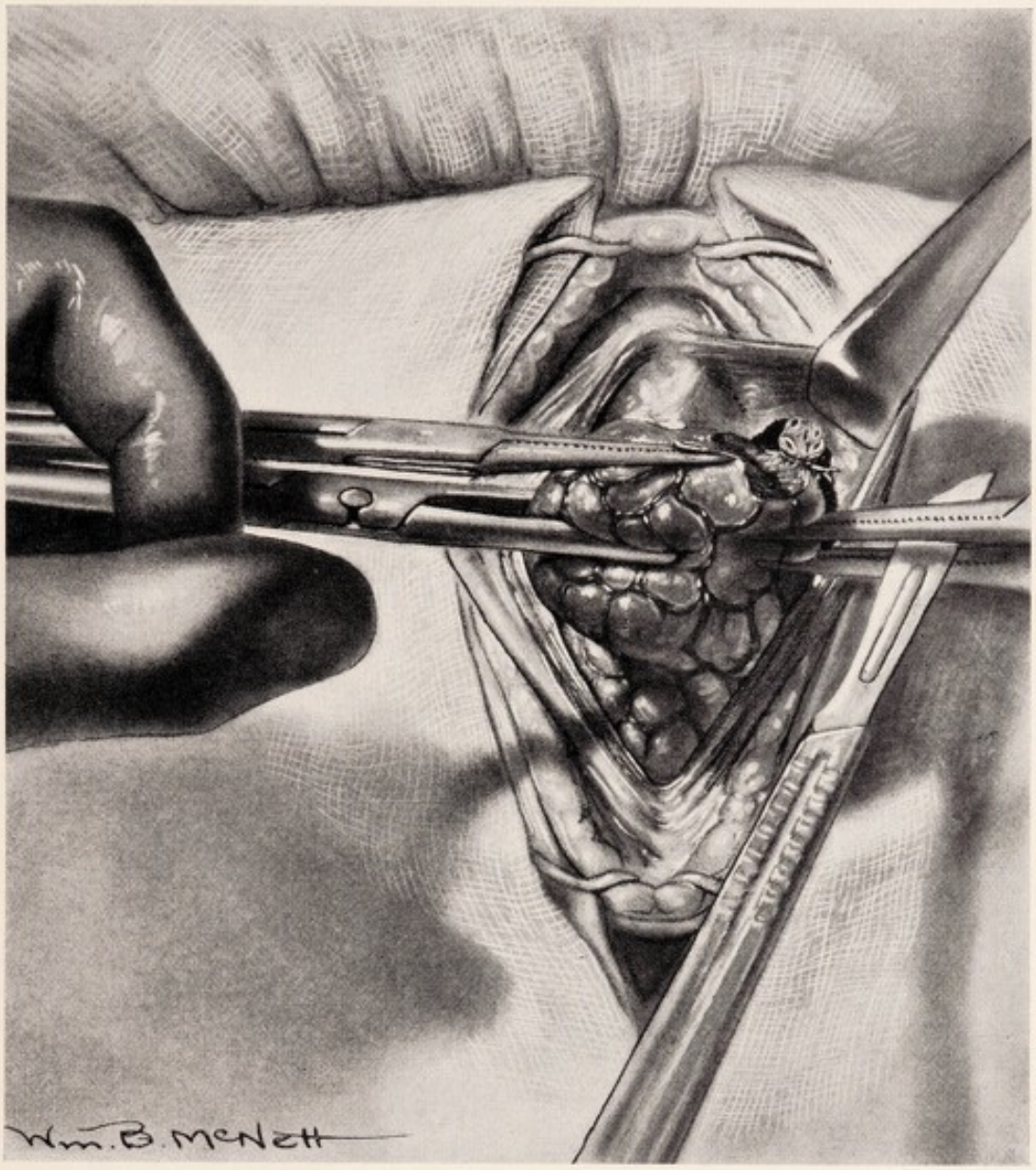


FIG. 83.—Vascular Stalk Severed.

itself will be brought about by traction on the upper pole which has previously been released. This flexion is maintained and rotation is produced by continued traction on the upper pole forward and mesially while dissection is continued downward along the posterior border of the lateral lobe. As the dissection proceeds, the flexed upper pole is drawn forward into the opening between the prethyroid muscles. As the superior pole presents itself in this opening, rotation toward the midline with continued flexion is effected. The middle portion of the thyroid pedicle, containing the branches of the inferior thyroid artery, comes into view. The severance of these branches and the gland tissue as far as the junction of the middle and lower thirds of the lobe, permits further rotation and

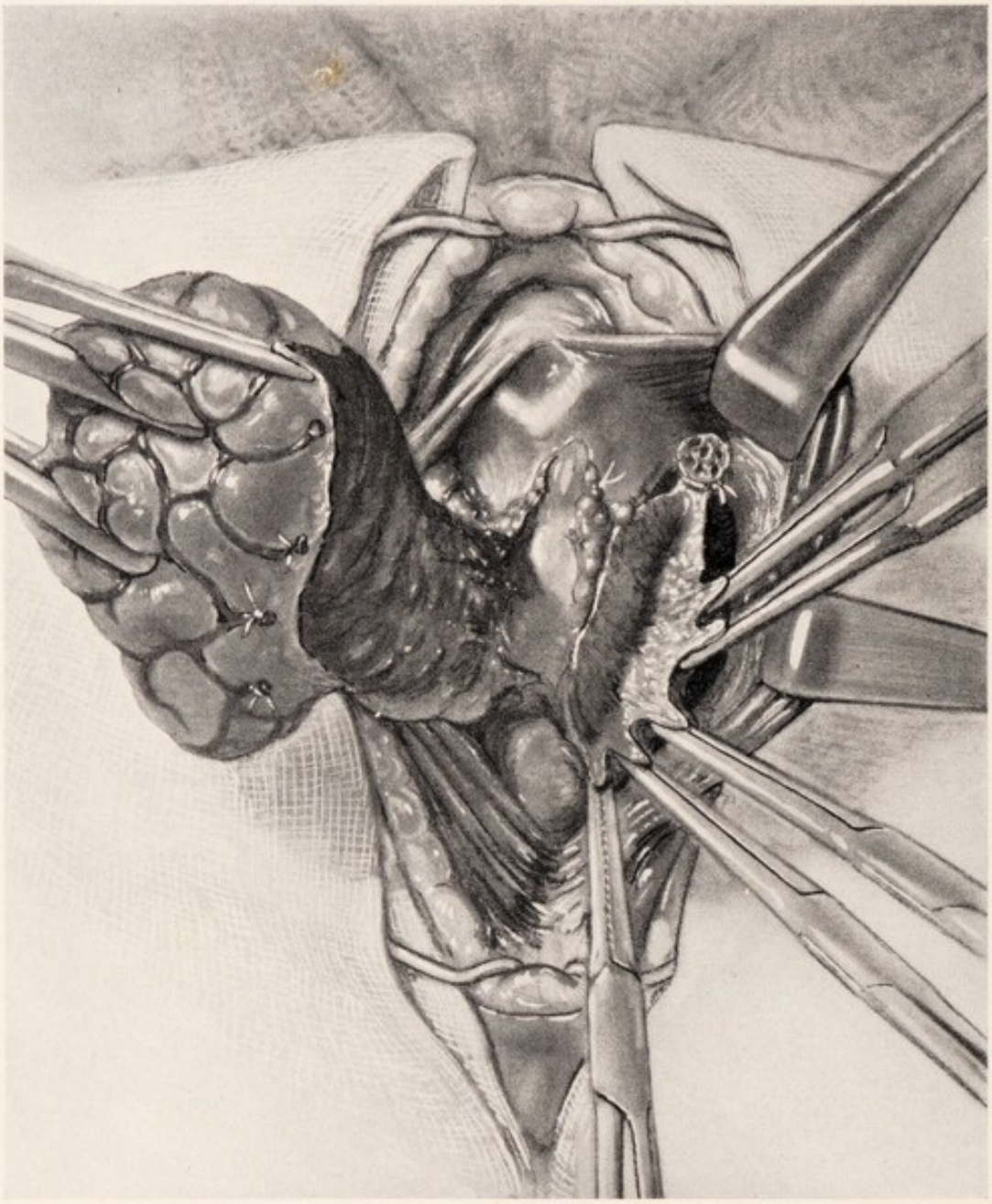


FIG. 84.—Lateral Lobe and Isthmus Amputated. Branches Inferior Thyroid Artery Caught in Forceps.

extension and the lower pole is delivered through the small opening. As progress is made in the dissection and the attachments are loosened, traction is maintained on the gland, and the lateral lobe is drawn out through the opening in the prethyroid muscles.

With the delivery of one lateral lobe, the attachments across the lower border of the isthmus come into view. As these attachments are severed, the inferior thyroid veins and the thyroidea ima artery (when present) are cut and ligated, thereby entirely releasing the isthmus from

the trachea. The second lobe can then be removed by similar maneuvers and with much greater ease.

Hemostasis.—Throughout the steps of the operation just described efficient hemostasis is essential. Not only the blood vessels but also all the tissues that apparently carry lymphatics are caught in forceps and tied. Ligation of the lymphatics will prevent flooding of the wound cavity with lymph after the operation.

After the branches of the superior thyroid have been ligated, no important blood vessels will be encountered until the direct branches of the inferior thyroid artery are reached at about the junction of the middle and lower thirds of the lateral lobe.

Delivery of the Lower Pole

Occasionally conditions present at operation make it advisable to deliver the lower pole first. In this case, after the gland is mobilized, the structures at the lower pole are severed between forceps and the proximal ends ligated; traction now applied upon the forceps attached to the lower pole will flex the lateral lobe and bring the posterior border of the gland into view; the successive steps in dissection of the lobe from below upward are next undertaken. The procedure is the same as that described in connection with delivery of the upper pole **with this difference:** after the structures at the lower pole are severed, it is usually advisable to carry the dissection across the lower border of the isthmus approximately to the midline before delivery of the lateral lobe. The ligation of the superior vessels is facilitated when the lower pole is delivered first since the lateral lobe is out of the way by the time the upper pole is reached and consequently there is room to pass the ligatures easily.

Residual Gland

Amount

The question as to the amount of gland to be left cannot be determined by any rule of thumb, such as those specifying an amount equal to one-fourth, or one-sixth, or one-eighth of the normal gland. All of the diseased portion of the gland must be removed and all that is healthy should be left. A small piece of normal tissue is of more value than a large piece that is diseased and non-functioning. It is never safe to leave a large mass in one piece since there will rarely be an adequate blood supply after the interference with the blood vessels which has been necessary during operation, and, where the circulation is impaired, atrophy or necrosis will usually take place.

Location

Removal of all gland tissue at the superior pole, the pyramidal lobe, and the isthmus is deemed advisable for the reason that if allowed to remain it will proliferate, as gland tissue left elsewhere does. An asymmetrical proliferation in this location is undesirable, since it forms a nodule and constitutes an obvious deformity. The tissue left should be near the thyroid pedicle of the lateral lobe. In this comparatively deep-seated location, a slight deformity due to proliferation will not be noticeable.

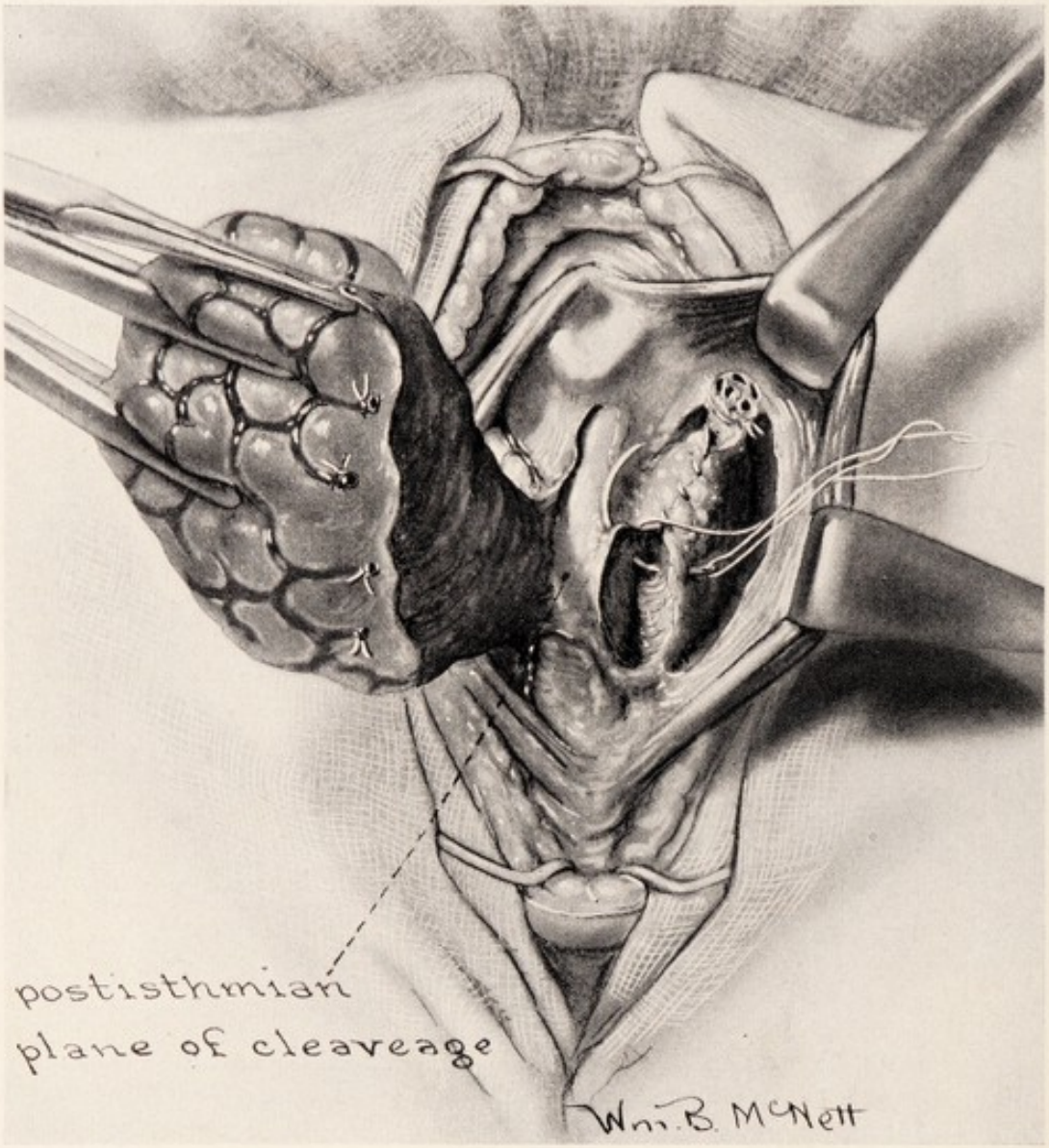


FIG. 85.—Control of Hemorrhage from Severed Branches of Inferior Thyroid Artery and Severed Inferior Thyroid Veins and Suture of External Border of Stump to the Severed Superficial Layers of the Pretracheal Fascia.

It is important that some gland tissue should be left over the thyroid pedicle—the region usually called the danger zone—for the protection of the recurrent laryngeal nerves. Fortunately the tissue in this region is usually normal; it may be left either in a thin layer or in numerous small bits. Larger portions may be allowed to remain without fear of atrophy only if the dorsal branch of the superior thyroid artery has been left intact and the branches of the inferior thyroid have been ligated on the surface of the stump of the gland. Experience has shown that the practice of leaving only small portions of healthy substance near the pedicle, where they will have an adequate blood supply, minimizes the number of

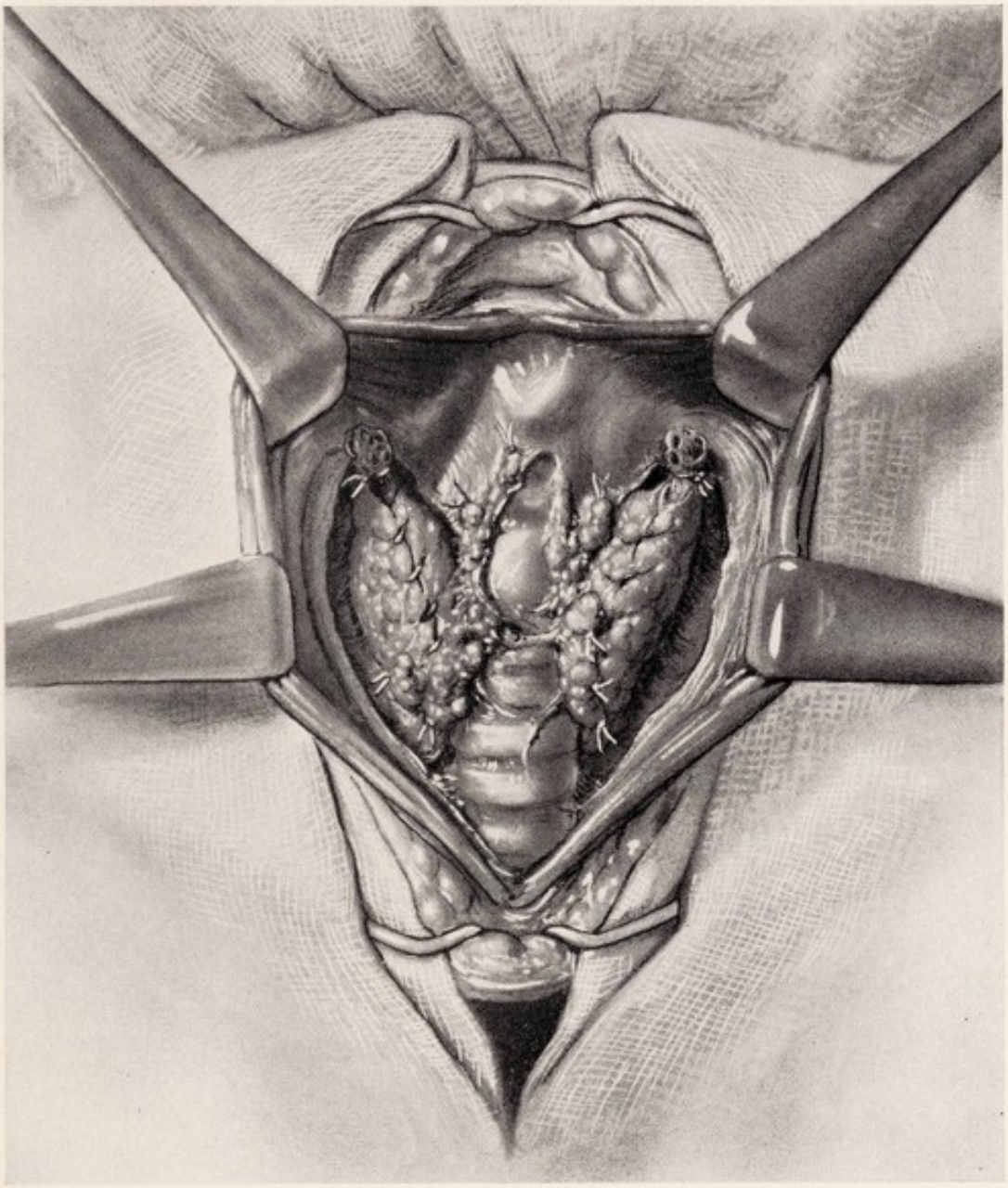


FIG. 86.—Stumps of the Gland.

recurrences and of sequelae such as hypothyroidism, myxedema, and recurrent nerve paralysis.

Closure

Care of the Stump

The stump may be covered either with the capsule or with the prethyroid fascia. The first method, preferred by many, entails the risk of a constriction of the remaining portion of the gland which may be sufficient to cause degeneration of the gland tissue. The prethyroid fascia, if it has been properly preserved, will make a far better covering for the raw sur-

faces of the gland. Since this fascia is elastic, it will not cause too much compression nor interfere with the movements of the gland and trachea.

Control of Oozing

After the stump has been suitably attended to, we must assure ourselves that the wound is dry. **This is a matter of great importance.** We must make certain that all oozing has been controlled. If the operation is being done under local anesthesia, the patient's chin should be flexed, the head thrown forward and the patient instructed to cough and swallow. It may be that a blood vessel has escaped us. It may not bleed while the neck is extended, since the muscles, on stretch and exerting pressure, act like a ligature or clamp to prevent oozing. As soon as the chin is flexed and the head thrown forward, the muscular tension on the vessels is relieved, and oozing, if there is to be any, will occur. If the patient is having a general anesthetic, he should be permitted to become partly conscious and should be encouraged to cough or swallow. We must be on the alert to lower the head of the table immediately, in case indications are that he is about to vomit, lest vomitus be inspired. After the patient has struggled a little in the efforts of coughing and swallowing or of vomiting, careful inspection is made for oozing. If the wound remains dry, we may feel assured that all blood vessels are controlled. The patient should be required to speak. If the voice tones are clear, **then** the operator may be certain that no damage to the recurrent laryngeal nerve has occurred, and may proceed to close the wound without hesitation.

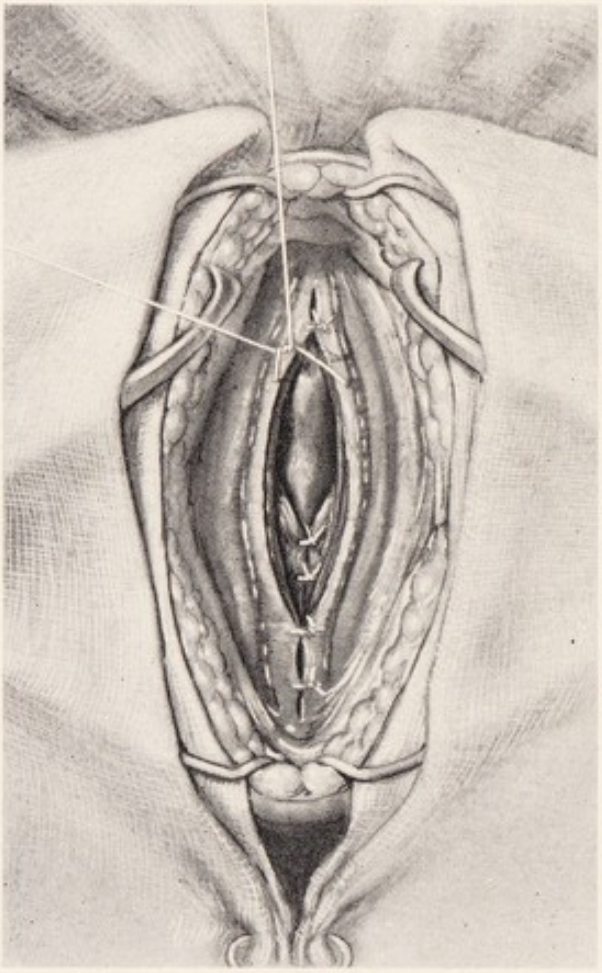


FIG. 87.—Closure Margins of Prethyroid Fascia and Sternothyroid Muscle Sutured in Lower Portion of Wound.

Drainage is sometimes considered advisable for the purpose of providing a tract through which any serum that may accumulate can find its way out through the muscles to the under surface of the flap. This may be accomplished either by a drain placed above Burns' space—not

lower—or by an opening one-half or three-quarters of an inch long, left unsutured and prevented from complete closure by a buttonhole stitch of plain catgut on each side.

Methods of Closure

Before the final steps in the closure, the prethyroid muscles and cervical fascia above the isthmus are brought together with fine catgut—size No. 000, or 00 plain, is large enough. If the sternothyroids have been separated along the posterior wall of Burns' space, their edges, with the fascia covering them, should be coapted to the level of the lower border of the isthmus. The cervical fascia over Burns' space is then neatly sutured and the buttonhole stitches are placed at the level of the isthmus so as to preserve a tract through which serum may escape from the visceral compartment to the superficial plane of cleavage.

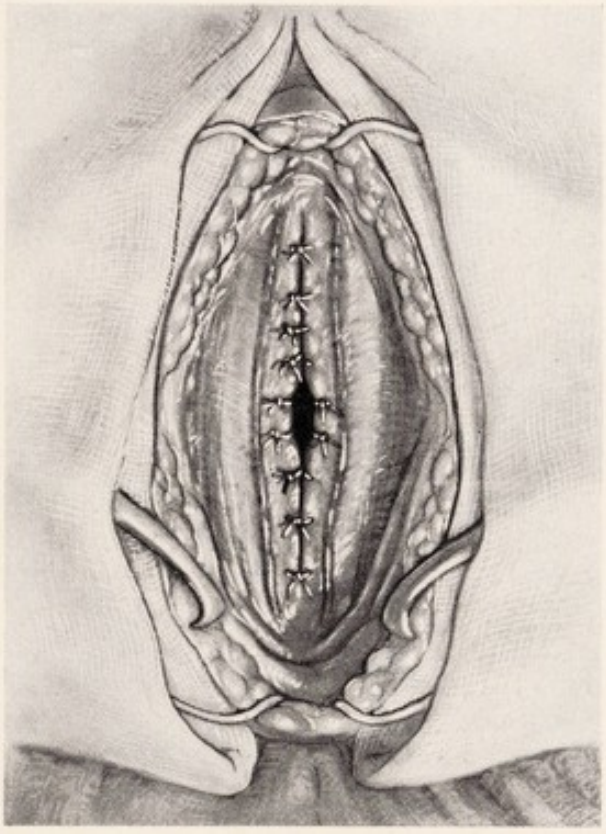


FIG. 88.—Prethyroid Muscle and Cervical Fascia Coapted except at Level of Upper Border of Isthmus. Opening 3/8ths to 1/2 inch long (button-holed) left for escape of serum to underside of flap.

The self-retaining retractors are next removed and the skin flaps brought together with clips, subcutaneous suture, or steeple sutures of horse hair. Many operators make a practice of suturing the thin layer of subcutaneous fascia as well as the skin. We do not consider this necessary, since the skin clips properly used will bring the edges of this fascia together, as well as the edges of the skin.

MODIFICATIONS IN TECHNIC

The operation described is our standard procedure **for the usual case** in which a subtotal thyroidectomy is indicated. From time to time variations in technic are necessary to meet the requirements of the individual case.

Variations in Approach to the Gland

In raising the superficial flaps some operators, notably Arn of Dayton, Ohio, and Hertzler (133) of Halstead, Kansas, routinely utilize the premuscular instead of the superficial plane of cleavage. The skin incision

is made according to the method already described and an area of the superficial fascia half an inch or more in width is exposed. The superficial fascia, platysma muscle, and the superficial layers of the deep fascia down to the premuscular plane of cleavage are separated by sharp dissection in line with the skin incision. The anterior jugular veins at this level lie between the superficial and deep fascia and are cut between forceps or ligatures. By sharp dissection, the premuscular plane of cleavage is followed upward and downward, thus raising the superficial fascia and the superficial layers of the deep fascia with the skin flaps, and thereby exposing the anterior surface of the prethyroid muscles. Separation of the prethyroid muscles in the midline completes the approach to the gland.

The only advantage of this method of approach to the gland over that previously described is that less retraction is necessary for the exposure of the upper pole. This advantage is counterbalanced by the fact that the procedure is successful only in the hands of a highly skilful operator. Moreover, the necessity of suturing the divided fascia and the danger of a deep-seated infection are disadvantages not to be underestimated.

Section at the Isthmus

Section at the isthmus, as practiced by Kocher, is sometimes indicated as the first step. For instance, when an adenoma is present in the isthmus, it may be well to separate one lateral lobe from the isthmus completely, and then dissect the pyramidal lobe and isthmus, including the adenoma, from the trachea and remove them with one lobe. In this procedure the dissection is usually made from within outward; the other lobe is removed in the same manner.

Some operators, notably Crotti (134), separate the isthmus as the first step routinely. After the exposure of the gland, they pass a forceps or scissors between the isthmus and trachea and, following the postisthmial plane of cleavage by blunt dissection, separate the isthmus from the trachea, then divide the isthmus and deliver each lateral lobe from the inner side. This technic accomplishes the same end as the separation of the upper border of the isthmus and the pyramidal lobe from the larynx and trachea as done in our operation. The question then arises, "Why not cut the isthmus in every case? Why resort to the more tedious technic previously described?" We may answer that if the isthmus is small, section of the isthmus as the first step may be acceptable. On the other hand, if it is large and vascular, serious hemorrhage may take place during the removal of the first lobe. The severed isthmus bleeds profusely and control with forceps is difficult. The fact that the goiter is removed in two pieces instead of in one is also a point against this technic, since most operators, other things being equal, prefer to remove the specimen intact.

A variation of this technic used by some operators in recent years is to sever the lateral lobe from the isthmus through what they term the bloodless area, just external to the junction of the median and lateral lobes. After removal of the lateral lobes, the isthmus is removed if necessary.

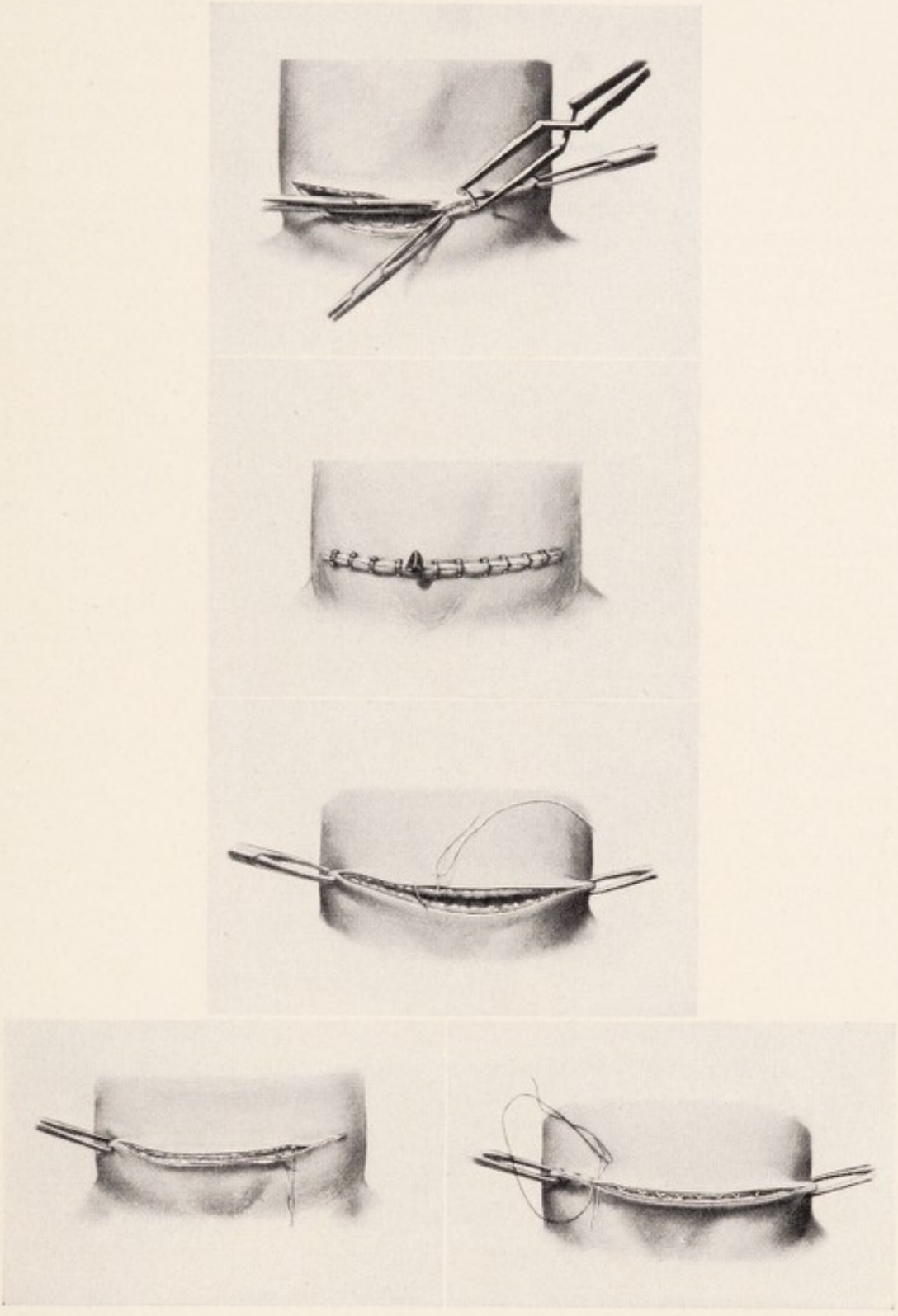


FIG. 89.—Closure—Skin Clips and Subcuticular Suture.

OPERATION FOR INTRATHORACIC GOITER

In the more serious cases of intrathoracic goiter, the surgeon may have need of all the judgment, skill, and experience at his command to carry through the operation acceptably. Throughout the course of the operation one must be on the alert for sudden accidents and disquieting complications. Crotti in his book *The Thyroid Gland* very aptly says: "Intrathoracic goiter surgery is one of the most thrilling there is. If one is seeking surgical emotion, it is surely in that field that he will find what he is looking for."

Preliminary Steps

The preliminary steps of the operation are identical with those already described in our usual operation. The upper pole is exposed and the blood vessels are ligated in the usual way. The upper pole and the upper portion of the lateral lobe are released; the inferior thyroid veins and all structures connecting the lower pole and the trachea are severed and the proximal ends ligated. **We are operating, remember, on the side on which the intrathoracic goiter is located.** All the attachments of the lateral lobe on this side are first released. Great care must be exercised to avoid undue traction which may result in tearing off the part of the lateral lobe above the clavicle from the intrathoracic projection. This would be an unfortunate accident and would unnecessarily complicate the operation.

Methods of Approach

Special cases of intrathoracic goiters will require variations in the method of approach. What shall we do for instance, when we find an intrathoracic mass on one side and a large supraclavicular adenoma on the other? The trachea may be curved into an S-shape and flattened from side to side by the tumors pressing in one direction in the cervical region and in the opposite direction in the thorax. More room for the removal of the thoracic tumor is afforded and the operation is expedited if the cervical tumor is removed first. Dangerous respiratory obstruction from collapse of the trachea in a position inaccessible to tracheotomy may occur, however, when the cervical tumor with its stabilizing tendency is removed. In view of this danger—if there is appreciable tension on the isthmus and other structures connecting the supraclavicular lobe on one side, and the intrathoracic prolongation on the other—we consider it far safer to remove the intrathoracic goiter **first.** This is particularly advisable if the intrathoracic portion is on the right side, or is in the midline in the substernal space. No great difficulties are encountered if the lateral lobe, on the side of the intrathoracic mass, is completely released superiorly, and from the trachea, before an attempt is made to displace or remove the intrathoracic projection.

There may be occasions, as Lahey (135) notes, when removal of part of the sternum is indicated, yet in a series of over fourteen thousand cases we have never found it necessary to resort to this somewhat drastic measure.

Delivery of the Mass

When all of the attachments of the lateral lobe have been released, we are ready for the delivery of the incarcerated mass in the thorax. We must first see that the mass is loose and free; if it is adherent to the pleura, the adhesions are cautiously separated with the gloved finger. For the delivery proper we again resort to obstetric maneuvers, using manipulations similar to those employed in the management of the aftercoming head. The superior portion of the gland is rolled down over the clavicle and the intrathoracic tumor is delivered by rotation rather than by traction. The patient can help considerably if the operation is being done under local anesthesia, or if permitted to come out a little from a general anesthesia. If the patient coughs and strains, the increased intrathoracic pressure aids very materially in forcing the mass up through the small opening. Sometimes the tumor pops out very readily and the balance of the operation is much simplified.

No concern need be entertained regarding the possibility of serious hemorrhage if the blood supply has been adequately controlled before the attempt is made to lift the mass from the thorax. In case the tumor mass is too large to pass through the upper aperture of the thorax, we must resort to certain expedients. The usual way out of the difficulty is to break up the gland substance; a procedure usually called morcellement. A finger is thrust into the mass from above, the inside of the mass is broken up, and perhaps some large nodules are enucleated. In this way a sufficient amount of material may be evacuated to permit partial collapse of the tumor. If thus diminished in size, the tumor may be drawn through the upper aperture and delivered. If a cyst is the cause of the obstruction, it may be punctured and the contents aspirated.

As the mass appears in the operative field, care should be taken that all bleeding points on the pleura or other structures to which the mass may have become adherent, are conscientiously caught and tied. The final release of the pleural sac is not permitted to occur until the tissues immediately surrounding the tip of the mass are caught with forceps so that every bleeding point in the cavity left may be meticulously ligated. Some surgeons advocate drainage as there is an extensive dead space left at the lower end of the wound. If very careful attention has been given to the question of hemostasis, drainage of the intrathoracic cavity will not be necessary.

LOBECTOMY AND STAGE OPERATION

Technic for Lobectomy

Lobectomy is sometimes indicated for unilateral goiter, or as part of the multiple stage operation. The lobe may be removed in exactly the same manner as that already described, but if a second operation is to follow, certain other considerations come into prominence. **It is highly desirable** that the approach to the second lobe should be through a field which is not obstructed with scar tissue—preferably through an entirely new field. **It is also important** that this lobe shall have been disturbed or

traumatized as little as possible by the first lobectomy. The operation which we have used for some years meets both of these requirements.

Exposure

Using a technic similar to that employed in subtotal thyroidectomy, the incision is made and the flap raised. The succeeding steps in the exposure of the lobe are different. On the side to be removed, the superficial

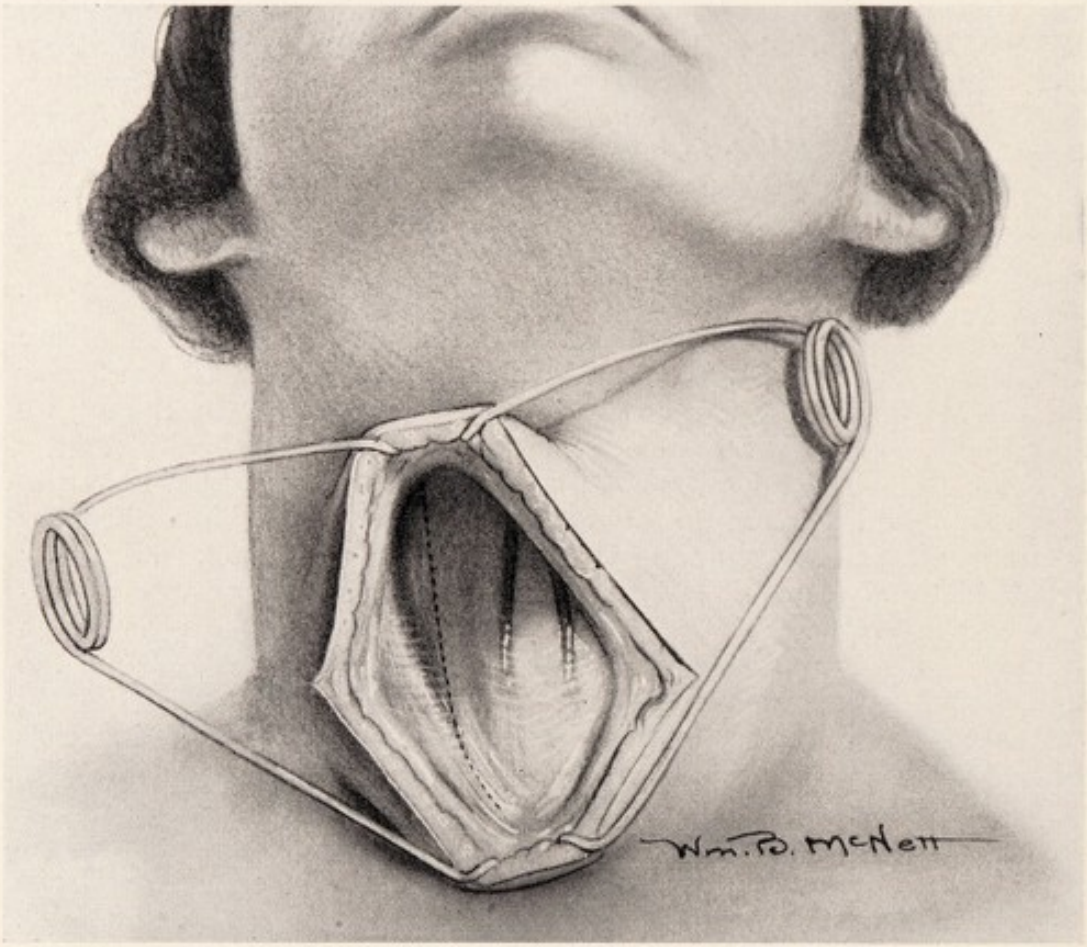


Fig. 90.—Incision to Superficial Plane of Cleavage. Flap Raised Following Superficial Plane of Cleavage to a Point above the Upper Pole.

plane of cleavage is followed to a slightly higher point than on the other side. The longest plane of separation is along the anterior border of the sternomastoid, from the suprasternal notch to the level of or slightly above the thyroid cartilage. At the lower angle of the incision, the hooks of the spring retractor are placed in the midline, while at the upper angle the hooks are placed lateral to the thyroid cartilage on the side to be removed. The anterior border of the sternomastoid muscle is freed by an incision through the cervical fascia, from the sternal notch to the upper angle of the opening. The sternomastoid is next retracted slightly outward and the prethyroid muscles incised in the direction of their fibers down to the gland.

Care should be taken, in mapping out the separation of the muscle fibers, that the upper angle of the opening in the muscles is mesial to the omohyoid. The muscles are retracted outward and inward respectively and the anterior surface of the lateral lobe is exposed. Approach to the upper pole is now easy. The vascular pedicle is ligated and severed, and traction is made on the flexed upper pole. As the pole makes progress through the opening in the muscles, the dissection is continued downward

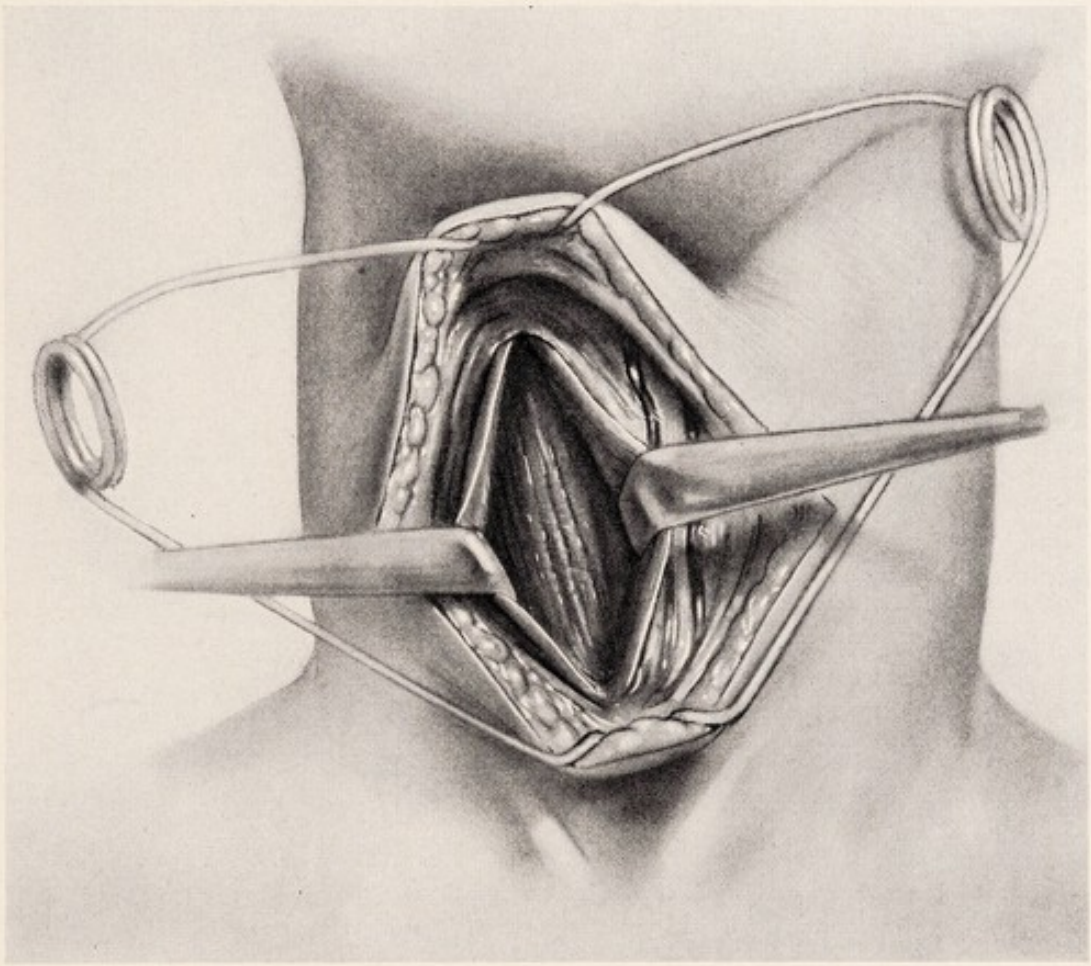


FIG. 91.—Anterior Border Sternomastoid Muscle Exposed by Incision of Fascia.

along the posterior surface, and an easy approach to the veins at the lower pole is provided. Severing the blood vessels at the lower pole completes the delivery of the lobe.

Removal.—Removal of the lobe may be completed by severing its connection with the isthmus or by proceeding to remove the isthmus with the lobe if this is required in the particular case. If the latter procedure is indicated, the lobe is rotated anteriorly, and the dissection continued along the postisthmial plane of cleavage, around the anterior segment of the trachea until the junction of the isthmus with the opposite lobe is exposed. The isthmus is then severed; this should always be done

between ligatures rather than clamps since the delicate blood vessels in this location may easily tear and cause troublesome hemorrhage.

Closure.—The closure is easy: the bleeding points, which have been clamped, are tied, and very few stitches are required to replace the muscles in their normal position since none have been cut.

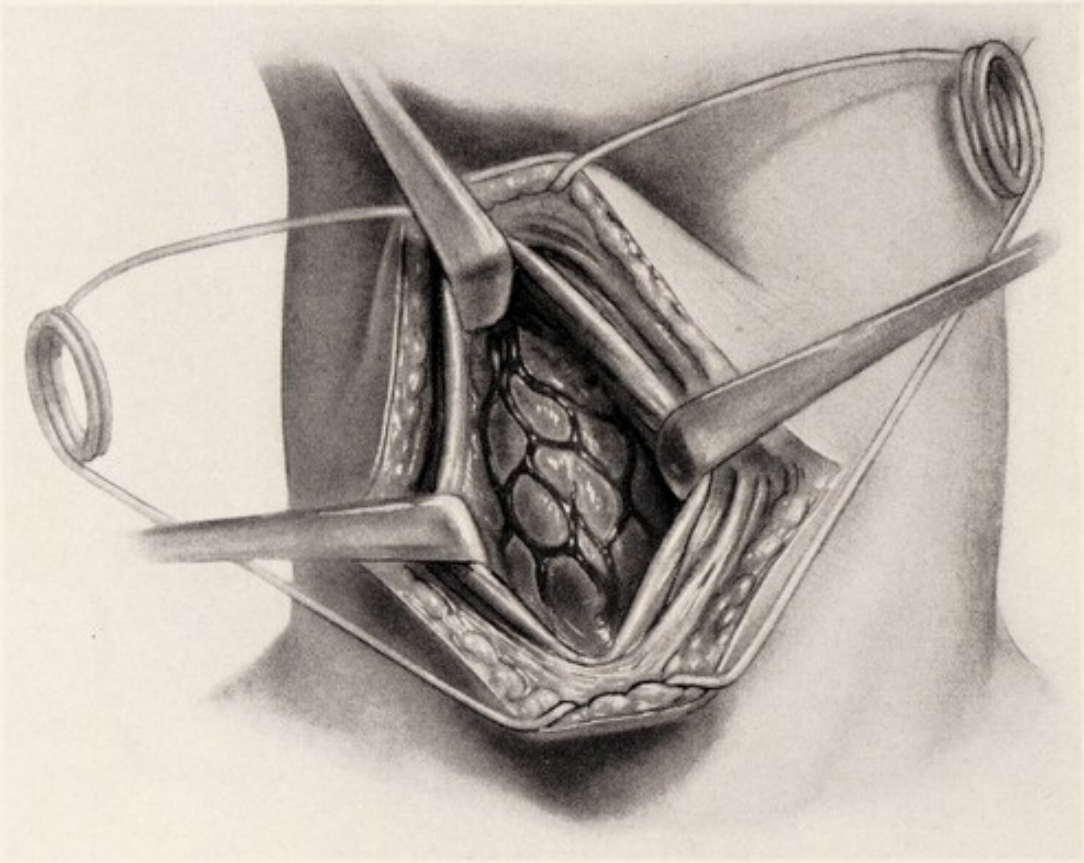


Fig. 92.—Sternomastoid and Omohyoid Muscles Retracted Laterally; Sternohyoid and Sternothyroid Retracted Mesially. Lateral Surface of Lobe Exposed.

Advantages of the Operation.—Briefly summarized, the distinctive points of this operation are: first, a line of incision which avoids important blood vessels and nerves; second, an incision which admits of easy removal of one lobe; third, no traumatism of the other lobe; and fourth, preservation of an undisturbed field for the second operation.

Multiple Stage Operation

The most important consideration in thyroid surgery is that **the operative procedure be limited to the endurance of the patient.** The risk as presented by the patient in terms of "hazard" for the proposed surgical procedure should be the measure of what we dare to do. Fortunately the most extensive thyroid operations may be done in successive stages, each stage being a minor operative procedure. The extent of the surgery done

in each stage and the number of stages will depend upon the individual case. When patients are approaching the moribund state, it may be necessary to resort to several stages such as:

First stage: Raising the flap.

Second stage: Approach to the lobe.

Third stage: Ligation of the vascular stalk.

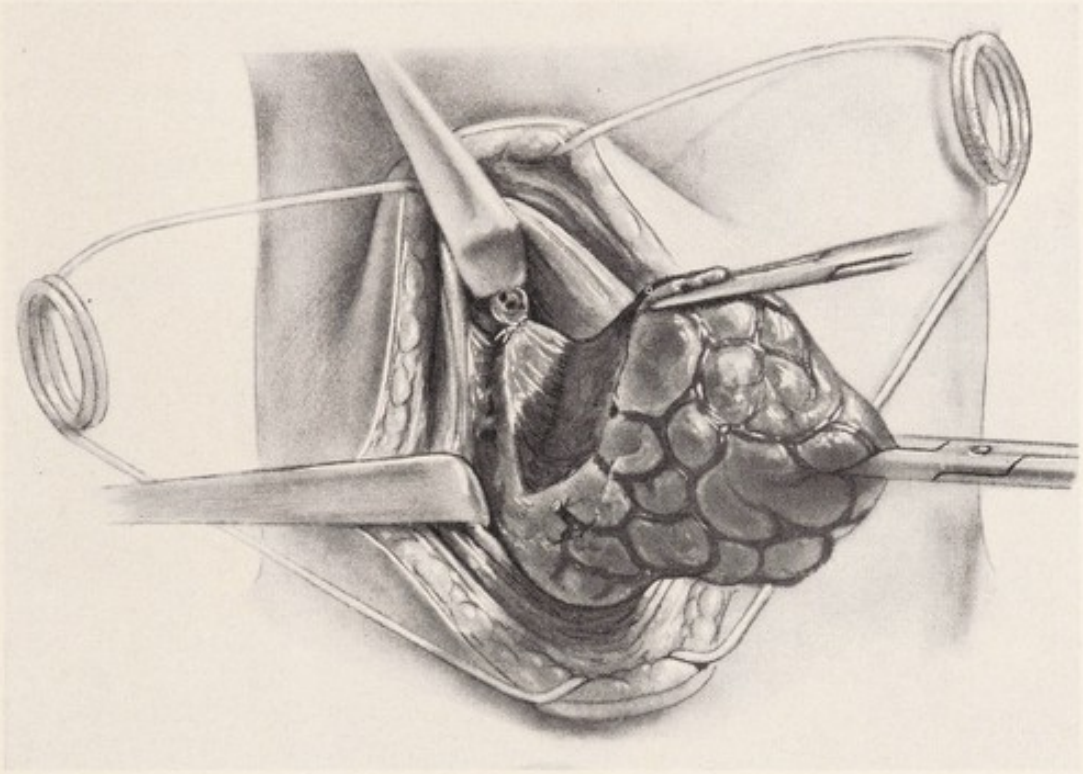


Fig. 93.—Superior Vascular Stalk Ligated. Lobe Being Delivered by Flexing Mesial Rotation and Dissection.

Fourth stage: Ligation of the inferior artery.

Fifth stage: Lobectomy.

Sixth stage: Lobectomy.

In some cases it is impossible to determine before the operation how much may safely be done. The condition of the patient should be watched and the operator be ready to discontinue the operation on the completion of any one stage. The operation should be so planned that its course may be determined by indications that arise as operation proceeds. In the majority of cases a lobectomy can be done at the first operation. Local anesthesia is more easily effected than in complete subtotal thyroidectomy and the lobectomy itself can usually be done in less than ten minutes.

The second lobe should be removed as soon as the condition of the patient warrants the operation. If it is not removed within four or five months, the toxemia will usually return.

OTHER OPERATIVE PROCEDURES

Enucleation

A single adenoma, especially if it is localized and definitely demarcated, may be enucleated by blunt dissection with very little disturbance of the other portions of the gland. The cavity in the gland may be obliterated by a few plain catgut sutures which will also serve to control any

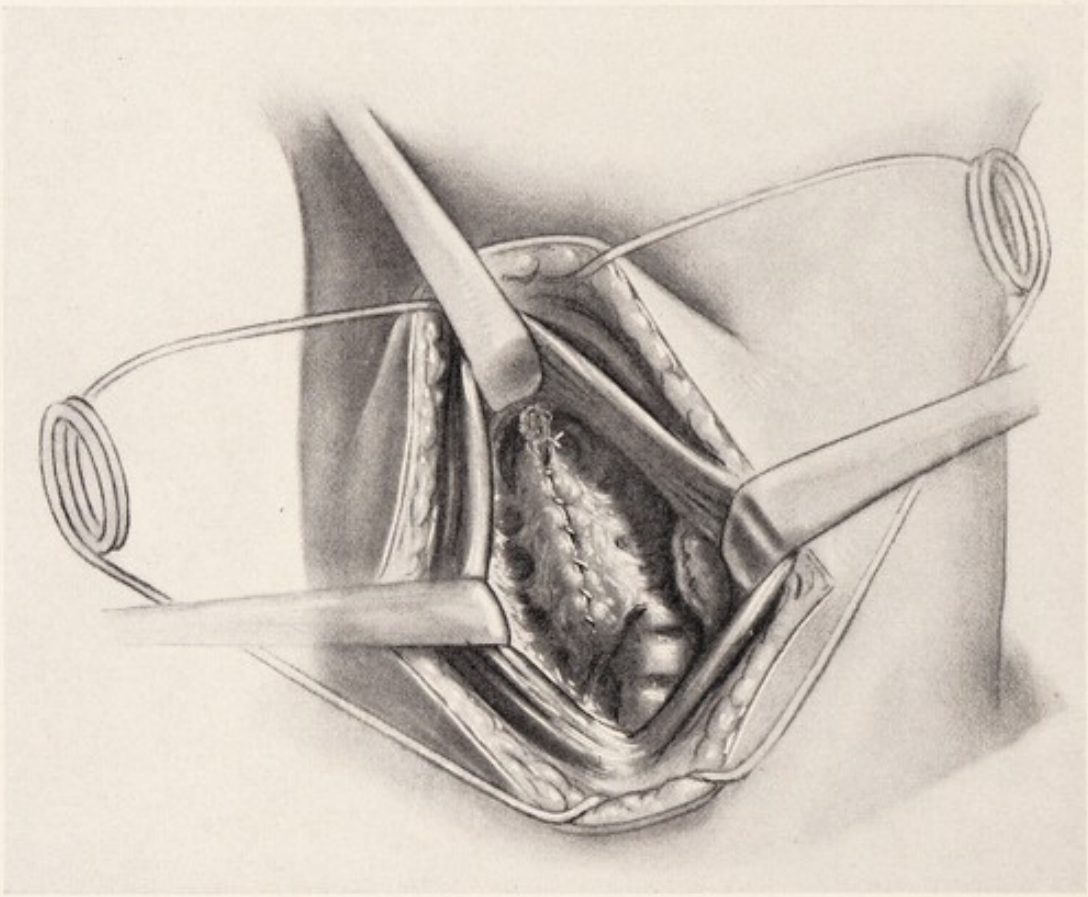


Fig. 94.—Lateral Lobe and Isthmus Removed, Ready for Closure.

tendency to hemorrhage. The procedure is very simple and attended with practically no postoperative discomfort. As a rule, it is not necessary for these patients to remain in bed for more than twenty-four hours after the operation.

In case of fetal adenoma, the tumor is definitely localized; sometimes it has a line of demarcation between it and the surrounding structures. The exposure should be made and the adenoma enucleated in the manner described above. If multiple, the various adenomas may be enucleated, or, if they are too numerous, a resection of the portion of the gland containing all the adenomas may be made.

Resection

Except for the fact that more gland tissue is left, the technic for resection is identical in every respect with that used for subtotal thyroidectomy. In resection the preservation of an adequate blood supply is of even greater importance, since there is more gland tissue left. The ligation of the upper pole should not include the dorsal branch of the superior thyroid artery; the branches of the inferior thyroid should be ligated on the cut surface of the gland. As in the case of subtotal thyroidectomy, it is advisable to leave the gland tissue near the thyroid pedicle; it is not advisable to leave a large lump of gland elsewhere, for reasons already given.

COMPLICATIONS OCCURRING DURING OPERATION

Hemorrhage

Middle Thyroid Vein

Hemorrhage from the middle thyroid vein is one of the most common complications occurring during goiter operations. If control of the proximal end of the torn vessel is lost, it retracts outward and is sometimes difficult to find. The proximal end is very short and, because there are no valves near its entrance into the internal jugular, bleeding from it may be profuse. When this complication occurs, the internal jugular should be sought and identified; the middle thyroid can then be readily found at its junction with the jugular and can be ligated at this position.

Inferior Thyroid Veins

The tearing of the inferior thyroid veins and the retraction of their proximal ends downward is a common complication. When this occurs, great care and patience must be exercised in the discovery and identification of the ends of the vessels. If the attempt fails, the hemorrhage must be controlled by packing, which is a poor alternative.

Under no circumstances should the operator attempt to control hemorrhage in this location by mass ligation. The inferior thyroid veins in the lower part of their course lie close to the recurrent nerve and one of them is sometimes slightly posterior to this nerve. An attempt at mass ligation of the vessels will greatly endanger the recurrent nerve. Tearing of the inferior thyroid veins can be prevented by careful ligation of these vessels before they are subjected to any great tension.

Inferior Thyroid Artery

The operator may lose control of the terminal ends of the branches of the inferior thyroid artery. Considerable difficulty may be encountered in the attempt to identify and recover them. Again, as in the case of the veins, we must keep in mind the dangers of mass ligation. An attempt to get blindly under the vessels with a needle will endanger the recurrent nerve. In the face of this complication it is best, even though we sacrifice the blood supply, to ligate the inferior thyroid artery, at some distance

from the recurrent nerve, at a point just mesial to the carotid sheath. By separation of the fibers of the pretracheal fascia at this point, the artery can be brought into view and ligated without danger to any important structure. This controls arterial hemorrhage at all points near the lower pole.

Superior Thyroid Artery

Hemorrhage from the superior thyroid artery may be quite spectacular, and may easily occur if we lose control of the branches of this vessel while manipulating the upper pole. If all the branches should be released at the same time, they will retract upward, under the flap, to a point which makes their recovery most difficult. Rather than lose time in a vain search for the branches, it is better practice to ligate the superior thyroid, proximal to its point of division. This may be accomplished in either of two ways.

The line of separation of the upper flap along the superficial plane of cleavage may be extended sufficiently on the side of the hemorrhage to expose the lower angle of the carotid triangle. A finger is then introduced along the course of the vessels, and a curved needle carrying a No. 1 catgut ligature is passed near the anterior border of the sternomastoid, just above the inferior angle of the superior carotid triangle, inward through the fascia and the platysma. It is swept around the tip of the finger behind the superior thyroid artery, between the finger and the larynx, and finally brought out through the fascia and platysma. The ligature includes the superior thyroid artery, some platysma and fascia fibers, and occasionally some of the external fibers of the omohyoid muscle. In order to avoid the risk of damage to the carotid artery and jugular vein in this procedure, the carotid artery should be held outward with the finger. The ligature should be tied loosely, for extreme tension is not required to control the artery. A ligature of No. 1 plain catgut will be absorbed in three to five days with no serious damage to included muscular fibers.

The second, perhaps a safer procedure, is to raise the flap high enough to expose the fascia over the superior thyroid, above the inferior angle of the superior carotid triangle, and proceed with the ligation of the trunk.

Complications Other Than Hemorrhage

Pleura

Damage to the pleura may occur during the process of its dissection off the tumor in cases of intrathoracic goiter. Any tear should be repaired according to the usual procedure. Following traumatism to the apical pleura, symptoms differing in no essential from those usual in pleurisy present themselves. The pain, as in other forms of pleurisy, is usually referred to the region of the seventh and eighth ribs. The pleurisy disappears as a rule within a few days although it may persist for several weeks. Effusion in the pleural cavity occurred in seven of our cases following damage to the dome of the pleura; in two of these cases, the effusion persisted for more than two weeks and had to be aspirated. In the other five instances, the fluid was absorbed without sequelae of any kind.

Recurrent Laryngeal Nerve

Damage to the recurrent nerve has always been a nightmare, the *bête noire* in the path of the thyroid surgeon. In the early days of thyroid surgery the complication was quite frequent. Billroth, for instance, is said to have had the unfortunate experience of having twenty-three cases of laryngeal paralysis in seventy-one goiter operations. At the present time serious injury to the recurrent nerve is rare, owing largely to the observance of the following precautions:

(1) A laryngoscopic examination should always be made prior to operation.

(2) In case of hemorrhage from the inferior thyroid vessels, mass suture should not be used to control the bleeding.

(3) After the vascular stalk has been severed, extreme forward traction on the gland should be avoided.

(4) The gland tissue to remain should be left in connection with the thyroid pedicle over the recurrent nerve.

(5) The operator should be on the alert to recognize promptly any evidence of injury to the nerve.

Prompt action at the first indication of this last-named complication will avoid serious consequences. When a suture is inserted that might by any chance include the nerve, the patient's respiration should be carefully watched as the suture is tied, and, if any change is noted, the suture should be promptly removed. Unless the patient is too deeply anesthetized, inclusion of the nerve in the suture will be followed immediately by change in the character of the respiratory sounds. If the nerve is surrounded by considerable tissue when it is grasped by the ligature or clamp, there will be less pressure on the nerve and less damage. In case of doubt, the patient should be permitted to come out from under the anesthetic to such an extent that he can speak. In the event that the nerve is severed and diagnosis of the complication is made during the operation, the cut ends should be brought together and sutured with very fine silk or catgut.

Trachea

With modern methods, collapse of the trachea is a comparatively rare complication. We should be prepared for it, for tracheal collapse is exceedingly disturbing. In our early experience, occasionally we had the unfortunate complication of tracheal collapse. This occurred seven times in our first five hundred goiter operations. In each case intratracheal catheterization was done and not one of the cases was lost. It will readily be seen that if the gland is dislocated before the short attachments to the trachea and larynx are severed, the trachea and esophagus must follow every movement of the gland. In the anterior rotation of the lateral lobe, pressure is exerted on the anterior surface of the trachea while the posterior surface is placed under tension; thus the trachea is subjected to both torsion and pressure.

If the occlusion of the trachea is complete, the patient may succumb very promptly unless the condition is immediately relieved. Sometimes

the replacement of the lobe will give relief. If it does not, tracheotomy or intratracheal catheterization with an open end catheter must be immediately performed. To insert the catheter, the epiglottis is lifted and the catheter is guided by a finger into the larynx and trachea to a point below the obstruction. This method is preferable to tracheotomy in cases in which the obstruction is of temporary character. After the goiter is removed, and before closure is begun, the catheter is removed and at once it becomes evident whether the collapse was temporary or is permanent. If collapse is still present after the removal of the catheter, a tracheotomy is indicated while the wound is still open and the approach prepared.

In goiters of long standing, particularly in the cases that have been complicated by pressure symptoms, the rings of the trachea may be more or less soft. In these cases, after a goiter has been removed the walls of the trachea may flap or collapse on inspiration and cause serious respiratory obstruction. We have tried to avoid tracheotomy in these cases by various expedients. Forcible extension of the head in a forward position may be effective. In some cases positive pulmonary pressure from a gas machine will hold the walls of the trachea apart and prevent collapse until the wound can be closed. Usually the respiratory difficulty disappears after the wound is closed and the patient regains consciousness. Sometimes suturing of the tracheal wall to the prethyroid fascia will, by the mild traction exerted, prevent collapse.

In cases which are not relieved by other procedures tracheotomy should be done before the patient is too exhausted. The tracheotomy should be done at a low level and a fenestrated tube should be used to enable the patient to respire through the larynx before the tube is removed.

If relief from respiratory obstruction is not immediately obtained upon insertion of the tube, we will find that one of four conditions is at fault: the caliber of the tube is too small; the tracheotomy has been done too high; the tube is not of the correct shape for the condition; or the obstruction is situated in the thorax below the tube. Often by changing the tube for one slightly larger and longer, immediate relief is obtained. In some cases, the tracheotomy tube can be removed within twenty-four or forty-eight hours and respiration can be adequately carried on without its help. In other cases, it is advisable to leave the tracheotomy in place for from five to seven days.

Vomiting

Vomiting during the course of an operation may endanger the life of the patient from obstruction of the respiratory tract due to inspiration of the vomitus. The danger may be obviated in great degree by lowering the head of the table when the patient vomits. In case large quantities of material are vomited, the head of the table should be lowered until the patient is in the Trendelenburg position. Should the patient, while under general anesthesia, inspire vomitus, he should be permitted to come far enough out of the anesthesia so that he is able to cough and

clear the bronchi of such material. This complication rarely occurs during local anesthesia.

PROCEDURES FOR CONDITIONS OTHER THAN GOITER

LIGNEOUS THYROIDITIS

Ligneous thyroiditis, a condition in which the gland is rigid, hard and firmly adherent to the surgical capsule, requires a modification of technic. Since it is not always diagnosed beforehand, the surgeon must be prepared to recognize the condition at the time of operation and alter his procedure accordingly. Sharp dissection in these cases is attended with great difficulties. The gland cannot be displaced without undue traction; flexion or rotation and dislocation are impossible.

Although sharp knife dissection is not practicable, the gland can be easily and safely destroyed by the use of cautery. There are various forms of cautery irons which may be used for the purpose provided they are not used too hot. Small irons, ground or hammered into a shape to suit the preference of the surgeon and heated over a gas flame, may be successfully used. J. F. Percy (136) has devised an electric cautery which is quite satisfactory except for the fact that the point of greatest heat is not at the tip and consequently it is difficult to protect the edges of the muscles and the overlying structures from damage.

The aim of the procedure is to destroy one-half to two-thirds of the gland by slow cautery and heat the balance. The part that is to remain should not be cooked to such an extent that its vitality is destroyed. One of the fortunate features of cautery in this condition is that gland tissue which is heated but not destroyed shows a prompt tendency to return to normal. The passage of heat through the gland should be just perceptible to fingers placed at the posterior borders. Great care should be taken at the upper pole; the comparatively large vessels at this point should be cooked but not destroyed. The upper pole should be rolled forward by the finger and the cautery thrust into the center of the mass so isolated. No ligature is necessary as cautery controls all hemorrhage.

Following this treatment with the cautery, drainage should be instituted. The wound heals with surprising rapidity; recovery in these cases is prompt and complete.

MALIGNANCY

Many surgeons are of the opinion that nothing can be done for malignancy that can be diagnosed before operation. The earlier the case is seen, the better the prognosis; yet even the case that has advanced beyond the primary stage does not, we think, warrant our withholding such palliative surgical measures as may make the patient more comfortable or prolong life if even for only a short time. Deep x-ray therapy by itself apparently gives only very fleeting benefit; it does not often relieve the rigidity, pressure symptoms, dysphagia, and marked disturbance of respiration. The same objection may be cited relative to radium treatment.

We have found that a combination of operation, radium, and x-ray treatments often gives surprisingly good results. The sequence is: operation, followed by radium left in the wound, followed in turn by deep x-ray treatment.

In malignancy the same difficulties are encountered in cutting operations on the gland as are met with in the case of ligneous thyroiditis. Another serious objection to knife dissection is the almost inevitable certainty that cancer cells will be disseminated. In malignancy there is frequently severe infiltration of the muscles of the neck and the other adjacent structures; in our experience any cutting operation, when the malignancy has extended beyond the confines of the gland, is unsatisfactory and ineffective. These objections do not apply to the use of the cautery. The gland is exposed by the method already discussed and then is destroyed by cautery with slow heat—the cautery iron not being allowed to become cherry red. In this way no hemorrhage is encountered.

Before the gland proper is attacked, all overlying muscles and other adjacent structures that are infiltrated and adherent to the thyroid are dissected off with the cautery. Then the major portion of the entire thyroid mass is destroyed by cautery. The iron should be only hot enough to char. After the major portion of the gland has been destroyed, the rest should be carefully heated to a temperature that causes the tissue to appear white. The temperature of the cautery iron may be tested by touching a drop of water with it; it should be hot enough to boil the water but not hot enough to sizzle. The greater the distance from the malignancy that non-destructive heat is conducted, the better will be the results.

The prethyroid fascia connecting the carotid sheath with the gland should be dissected off the carotid sheath **with the cautery.** Special attention should be given to the rigid tissue which is often encountered near the lower pole of the gland. Frequently some small hard nodules are palpable in this location and in the thyrothymus tract. These and the group of lymphatics in Burns' space should be entirely destroyed. It is usually advisable to destroy the sternothyroid muscles completely and heat the sternohyoids perceptibly.

The next step is the placing of the radium needles. Four 12.5 milligram needles, screened with 1 millimeter of copper or 2 millimeters of silver, are placed in the depth of the wound, one near each upper and one near each lower pole. The wound is lightly but firmly packed with gauze in such a manner that it will not be disturbed by the removal of the radium needles. No closure is attempted except at the angles of the skin incision, where clips are used to bring the skin together, leaving an opening for the exit of the gauze packing and the strings attached to the radium needles. This opening is in the midline and is usually about three inches in length.

The 50 milligrams of radium distributed as described are allowed to remain for twenty-four hours. After forty-eight hours the gauze is removed and lightly replaced.

The whole operative procedure is carried out with few difficulties

and with surprisingly little shock to the patient. In the majority of instances, the patient will be breathing more easily and the pressure symptoms will have been partly relieved by the time the operation has been finished.

On the fourth day, the x-ray exposures are begun. Deep exposure of the anterior cervical region to roentgen ray is the first step. Successive areas are exposed until the entire cervical region and upper thoracic regions have been treated. Especial care is taken that the supraclavical glands on each side and the mediastinal region receive maximum exposure. Close attention is also given to the posterior occipital and mastoid region and cross fire is directed at the sides and processes of all cervical vertebrae.

After an interval of four or five weeks, the deep exposure of the entire region to the roentgen ray is repeated. Within a period of four months all of these regions should have three maximum exposures.

What are the results with this combined routine of radical operation, radium, and x-ray? In the six years from 1922 to 1927 inclusive, this procedure was followed in nineteen cases of malignancy that were diagnosed before operation with the following results: Seven of the nineteen died within a few months after operation. Five had recurrence within eighteen months—the metastases in three of the five cases occurring in the posterior occipital region. One died seven years after operation from cancer of the liver. Another died five years after operation from malignancy of the lungs. Of the other five, four died from other diseases—two, four, six, and seven years after operation—and one is still living nine years after operation with no symptoms of recurrence. Although in the majority of cases the ultimate results are far from satisfactory, the procedure is justified by the temporary relief experienced and by the fact that in some cases the patient remained free from symptoms of recurrence over a period of years.

CHAPTER XV

POSTOPERATIVE MANAGEMENT

POSTOPERATIVE CARE AND TREATMENT

In cases of simple uncomplicated goiter, the postoperative care and treatment differ little from the ordinary routine following any surgical operation. In toxic goiter, the after-care and treatment of the patient play a definite rôle in the successful management of the case. In either, the postoperative care begins at the moment when the operation is completed.

The promptness and dexterity with which the dressing is applied and the patient moved from the table to the cart, and the expeditiousness and skill exercised in transporting the patient from the operating room to the bed are matters of great importance from the standpoint of the future comfort and well-being of the patient. Attention to details, sympathetic understanding, and the interpretation and appreciation of apparently trifling indications of discomfort enables the attendant to prevent much unnecessary suffering.

Dressing of the Wound

The dressing of the wound so that it is adequately protected from contamination and irritation is of grave importance. If the dressing is too large it is uncomfortable. A small dressing, changed frequently, is better than a large one changed infrequently. The dressing should be absorbent, soft and non-irritating; about one inch in thickness and of sufficient size to cover the anterior surface of the neck.

A well fitted dressing that provides a certain amount of support will add greatly to the postoperative comfort. The use of adhesive tape, which always causes some irritation when applied to the freely movable skin of this region, should be avoided when possible. The dressing may be comfortably and securely held in place by a moderately stiff towel, folded to a width of two and one-half or three inches, brought around the neck from behind and crossed in front over the dressing. The ends are brought downward and outward, and held by pins to a binder around the thorax. The towel, applied in this way, holds the dressing in place, and gives support to the neck without producing pressure over the trachea in the midline. The binder around the thorax always adds to the comfort of the patient. In women with large breasts the weight of the breast often pulls the skin down in the region of the scar and produces tension upon the sutures or clips. The thoracic binder prevents the breasts from falling down and causing tension on the wound margins.

The Patient in Transit

In moving the patient from the operating table to the bedroom, five considerations are of importance:

(1) The patient who has had a general anesthetic should, if possible, be moved to the wheeled stretcher and should be on the way to the bedroom before regaining consciousness.

As a rule, in cases of toxic goiter at least, it is advisable to change the garments before the patient leaves the operating room. During anesthesia, the patient is apt to perspire rather freely and on this account it is desirable to provide fresh clothing as soon as possible.

If a local anesthetic has been given, the patient, on termination of the operation, should be transferred immediately to the stretcher and started on the way to bed. The transference should be made as carefully and as tenderly as possible. Sudden movement or jarring causes pain and the toxic patients, at least, are especially fearful. Nothing tries the fortitude of the patient more than unnecessary delay in the operating room.

(2) The mental attitudes of thyrotoxic patients must be taken into consideration during transit of the patient from the operating room. No unnecessary noises should be permitted in the hallways or elevators. It must be remembered that under the circumstances the patient's hearing is sometimes very acute and loud talking, indiscreet remarks, or jarring noise, may sound many times as loud to the patient as to the attendants.

(3) A sufficient number of attendants should accompany the patient to guarantee proper care in the event of such complications as transient delirium or vomiting.

(4) The preparation of the bedroom should have been attended to before the patient returns. The bed should be ready with the covers laid back. The confusion and delay attendant upon turning down covers, smoothing sheets, moving heat pads, or adjusting the position of the bed, are very trying to an anxious patient. The shades should be drawn to the proper level; even the raising of a shade after the patient is in bed may be sufficiently disturbing to make necessary an extra dose of sedative.

The laying out or preparation of paraphernalia for hypodermoclysis or proctoclysis may also constitute a disturbing element. Arrangements for such procedures should have been completed in every detail if there is a possibility that they will be required.

(5) In the transit from operating room to bedroom care should be taken that sudden changes of temperature be avoided. Enough blankets should be used on the stretcher to prevent discomfort due to drafts or lower temperature in elevators or corridors.

Patient's Position in Bed

It is customary in some clinics to place the patient immediately in the Fowler position. In our opinion, this should never be done until the patient regains consciousness. The reason, of course, is that such a position increases the danger of inspiring vomitus. After a few hours the head

of the bed may be raised and the patient placed in the Fowler position or even turned on one side. Whatever position is found to be most comfortable should usually be permitted. The patient should not be allowed to remain in the same posture for more than two or three hours at a time. Even during sleep the position should be slightly changed at intervals. Early attention to this detail will add much to the comfort of the patient and be a factor in the prevention of postoperative backache. Backache after operation is most often due to unusual movement of the joints in the vertebral column during complete relaxation under general anesthesia, but it is sometimes encountered in patients who have been permitted to remain in the Fowler position for many hours at a time.

Stimulation

In the routine case stimulation is seldom required. Occasionally a decided fall of blood pressure or a delay in recovering from the anesthetic may be an indication for use of a stimulant. A lowered blood pressure calls for the administration of adrenalin and pituitrin. Cyanosis of any degree, if accompanied by restlessness or stupor, is an indication for a respiratory stimulant. Caffein sodium benzoate, strychnia, and adrenalin are each of some value as respiratory stimulants. Nothing is so prompt and reliable in action as an 8 per cent mixture of carbon dioxid in oxygen given by inhalation.

Heart stimulants are rarely required. Arhythmia, cardiac insufficiency due to fibrillation, valve lesions and broken compensation are indications for digitalis or similar remedies. It should be remembered that the rapid pulse due to the toxemia in thyrotoxicosis is not influenced by digitalis.

In case there is urgent need for prompt general stimulation, the hypodermic administration of 7 to 20 grains of caffein sodium benzoate and the intravenous administration of normal saline solution will usually produce quick results. Intravenous stimulation is the mode of preference; not only is it promptly effective but in well organized hospitals with the facilities available it may be given with ease and causes a minimum of discomfort.

Whiskey, in our experience, is a stimulant of value when administered orally but ineffective when administered by proctoclysis. The patient in need of stimulation can usually be induced to drink a toddy composed of equal amounts of whiskey, glucose syrup and hot water as he is regaining consciousness. No other stimulant equally allays the mental apprehension, dilates the superficial capillaries, stimulates the secretion of urine and adds to the sense of well-being of the patient.

Control of Pain and Nervous Symptoms

For the period immediately following operation the narcotic or sedative given previous to operation is usually sufficient to control any discomfort or nervousness. Should the patient become restless and be unable to sleep, it may be advisable to resort to morphin given hypodermically.

It is desirable, if possible, to insure a good night's sleep for the patient on the first night subsequent to the operation. Some surgeons advise the hypodermic injection of a narcotic immediately upon the return from the operating room, with repetition of the injection as required to keep the patient in a light stupor for the first twenty-four to forty-eight hours. In our opinion narcotics should be used only if other means fail to keep the patient from becoming restless and excited. If morphin causes vomiting or nausea, codein or pantopium hydrochloricum should be substituted. Except in the presence of actual pain, codein is almost as efficient as morphin. Pantopium hydrochloricum is slower in action but almost as effective.

In many clinics it is customary, especially when respiratory symptoms are present, to combine 1/150 or 1/200 grain of atropin with each $\frac{1}{4}$ grain of morphin. This is of distinct advantage in comparatively rare cases in which the accumulation of mucus in the bronchi is excessive. It may also be of advantage in the case of the patient who experiences pain or difficulty in swallowing. Such patients will delay swallowing as long as possible and consequently a large amount of saliva will accumulate in the mouth. Some of this saliva escapes into the throat and enters the larynx. The use of atropin will check the excessive salivation and make the patient more comfortable.

In the usual case, atropin, by checking the secretion of mucus, leaves the trachea and bronchi in a dry state which obviously invites irritation. We are quite convinced that atropin, given as a routine medicament, will in many cases be followed by aggravation of the tracheal and bronchial irritation with consequent delay in the disappearance of the respiratory difficulties. The administration of 1/150 or 1/200 grain of hyoscin with morphin increases and prolongs the effect, and reduces the nausea and discomfort that follows the use of morphin alone.

Sedative

If the patient cannot sleep the first few nights after operation, there is no objection to the use of carefully selected hypnotics given in proper dosage. Barbital, phenobarbital, sodium amytal, or bromids may be given. Barbital is usually given in dosage of 5 to 10 grains; phenobarbital in dosage of 2 to 4 grains; sodium amytal in dosage of $1\frac{1}{2}$ to 3 grains; bromids may be given by proctoclysis in dosage of 40 to 60 grains. Usually, by the judicious use of these sedatives the patient can be made comfortable and the use of narcotics dispensed with after the first night.

Idiosyncrasy

When the existence of an idiosyncrasy to a certain drug is discovered, another remedy should be substituted. Pantopium hydrochloricum will sometimes relieve the discomfort and produce sleep when morphin is followed by extreme restlessness and sleeplessness.

Cough

Pain and discomfort resulting from cough, increase the apprehension and nervousness of the patient. The patient with mucus in the trachea

and bronchi, who is distressed by persistent coughing, is relieved by ½ grain of codein sulphate, by mouth, or steam inhalations of compound tincture of benzoin.

Vomiting

Great care should be taken to prevent the possible inspiration of vomitus during unconsciousness. Use of the Trendelenburg position is sometimes resorted to if vomiting is copious. Gastric lavage is the most dependable measure for the control of persistent nausea and vomiting. Hyoscin (1/200 grain) held under the tongue for twenty minutes will frequently relieve the nausea and vomiting following the administration of narcotics. If the patient is unable to hold the tablet under the tongue for the required length of time or if one tablet is not effective, the dose may be repeated in one hour. The effect of hyoscin upon the patient's mental condition is usually very beneficial.

Temperature

Thyrotoxic patients should not be covered too warmly after operation. In the majority of goiter cases there seems to be some disturbance of the mechanism for the elimination of body heat. A postoperative elevation in temperature is more constant in severe cases of Graves' disease when the thyroid tissue has been unduly traumatized during operation. The earliest indication of an on-coming thyrotoxicosis is a rise in temperature. In severe cases there may be a rise from 100 to 107 within an hour.

It is important, particularly in toxic cases, that the temperature be accurately taken every hour until the danger of thyrotoxicosis is over. Even in atoxic cases the temperature should be taken every three hours during the first afternoon and night and every six hours during the next five days.

The rectal or vaginal method should be used routinely for all temperature readings since the oral method is not reliable. Occasionally the oral temperature is close to normal when the rectal temperature is 105 to 106 degrees.

Dehydration

Dehydration favors the development of postoperative thyrotoxicosis. It is important, especially with thyrotoxic patients, to overcome as soon as possible the dehydrating effects of excessive perspiration and temporary abstinence from liquids by mouth entailed by operative procedures. As a routine measure, during the first twenty-four hours following operation, at least 1500 cubic centimeters of fluid should be administered either intravenously or by hypodermoclysis or proctoclysis. The last named method is usually reliable if started before the patient regains consciousness. If, as sometimes happens, this method causes gas distention and pain in the large bowel, an enema will usually give relief. There are numerous solutions in use for overcoming dehydration and opinions vary as to their relative value. Lugol's solution may be added to the normal saline usually employed. Other solutions, such as glucose

or lactose, may be used alone or in combination with normal saline solution. It is important to have the liquid for proctoclysis at body temperature since a difference in temperature, when the solution comes in contact with the rectal mucosa, may stimulate peristalsis or irritate the rectum and thus prevent retention. The administration of fluids by mouth should be resumed as early as possible.

Sutures

If scarring is to be prevented the early removal of sutures is of great importance. If equisetine sutures are used they should be removed on the second day; dermol may be left till the third day; and horse hair, if not drawn too tight, may remain five days without danger of scar formation. If skin clips are used, some may be removed on the second day and all by the fourth day.

Dressings

The postoperative dressing should, as a rule, be examined every few hours and changed if soiled. A dressing soaked with drainage and serum is extremely uncomfortable and invites infection. Occasionally, even in clean cases closed without drainage, some serum is discharged during the first few hours after operation. When drainage has been instituted, the dressings should be changed at shorter intervals.

On the slightest indication of infection, hot wet dressings should be applied to the wound. When a wet dressing is indicated, gauze, wet with a *saturated* solution of boric acid, makes an excellent one. These wet dressings, changed every four or five hours, usually bring about resolution and drainage within a few days.

Drainage

Drainage, when employed, should be discontinued early. The drain ordinarily should be removed on the evening of the day on which the operation has been performed. At all events it should not be allowed to remain longer than the morning after operation. It has served its purpose as soon as a tract has formed for the escape of serum from the deeper parts of the wound. (After an extensive operation with considerable trauma of the tissues, a copious discharge of serum may be expected and it may be advisable to leave the drains in place for forty-eight to seventy-two hours.)

Diet

If the operation has been done under local or light gas anesthesia, fluids may be administered by mouth shortly after operation. Orangeade, orange albumin, prune juice, pineapple syrup or juice may be freely given. We favor as a postoperative drink orangeade made with fresh orange juice, glucose syrup, and water. The patient should be urged to swallow liquids immediately after operation. Pain from swallowing is sometimes complained of at first. This pain is less noticeable if the patient can be induced to swallow before the effect of the local anesthesia has dis-

appeared. Following general anesthesia, if the patient can be made to swallow a few times before regaining full consciousness, he will experience less discomfort afterwards.

On the day of operation, the patient may be given fruit juices, toddy, or bouillon. The second day, the thyrotoxic patient is continued on liquid diet; on the third day, the diet is semiliquid—soup and soft foods. On the fourth day, the patient may be placed on regular diet excluding, however, highly seasoned foods, tea, coffee, and meat. Excessive use of stimulating foods and meat should be restricted for a period of at least six months.

Cathartics

Cathartics should not be given, except in extreme cases, before the fourth day. Enemas may be given at any time.

Nursing

The psychic element is not always sufficiently considered in the postoperative management of the thyrotoxic patient. It must be recalled that the toxic goiter patient is an extremely sensitive creature and that his or her reactions are still more accentuated and disturbed consequent on the operation. Accordingly every effort should be made to promote a reposeful postoperative environment. Disturbing influences should, as far as possible, be excluded. In many instances it is advisable that the patient receive no company for a day or so after the operation or that such visits as are allowed be very brief. Protection of the patient from family solicitude is in certain cases one of the difficult phases of the postoperative problem.

Bed and Hospital Stay

The duration of the bed and hospital stay will vary according to the severity of the case and the nature of the operative procedures.

No set rule can be made in regard to the time at which the patient may be allowed to get up. This decision will depend more upon the condition of the heart than on any other consideration. We may presume that the longer the toxemia has been present the greater the amount of myocardial damage, and the longer must be the period of the bed stay. It is more prudent to remain on the safe side. In the case of patients who have been digitalized previous to operation, care should be exercised that they leave bed only after careful examination. It is, perhaps, safer to keep such patients in bed until they have again been digitalized. The drop in the basal metabolic rate may also offer a valuable index. In a general way it may be said that the greater the drop in basal metabolic rate and pulse rate, the longer the time required before the patient is permitted to get up.

The duration of the postoperative hospital residence will also depend upon the nature and extent of the operative procedure. If the prethyroid muscles have not been cut, there is no indication, from the standpoint of the operative wound, to keep the patient in the hospital longer than seven days. In advanced toxic cases, a patient, who after a lobectomy

might be able to return home safely and comfortably on the eighth or tenth day, would not be in condition to leave the hospital until the fourteenth to the twenty-first day after a complete, subtotal thyroidectomy. Mild cases should not be kept in bed too long. It will be found that some patients, when allowed to remain in bed, become rather reluctant to be up and about.

In the average case the patient may be allowed to sit up in bed on the second day; on the fourth may be permitted to be out of bed in a chair for an hour or two; and on the sixth or seventh day be allowed to return home. Few uncomplicated cases need to remain in the hospital longer than ten days after operation. If the operative procedure has been well within the patient's limitations, recovery will be prompt and certain. If the procedure has severely taxed the patient's endurance, considerable time may be required for recovery.

Postoperative Home Routine

The patient, who is returning home after an operation for hyperplastic goiter, should be impressed with the very great importance of tranquility and rest in the home environment; should be cautioned to avoid social gatherings, theaters and other occasions of excitement or stimulation; should be advised to retire early and arise late, and in addition to take an afternoon rest period of a couple of hours. The patient should be made to realize that the operation is only one necessary step and not the final step in recovery and should be told that frequently there are certain residual symptoms which the surgeon's knife cannot reach and that the elimination of these unpleasant symptoms is a task that requires time and lies within the province of the patient.

Medication, in the average mild case, is unnecessary. In cases attended by heart complications, the medication will depend on the symptoms present.

Some authorities advise that patients operated on for simple goiter be given an iodin preparation in careful doses over a considerable period of time to prevent a recurrence due to compensatory hypertrophy. This should be done if an iodin deficiency is present, but is useless otherwise. In the author's experience many more patients who have had simple goiters removed need thyroid than need iodin. The administration of either should be for definite indications rather than as a routine. In mild cases we believe iodin is not required as a routine postoperative medicament. There is no objection to its use in moderate dosage, especially if it be administered intermittently. Moderate dosage from the first to the fifth, and from the fifteenth to the twentieth of each month, is tolerated by most patients over long periods of time.

POSTOPERATIVE COMPLICATIONS

Shock

Owing to improved operative technic and careful postoperative treatment, shock is now rarely seen. If shock should occur the extremities should be bandaged and the foot of the bed or table elevated. If the

patient is afebrile, hot applications are in order. Morphin is beneficial in all cases as is also proctoclysis. In addition fluids may be given by hypodermoclysis and intravenous injection. Adrenalin is effective in those cases with lowered blood pressure. If symptoms of anoxemia or atelectasis are present, respiratory stimulation should be instituted. Blood transfusion is a most efficient measure and, if indicated, should be done immediately.

Acute Thyrotoxicosis

The severe attacks of postoperative thyrotoxicosis so common in former years are rarely encountered today. The introduction of preoperative iodin medication, the improved surgical technic, the substitution of local and nitrous oxid analgesia for general anesthesia, and the more scientific postoperative care have all been factors in the successful prevention of postoperative thyrotoxicosis.

Prevention is more important than treatment. Each severely toxic case should be regarded as a potential victim of postoperative thyrotoxicosis and measures should be instituted previous to and continued after the operation to prevent this complication. Dehydration should be forestalled by forcing fluids. The administration of Lugol's solution should be continued. If it is not tolerated by the mouth, it may be given in solution by proctoclysis, or sodium iodid may be given by the intravenous method.

The first indication of acute postoperative thyrotoxicosis, a slight elevation of temperature, should be watched for. If the temperature rises more than two degrees above normal, artificial elimination of body heat should be begun. An ice cap to the head and one over the region of the heart should be applied, a sponge bath or alcohol rub given, and all covers, except the sheet, should be removed, and the patient exposed to the breeze from an electric fan.

If, notwithstanding measures of prophylaxis, an acute thyrotoxicosis should develop, prompt measures of relief should be instituted. The thyrotoxicosis is usually evidenced early, by tachycardia, hyperpyrexia, marked restlessness, and such gastro-intestinal disturbances as nausea, vomiting, and diarrhea. The psychic symptoms may be pronounced; the extreme physical and psychic restlessness may be followed by mania and this in turn by stupor. In other instances the stupor may be pronounced throughout the entire attack. The rise in temperature may be alarming and sudden. The writer has seen the rectal temperature rise from 102 to 108 within one hour. The immediate danger in the severe case is from the high temperature and it is imperative that this be promptly reduced. The patient may be packed in turkish toweling wrung out of ice water, or a series of ice bags may be placed about the patient outside of the sheet, or again the patient may be covered with a thin rubber sheet with ice packed about outside of this sheet. These measures will, if started in time, be effective in eliminating the excess of body heat.

The Cold Tub Bath

In some cases the sudden onset of a temperature of 106 or 108 makes necessary an immediate artificial elimination of body heat. In these cases

immersion of the patient in a cold bath is the most prompt and successful measure at our command. The water in the tub should be cooled by the addition of ice. A cold vaginal douche or cold enema, given while the patient is in the tub, adds greatly to the effect of the bath. During the bath massage of the body and passive movements of the limbs should be continuous. The massage and passive movements will be helpful in obviating the shivering and discomfort. Ordinarily the patient should be left in the cold bath about fifteen to twenty minutes, but if there is evidence of much discomfort and excessive shivering removal from the bath should not be delayed.

After being taken from the bath, the patient may ordinarily be placed on the bed and exposed to the breeze from an electric fan. The massage and passive movements of the limbs are energetically continued until the patient is comfortable. The rectal temperature is now taken and usually it will be found to have dropped to 103 or 102 degrees. Every effort should be made to keep the rectal temperature below 104. After the heat is eliminated, the stupor and restlessness disappear, the thready pulse of 160 or more slows down, cyanosis becomes less intense and the patient's general condition improves in proportion to the reduction of the temperature. When the temperature drops below 103 it usually means that the attack is over. A second attack, which is less serious and more easily managed, sometimes occurs six to fourteen hours following the first one.

The Ice Pack

Some authorities prefer the ice pack to the cold bath. The temperature is not lowered so rapidly with the ice pack as with the cold bath but it may be used with less physical disturbance of the patient. The technic of its application is not difficult. The patient is wrapped in a sheet and covered with a thin rubber blanket—the mattress is usually covered with a rubber pad—100 pounds or more of crushed ice is packed as tightly as possible about the patient and an ice cap is applied to the head. The temperature will frequently drop two degrees or more per hour. Thin individuals particularly may react quite rapidly to the cold and the fall in temperature may be sudden and continuous. It is consequently advisable that the patient be closely watched and that the rectal temperature and the pulse rate be taken at frequent intervals.

Medication

Iodin given in proper dosage and under proper conditions during the preoperative period and immediately following operation is the most reliable measure for the prevention of postoperative thyrotoxicosis. It is also the most dependable drug for the treatment of the thyrotoxicosis.

At the onset of symptoms, if no iodin has been given previous to operation and there is consequently no contra-indication to its use, Lugol's solution in doses up to 100 minims may be given by proctoclysis or 20 to 30 grains of sodium iodid may be given intravenously. If the condition is not brought under control by the one dose, it may be repeated in four to six hours.

In addition to the hydrotherapeutic measures discussed, the patient with acute thyrotoxicosis should be subjected to energetic support treat-

ment. If seen in the height of the attack with a rectal temperature of perhaps 107 or 108, pulse so rapid that it cannot be counted, marked cyanosis, rapid respiration, restlessness, delirium, mania or stupor, stimulation should be immediately resorted to; one-thirtieth or one-twentieth grain of strychnin given hypodermically at the time the patient is placed in the cold bath is effective in stimulating respiration. Caffein sodium benzoate, given hypodermically as advised by some surgeons, has seemed to us to exercise a rather detrimental effect in severe, acute thyrotoxicosis. We have found whiskey, administered in the following way, of value in critical cases: The stomach is first washed out with cold normal saline solution and then four to six ounces of whiskey diluted with an equal quantity of water is introduced into the stomach by means of the stomach tube. This treatment has, in our opinion, saved several lives that would otherwise have been lost. Following the acute attack, fluids should be forced in order to correct the dehydration present.

Infection

In the early days of goiter surgery the operation was only too frequently followed by severe local infection which terminated in a fatal pericardial inflammation, empyema, or mediastinitis. In the surgery of today a severe infection after a goiter operation is unusual. The blood supply of the region is so abundant that, with proper asepsis, infection is less likely to occur than in other parts of the body. When it does occur, it is easier to control. Nevertheless, infection is an occasional unpleasant sequel to operation and may, in rare instances, be serious.

Infection may be of the following types:

(1) **Mild superficial infection** occurs in the superficial tissues along the line of incision. It is usually caused by staphylococci and reacts promptly to efficient drainage.

(2) **Deep spreading infection in the nature of cellulitis** may, if drainage is not instituted, spread from Burns' space outward into the axilla or from the visceral space downward to the mediastinum. For these conditions the wound should be freely opened, the prethyroid muscles separated, the infected cavity irrigated with some solution such as Dakin's, and effective drainage instituted.

(3) **Abscess formation** is sometimes noted, comparatively late in the period of convalescence; it may be first observed some two or three weeks after the operation. The abscess may be due to infection of a hematoma or of a pool of serum imprisoned in the tissues. It is more often due to the presence of a ligature that has not been absorbed. The possibility of this complication arising from the use of silk or chromic catgut ligatures is an argument in favor of the use of fine plain catgut ones. Incision and evacuation of the abscess will result favorably.

In this connection it is pertinent to emphasize again the danger of sewing together the prethyroid muscles in such a way that little pools of serum or blood may be imprisoned behind them. If precautions are taken

to avoid this undesirable condition, deep infections will be rare and the occasional mild superficial infections are not matters of serious consequence.

Patients, having infected tonsils or teeth, or focal infection such as acne, should receive special consideration. They are more prone to postoperative infection and should receive every possible aseptic safeguard, both during the operation and afterward, to provide against this eventuality.

Hemorrhage

Prevention is the important consideration. Bleeding points should be securely and conscientiously tied at the time of operation. We have never seen postoperative hemorrhage due to the weakening of a suture by absorption. All cases that we have seen have been due to slipping of the ligature off the blood vessels, to the knot becoming untied, or to general oozing from all cut surfaces. The ligature may have been on one of the main trunks or on an apparently small unimportant vessel. It is a worth while precaution to see that the superior thyroid artery is securely tied with two sutures, tied separately.

Postoperative hemorrhage may be noted either in the shape of small continuous oozing or as a brisk hemorrhage from a large vessel. In the latter eventuality no time is to be lost. The necessary operative procedures will have to be carried out in the room. The surgeon should not even waste minutes in an effort to provide all the customary aseptic safeguards. Frequently time cannot be spared to anesthetize the patient completely. The first and most urgent objective is to find the bleeding point and stop the hemorrhage before it is too late. The wound must be opened at once, the bleeding point caught, and the hemorrhage controlled. This done, time may be taken to prepare the operative field as desired and to carry out the further measures necessary. After the bleeding vessel has been tied, the wound may be packed loosely with gauze or may be closed as it was following the original operation.

The chief danger in these sudden hemorrhages is not so much the loss of blood as the probability of interference with the function of respiration. The increasing volume of blood in a closed wound may rapidly cause compression of the trachea and suffocation. It is this danger of suffocation which frequently causes the emergency and makes the prompt opening of the wound and the evacuation of the extravasated blood the necessary consideration.

Oozing, while not so dramatic, is sufficiently serious and practically every case of oozing that persists for ten or twelve hours will demand the reopening of the wound. If the oozing is from a vein or small artery, it may be controlled by gauze snugly packed in the wound. If, in spite of the packing, the oozing continues, the gauze must be removed and the bleeding point or points searched for and tied. Oozing may also, though in a more gradual manner, bring about compression of the trachea and dyspnea. A hematoma may form on the first day but it is more frequently noted on the second or third. Some writers believe that a hematoma which

does not cause dyspnea or pressure may be left without detriment to the patient. We believe that it is better practice to evacuate all blood clots of any size.

Oozing from all cut surfaces presents a different problem. It can usually be controlled by packing and the administration of coagulants. Intramuscular injections of the patient's blood seems to be effective in some cases. The oozing can, in almost every case, be promptly controlled by a transfusion of 250 cubic centimeters of whole blood.

After a severe hemorrhage the condition of the patient is sometimes critical. Hemorrhage, affecting as it does a patient already weakened by thyrotoxicosis and operation, constitutes a grave emergency. The condition sometimes calls for a blood transfusion at the earliest possible moment. In addition to the blood transfusion, such measures as are customary in hemorrhage cases should be resorted to.

Cardiac Failure

Many deaths have been attributed to cardiac failure which, if analyzed more thoroughly, would have been found to be due to other causes. There is a great temptation to classify the sudden deaths from embolism as due to cardiac failure. Traumatism of the anterior jugular vein or its obstruction by pressure in retraction during the course of operation may result in coagulation of the blood in the vessel. When the pressure is removed and the blood pressure, following the operation, ri es especially during vomiting or coughing, the blood clot in the vein may be released and carried down into the general circulation. Such a complication is likely to result in death from embolism.

A considerable pe:centage of such deaths may be prevented if the anterior jugular veins are ligated early in the operative procedure. When cardiac incompetency is present, great care should be exercised regarding the intravenous or subcutaneous method of fluid administration. Unless the cardiac complication is due to toxemia, the indications are for restriction of fluids rather than for their administration.

Recurrent Nerve Disturbances

Occasionally voice disturbance which was present previous to operation clears up very quickly after the goiter has been removed. In such instances the trouble was caused by pressure irritation on the recurrent nerve. With the pressure relieved, the nerve resumes its normal function with natural improvement in voice production. During operation the nerve is sometimes cut through, crushed or caught in a ligature. The consequent paralysis may be partial or complete, depending on the degree of injury and whether the lesion is unilateral or bilateral. In partial paralysis there is usually very little alteration in the speaking voice but the defect is obvious upon coughing. When paresis is present, the cough will not show the usual clear, resonant timbre.

During the course of operation the patient should be observed for evidence of injury to the recurrent nerve. If injury to the nerve is recognized during operation, the nature and extent of injury should be deter-

mined. If caught in a ligature or by a forceps, the nerve should be released. If cut, an attempt should be made to identify the ends and suture them.

After operation the condition may be recognized by a crowing sound which gradually, over a period of a few hours, becomes worse. This sound is present during sleep as well as when the patient is awake. If the condition is recognized, for the first time, after operation, an attempt should be made to determine the nature and extent of injury. If the nerve has been destroyed, the surgeon must decide whether or not an attempt should be made to repair the nerve by suture. Frazier (137) of Philadelphia and others report encouraging results even in old cases from suture of the nerve.

If the nerve has been enclosed in a ligature, the surgeon must decide which affords the best chance for relief: removal of the ligature or reliance upon the possibility that the ligature will be absorbed before permanent damage to the nerve has occurred. If the nerve has been traumatized, as for instance by being crushed by forceps, the symptoms may not develop until several hours have elapsed. A nerve that has not been traumatized too seriously will usually regain its function in four or five weeks. In some serious cases the period for restitution of function may be as long as a year.

Recurrent laryngeal nerve disturbance due to compression by cicatricial tissue does not develop until two to four months after operation. Injury to the nerve from this cause is, in our experience, rare.

Functional Voice Changes

Occasionally a nervous patient will develop functional aphonia. Laryngoscopic examination demonstrates no change in the vocal chords and the surgeon need not concern himself with the matter. The voice will usually return in a few days after the patient is informed of the character of the condition.

Change or alleged changes in the quality and timbre of the singing voice may be a matter of concern for the surgeon. The temperamental artist may decide that his voice is altered for the worse in quality and resonance when as a matter of fact there is no change. The effect of the removal of a goiter on tone production should be favorable.

Respiratory Complications

Postoperative respiratory obstruction may be due to any one of several causes. We should first think of obstruction due to pressure from a hematoma or from gauze packed too tightly. Removal of the gauze or of the clot will eliminate this difficulty.

Respiratory obstruction may sometimes be due to slight edema of the larynx and trachea. For this type of obstruction, steam inhalations, and atropin given hypodermically, are valuable.

Occasionally we note respiratory obstruction due to a hemorrhagic infarct inside the trachea. Intratracheal infarct is due to the tearing off of one of the branches of the intralaryngeal branch of the superior thyroid

artery. This artery enters the larynx and descends beneath the mucous membrane of the larynx and trachea giving off small branches that perforate the walls of the trachea and are distributed to external structures. By traction on the goiter, a branch is sometimes pulled in two at the point where it passes through the opening in the wall of the trachea. The proximal end retracts and hemorrhage occurs.

The infarct is situated between the mucous membrane and the tracheal ring. It produces not only some mechanical obstruction from its actual size and location, but there usually occurs a degree of infiltration and edema in the mucous membrane of the entire surface of that segment of the trachea. The respiratory obstruction consequent on this infarct will not be influenced by such measures as inhalations or atropin.

The dyspnea occurring soon after operation and the blood tinged mucus brought up make the diagnosis. As regards treatment, nothing will afford relief except tracheotomy. A hemorrhagic infarct may be absorbed in four to six days but in the meantime the patient must have relief.

Respiratory obstruction may be due to collapse of the trachea. The tracheal rings, softened by long pressure of the goiter, collapse during the maneuvers of the operation. The collapse is usually accompanied by flapping of the tracheal walls and the obstruction affects only inspiration. This type of obstruction is sometimes partially relieved if the patient assumes a suitable posture and practises slow and careful breathing. The best position for breathing seems to vary with the individual; as a rule, holding the head forward with the chin up gives the most comfortable position. Sometimes the patient can breathe comfortably lying on his side. Distention of the trachea by blowing into a bottle from time to time sometimes seems to increase comfort. This type of obstruction will as a rule, improve spontaneously after a few hours. Meanwhile, during the period of discomfort, sedatives may be used; the best perhaps is codein in dosage of $\frac{1}{2}$ grain. Atropin seems to aggravate the dyspnea when the obstruction is due to collapse of the trachea.

In urgent cases more strenuous measures must be resorted to. If the tracheal collapse is noted at the time of operation, a suture or two may be passed through the collapsing walls uniting these to the muscular layer. The type of suture used and the method of application should insure that the trachea be held in contact with the muscles until it has become sufficiently adherent to prevent further collapse.

Intubation tubes cannot be used for tracheal collapse owing to the fact that the obstruction lies at a lower level than that which can be reached by the tubes. Tracheotomy affords immediate relief and should be resorted to before the condition of the patient becomes critical. The tube can, as a rule, be removed in forty-eight hours and the convalescence is usually prolonged not more than two or three days by the tracheotomy.

Bronchitis and tracheitis are occasional postoperative incidents. For these conditions, steam inhalations or inhalations of compound tincture of benzoin from a croup kettle are helpful. Pneumonia and pulmonary edema very rarely follow an operation performed under local or gas anes-

thesia. Pulmonary embolism may occur following operation and is attended by considerable respiratory difficulty. It is usually unilateral and is not complicated by definite symptoms of obstruction.

In old asthmatics, respiratory difficulty due to spasm of the larynx is sometimes distressing. These cases are usually given prompt relief by the administration of adrenalin.

Genito-Urinary Complications

Urinary complications are seldom encountered in the young. In older persons, men especially, one may expect retention in the bladder. Catheterization should be reserved for a last resort and various measures should be tried in an effort to procure relief without it. Many old men will void if they are permitted to sit up on a commode. If the operation has been performed without the cutting of muscles, the patient can as a rule get out of bed on to a chair commode, at any time after operation without danger. If the prethyroid muscles have been cut, it is perhaps better to resort to the catheter although one catheterization may make repetition of the procedure necessary and, if cystitis follows, it is a serious complication.

Parathyroid Deficiency

Parathyroid deficiency is a serious complication, or at least, one that is difficult to manage. The parathyroid deficiency may appear immediately after operation or may not be evidenced until after the patient has returned home. The treatment will be discussed in the chapter on the Parathyroid Glands.

Thyroid Deficiency

Transitory myxedema sometimes occurs following operation owing to decreased function from inflammatory reaction in the traumatized gland. The symptoms of this type of myxedema appear about two or three weeks after operation and disappear within three or four months. Temporary thyroid medication is indicated. Equally important is the stimulation of elimination. One grain of calomel given in broken doses on each fifth day and followed by a saline laxative on the day following has, in our hands, given good results. A change of climate for this type of patient is often quite beneficial.

If the transient myxedema is due to disturbances of the blood supply to the portion of the gland remaining, clinical improvement will be slow and gradual. The maximum improvement may not be reached for more than six months. In these cases thyroid medication is imperative to tide the patient over the interval.

In some cases, deficiency of thyroid function is of long standing and is not the result of the goiter operation. In other cases, the operation is in all probability responsible. In either event, it is of utmost importance that the extent of the deficiency and the amount of thyroid required to correct it be discovered. The amount needed to maintain perfect health usually becomes smaller during each of the first five years subsequent to the operation. Of fourteen patients who have been under observation for

more than fifteen years since operation, five require only 10 grains of desiccated thyroid per week and nine require only 5 grains per week for the maintenance of perfect health.

Fixation of the Scar to the Trachea

In rare cases the scar becomes attached to the trachea, particularly if drainage has been prolonged. Owing to this attachment, the scar will be seen to rise and fall during the act of swallowing and for this reason becomes much more noticeable. In addition, the patient complains of an unpleasant pulling or dragging sensation. Treatment consists in excision of the scar tissue, and approximation of the separated fascia and muscles in such a way that the overlying skin is free. The operation is not difficult and good results may be expected.

Unsightly Scar

An unsightly scar constitutes a reproach to the surgeon and is a result to be avoided. The proper technic for the incision as already described will minimize this possibility.

Gradual hypertrophy of the scar tissue follows operation and continues for three or four months during which time the scar becomes thicker, red, sensitive and inelastic. The hypertrophy ceases and gradual atrophy of the scar tissue normally begins at about the third or fourth month. The scar gradually changes from red to white and becomes finer and more elastic. The atrophic process may continue over many months or even years and finally only a fine, white, elastic, mobile scar remains. In some instances, when the hypertrophy is stimulated by an irritation such as infection or drainage, the hypertrophy continues and atrophy does not occur. If the hypertrophy is not checked, an unsightly scar or possibly a keloid will be the result. Should the hypertrophy be excessive or continue longer than twelve weeks, x-ray or radium treatments should be instituted. If started in time only light doses are required but if the scar has become thick, rigid and sensitive, especially if keloid formation has occurred, larger dosage is necessary for satisfactory results.

Irregularity of Contour

In large goiters of long duration the relationship of the tissues and the structures of the neck have been definitely altered. A certain amount of tissue absorption has taken place and in some instances the normal contour has been permanently lost. Occasionally a female patient is disappointed if the operation does not give her a perfect neck of classic outline. It is well to bear this in mind and to advise such patients before operation that the removal of the goiter may not entirely meet the expectation of the patient as regards beauty and symmetry.

CHAPTER XVI

HYPOTHYROIDISM

The direct effect of thyroid deficiency is the retardation of all the vital processes. The indirect effects, through this retardation of the vital processes, are the subthyroid syndromes: myxedema, cachexia strumipriva, and examples of repressed differential development (cretinism, infantilism, deaf mutism, deformities and subnormal mentality). These syndromes vary in intensity with the degree of thyroid insufficiency, the suddenness with which the thyroid deficiency occurs, and the age and stage of development of the individual at the time that thyroid function was diminished or abolished.

All the vital processes, physical, mental and emotional, are dependent upon thyroid function. In adult life the repression of these is manifested by subthyroid syndromes such as lowered metabolism, myxedema and cachexia strumipriva. The repression of the vital processes of the mother by thyroid deficiency affects the child in utero greatly. This is evident after birth. This evidence consists of retarded or disturbed differential development such as cretinism, deaf mutism, deformities and subnormal mentality. Thyroid deficiency in childhood and youth produces both the subthyroid syndromes seen in the adult, and various degrees of retarded or disturbed differential development.

Hypothyroidism may be due to functional insufficiency of the gland itself, or may be due to a deficiency in the available supply of iodin or other constituents necessary for the elaboration of the thyroid hormone. Functional deficiency of the gland may be due to athyroidism, destruction of gland tissue by disease, or surgical removal.

When due to athyroidism, it dates back to infancy and is attended by disturbances of differential development. In a large percentage of cases of athyroidism, the defective development of the gland itself is the result of retarded development of the gland during fetal life in the mother.

When due to destruction of the gland by disease, the deficiency appears later in life and is usually accompanied by gross degenerations such as large degenerated adenomas.

When due to surgical removal of gland substance, it follows the operation within a few weeks.

As the various manifestations of hypothyroidism or athyroidism are considered, usually, as clinical entities, the following hypothyroid states will be discussed separately.

1. Myxedema { Postoperative (Cachexia Strumipriva) / Spontaneous
2. Cretinism
3. Mild, almost imperceptible, types of hypothyroidism

4. Incomplete, undeveloped or fruste types of myxedema
5. Infantile type of myxedema
6. Cretinoid conditions
7. Co-existent hyperthyroidism and hypothyroidism

MYXEDEMA

The result of hypothyroidism, appearing after differential development is more or less complete, is a condition called myxedema which is characterized by a retardation of the vital processes, and by certain trophic manifestations. The retardation of the vital processes is evidenced by a low rate of metabolism, mental apathy, and physical sluggishness. The trophic disturbances affect the teeth, nails, hair and skin.

The name was derived from the edematous condition of the skin but all the tissues of the body are affected. The characteristic infiltration can be seen in swelling of: the subcutaneous tissues of the face, supraclavicular region, neck and the mucous membranes of the orifices of the body. The mucous membranes, peritoneum and such organs as the brain, the kidneys, the suprarenals, and the gonads are also affected by the mucinous infiltration. The peritoneum covering the mesentery of the intestines and the broad ligaments is light in color and obviously thickened. The swelling of the mesentery from the infiltration is so marked in severe cases that one might interpret it as evidence of inflammation were it not for the light pale color of the peritoneum and the absence of free peritoneal fluid. The peritoneum covering the intestine is thickened at the mesenteric margin but over the rest of the circumference of the intestine it is pale, glistening and very fragile.

Myxedema may be postoperative or spontaneous. The term suggested by Kocher (138), cachexia thyreopriva, is usually applied to myxedema that follows the surgical removal of the thyroid. Postoperative myxedema generally occurs at a later period in life than spontaneous myxedema and is more amenable to treatment. Spontaneous myxedema results from atrophy or loss of function of the thyroid from disease.

SPONTANEOUS MYXEDEMA

Onset.—The onset is usually insidious and the symptoms are frequently first noted in middle life. Women are much more frequently affected than men. The patient may have had a simple or nodular goiter of several years standing. The patients often complain first of a tired feeling and languor, dyspnea and palpitation on exertion, swollen face, hands and ankles, increased weight, and dry scaly skin. Objectively, they present evidence of mental sluggishness, indifference, poor memory, lack of interest, irresolution, and apathy. Frequently, owing to this apathy and indifference, it is quite difficult to obtain anything in the form of a reliable history from the patient. Very often, the myxedematous patient complains of cold and chilliness. He lacks initiative and is disinclined to exertion.

Physical Signs

The Skin and Appendages.—The skin changes are quite characteristic. The skin and subcutaneous tissue are thickened and infiltrated with a mucin-like substance. It is to this last named fact that it owes its name.

The edema in myxedema is at times marked, but differs very materially from the true edema due to other causes. The chief characteristic of the edema is that it does not pit on pressure. The eyelids are pouchy and swollen, and the eyes seem small and lusterless. The edema, if it may so be called, is really an expression of a greatly slowed metabolism. Owing to the imperfect cell catabolism, cellular debris accumulates in the skin and other tissues and gives rise to the characteristic thickening. This thickening is often most noticeable in the face. The features are coarse, heavy and swollen. The skin is scaly, dry, and rough. The ears are thickened and frequently present a cauliflower-like appearance. Due to the mental and skin changes, the face presents a heavy, apathetic, infantile appearance. The nose is thick and coarse, the lips are thick and sometimes of a negroid type; puffiness under the eyes is frequently noted.



Fig. 95.—Hypothyroidism (5 Year Old Child).

The complexion is white and pasty with patchy areas of cyanosis or pigmentation. Fatty deposits are rather characteristic, particularly supraclavicular pads of fat and marked deposits of fatty tissue in the loins, abdomen, and hips. Itching is often severe and may be almost intolerable. The nails are brittle and the hair is coarse and scant. This applies to the hair of the axilla and the pubis as well as to the hair of the head. The hair is often prematurely gray and when of normal color is dull and lacking in luster. Leopold Levy describes an eyebrow sign, i.e., sparseness of the hair at the outer third of each eyebrow.

The hands are thick and spade-like. The fingers are stubby and thick. This appearance of the hands is characteristic. The feet are also at times apparently thick and swollen.

Some degree of relaxation of the articular ligaments is sometimes noted. "Double joints" are often observed and marked hyper-extension of the fingers is at times noticeable. Scaly or icytyotic rashes are frequently noted on the inner surfaces of the forearm and legs.

Systemic Involvement

The Nervous System

There is no definite involvement of the motor nerve. Sensory disturbances are frequent and sometimes annoying. Headache is quite frequent. It is sometimes occipital but for the most part frontal; occasionally it may be generalized. The headache is said to be most noticeable in the morning. Other sensory disturbances are giddiness, roaring and buzzing in the ears, unusual noises, such as ringing of bells, etc.

The patients are usually drowsy but the drowsiness is more marked after meals. They are unrefreshed by slumber and feel listless and apathetic even after long hours of sleep.

The mental and psychic changes are constant and characteristic. There is lack of memory, lack of initiative and disinclination for effort, confusion of ideas, indifference, apathy, lack of confidence, inferiority complex and sometimes irritability. Melancholia is not infrequent and other of the major psychoses are sometimes seen.

The Osseous System

Considerable infiltration of the joints and ligaments is typical. Joint crackling, similar to that seen in chronic rheumatic conditions, is frequent.

Gastro-Intestinal

Gastric disturbances are frequent, constipation being the rule. The digestive and assimilative processes are below normal. Symptoms of intestinal stasis are often present. Hertoghe (139) believes that the gastro-intestinal disturbances are largely due to the fact that the tissues of the intestines suffer from infiltration as do the skin and subcutaneous tissues. This infiltration, in turn, causes some degree of bowel paresis with constipation and other secondary symptoms.

The tongue is coarse and thick and often heavily coated. The difficulty in speech, which is sometimes noted, may perhaps be due to the thickening of the superficial tissues in the tongue.

Cardiovascular

The pulse is frequently slow and small. In late cases it may be rapid and small or irregular due to myocardial changes. The blood pressure is low in the early cases but hypertension is common in the late cases. The pulse pressure is usually low even in the cases with hypertension. The heart changes are not characteristic.

The Blood

Frequently a secondary anemia of moderate or mild degree is present. Some diminution in the number of the red corpuscles is noted with a corresponding proportional decrease in the hemoglobin content. There is often a leukopenia with an increase in the number of lymphocytes. The coagulability of the blood is sometimes reduced.



FIG. 96A.—A Family Group in which Goiter was Endemic.



FIG. 96B.—A Family Group in which Goiter was Endemic.

The Special Senses

Disturbances of the functions of the sense organs are rather frequent. Deafness of varying degrees is not uncommon; tinnitus and other auditory disturbances have already been referred to. Vision, taste, and smell are frequently impaired. Touch and cutaneous sensibility are often decreased. This impaired sense of touch in the feet and hands is perhaps the explanation of the uncertain, peculiar walk and the clumsy movements of the hands often observed in these patients.

Basal Metabolism

The basal metabolic rate is lower. Plummer (140) has made careful study of the basal metabolism in myxedema and finds a relationship between the basal metabolism and the appearance of edema. He finds that edema does not appear until the metabolic rate has fallen to minus fifteen or minus seventeen. Plummer claims that this relationship is rather constant and feels that, when the basal metabolism is below minus twenty, if edema is not present the diagnosis is doubtful.

It must be remembered that several other conditions, as pituitary involvement, malnutrition, inanition, may be accompanied by a fall in the metabolic rate.

It may be interesting here to note the observation which Plummer (141) has made regarding the degree of thyroxin deficiency in myxedema. He has demonstrated that the tissues of the normal body, exclusive of the thyroid gland, contain about 14 mg. of thyroxin.

He has further shown that the tissues use daily between 0.75 and 1.0 mg. of thyroxin, and perhaps as the most interesting demonstration of all, has shown that approximately 22 mg. of thyroxin given by the intravenous route will raise the metabolism of a case of myxedema to the normal level.

Further metabolic studies in myxedema and other hypothyroid conditions are indicated. It will doubtless be shown that reduced metabolic rate is as characteristic of hypothyroid conditions as increased metabolic rate is of hyperthyroid conditions. Furthermore, with a more refined technic and more conscientious observations, study of the metabolic rate will probably prove of considerable import in the diagnosis of obscure hypothyroid conditions, which at the present time escape observation.

Treatment

The prognosis for the specific treatment of myxedema will depend on the amount of visceral damage already present. Thyroid extract can only supply artificially the equivalent of the thyroid hormone which is essential to proper function of the organs; if these organs are broken down, it cannot reconstruct them.

In every case of myxedema we must be exceedingly cautious in instituting thyroid therapy. If serious cardiovascular trouble is present, the heart should be put in the best possible condition before the gland preparations are given; a short period of rest in bed is advisable; digitalis or strophanthus may be indicated in a particular instance to improve

the heart function. If anemia is present and severe, it is advisable to put the patient on a preliminary course of treatment for this condition.

The initial dosage in myxedema of long standing must be very small; here in contradistinction to cretinism one must err extremely on the side of caution; one should not be in too much of a hurry to bring the basal metabolism up to normal; in fact, the patients very often feel better if the metabolism is allowed to remain, consistently, a trifle below normal. This point is not generally grasped, and yet it has considerable significance; the patient has had perhaps for years a greatly depressed metabolic rate, and we should realize that bringing it up to normal within a short period of time is apt to be fraught with considerable physiologic upset.

After we have once determined a maintenance dose at which the patient is relieved and comfortable, the rest is usually easy, and the treatment will be along the lines already sufficient indicated.

POSTOPERATIVE MYXEDEMA

Cachexia thyreopriva or postoperative myxedema may appear in a few weeks, months or even years after thyroidectomy. In the cases in which the condition does not develop for years after operation it is usually due to further destruction of gland by disease and is chronic. Some degree of hypothyroidism, accompanied in some cases by myxedema, not infrequently appears about the second or third month following operation. In 98 per cent of these cases the myxedema is transient disappearing spontaneously in three to six months after its onset. In the other 2 per cent of cases, it is chronic, persisting for years. With the passage of years, however, less thyroid medication is required, even in the chronic cases, to control the symptoms.

In mild cases the edema may spontaneously disappear and all the symptoms may improve or become stationary with the exception of a progressive increase in weight. The progressive increase in weight is often accompanied in these cases by a slow rise in blood pressure and cardiovascular changes. For this reason every effort should be made to effectively correct, by replacement therapy, even the milder degrees of postoperative hypothyroidism.

In severe untreated cases the symptoms are more pronounced. The basal metabolic rate may drop to minus forty or even minus fifty. With the drop in the metabolic rate the edema extends to other parts of the the body. The patient becomes apathetic and melancholy. Psychoses are sometimes present, especially in the morning. In severe cases the weight may not be increased although the myxedematous infiltration is pronounced, the face being puffy and pale yellow and the tongue and the mucous membrane of the nares, pharynx and larynx thickened and edematous.

Treatment

The only effective treatment for postoperative myxedema is the correction of the thyroid deficiency by the proper administration of thyroid. The earlier thyroid medication is instituted the easier it will be to control the myxedema. The regulation of the dose is of the greatest

importance. In early cases large doses may be given from the first and continued until mild symptoms of hyperthyroidism appear. In the severe or chronic cases the stimulation of the vital processes must proceed with caution. In late cases with cardiovascular disturbance it is safer to begin the thyroid medication with very small doses—not more than $\frac{1}{4}$ grain of desiccated thyroid three times daily and increased slowly; a monthly increase in dose of more than $\frac{1}{8}$ grain is rarely indicated.

In the early cases, with no cardiac weakness, treatment may be commenced with one to five grains of desiccated thyroid given three times daily. Under such treatment the length of time required for tachycardia, flushing or other symptoms of hyperthyroidism to appear affords a basis for the estimation of the approximate amount of thyroid required to correct the deficiency. Upon the appearance of symptoms of hyperthyroidism the thyroid medication should be discontinued for a period of two weeks or more and then resumed in smaller doses.



Fig. 97.—Sarcoma (9 months).

The amount of thyroid administered should be increased slowly or decreased promptly according to the indications of results obtained until the proper dose for correction of the deficiency is determined. After the tone of the heart muscle is improved the dose may be increased in size and given at more frequent intervals until the deficiency is corrected. It may require many weeks or months to safely bring the chronic myxedematous patient back to a normal metabolic condition.

CRETINISM

Cretinism is the most severe manifestation of disturbed differential development from hypothyroidism. It was early recognized, in Switzerland and some other endemic goiter regions, that there was some relation between the incidence of cretinism and the incidence of simple colloid goiter, in a community. It was thought that the cretin usually had goitrous parents, grandparents and great grandparents. In endemic goiter regions it is sometimes a familial disease, and in such cases the incidence of cretinism and colloid goiter are both high during succeeding generations.

In America, as in the British Isles, the incidence of endemic cretinism is low, and the cases seen are of the sporadic variety. The condition is usually congenital but may be unnoticed until the child is several months old. In the majority of cases seen in this country the thyroid is in an

infantile or undeveloped state. The small thyroid has been in many cases thought to be an atrophied or diseased thyroid. Histologically, it resembles the undeveloped gland of the fetus and is usually very small in size unless colloid distention or cystic degeneration has occurred.

Stature

Nanism or dwarfism is one of the characteristic and striking signs of cretinism. This impairment in physical development is the essential differential feature in athyroidic conditions in the child and in the adult. The impetus to skeletal development is not present and the bony framework remains undeveloped and infantile. Frequently, even in adult life the cretin is only three feet tall or less. The limbs are short, the abdomen protuberant. The condition of "pot-belly" is common and very noticeable and is sometimes associated with large umbilical hernia.



Fig. 98.—True Cretin.

The Bones

The bones often present changes quite similar to those seen in rickets. They are broad, thick and show various degrees of deformity. The spine is frequently involved and kyphosis and scoliosis are frequent. The skull of the cretin is broad and low. The tables are thick and the delayed closure of the frontenals is the rule. The inferior maxilla is heavy with a suggestion of prognathism.

Facies

The facies is quite characteristic and usually will of itself establish a diagnosis. The head is large and disproportionate to the size of the body. The face is dull, expressionless, with eyes vague, and lusterless. The forehead is low and wrinkled. The lips are thick, the mouth often held agape, frequently with the tongue protruding. The tongue is large, thick and frequently cannot be held, even with effort, in the aural cavity. Together with protrusion of the tongue, there is a constant drooling of saliva. The other features are also often distinctive, the "saddle-nose," the averted and thickened ears, and the flabby cheeks. The eyelids are thick and heavy, the hair is coarse, dental caries is the rule. The fontanelle may remain open until the tenth year, and may not be closed even in adults. The neck is short and thick, and fatty pads are often noted in the supraclavicular regions, between the scapulae, or in the axillae. They are usually symmetrical and often the size of a small hen-egg.

Extremities

The extremities are short and stubby, toes are often swollen and painful, the gait is wabbling and awkward. The cretin usually walks late and may be four or five years old before he takes his first step. The extremities, indeed the whole body, feels cool, and the temperature as taken by rectum is below normal.

Genital Apparatus

The genital apparatus does not develop and remains infantile throughout life.

The Mentality of the Cretin

In congenital athyroidism, the degree of idiocy is the most extreme imaginable. There is apparently no glint or scintilla of intelligence. The level of intelligence is debased below that of the lower animals. They do not recognize their parents, are apparently totally insensible to their environment, and are unresponsive to kind or unkind treatment. They will not feed themselves, and will starve even with the food within their reach. Their functions and reactions are suggestive of vegetative rather than animal existence. So striking is the absence of normal animal reactions in this type of cretin that Roesch has called him the "manplant." His reflexes, superficial and deep, are diminished; he is often loath to move and will remain in an uncomfortable position with the sunlight directly in his eyes for a long period. The cretin of this type is often inclined to be drowsy and sleeps a great part of the time. He is impervious to all impressions or stimuli from his environment and cannot be taught even the most rudimentary conceptions of cleanliness and hygiene. Fortunately most cretins of this type die young, in fact in the first few years of life.

Lesser Degrees of Idiocy

In the cretins who have not been totally deprived of thyroid secretion from birth varying degrees of intelligence are seen.

They are still idiots, dull, placid, undisturbed by conditions and events to which the normal child would react. Many of them will smile and reach for playthings; they recognize their parents and seem appreciative of kindness. They can be taught cleanliness and health habits. They are good natured, apparently fairly content, and as a rule are not excitable or troublesome. At the age of fifteen or eighteen, they may show the mentality of a two or three year old child.

Unless administered very early, thyroid extract will not have, by any means, as striking an effect on the mental as on the physical symptoms. Theoretically if thyroid extract is administered from birth or soon after, and if its administration is conscientiously and scientifically adhered to, the child should develop an approximately normal mentality. Practically, however, these ideal conditions are never met, and the cretin child even after the administration of thyroid extract over prolonged periods, will always show some degree of mental defect.

The intelligence of the individual cretin varies within very wide limits. There is perhaps a greater intelligence chasm, between the "man-plant" and the high grade cretin, than there is between the high grade cretin and the normal human. The point at which the intelligence, as well as the physique, ceases to be cretin and becomes cretinoid is vague, just as the point at which a subthyroid condition may be termed myxedema is vague. Many of the cretins can absorb considerable teaching of a simple nature, and may be taught to perform simple tasks and make themselves useful in many ways.

They do not offer as great an economic problem as one might suppose as many of them die in childhood. Quite a few, however, live to adult life and, in rare instances, to the age of sixty or over and, of these, some are able to care for themselves adequately, both physically and financially. Impairment of the special senses is often an additional handicap to overcome and a further bar to their usefulness. The hearing is frequently impaired, indeed often they are quite deaf, and sometimes both deaf and dumb.

Sometimes they show a rudimentary speech faculty. Their speech is garbled, fragmentary, stumbling and unintelligible to all but their immediate relatives or parents, who have learned by experience to interpret the mumbled sounds.

Response to stimuli of all kinds is lessened. This applies to physical as well as to psychical stimuli. Their cutaneous sensibility is lessened, and is sometimes quite noticeable.

The Course

The course is progressive and the development of the symptoms very variable, depending on the total or partial absence of thyroid secretion and the age at which this thyroid secretion develops. The endemic cretin is long-lived, and the condition, mental and physical, may remain unchanged for years. He may be physically active and show varying degrees of intelligence. In the case of the cretin suffering from congenital athyroidism, this arrest of the symptoms over a period of years is not noticed. The symptoms become intensified and the patient usually dies young.

Treatment

The cretin of course should have been treated through his ancestry; his grandparents and forbears should have received treatment for their goiter conditions.

The cretin, however, is here; what can we do for him? We can do much if we have the case under observation sufficiently. The sooner we see the cretin after birth, the better the outlook. This principle is particularly true as regards the development of the mental faculties. As regards the physical development, the thyroid preparation, seems to act on it as does the rain on a withered shrub; growth and physical development recommence appreciably and almost immediately; the physique was in "hibernation" and was awakened by the stimulus of the thyroid

hormone. In suitable cases and sufficiently early, the definite improvement in such a short time might almost be termed miraculous.

Osler, who seems to describe everything a little better than anybody else, speaking of the improvement in such cases subsequent to the use of thyroid extract, says "Not the magic wand of Prospero, or the brave kiss of the daughter of Hippocrates, ever affected such a change."

Can the born cretin ever be brought up to normal mentally and physically? This is, of course, a difficult question to answer; we do not know the exact ratio of mental to physical development of the fetus in utero; we must assume that the ten months in utero constitute a most important period in psychical development. We see individuals who were alleged cretins at birth, and who apparently have reached a fairly normal maturity, both mentally and physically. We are not absolutely assured, in many instances, as to the correctness of the diagnosis (as to whether the child was totally deprived of the thyroid hormone); nor have we any standard by which to measure the individual in question. Our only standard for the alleged cretin baby, would be a mirror image of himself (a complete mental and physical duplicate) with the presence of normal thyroid function reversing the picture.

Undoubtedly, however, we do see very great improvement; even if we cannot attain perfection, we can hope in many instances, to convert a potentially useless idiot into a useful member of society, able to care for himself and make his way acceptably through life. This is a sufficiently brilliant objective and worthy of our best efforts.

In treating the cretin we should err on the side of boldness rather than caution. We should at first push the dosage until definite evidence of the pharmacological action of the thyroid preparation is noted—we may have had foisted on us in a particular instance, a drug of reduced potency, and time is too precious to waste; every day counts. We should push medication until we note a little nervousness, tremor, tachycardia, and rise in temperature. From the information derived we can estimate the approximate dosage required for the individual case.

The usual initial dosage, for the cretin child under one year is ½ grain of the desiccated gland daily; between one and two years, 1 grain of the dried gland daily, and in older children 2, 3, 4, 6 or more grains daily depending on the age and the effect.

It will be found that for the growing cretin the dose will have to be changed two or three times or more to meet the increasing demands of the growing organism.

Holt advises the preparation of thyroid extract put out by Burroughs Wellcome and Company in doses of ½ grain at first, once or twice a day; later as tolerance grows the dose may be gradually increased to 5 or 6 grains.

After the period of growth has passed, the dosage can usually be decreased and a definite maintenance dose determined upon. The maintenance dose varies within wide limits and may range from 1½ or 2 grains of the desiccated gland to 6 or 8 grains a day. If the thyroid extract is used, the daily maintenance dose varies, from ½ or 1 grain daily to 2 or 3 grains.

If thyroxin is used intravenously from 1/185 to 1/85 is advised as the maintenance dose.

It is of the utmost importance to continue the medication according to schedule. If the thyroid medication is stopped, the results are soon evident, and mental and physical retrogression is soon noted. The retrogressive change is obvious in two to eight weeks. Some writers speak of retrogressive change definitely apparent in a day or two after thyroid therapy has stopped. The dosage must indeed be very finely drawn and the hormone balance very delicate if deprivation symptoms are so soon noted.

The changes resultant on thyroid medication are often remarkable enough; the cretin whose growth had become arrested, commences to grow again and may gain four to six inches in a year; the size and shape of the head tend more towards the normal; the idiotic expression becomes less marked and is finally lost; the thickening of the skin and coarsening of the hair disappear; the muscular power is improved, and the patient shows inclination to walk; later physical hyperactivity is often noted and must be checked.

Mental improvement also takes place, but not pari passu—not with equal strides; however, the improvement even in this respect is often remarkable enough: the child learns to talk and is able to go to school. Practically, although always in a more or less retarded grade, he is in a position to gain some degree of education and get something out of life. Occasionally one of these "salvaged cretins" shows special aptitudes along certain lines, music for instance, and may in rare instances, become surprisingly proficient.

MILD, ALMOST IMPERCEPTIBLE TYPES OF HYPOTHYROIDISM

Probably the number of sufferers from the very mild types of hypothyroidism is legion. Probably also many obscure ailments of a temporary nature are due to a temporary diminution of the secretion of the thyroid glands.

It would be far-fetched and visionary to attribute the characteristic temperaments of the different age periods to changes in the structure of the thyroid gland and in the character of the thyroid hormone. Nevertheless there is an interesting thought hidden in this conception. In youth we have a fresh and active thyroid and we have exuberance, idealism, ambition, energy, combativeness, optimism, hope; in old age we have a sclerosed and worn out gland, and we have indifference, apathy, forgetfulness, pessimism,—in short, worn out emotions as well as a worn out thyroid.

It is difficult in most instances, or even impossible to clinically recognize the mild types of hypothyroidism. It is only through the medium of thyroid therapy that the underlying condition of thyroid insufficiency becomes evident. Some obscure chronic or subacute condition which has resisted all treatment becomes readily amenable to opotherapy. It may be a question of chronic headache, constipation, flatulence, vague joint or muscle pains, chronic rheumatism, dysmenorrhea,

amenorrhea, chronic skin lesions, or in fact any number of vague disorders for which not a signable cause is apparent.

The expression "Hypothyroid Temperament" is used by the French writers to describe those individuals who show a leaning toward hypothyroidism. They may give no distinct evidence of hypothyroidism, but they convey the impression that they, either potentially or actually, are laboring under the handicap of insufficient thyroid secretion.

This disorder may be of long standing and may have tried severely the endurance of the patient and the patience of the physician. Finally the administration of thyroid extract is decided upon as a last resort and both the patient and the physician are agreeably surprised.

Hertoghe, especially has made a very exhaustive and scholarly study of these mild hypothyroid conditions and the reader is referred to his works for a complete survey of the subject (139).

These mildly hypothyroid individuals show no definite group of symptoms upon which one can base even a tentative classification. The patient may be over weight, and complain of no other symptoms. The reduction in weight on the administration of even small doses of thyroid extract may be so prompt and so satisfactory that the question of hypothyroidism is immediately raised.

A school child, for instance, may present a goiter of puberty and simultaneously experience some difficulty in keeping up with his classes. He does keep up, however, but is quite conscious of the effort. A little thyroid extract, given for the simple goiter, has the effect of reducing the size of the goiter, almost immediately the child learns faster and experiences no effort in keeping up with his classes. Innumerable instances might be given in which obscure disorders have immediately cleared up on the exhibition of thyroid preparations showing definitely that insufficiency of the thyroid hormone was the basis of the condition.

To summarize:

Mild hypothyroid disorders are much more common than the usual conception.

These mild hypothyroid conditions present no definite clinical syndromes and must be suspected rather than demonstrated.

A vague chronic disorder for which no demonstrable cause can be found, should arouse suspicion of hypothyroid origin and should be given the benefit of treatment with thyroid preparation.

Conditions not usually associated with thyroid disorders, as chronic rheumatism, dysmenorrhea, constipation, may be directly due to insufficiency of the thyroid hormone. This should be kept in mind in chronic conditions of this kind which have resisted other forms of treatment, and the patient should be given the benefit of opotherapy.

INCOMPLETE, UNDEVELOPED OR FRUSTE TYPES OF MYXEDEMA

The incomplete or fruste type of myxedema is probably much more common than the fully developed or classical type already described. The incomplete cases present some of the characteristic symptoms of myxedema but fall short of the complete clinical picture.

The fruste form of myxedema may appear after operation or may occur spontaneously. The patient gains in weight, the mentality becomes a little dulled, ambition and energy is decreased, the skin symptoms may be very slight, barely noticeable, or even entirely absent. The basal metabolic rate may be slightly lowered.

The course of the fruste type of myxedema may be exceedingly chronic. The disease may remain stationary in the fruste stage for months or even years without noticeable change; there may be present enough thyroid secretion to keep the individual at a definite sub-thyroid level, without allowing the condition to progress to the stage of typical myxedema. Individuals with the fruste type of myxedema react very well to thyroid medication.

INFANTILE MYXEDEMA

Infantile myxedema develops during childhood before physical or mental maturity is attained. Consequently, as we would expect, in addition to the symptoms of myxedema, as already described, we note skeletal changes, sometimes amounting to dwarfism, and in addition mental change or retardation of varying degree. The amount of mental and physical deterioration will depend upon the age which the thyroid hypofunction occurred, as well as upon the degree of thyroid insufficiency.

CRETINOID CONDITIONS

As mild hypothyroidism is much more common than typical myxedema, so also cretinoid conditions are much more common than true cretinism. In certain localities, in which goiter is highly endemic, cretinoid degeneration is almost the rule. In some European countries in the past, cretinism at times reached a level of sixty or more per hundred thousand. With this high level of true cretinism, it would be difficult indeed to estimate the incidence of cretinoid degeneration in the community.

In some localities it was said to be difficult to find an individual of perfectly normal physical and mental development. Almost the whole population showed some evidence of cretinoid degeneration. This cretinoid degeneration may be evidenced either in the mental or physical development. Slight degrees of mental retardation may be the rule and the majority of the school children may be very slightly, almost imperceptibly below the normal standard. Cretinoid degeneration is reflected in the character and disposition, and it seems true that in many communities very many individuals are jealous, envious, quarrelsome, without ideal or ambition.

In highly endemic communities cretinoid degeneration is also evidenced in rather frequent impairment of the special senses. Impairment of hearing, often amounting to total deafness, is common; deaf mutism is also not infrequent; speech disturbance, as stammering, stuttering, faulty enunciation are common.

Cretinoid degeneration in endemic communities is evidenced in a poorly developed general physique. The stature is often below normal. The musculature is not well-developed. Evidence of defect in skeletal structure is noted, as kyphosis, scoliosis, rachitis, etc.

CO-EXISTENT HYPER- AND HYPOTHYROIDISM

Hypothyroidism or even severe myxedema is sometimes seen with co-existent Graves' disease as well as with co-existent degenerated adenomatous goiter. It is easy to understand the appearance of myxedema due to destruction of normal gland tissue by adenomatous degeneration. It is more difficult to conceive of myxedema in the presence of Graves' disease. Yet we occasionally encounter cases in which both are present.

Sometimes myxedema will appear before the thyrotoxicosis has entirely subsided. We have encountered several severe late cases of Graves' disease with plus 30 to plus 40 basal metabolism and characteristic symptoms of myxedema. These patients respond well to the administration of a good preparation of thyroid. The fresh gland is much more effective in these cases than any extract or other dried preparation. However, the Graves' disease is usually of long standing and the areas of gland involved have reached the stage of fibrosis popularly called "burnt out" and are non-secreting so far as normal thyroid hormone is concerned before myxedema occurs.

If the thyrotoxic patient has the resistance to last through several years of the toxemia of Graves' disease, if she is fortunate enough to last through the crisis and other accidents of the disease, she may reach a stage of comparative tranquillity in which most of the symptoms of exophthalmic goiter have disappeared. Furthermore, on the vestiges of exophthalmic goiter, there may be implanted a definite syndrome of hypothyroidism.

Of all the symptoms of hyperthyroidism only the exophthalmus and goiter heart may remain, and with this exophthalmus and goiter heart we may note the gain in weight, the mental dulness, the lowered basal metabolism, and even the skin changes of myxedema. In some instances, hypothyroidism seems to follow in the path of hyperthyroidism or thyrotoxicosis. In other words, the symptoms of hypothyroidism do not usually appear until the sequelae are the only evidences of Graves' disease remaining. This can be readily understood if we consider the pathological sequence of the changes that occur in the gland in Graves' disease.

The end result of hyperplasia is sclerosis, a condition popularly called "burnt out gland." The hyperfunction and stimulation over a period of years lead to fibrosis of the secretory elements and we have consequently an absence of all thyroid secretion from the area of gland tissue involved. This theory explains well enough the type of case in which the symptoms of myxedema or hypothyroidism appear after the evidence of hyperthyroidism or thyrotoxicosis has vanished. Normal secretion from the affected areas that have been "burned out" cannot occur. The unaffected areas are too small in extent to provide enough thyroid hormone to prevent myxedema.

Between the disappearance of the symptoms of Graves' disease and the onset of the symptoms of myxedema the patient may enjoy a period of normal health. Gradually, however, the patient gains weight, and gradually takes step after step down the "hypothyroid ladder."

The instances which show an actual co-existence of hyperthyroid and hypothyroid symptoms are not so easy of explanation. If Graves' disease is due merely to a hypersecretion of thyroid hormone, it is difficult for us to understand how we can have simultaneously the symptoms of hyper- and hypo-secretion in the same individual from the same gland. We must have in the system at any one time either too much thyroid secretion, a normal amount of thyroid secretion, or too little secretion. We cannot, obviously, have too much and too little secretion in the tissues of the same individual at the same time.

We can only explain these cases which show a blending of the syndromes of Graves' disease and hypothyroidism, if we accept the hypothesis that Graves' disease was due to a qualitative change in secretion, rather than to a hypersecretion. If we accept this theory we can readily see that while the total amount of secretion may be lessened, we may nevertheless have a sufficient amount of vitiated secretion to maintain a continuance of some of the symptoms of Graves' disease. The amount of vitiated secretion necessary to promote a continuance of toxic symptoms may conceivably be very small, even infinitismal and for this reason, may offer no bar to the development of hypothyroid symptoms.

THYROID IN CONJUNCTION WITH OTHER ENDOCRINE PREPARATIONS

Certain long standing cases of hypothyroidism are undoubtedly followed by hypofunction or dysfunction of certain of the other endocrines. The connections between the thyroid and the pituitary has been demonstrated among others, by Benedict (142) and Homans (143) who found a gradual fall in the basal metabolism following the extirpation of the anterior lobe of the pituitary in dogs. In myxedema according to Dock (144) the hypophysis is often enlarged, atrophied or shows evidence of degeneration.

When other endocrine preparations are indicated the writer prefers to administer them separately, so that the new preparation may be added or withdrawn at will and the effects estimated. In some cases of cretinism, refractory to thyroid therapy, the writer has found that if 10 grains anterior lobe of the pituitary is added, favorable results may be noted. The same results were obtained in a few cases by giving whole pituitary 20 grains by mouth.

Corpus luteum is also useful in conjunction with the thyroid preparation in the treatment of hypothyroid girls who show evidence of delayed puberty or scanty or irregular menstruation.

Iodin and Thyroid Gland Preparations

The addition of small doses of iodin will sometimes turn the tide, when thyroid itself has failed. It may be given in the form of iodostarin or syrup of hydrictic acid.

Dosage.—No two writers seem to agree about the amount of the gland to be given under certain circumstances or as to the method of its administration. Some advise continuous, some advise remittent ad-

ministration; some advise rather large initial dosage; some advocate extremely small doses at first, testing out very carefully and gradually the tolerance of the individual patient.

All are agreed that each case represents an individual study, that the dosage will have to be worked out for the individual using careful and frequent basal metabolism estimations as a control.

In treating any hypothyroid condition, we must in fixing the dosage, keep two considerations in mind.

We must ascertain:

(*a*) *The initial dosage*—The dosage necessary, either in the form of one large dose, or repeated small doses—to bring the basal metabolic rate to normal.

(*b*) *The maintenance dosage*—The amount to be given daily, weekly or at other intervals, in order that the basal metabolism may remain at the normal. For instance 2 grains of the desiccated gland twice or three times a day may, in a particular case, bring the basal metabolism to normal in six or seven days. A smaller dose may bring it to normal in ten or twelve days or longer depending on the size of the dose.

After the basal metabolism has once reached normal it may only be necessary to administer a grain of the dry gland once a day to keep it at this level.

The experience of the writer is against large initial dosage, especially if there are any cardiovascular complications present. If large initial dosage is practiced, and untoward symptoms result, the patient may be seriously and permanently prejudiced against the treatment. If as a result of careful examination it is determined that cardiovascular disease or serious hypertension is present, we should proceed very cautiously—giving perhaps $\frac{1}{8}$ grain or 1/10 grain of the extract once a day or even once in two days.

As the tolerance is determined we gradually increase the dosage. Trying to bring the metabolism, in a case of myxedema complicated by cardiovascular degeneration, to normal in a few days, is about as reasonable as asking a man of sixty to run a mile race.

Writer's Method of Administration in Cases of Mild Hypothyroidism.—The cases of mild hypothyroidism which we usually see, do not show as a rule, cardiovascular degeneration or hypertension, and for such cases, the following method in our hands has met with good results.

Desiccated gland in doses of 1 grain is given three times a day for five days from the first to the fifth and from the fifteenth to the twentieth of each month. This dosage is increased half a grain a dose for each period of administration and continued in this increasing ratio, until mild symptoms, as moderate tachycardia, slight nervousness, slight irritability, and wakefulness are noted. When these symptoms appear, medication is stopped for one month.

The patient is then put back on the desiccated gland, at two-thirds of the dosage at which symptoms appeared. If symptoms of hyperthyroidism should again appear, the medication is again stopped for a month, and again started at two-thirds of the last dosage.

As improvement is noted, this dosage is further decreased until the proper maintenance dose is determined. This maintenance dosage varies considerably; as a rule we give a weekly maintenance dose and it ranges from 5 to 20 grains of the desiccated gland. The dosage must occasionally be cut rather fine. We have had patients who did not seem to recover well on 5 grains a week of the desiccated gland but who showed symptoms of hyperthyroidism on 10 grains a week. As the slight symptoms were unaccompanied by any material rise in the metabolic rate, the question of psychic influences must be considered.

Frequent basal metabolism estimations are made during the course of the treatment. We find, from experience, that the patients seem to do better and feel better if the metabolic rate is kept just a little below the normal. We are satisfied if the patient is subjectively and objectively improved, and has reached a two-third or three-fourths correction of the metabolic error.

Some writers advocate a daily maintenance dose, advancing as an argument for this procedure, that the thyroid secretes its hormone every day, not twice a week or once a week. One might answer that the thyroid pours out its secretion not once or even twice a day but every hour and every minute. Quite manifestly we cannot supply the thyroid hormone in anything like the same way in which nature does. After a sufficient period of study and observation, it is just as rational and effective to administer a weekly as a daily dose. In fact the weekly dose, by eliminating cumulative action, enables the observer to more accurately determine the smallest amount of the thyroid preparation, which will adequately meet the needs of the organism.

Each physician who is on the lookout for cases of hypothyroidism, will find sufficient material to work with and will soon develop his own scheme of administration and dosage. The family physician will find it advantageous to bear in mind the possibility of hypothyroidism in connection with the following life periods and conditions: Puberty, Pregnancy, Infectious disease, acute or chronic, Operations, The menopause, and Simple Goiter.

Treatment of Associated Condition

Sometimes an associated condition as anemia, a neurosis, or a gastro-intestinal disturbance needs correction. We should be on the watch particularly for an associated anemia, and a complete blood count should be done in every case. McKenzie observed three cases in whom a diagnosis of pernicious anemia had been made prior to the determination of the basal metabolic rate. Heart and kidney cases must receive proper attention. The possibility of associated endocrine disorders must be borne in mind, and if their presence is suspected, the indicated gland therapy must be instituted. The diagnosis of associated or secondary endocrine disturbance may be founded on guess work, may be, in fact, little better than a surmise. Nevertheless, taking into account the fact that the extent of our present knowledge as regards the ductless glands leaves much to be desired, we must not be too arbitrary, and we should be inclined to give the patient the benefit of the doubt.

Adjuvant Therapy, in the Mild Hypothyroid Disorders

The use of iodin as an adjuvant in the treatment of the mild hypothyroid conditions has been referred to. We seem to get better results when thyroid or iodin preparations are given intermittently than when given continuously. Better results seem to follow their administration separately than when given together. Iodin may be given one week and thyroid the next, alternating them weekly, or a favorite method of ours may be adopted. Thyroid is given from the first to the fifth and from the fifteenth to the twentieth of each month and iodin is given from the fifth to the tenth and from the twentieth to the twenty-fifth of each month. Probably the good effects noted on the administration of such tonics as syrup of ferrous iodide is due to the iodin content of the preparation and its stimulating effect on thyroid function.

Some writers advise the use of arsenic in one form or another, and it is doubtless useful in many of the cases accompanied with anemia. Others advise the free administration of alkalis, under the belief that the action of the thyroid preparation will be enhanced if the alkalinity of the blood is increased.

Diet.—For these cases there is no tangible evidence to show the advantage of animal over vegetable diet or vice versa. The most rational procedure, probably, is to place the patient on a full diet of the food to which he is accustomed, and which he likes. A generous allowance of fish seems to be indicated, and the patient should have fresh fish or other seafood at least once a week.

Non-Medicinal Treatment

Hydrotherapy.—Owing to the sensitiveness to cold, of which these patients frequently complain, it is generally believed that hydrotherapy is contra-indicated. If properly supervised, however, hydrotherapy can be used with benefit. The salt rub, sprays, and douches of various kinds will bring about a gradual tolerance for lower temperatures, and should, when properly managed, be effective in producing the desired reaction.

Mechanotherapy.—Mechanotherapeutic procedures, which increase the oxidizing powers of the individuals, by increasing muscular activity, without effort on the part of the patient, is said to be of value in some instances. Various light, electric and thermal methods of treatment have their advocates. With the exception of the actinic ray, which on general principles should be beneficial, if the others have a field of usefulness at all, it must be a limited one; if the patient's illness or disability is due to thyroid failure, and if it reacts favorably to thyroid therapy, the thyroid preparation in itself will be sufficient, and the results without complicating physiotherapeutic apparatus will be sufficiently gratifying.

Scope of Opotherapy

Many individuals, owing to thyroid failure of varying degree, go through life without realizing to the full their latent possibilities. These individuals are immature, have not reached their final stage of differ-

ential development, mental or physical; there are heights which they just fail to climb, peaks which they just fail to reach; they stop just short of success; they drag along in the rut of mediocrity; their friends know that they should do better, they themselves know that they should do better; they lack something for the final push; they cannot realize to the full on their probable or possible inherent qualities and possibilities.

The writer believes that many cases of waywardness and backwardness in childhood and young adult life are due to hypothyroidism, often of comparatively mild degree—and is strongly convinced that the endocrinologist, in caring for these thyroid insufficient children, will find one of his greatest fields of usefulness.

This is, however, not the only field. There are many types of mild thyroid failure in which opotherapy, the only efficient method of treatment, is indicated. The writer, from the point of view of specific therapeusis, is inclined to use the following entirely arbitrary classification.

Thyroid therapy is indicated in:

1. Thyroid deficient children and young adults, who as a result of thyroid deficiency are mentally and sometimes physically retarded.

2. Vague chronic disorders of indefinite origin associated with a lowered metabolic rate. Many patients that have gone "the rounds" from doctor to doctor will be greatly relieved or cured by thyroid extract.

We have found vague chronic complaints commonly associated with lowered basal metabolic rates, and the use of thyroid preparations in such cases has brought about satisfactory and sometimes amazing results.

The following symptoms and syndromes were found frequently associated with a lowered metabolic rate:

Fatigue
Headache
Constipation
Dizziness and vertigo
Partial loss of memory
Indifference and loss of interest
Scanty or irregular menstruation
Dyspnea on exertion
Tooth decay
Excessive appetite for sweets in children
Cold and numb extremities
Chronic rheumatism
Arthritis
Skin disease (acne vulgaris, recurring furunculosis, psoriasis, eczema, ichthyosis)
Delayed sexual development

These patients in some instances show only a very slight lowering of the metabolic rate. In some instances it is minus ten or even less. Many are inclined to consider a minus ten reading as within the limits of the normal. We are, for our part, inclined to attach significance to even a slight minus reading, if accompanied by other signs suggestive of mild hypothyroidism. Experience with thyroid therapy in a large number of such cases has convinced us that we are justified in this assumption. A slightly depressed metabolic rate has in itself no significance; it has significance when, in addition, there are symptoms present definitely suggestive of mild hypothyroidism.

The physician who is inclined to invariably associate hypothyroidism with obesity, would be surprised to note that in many of these cases the weight is below normal.

3. Thyroid extract is useful in certain types of nephritis and heart disease, even when the diagnosis of myxedema is not made.

It is particularly useful in cases with edema; it promotes diuresis and in cases in our experience caused rapid disappearance of the edema. In some of the kidney cases, it seemed efficient in lessening the degree of albuminuria. Whether the beneficial effect of thyroid extract in such cases is due to direct action on the cardiovascular apparatus, or whether it is due to the influence of the thyroid preparation on cell metabolism, is difficult to say.

The dyspnea attendant on the edema will have a tendency to influence the metabolic rate, will perhaps even give a comparatively high plus reading; under such conditions and in the absence of other signs of myxedema or hypothyroidism, it is difficult to make a diagnosis. It may well be, however, that some or all of these cardiac or renal cases that react favorably to thyroid extract are really on a myxemic basis and that the improvement must, consequently be attributed to the specific influence of the preparation given.

In certain cases of angina pectoris, even in some instances in which the metabolic rate is not sufficiently low to suggest myxedema, the administration of thyroid extract in very careful dosage is productive of good results.

4. In only a very small percentage of obesity cases is there any indication for thyroid therapy. Most of the obese come by their obesity honestly, without the aid of the endocrines, and through the route of excessive or ill advised dieting. The obese individual who "has an appetite like a canary bird" is in many instances a myth. Personal observation or honest discussion with members of the family will elicit the fact that the patient from all appearances is receiving more than his just number of calories, and that in addition, he is taking very little exercise. When the adiposity is marked, myocarditis of varying degree is almost invariably present, and we must consequently be very cautious in the administration of thyroid extract.

It has been our custom to give thyroid only in these cases of obesity which show a definite, though perhaps slight, lowering of the metabolic rate. We have found that some extremely obese individuals, while showing none of the other mental or physical signs or symptoms of myxedema have nevertheless a definitely lowered metabolic rate (on the average about minus 10 to minus 12) and it is in cases of this kind that we secure our best results in safe weight reduction. In about only 3 to 5 per cent of the cases of obesity that we see is there any indication for opotherapy.

It is quite possible, of course, that certain cases of obesity are due to hypofunction of the pituitary or other endocrine glands. In cases in which it seemed probable that the adiposity was due to associated dysfunction of the thyroid and other endocrine gland, our results (perhaps due to menorrhagia and dysmenorrhea) with the specific extracts were not encouraging.

5. Several of the endocrinologists have called attention to the rôle of thyroid preparations in removing the bane of sterility in women. In

view of the close connection and co-relationship that exists between the thyroid and the sexual and generative apparatus, it may be reasonably argued that there is some basis for the value of opotherapy in this connection. From the point of view of specific therapy, it is probably somewhat on the same plane as obesity. Doubtless a certain number of cases of sterility are due to hypoplasia or incomplete development of the generative organs consequent on hypofunction of the thyroid. In such instances, if treatment is started sufficiently early in life there is no reason why a favorable result may not be anticipated. Later in life, however, after the generative organs have undergone fibrotic and degenerative change it is difficult to see how opotherapy could be of any benefit.

In our own experience, we have failed much more often than we have succeeded; indeed, this a mild way of putting it. I can find, from a total of several hundred cases, only nine cases in which pregnancy in a previously sterile woman could, with any show of reason, be attributed to the use of a thyroid preparation. We have had our best results in sterile women who gave a history of late or incomplete puberty change—in most instances of women who did not menstruate until the age of eighteen or nineteen and in whom the flow had been brief, irregular or scanty.

CHAPTER XVII

PARATHYROID GLANDS

HISTORICAL

Before 1880, when Sandstrom (145) first recognized the parathyroid glands as separate and independent structures, they were seen and described but considered as lymph glands or accessory thyroids, and given little or no attention. When they were described they were considered embryonic thyroid rests until about 1895 when Kohn (146) vigorously opposed this view and strongly contended that they were independent structures. He supported his contention by reports of a very complete anatomical study of these glands in the dog, cat and rabbit. He placed the anatomy and histology of these glands on a definite basis and, by his very thorough reports on the parathyroids of mammals, established the fact that they were independent structures morphologically, and functionally different from the thyroid gland.

In 1891, Gley (147) definitely showed that the symptoms resulting from thyroidectomy, alone, in rabbits, were entirely different from those following thyroidectomy which included the parathyroids. Vassale and Generali (148) in 1896 showed that parathyroidectomy without thyroidectomy, in dogs and cats, caused fatal tetany, while, if one parathyroid remained functionally active, tetany did not occur. Despite this great amount of work, both on the anatomy and physiology of these bodies, it was generally assumed, until about 1910, that the thyroid and parathyroids were closely related organs. These organs—recognized but not considered until 1880; accepted as embryonic thyroid rests, lymph glands or accessory thyroids until 1895; not generally accepted as definitely independent structures until about 1910; and which for a long time appeared comparatively unimportant (from an anatomical point of view)—were finally proved to possess, when thoroughly studied from an experimental point of view, an importance in the life of an animal equal to that of any other functioning organ.

EMBRYOLOGY

The parathyroids arise as paired structures, from the entoderm of the third and fourth branchial clefts, in close association with the corresponding anlagen of the thymus gland. They become separated from the thymus as this organ develops caudally, and while their association with this organ is embryologically and possibly physiologically a more fundamental one than with the thyroid, their topographical relations to the thyroid are of more practical value and descriptions regarding their location are usually phrased in reference to the thyroid. The pair arising from the third cleft (first described as "outer" parathyroids because in cer-

tain animals they were situated outside the thyroid) pass backwards and come to rest behind the lower border of the thyroid, forming the inferior bodies. The pair arising from the fourth cleft (first described as "inner" thyroids because in certain animals they were found within the thyroid lobe) come to rest on the lateral portion of the thyroid and form the superior bodies.

In man four parathyroids (the two pairs) are usually found, although reports of nothing but parathyroid tissue diffusely imbedded in areolar tissue of thyroid to twelve (Erdheim) (149) actual parathyroids have been described. It is often difficult to demonstrate the four parathyroids, even by experienced searchers. Von Verebély (150) reported that he found four parathyroids each in 108 out of 138 dissections. This points to the possibility that frequently one or more parathyroids are congenitally absent, or fail to develop. Complete aplasia, however, has never been proved, and we doubt such a possibility because it is incompatible with life, even during the fetal period. MacCallum is most likely correct when he says "Because in a space extending from the basis of the skull to the diaphragm we do not find a little gland the size of a lentil, have we the right to deny its existence?"(151).

ANATOMY

Because of the great variation in number, form, size and location, the weight and shape of these bodies also vary greatly. When they are in a location free from pressure, they are slightly flattened, oval bodies of soft consistency averaging 5 to 7 mm. in length, 2 to 4 mm. in width and 1.5 to 2.5 mm. in thickness. They vary in color from a light yellow red to brown red, and become somewhat darker with age. The color is largely due to intra- and extra-cellular lipoids, although Erdheim has demonstrated hemosiderin pigment in parathyroids of infantile tetany where capillary hemorrhages into the parathyroids may be found.

While the position and number of parathyroids vary, and even accessory parathyroids are of frequent occurrence in all mammals, these bodies are usually recognized in pairs—the two superior and the two inferior parathyroids. They are most frequently located on the posterior lateral angles of the thyroid lobes; the superior at the junction of the upper and middle thirds, and the inferior at the junction of the middle and lower thirds. They usually lie in a small groove or depression formed by the entrance of a radical of one of the thyroid arteries.

The superior parathyroids are the more constant in position. They are usually wholly outside the glandular capsule and the inferior laryngeal nerve passes up internally to them. The inferior parathyroids generally lie more laterally than the superior ones and are external to the inferior laryngeal nerve and the inferior thyroid. While these positions are fairly constant, a great many variations are encountered, especially of the inferior pair. These may be found at the extremity of the lower pole, under the lower border of the isthmus, in the pre- or peritracheal fatty tissue, or even imbedded in the thymus gland.

According to Halsted and Evans (152) the parathyroid glands have a very large blood supply, derived from branches of the inferior thyroid

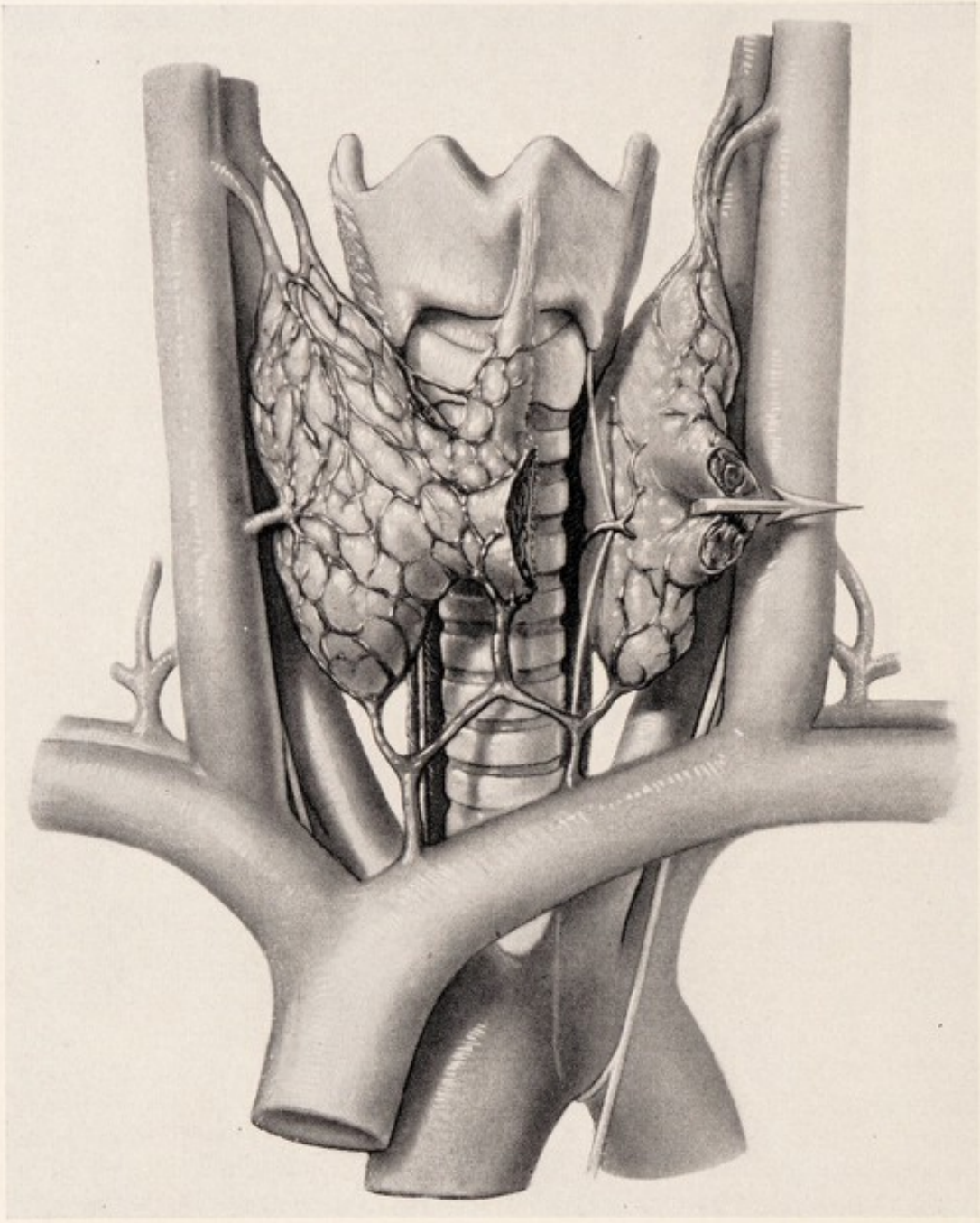


FIG. 99.—Parathyroid Glands, Recurrent Laryngeal Nerve Showing True Gland.

artery. The artery enters the gland at the hilus and immediately divides into numerous branches which run into the septa. The main vein leaves the gland at the hilus and fails to run any further constant course. A very striking characteristic of the human parathyroid is the anastomosing net work of large sinus-like collecting veins beneath the capsule.

The nerve supply to the parathyroids, according to Rhinehardt (153), is very scanty. He believes that all fibers present could be accounted for

as vasomotors. These are non-medullated nerves entering with the artery and a few fibers seem to run in the connective tissue between the cell columns, but none of these leave the connective tissue to penetrate into the cell groups.

The parathyroids in man are rarely actually embedded in the thyroid although Wellbrock described the occurrence of accessory parathyroid glands in about 8 per cent of cases while examining 1056 thyroid glands immediately after removal at the Mayo Clinic (154). Accessory parathyroids are frequently found in all mammals if extensive search be made. This occurrence is explained by the fact that these bodies arise from four different embryological sites and that the branchial cleft region undergoes such great structural change during development that fragments of parathyroid anlagen could be broken off and irregularly distributed.

Shapiro and Jaffé (155) demonstrated accessory parathyroids in 12 per cent of cats, by examination of a single histological section taken from the thymus area. Nicolas and Swingle (156) found them in thymuses of 35 per cent of the cats they examined. The most common sites for accessory parathyroids are:

1. In or about the thyroid lobes.
2. In upper portion of thymus.
3. In the intervening tissue between the thyroid and thymus.

The different results reported from parathyroid extirpation may be explained by the frequency of accessory parathyroids.

HISTOLOGY AND TYPE

Microscopically the parathyroids are seen to be made up of a parenchyma composed of closely packed, relatively large cells within a supporting stroma which is derived from fine connective tissue strands extending in from the capsule and forming a delicate uniform reticulum. This uniformity, which gives the gland a compact and uniform outline, is maintained throughout early life. Later the stroma becomes septa-like and gives the gland the anastomosing strand appearance characteristic of young adults. Still later in life, as the stroma bands become more prominent, the gland takes on a definite lobulated appearance. Thus we divide the parathyroids into three groups as first suggested by Welsh (157):

1. The compact uniform type of early life.
2. The anastomosing strand type of adult life.
3. The lobular type of later life.

Occasionally in parathyroids of adults all three types are seen in the same gland; this observation has been interpreted as "overlapping" of the types. The cells which make up the parenchyma are of two types: chief cells described by Noodt (158), and large oxyphilic cells described by Welsh (157). The chief cells appear to be the essential ones representing the only type present in man up to about the tenth year and in other species, as the dog and cat, the only type present throughout life. They

have clear, poorly staining, non-granular protoplasm with relatively large, pale nuclei often eccentrically placed.

The oxyphil cells usually begin to appear in late childhood, are much longer than the chief cells, occur singly or in groups, and are characterized by large amounts of granular protoplasm which stains intensely with acid dyes. Their nuclei are much smaller than in the chief cells and the chromatin stains deeply.

There is a third group of cells sometimes described as dark chief cells, but they are probably a sub group of the chief cells. The prevailing opinion is that the dark chief cells and the oxyphil cells indicate different stages of secretory activity, and that the oxyphil cells are the ripened and mature cells which eventually undergo degenerative changes and disappear.

The mode of secretion of the parathyroid cell has been disputed and to present date no definite conclusions have been demonstrated. Cowdry (159) found great variations in the cytoplasmic location of the Golgi apparatus. Glycogen is usually present in both the chief and oxyphil cells, occurring in large quantities in the former, and in very small quantities in the latter. This glycogen content appears to be independent of age, sex, and disease and is usually resistant to destruction. Colloid, histologically a homogeneous protein mass taking acid dyes and morphologically resembling that present in the thyroid, is frequently seen in the parathyroids of adults. It is well known, however, that any albuminous material in closed cavities may assume the appearance of colloid.

The appearance of colloid containing follicles was cited by older writers in supporting the view that the parathyroids were functionally related to the thyroid. Erdheim (149) as far back as 1903, in studies of the parathyroid in myxedema, disproved this contention. Similarly, the early literature contained references to the presence of iodin in significant amounts in the parathyroids. This was taken as an assumption that the iodin was contained in the colloid of the follicles just as in the thyroid. Estes and Cecil (160) have shown that parathyroids, not contaminated with thyroid tissue, do not contain iodin in any greater concentration than that of the body tissues in general, exclusive of the thyroid. This presence of colloid in the parathyroid gland is explained either as a degenerative process or as a stasis of albuminous material in the spaces formed by the differentiation of the columns of cells into follicles.

Vincent and Jolly (161) showed that differentiation into follicles may be increased, during compensatory hypertrophy, in dogs. Whatever the exact composition of the parathyroids may be, it has definitely been proved that they are highly resistant to putrefaction and post mortem changes. Parathyroids of dogs and rats show well preserved histological details after having been kept in various solutions and infusions, while thyroid tissue subjected to the same treatment is histologically unrecognizable. On the other hand, in sharp contrast with the thyroid or thymus, parathyroid tissue has very slight regenerative capacity. Some hypertrophy is seen in pregnancy, lactation tetany, and low calcium diet in young animals, but even after removal of three parathyroids in dogs,

cats, or rabbits, the remaining gland may undergo no obvious enlargement, despite the fact that the animals remain in good health. Marine (162) has shown that hypertrophy is more readily produced in birds particularly when fed on a very deficient diet.

EFFECTS OF EXTIRPATION

In all species of animals in which removal of the parathyroids has been done, there followed a fatal symptom complex characterized by hyperexcitability of the nerves, beginning within two or three days, which proceeded to tonic and clonic spasms of the muscles. Marine (163) has shown that under certain conditions of vital nutrition the tetany in dogs may begin within four hours and end fatally in seven hours after parathyroidectomy. Particularly in cats, and to some extent in other animals, there are two distinct clinical manifestations of parathyroid tetany following parathyroidectomy: (1) typical tetany with tachycardia, tachypnea and muscle twitchings, and (2) a slowly progressing lethargy and coma. There are other forms of tetany which differ markedly, both from parathyroid tetany and from each other, but with the exception of tetany of pregnancy and lactation there is as yet no proof that they are directly related to parathyroid insufficiency.

There is a possibility, as noted by MacCallum (164) that while the other clinical types of tetany appear to differ in their etiology, the final changes in the blood which bring about the symptoms may be due to lack of parathyroid hormone. Parathyropriva tetany is the best understood form of tetany and its relationship to the parathyroid has been arrived at after considerable dispute. Much of the conflictive evidence has been due to the fact that under favorable nutritional condition, very small fragments of, or accessory parathyroids are sufficient to prevent tetany, while under similar unfavorable conditions typical parathyroid tetany may develop with all parathyroids intact.

Pappenheimer and Minor (165) have recorded similar observations in human rickets. They believe that in human rickets there is actual hyperplasia, and that the type of all remains unaltered during hypertrophy and hyperplasia. Hyperplasia of the parathyroids is seen in diseases other than rickets. Klemperer (166) noted such an occurrence, associated with extensive bone metastases, in a case of carcinoma of the breast. Kerl (167) reported enlargement of ten parathyroids in adenoma like formations in cases of osteomalacia and osteoporosis. Adenomatous hyperplasia of the parathyroids has been reported by Barker (168) either independently or associated with chronic nephritis.

While parathyroid tissue does not regenerate very well its autotransplantation is easily accomplished in ordinary laboratory animals, and proof of the function of such transplants in any part of the body has been furnished by Halsted (169). His view, however, that it was necessary to create a parathyroid insufficiency before autografts would take, has been disproved by Manley and Marine who obtained many accidental transplants of parathyroid in rabbits in transplanting a considerable portion of the thyroid lobe where the parathyroids were intact.

SURGICAL PRECAUTIONS

This may be as good a place as any in connection with the consideration of the surgical anatomy to discuss the surgical precautions necessary. We know, of course, that complete removal of all parathyroid tissue will result in tetany. Gley, in a series of reports starting in 1891 (170), first drew the attention of the profession to this serious complication. How much parathyroid tissue may we remove? How are we to identify, how are we to know that no parathyroid tissue is left? We have repeatedly, unintentionally, removed three or four parathyroids. No evidence of tetany was noted and the patients made uneventful recoveries. In one instance seven distinct parathyroid nodules were noted in the removed specimen; no tetany and no symptoms of calcium deficiency resulted. It is not, of course, a question of how much parathyroid tissue is removed, it is a question of how much parathyroid tissue is left. If even only one small parathyroid is left, it will undergo hypertrophy and we have reason to assume, will be ample to supply the parathyroid function. It should, of course, be the surgeon's objective to remove no parathyroid tissue at all.

With this objective in mind, it is particularly essential that undue traction is not employed. If undue traction is used, the little parathyroids, which are often extremely difficult to identify, may be dragged off adherent to the specimen. As noted, the glandules are sometimes no larger than a mustard seed and, consequently, extremely difficult to differentiate in the operative field. The surgeon, consequently, as his first safeguard, must be particularly careful to make his dissection without undue traction. Another safeguard lies in the correct identification of the posterior plane of cleavage discussed in our chapter on Surgical Anatomy. As long as the dissection is not carried internal to the mesial margin of the plane of cleavage, there is little likelihood that the parathyroids will be accidentally removed.

We have discussed Millzner's (171) suggestions with reference to leaving the lateral and anterior portions of the capsule. According to his technic, as soon as the lobe is mobilized, the anterior and lateral part of the capsule is carefully inspected. An effort is made to recognize and protect any parathyroid tissue seen. A suture is inserted through the anterior capsule to serve as a mark of identification, clamps are then applied in such a way that the lateral capsule may be stripped off the lobe from before backward; as soon as a large amount of thyroid capsule is thus preserved, the resection is done according to the usual technic.

We are not quite convinced of the necessity of this measure. In thyroidectomies, until recent date, no especial attempt had been made to preserve the anterior and lateral capsules. The parathyroids in these locations were unquestionably removed. Nevertheless tetany occurred only in very rare instances and, in these instances, we are convinced rough manipulation and too thorough dissection posteriorly resulted in the removal of the deeper lying parathyroid nodules.

As a further measure of precaution, it is recommended that the inferior thyroid artery be tied external to the thyroid fascia.

The Immediate Transplant

It has been our custom to have the specimen examined immediately on removal for adherent or implanted parathyroids. If a nodule is found which seems to be parathyroid substance it is our custom to immediately reimplant this nodule in the stump of the gland.

We have done such autotransplantations in some fifty or sixty cases. We have no means of knowing how efficacious this procedure was, or whether, as a matter of fact, it was at all or not necessary. In each case in which it was done, no symptoms of tetany followed. In none of the cases, however, had we any reason to suspect that other parathyroid tissue was not present. Furthermore, as it was not possible or advisable to resort to microscopic examination, we were not sure in every instance whether the implanted nodule was really parathyroid tissue or not. Lymph nodes, small nodules of thyroid tissue, or even small masses of fat may have been mistaken for parathyroid glands.

In some instances in which a small section was taken for later microscopic study, it was found that the autotransplant was not parathyroid substance.

Lahey (172) and others make the autotransplant into the fibers of the sternocleidomastoid muscle rather than the stump of the thyroid. They advise that a small incision be made in the aponeurosis of the belly of the sternocleidomastoid and by separation of the muscle fibers a little pocket may be made into which the parathyroid nodule is placed.

POSTOPERATIVE TETANY

Incidence

A survey of the literature makes it at once apparent that it is difficult or impossible to gain any really accurate conception as to the incidence of postoperative tetany. Several factors contribute to the lack of basically sound statistics in this matter.

In the first place it has been alleged by some of the medical writers that surgeons are not apt to chronicle such unfortunate accidents. For instance, Berkeley (173) states, "Surgeons are naturally apt to deny to such unfortunate accidents the publicity they give their successes and statistics are hard to find." In the second place, many surgeons do not make mention of the milder forms of postoperative tetany. In our series we have recorded as tetany any case in which the symptoms, even though transitory, were sufficiently exclusive. Gibson (174), for instance, writing on the postoperative treatment of exophthalmic goiter in the Crile Clinic in 1922, states,

> A spurious form of tetany which appears after from two to twenty-four hours is not altogether uncommon. The symptoms are a slight tingling of the finger-tips; an itching of the nose. One may notice a slight pallor about the mouth and the fingers are flexed. There is also moderate spasticity of the muscles of the forearms and lower extremities. This condition is due to a transient cessation of the normal physiologic function of the parathyroid bodies produced either by trauma of their nerve supply or by the edema which results from operative procedures in their immediate vicinity.

In the third place, statistics covering a large number of cases for a long period of time, extending back, for instance, to the pioneer days of goiter surgery will, of necessity, show an uneven growth of tetany incidence. The number of cases of postoperative tetany will naturally be greater in the series of patients operated in the early days. Tetany was quite frequent in those days when total thyroidectomies were the routine procedures. In early cases it was a quite common complication. Kocher, on the contrary, saw it only five times in his last 1000 operations.

With reference to our own figures, we have had twenty-nine postoperative tetanies from a total of 15,000 operated. Twenty-seven of these twenty-nine cases occurred in our first 6000 operations which we completed in 1918; two cases occurred in our last 8000 cases. Of the twenty-nine cases of postoperative tetany two died. Both of these fatal cases occurred in our first series of 6000 thyroidectomies.

In addition to the twenty-nine cases occurring after thyroidectomy, we had two fatal cases of tetany following double ligation of the inferior thyroids. As noted elsewhere both these patients had been, prior to operation, subjected to radical x-ray treatment.

The incidence of postoperative tetany in our case may seem unusually high. It must be remembered, however, that we recorded all cases in which the diagnosis positively could be made, including the mild cases which cleared up promptly in a few days.

We believe that if similar procedures were followed in other clinics, if all cases both mild and severe were recorded, that tetany incidence would be considerably higher. In confirmation of this belief, the author considers it not inappropriate to state that he has treated, in his practice, some sixty-four cases of postoperative tetany that had not been operated in his clinic. Some of these, in fact many of these, had been carried along for a period of three or four months after operation and, when first seen by the writer, were still in serious condition.

Etiological Considerations

The immediate cause, of course, of postoperative tetany is the removal or injury of all parathyroid tissue or the removal or injury of so much parathyroid tissue that the amount left is insufficient to produce the requisite amount of hormone.

Postoperative tetany may be due to:

1. Oblation or removal of all parathyroid tissue or of so much parathyroid tissue that sufficient hormone, in the absence of compensatory processes, is not available.

2. To crushing injury of parathyroid substance from a hemostat or otherwise.

3. To interference with the parathyroid arteries either through crushing or accidental ligation.

4. To the involvement of remaining parathyroid tissue in the scar tissue. The parathyroid substance may be strangled or pressure strangled in slowly contracting scar tissue so that the symptoms in a certain case cannot be evident for some time after operation.

5. To pressure edema on remaining parathyroid substance, causing temporary hormone insufficiency.

Symptoms

Onset.—The time of onset after operation varies somewhat with the individual case. In some of the milder cases, due to pressure edema, the symptoms may be evident right after the operation. In the case of slowly contracting scar tissue the condition may not be evident for a period of two or three weeks. Some state that postoperative tetany may occur months after the operation.

In the average case of postoperative tetany it may be stated that the mild symptoms appear between twenty-four and forty-eight hours after the operation. The symptomatology, if the case is to be progressive, reaches its maximum on the third to fifth day. Owing to this fact—that the clinical picture is complete on the third to fifth day—many writers are inclined to attribute the onset of the condition to this.

As regards the character of the onset we may say that this also varies. When early and severe, postoperative tetany may resemble experimental tetany in animals. There is great mental distress, restlessness, sometimes delirium. On the other hand the onset may be quite gradual with gradual spread of the symptoms and without evidence of great mental distress. The first sign noted frequently is a pricking sensation or stiffness of the fingers.

Altered Nerve Reactions.—The symptoms most characteristic of tetany are those symptoms characteristic of spasmapholia in general—increased mechanical excitability of the nerves and altered electrical reactions. The altered electrical reaction of tetany was demonstrated by Erb (175). In tetany there is an increased excitability of the nerves to the galvanic current. A current strength of 5 milliamperes or less, powerless to produce a contraction on cathodal closing in a healthy individual, will cause such a contraction in an individual suffering with tetany. It is also noted that the anodol opening contraction is produced with less current than an anodal closing contraction. The electrical excitability is accentuated during the spasms.

Mechanical Irritability.—The mechanical irritability may be demonstrated by means of certain distinctive phenomena.

The Trosseau Sign.—The Trosseau sign may be demonstrated by exerting circular compression on the arm, using either a rubber band or merely exerting the pressure by entwining both hands around the arm. This compression exerting pressure on the nerves and blood vessels in the bicipital groove, causes spasmodic contractions and flexion of the forearm and wrist.

Chvostek's Sign.—This sign elicits the mechanical irritability in the facial group. It is demonstrated by a slight tapping or striking in front of the auditory canal or over the malar bone. Such procedure causes sudden clonic contractions of the facial muscles.

Spasms.—Spasms are the natural sequence of increased irritability. They may be clonic or tonic, are usually localized, rarely general. It is

occasionally in adults a more or less generalized tonic spasm throughout the body, including the muscles of the tongue and face. Such spasms, naturally, interfere with swallowing and respiration. Even with this generalized spasm, there is no interference with consciousness.

Localized Spasms.—The localized spasm, so-called carpopedal, is a characteristic feature of tetany. As noted quite early there are premonitory symptoms—numbness and pricking in the hand and perhaps the feet. As the spasm develops in the upper extremities, the phenomenon known as the "Accoucheur's hand" is produced. The spasm is bilateral. The thumb is drawn into the palm and the fingers adducted; the hand is flexed at the metacarpophalangeal articulations; the fingers are extended and the wrists flexed. In addition, sometimes the forearm is flexed and the whole upper extremity drawn close to the body.

When the spasm has spread to the lower extremities, the thighs and legs are extended; the knee joints are somewhat rigidly flexed, the thighs flexed and adducted; the foot is often in the position of talipes equinus or equinovarus; the foot is supinated and the toes in a state of plantar flexion.

Seen less occasionally are spasms of the diaphragm, rectum, bladder, esophagus and larynx.

Sensory Symptoms.—In cases associated with tonic spasms there is frequently parasthesia together with pain. Symptoms of hyperasthesia—burning and pricking sensations—are often noted. Numbness is not infrequent. Disturbance of the special senses—hearing, smell, taste—are noted from time to time.

General Symptoms.—During the spasms there is frequently, as might be expected, tachycardia associated with increased respiration. In severe spasms dyspnea and cyanosis may be noted. Gastro-intestinal disturbances, nausea, vomiting and diarrhea may be present.

The majority of these tetany patients in our series seemed to be dehydrated. They seemed unable to take large quantities of either fluid or liquid.

It seems to us that the mental condition of the patient in tetany has not been sufficiently emphasized. Neurasthenia and melancholia, at times, becomes marked and sufficient control of the patient is impossible without sanitarium environment and some special attendance. The patient remains conscious throughout the attack and, frequently, when the attack is at all severe, has a fear of impending death. This feeling, naturally, brings about a neurasthenic condition which makes treatment very difficult. We attribute two of the deaths in our series to the fact that the patients could not be subjected to proper control.

Course and Prognosis

The course varies greatly in the individual case. The mild forms, those due for instance to pressure edema, will clear up very quickly. On the other hand, in severe forms, the case progresses rapidly to a fatal termination. Even in mild forms the prognosis must be guarded as occasionally in these light forms sudden exacerbations arise which may terminate quickly in death.

In our series of cases the tetany, in the average case, cleared up within a few weeks. If the parathyroid substance left has been seriously damaged it may be three or four months or longer before the patient is free of symptoms. Patients convalescing from tetany, who are subjected to ordeal or shock or who suffer from nutritional disturbances, are liable to have recurrences.

It may be of interest to note the duration of the disease in our series of 31 cases: about 9 cases cleared up completely in 1 to 3 weeks; 7 cleared up in 4 to 5 weeks; in 5, the attacks lasted from 2 to 4 months; in 3, some symptoms were present after 5 months; in 2 instances, intermittent attacks of tetany were noted after a period of 8 to 9 months. For these cases change of climate to California was recommended with immediate improvement and ultimate recovery. The actinic ray was, we believe, the deciding factor in the recovery. In 3 instances, the course was still more prolonged; the symptoms lasted over a year—14 to 15 months to be accurate. The tetany in these three cases was quite severe and large doses of calcium lactate and parathyroid were required to control the symptoms.

Of the two deaths from tetany after thyroidectomy, one died four months and one about seven months after the operation. We feel that both patients could have been saved if it had been possible to keep them under perfect control. In both instances the symptoms were controlled absolutely when calcium lactate and parathyroid extract were given in adequate dosage. The psychic factor was the stumbling block; both patients were neurasthenics, would not take nourishment, and would not follow instructions. The mental condition rapidly deteriorated; their relatives were unfitted to care for the patients, and both patients and relatives refused the sanitarium treatment.

In the 64 cases which came under our observation and which had not been operated in our clinic some, probably about 10 or 15 cases, had been carried along for three or four months after operation. In several of these cases also, as in our own series, marked psychic and nervous symptoms were present. These patients could not be controlled in the hospital or in the home and were removed to a good nervous and mental sanitarium where they recovered.

As regards percentage mortality, in the 160 cases chronicled by Guleke (176), 25 per cent died. In our total of 33 cases, as seen, four, or 8.2 per cent, died. When death occurs, it is usually due to spasm of the glottis or the diaphragm.

Factors That Modify the Prognosis

There are several factors which influence the prognosis very materially.

1. The amount of parathyroid tissue left. This, of course, is the basic consideration. If all the parathyroid tissue has been removed death, in all probability, will occur eventually despite the most heroic treatment. The prognosis varies directly with the amount of parathyroid tissue remaining—the more tissue remaining, the better the prognosis. Even if due to transient edema or other cause, the remaining parathyroid sub-

stance does not immediately function, the outlook is still good. Parathyroid extract and calcium lactate will carry the patient along temporarily until function is reestablished.

Even when the amount of parathyroid substance left behind is quite small, the outlook, with suitable treatment, is comparatively good. The bit of parathyroid tissue left behind will rapidly hypertrophy and supply sufficient hormone for the needs of the organism.

2. The mild tetanies due to slight trauma or slight rushing will usually clear up rapidly.

3. Sunlight. We found in our series, particularly in the severe chronic cases, that sunlight influences the prognosis very favorably. A sunny climate, outdoor living in a bathing suit seems to be the deciding factor of recovery in several cases.

4. Treatment. Conscientious and careful treatment, with particular reference to the psychic factors, may bring about recovery in apparently hopeless cases. Patients that obviously have no chance, on the whole, must be conceded at least a good fighting chance when subjected to suitable treatment in a well equipped nervous and mental sanitarium.

TREATMENT

General Treatment

The matter of the general treatment of tetany deserves a word. We should not depend entirely on parathyroid extract and calcium lactate. We must take into account and properly treat the peculiar psychic condition of the patient. We must also attempt, in so far as possible, to keep up the nutrition to par. For the nervous patient bromide or luminol, in suitable doses, may be used.

It is very necessary to increase the food intake. Those patients are adverse to taking food and liquids and, in many instances, are more or less dehydrated. If sufficient food cannot be taken by mouth, proctoclysis or hypodermatoclysis should be given. In proctoclysis, the food should be given by the Murphy method. In hypodermatoclysis, it should be given very slowly, beneath the breasts.

After relief of spasms, in an effort to keep up the nutrition, glucose may be given by the intravenous method. As a further measure, nutrient enemas may be given.

Sunlight

The efficacy of sunlight in the general treatment of tetany is not generally realized. We have in our series of cases seen extremely beneficial results from its use. In the chronic cases, we have several times advised change of climate to California or Florida and have advised that the patients remain, as much as possible, in the sunlight, due precautions, of course, being observed as to full exposure.

Those who are not in a position to go away are advised similarly regarding out-doors and sunlight in the home climate and are, furthermore, subjected to carefully regulated dosage with the quartz lamp.

Diet.—A suitable diet is of considerable importance. It is difficult to get patients to take adequate amounts of food and drink. The diet should be well balanced with a preponderance of vegetables, particularly green vegetables. The meat ration should be low; indeed, some advise a meat free diet.

Hot Packs.—Hot packs as a measure of elimination have been advocated by some. They do relax the patient, but the packs tend to still further weaken the patient and, on the whole, we feel that they do more harm than good.

Blood Transfusion.—In the case of tetany following severe hemorrhage, blood transfusion is undoubtedly indicated.

Calcium

Calcium may be given by mouth, by rectum, subcutaneously or by the intravenous method. We have used both lactate and gluconate of calcium in our treatment. Our dosage and method of administration is as follows.

For mild cases: Oral administration of large amounts of calcium in either form is usually sufficient. The diet should be carefully supervised and some form of Haliver oil should be added.

For severe cases: It must be realized that the effect of the calcium is merely transitory and all we can hope to do is to maintain the blood calcium at the necessary level until such time as the remaining parathyroid tissue is hypertrophied. In severe cases intravenous injections should be resorted to. Calcium lactate in doses of one to two grams may be given. It may be prepared as an aqueous solution of a certain strength. It should be filtered, boiled for ten minutes in a water bath, then cooled to blood temperature and injected slowly. The surgeon should hit the vein accurately as calcium salts left in the tissues sometimes produces a painful induration or even an abscess. At the present time types of sterilized calcium salt solution are obtainable which are quite convenient to use.

Specific Medication

The question of parathyroid grafting has passed but little beyond the experimental stage. As previously noted, we have in many instances, made an autotransplant of a parathyroid which we accidently removed during operation. We generally inset such removed parathyroid tissue into the stump of the thyroid.

With regard to the heterotransplant, we have had no experience. Surgeons in the past have removed, for purposes of heterotransplantation, parathyroids from individuals recently dead by execution, suicide or some acute disease which would not contra-indicate the use of the gland. The thought has occurred to us several times that we would perhaps be justified in taking a bit of parathyroid substance accidently removed during an operation and transplanting it into a tetany patient. There are, however, certain obvious objections to this course and we have never resorted to it.

THE PARATHYROID HORMONE

In recent years, many workers have attempted to prepare an extract which would contain the active principles of the parathyroid gland. The preparation of a stable extract capable of accurate physiological standardization was a matter of considerable difficulty. Collip, through the medium of acid hydrolysis of parathyroid glands, has successfully prepared extracts which are effective in controlling, or preventing, tetany in parathymectomized animals. According to Collip (177) this active parathyroid extract is a specific for experimental parathyroid tetany in the same way that insulin is a specific in experimental diabetes. The function of the parathyroid hormone relates, in so far as we know it, to the proportion of calcium and phosphorus metabolism. The hormone when injected into dogs suffering from experimental parathyroid tetany causes a restoration of the blood calcium to normal level and causes the inorganic phosphorus if increased, to be decreased. The important physiological action, therefore, of the parathyroid hormone, as we see it at present, may be considered to be that of a blood calcium mobilizer. Relatively small doses of the extract will restore parathyreoprivic dogs to normal. The improvement in experimental animals is coincident with the rise in blood calcium. There seems to be a quantitative relationship between dosage and blood calcium rise.

Collip has also shown that the administration of the extract to normal dogs is effective in raising the blood calcium above the normal level.

The injection of the parathyroid hormone, then, has been shown to cause a definite mobilization of calcium in both the normal and the parathyroidectomized dog. If the amount of the hormone injected is excessive the blood serum calcium may be raised from the normal average of 10.5 mg. to 20 mg. per hundred cubic centimeters.

Overdosage.—We must remember that the human is not an experimental animal and that we must use with extreme caution a therapeutic agent the potency of which is, to a considerable extent, a variable factor. Even if we could accurately standardize the hormone in regard to its potency in experimental animals we must, for the time being at least, remain in the dark concerning its mode of therapeutic action and its potency in the human. There may be certain innate conditions in the individual human organism which render said organism unusually susceptible to the effects of hypercalcemia.

Large doses should not be used clinically, except in the face of urgent emergencies. The object of the hormone therapy is to restore the normal calcium level. In doing this, it must be remembered that we are shooting at a rather fine target and that we may easily overshoot with disastrous consequences.

The trend of symptoms noted in hypercalcemia are anorexia, diarrhea, vomiting, general atonia, apathy, drowsiness and, in the later stages, anuria and severe acidosis, coma and a failing circulation. Hypercalcemia is especially liable to result when the interval between injec-

tions is too short. In addition to the symptoms noted, there are certain tissue and blood chemistry changes associated with hypercalcemia. There is a great increase in viscosity with an associated decrease in volume; there is a decrease in the chlorides and an increase in urea and non-protein nitrogen. There is a marked increase in inorganic phosphorus in both the blood and in the serum. The alkaline reserve shows diminution; the osmotic pressure is increased 10 to 15 per cent; the blood calcium may be up to 21 mg. of calcium per 100 cc.

As regards the essential characteristic of the hormone we know comparatively little. Collip is of the opinion that it is a comparatively simple, organic substance. The extract, as finally prepared, is crystal clear and brings about no local reaction. The active principle is soluble in alcohol up to 90 per cent but is insoluble in ether. The extract, for purposes of injection, may be sterilized by immersion in a boiling water bath.

Modes of Administration.—The hormone may be administered:

1. By the intravenous route
2. By subcutaneous injection
3. By mouth

Dosage.—The matter of dosage is of very great clinical importance. It is necessary, if possible, to be able to use a properly standardized solution so that we may have some idea of the possible therapeutic effects and action.

Two methods of standardization are available. Collip's method is based on the production of hypercalcemia in the normal dog. The second method, proposed by Hanson (178), proposes that the parathyroid extract should be standardized against a known hypocalcemia. In other words, Hanson develops his standard units as a result of the treatment of parathyroidectomized dogs.

As regards the dosage itself, Hanson advises comparatively small doses given over twelve hours for five or six days. He advises for clinical work a dosage of from 30 to 60 units every twelve hours for five or six days. Following this period, a free interval of from seven to fourteen days is allowed after which the treatment may be repeated. In severe tetany following goiter operations, it will, of course, be necessary to continue the injections over long periods of time, "preferably keeping the calcium level slightly below normal rather than above normal."

Indications for the Use of the Hormone.—Parathyroid hormone basically, is indicated in conditions in which the blood calcium level is below normal. Its primary and most urgent indication, therefore, is in tetany in which the blood calcium level is lowered. The value of the extract in other conditions must be decided largely by further clinical and experimental work. It is known that blood calcium is lowered in such conditions as spasmophilia, nephritis, tropical sprue and in some cases of whooping cough.

McCann (179) found that in three patients with generalized edema and nephritis, the administration of parathyroid extract initiated a diuresis of water and salt lasting several days after the transient elevation of the blood serum calcium.

Lisser, Smith and Shepardson (180) record the treatment of a case of maternal tetany with Collip's parathyroid extract.

Aub has treated cases of lead poisoning with parathyroid extract with interesting results.

Gordon and Cantarow (181) quote a series of 347 patients with hemorrhage treated with parathyroid extract. They found most favorable results followed the administration of from 10 to 15 units every thirty-six hours for one to three doses.

CHAPTER XVIII

THYMUS

Research today has not established the significance of the undoubted relationship which exists between the thyroid and the thymus. We know, however, that some such relationship does exist; that goiter conditions are frequently associated with hyperplasia of the thymus and that this thymic hyperplasia at times becomes a question of moment to the thyroid surgeon.

We still, then, are free to speculate regarding the physiological connection between thymus and thyroid. Is the thymus, as some believe, wholly or in part responsible for the symptomatology of Graves' disease? Many authors, including Capelle (182), Bircher (183), Matti (184), and others, have been inclined to this hypothesis. It is believed by some that there is a definite thymogenic form of Graves' disease. Some writers have developed a schedule of differential diagnosis to distinguish the thymogenic from the thyrogenic form of Graves' disease. Experiments on animals have failed to link up the thymus as the positive factor in Graves' disease. Injections of thymus extract and thymus transplantation have, on the whole, not been successful in producing symptoms suggestive of thyrotoxicosis. A few writers report suggestive symptoms after such injections or transplantings; the weight of evidence, however, is in the opposite direction.

As regards the frequency of coincidence of hyperplastic thyroid and hyperplastic thymus, Blackford and Freligh (185), of the Mayo Clinic concluded as a result of 100 postmortem examinations of fatal cases of Graves' disease, that hyperplastic thymus is present in all cases in which the patient is under forty and in half the cases in which the patient is over forty.

Thymic hyperplasia seen in association with Graves' disease may cause the thymus at times to be quite voluminous, reaching from 60 to 250 grams.

In a general way the weight of evidence seems to indicate that the thymus does not bear a definite causal relationship to the onset of Graves' disease. It is, in the opinion of the writer, more logical to assume that the enlarged thymus in itself is an expression of thyrotoxicosis. It is even rational to suppose that the hyperplasia of the lymphoid tissue of the thymus is a compensatory reaction to the flooding of the system with toxins of thyroid origin. If we are willing to accept the fact that infection plays an important rôle in the production of thyrotoxicosis, we may see in the thymus hypertrophy, merely, increased lymphocyte production as a protective mechanism in the presence of infection.

Whatever the relationship of thyroid to thymus may be, we know that frequently the question of hyperplastic thymus is of interest to the

surgeon: we know that, under certain conditions, thymectomy is advisable or even necessary as a supplement to thyroidectomy.

ANATOMY

Location

The thymus, a grayish-pink organ composed of lobes and lobules, is located, usually, in the superior and anterior mediastinum extending from the level of the fourth costal cartilage upward; frequently it extends into the lower part of the neck. In children the upper extremity of the gland extends often 1–2 cm. above the midsternal notch. The thymus may reach the lower borders of the thyroid and the two glands are frequently connected by the thyrothymic ligament. The gland measures normally about 5 cc. in length, 4 cc. in width, and about 6 mm. in thickness.

Shape

The variability in the shape of the gland has been a matter of frequent observation. The gland is usually described as consisting of two lobes, though it has been described also by writers as being unilobar or trilobar.

According to Noback (186) the normal fetal thymus is broad in shape and is changed to the elongated shape usually seen only after the establishment of respiration.

It is usually found, in the normal gland, that the two lobes are placed in close juxtaposition along the middle line. An isthmus is not discernible. The lobes, as a rule, differ considerably in size and are occasionally united to form a single mass in which the lobar markings are not evident.

In part, the differences in description arise from the fact that the gland varies relatively and absolutely in size, weight, and position, depending upon the sex, general nutrition, age, etc., of the individual patient.

Weight and Size

Weight and size of the gland are subject to extreme degrees of variation depending upon the factors already noted. It is reduced in size by starvation and malnutrition. In lower animals, castration is said to increase the size.

The thymus in the new-born shows temporary loss of weight, probably coincidental with the normal weight loss characteristic with this period. Severe illness may also result in appreciable change of size. According to Cunningham, the female thymus weighs 20 per cent less than the male. This rather marked difference in weight is not borne out by other research. Hammar's (187) careful research has thrown into the discard certain conceptions, which we had, concerning the early atrophy of the thymus. His work indicates that the average weight at birth is in the neighborhood of 13 grams and increases to 37 grams at the age of fifteen. During adult life and middle age the gland proceeds to

atrophy and at the age of fifty-five weighs in the neighborhood of 12–15 grams.

Nerve and Blood Supply

The internal mammary arteries, with the inferior thyroid, constitute the blood supply. The nerve supply is furnished by the sympathetic and vagus.

Histology

The thymus has, as is usual with such structures, cortex and medulla. The cortex is composed largely of lymphocytes; the Hassall's corpuscles are the distinctive feature of the medulla. Research today has produced no definite evidence concerning either the origin or function of the Hassall's corpuscles. Jordan and Horsley state that "The histologic date consistently supports the interpretation of these thymic corpuscles as restricted areas of stenosis or occlusion of the lumen of medullary capillaries and precapillary arterioles resulting from endothelial cell hypertrophy concomitant with either disease or age involution" (188). According to other theories the Hassall's corpuscles are formed from the reticulum cells of the thymus and bear no direct relationship to the blood vessels.

Physiology

Notwithstanding the immense amount of research and experimental work performed within recent years, there still remains considerable doubt concerning the function of the thymus and its proper place in the physiology of the organism. That it has a place—and a place of considerable importance—we must concede.

We cannot consider it as a vestigial organ as is the appendix. Its development, the increase in size, pari passu with the development of the organism, precludes such an idea. True, it is not possible at the present time to attribute to the thymus a specific internal secretion. Neither is it justifiable to deny absolutely the possible existence of such a secretion. Recent writers, in our opinion, are too emphatic in their decisions to remove the thymus completely from the sphere of the endocrine glands. In the case of the thymus, the writer believes, with the means at our disposal at the present time it is extremely difficult (or impossible) to disprove the possible existence of a specific endocrine; the evidence is confusing and the data in support of either one side or the other unsatisfactory.

With this thought in mind—that the question of the thymus as an endocrine gland must remain, for the present, unsettled—we next proceed to consideration of the thymus as a lymphoid organ. Some believe that the thymus functions in the production of leukocytes and lymphoid cells in infancy and childhood at the time when such cells are especially needed. In addition to this rôle in the production of leukocytes in fetal life, others have attributed to the thymus the rôle of producing erythrocytes in fetal life. According to some experiments, thymectomy limits the growth and calcification of bone and renders the peripheral nerves more excitable to the galvanic current.

David Marine (189) presents some interesting experimental data; he adverts to the fact that Soli, in 1910, found that fowls, from whom most of the thymus had been removed, laid eggs with deficiently calcified shells. He recounts Soli's conclusion that the thymus of birds was concerned in some way with normal calcium metabolism. Marine proceeds to show that recent experimental evidence indicates specific chemical interrelationships between the thymus, thyroid, gonads, and the suprarenals. Marine's experimental work has confirmed work already done, demonstrating that thyroidectomy hastens the physiologic involution of the thymus. As further evidence of the interrelation between the thyroid and the thymus, he adduces the findings of many pathologists to the effect that atrophy of the thymus is frequently found in cases of infantile myxedema. "The conclusion seems evident," Marine insists, "that the thyroid gland is necessary for normal thymus growth and function."

Relationship with the Gonads

Gonadectomy delays involution of the thymus in both the male and the female. Paton and Goodall (190) in the case of the guinea pig; Soderlund and Backmann in the case of cattle; Lucien and Parisot (191) in the case of the rabbit—have shown that thymic involution commences at the time when spermatogenesis commences.

Relationship with the Suprarenals

Marine states, "Suprarenalectomy not only prevents thymus involution, but actually causes regeneration even of the highly involuted organ of old rabbits." It may be of interest here to present the summary with which Marine concludes his paper:

> Thyroidectomy hastens involution of the thymus. Gonadectomy delays this involution but does not cause regeneration. Suprarenalectomy not only delays involution of the thymus and lymphoid tissues, but actually causes their regeneration. Thyroidectomy prevents this reaction even after combined suprarenalectomy and gonadectomy.
>
> Suprarenalectomy plus gonadectomy is a more powerful stimulus for thymus and lymphoid regeneration than either of these influences alone.
>
> The combined effect of these two factors results in certain lymphoid and thymus hyperplasia in rabbits and rats which persists until regeneration of the accessory interrenal tissue corrects the physiologic defect.
>
> The syndrome thus experimentally produced resembles status lymphaticus and is believed to depend mainly on a partial loss of certain functions in the interrenal and sex glands rather than of the chromaffin tissue. The normal and abnormal lymphoid and thymic hyperplasias of infancy and childhood are believed to be manifestations of a functional underdevelopment of the interrenal and sex glands of varying intensity.
>
> The so-called lymphatic constitution which underlies or accompanies exophthalmic goiter and Addison's disease also appears to be dependent on a partial suppression of certain functions of the interrenal and sex glands (189).

Side by side with this summary of Marine's it may be of interest to give the summary which Short arrived at after a careful survey of the literature. Short summarized the experimental work up to 1924 and his summary indicates the following conclusions:

1. The thymus is not necessary for life.
2. Thymectomy has no effect on the growth and development of the skeleton and organs.
3. Castration delays the involution of the thymus.
4. A substance contained in the thymus when injected causes convulsions.
5. Thymus feeding to salamander larvae with or without parathyroids causes tetany.
6. Thymus hyperplasia follows double suprarenalectomy.
7. Thymic hyperplasia in thyrotoxicosis is secondary.
8. In birds a relationship exists between the thymus and the egg-producing mechanism.
9. So-called "thymic death" not due to tracheostenosis, probably bears no relation to the state of the thymus gland.
10. One, if not the primary function of the thymus gland, is to produce leucocytes.
11. The thymus may also have an anti-toxic function.

Pathologic Changes in the Thymus

Thymitis may occur as the result of metastatic infections. The thymus increases in size during the course of many of the acute diseases; on the contrary it atrophies in chronic conditions. Thymic tumors are relatively infrequent, fibromita, dermoid cysts, lymphomata, and malignancy are noted.

Surgical Relations

The thymus lies in the upper and anterior portion of the mediastinum, its posterior surface is in contact with the aorta, the innominate veins and arteries, the pulmonary vena cava, the trachea, the inferior laryngeal and phrenic nerves and the vagus. Its lateral surface is in contact with the pleura, its upper borders, in many cases, come in contact with the thyroid gland and similarly its lower borders and surface may come in contact with the pericardium.

Noback (186) found the thymus overlapped by the left lung in 80 per cent of the cases examined; and found the thymus overlapped by the right lung in all cases examined.

SYMPTOMS OF THYMIC DISORDERS

The symptomatology of thymic disorders has, to date, not been sufficiently covered by the internists. Our ideas of the subject are inclined to be vague.

In the first place, it may be advisable to say a word concerning the etiological factors operative in the production of thymic symptoms. Are the symptoms of thymic disorders due to a quantitatively or qualitatively changed thymic secretion as thyrotoxicosis is due to changed thyroid secretion? Or, on the other hand, can the symptoms be explained on the basis of pressure by the thymus gland on neighboring structures? Available evidence seems to indicate that the pressure factor is the preponderating cause of most of the symptoms. We must remember that in children the anterio-posterio diameter of the upper thoracic aperture is quite small. When the thymus is enlarged, it protrudes up into the neck and may

easily cause pressure of other organs at the level of the upper thoracic aperture.

The trachea at this point may be readily compressed from before backward. Hyperextension of the head will decrease the size of the superior thoracic opening and consequently, if an enlarged thymus is present, further constriction of the trachea will result. This fact will explain the onset of choking or suffocating spells in children consequent to hyperextension of the head. It will also explain why the suffocating and cyanosis are relieved when the child is held in the upright position, or with the head a little flexed. In crying the diaphragm and respiratory muscles are tensed; the contents of the mediastinum are pushed upward, the enlarged thymus is forced up into the unyielding bony ring of the thoracic opening where it causes pressure on the trachea and other important structures. The fact that crying often brings on breath-holding spasms or choking spells is also an indication that pressure is the prime etiological factor.

We must not, however, be too dogmatic; we cannot deny with absolute conviction the possibility of vitiated thymic secretion, or the rôle of such a secretion in causing at least some of the thymic symptoms.

It is also possible that the cause of thymic disturbance may be twofold, that some of the symptoms may be due to "thymotoxicosis" (vitiated thymic secretion) and that some of the symptoms may be due to pressure effects.

Latency.—It complicates the situation, both from the point of view of symptomatology and etiology, that many cases in which an enlarged thymus is demonstrated by the x-ray present no symptoms.

STATUS LYMPHATICUS

In this condition we have hyperplasia of the lymphatic system as a whole in addition to hyperplasia of the thymus. Patients with this syndrome are pale, flabby, show enlarged tonsils and adenoids and display a diminished resistance to infections. The generalized flabbiness, which is easily recognized but which is difficult to describe, seems to extend to the heart. Children of the thymo-lymphatic type are liable to heart paralysis and death after shock or sudden effort, etc. Sudden deaths of such children have occurred in the dental chair after an apparently light anesthetic, after swimming, diving, etc. These patients are supposed to show hypoplasia of the heart and vessels as well as general hyperplasia of the lymph tissues.

A word of caution is necessary. We are only too apt to accept deaths in children as "thymic deaths," for want of a better explanation. What is the cause of the so-called "thymic death"? Theory alone rules on the consideration of this question. Is the death due to the fact that the hyperplastic thymus has released a toxin which has gradually weakened the heart muscles? Is the sudden death due to the fact that this weakened myocardium has failed under stress of sudden effort or great excitement? More unlikely still, has the sudden shock suddenly liberated an excess of toxin which paralyzes the cardiovascular appliances? Is pressure, and pressure alone, the only factor?

It seems hardly rational to suppose that the thymus can enlarge suddenly and enlarge to such degree as to produce pressure sufficient to cause death. It is of course possible that an enlarged thymus, which does not cause lethal pressure while in the mediastinum, may cause lethal pressure upon vital structures if suddenly pushed up onto the intrathoracic opening surrounded by an unyielding bony ring. The mode of death, however, and the post mortem findings in most of these cases do not seem to corroborate this theory. Is the death due to acidosis? We can neither definitely affirm nor absolutely deny any one of these theories. Our inability to reach a conclusion on this subject is merely indicative of the mist which still hides in uncertainty the whole subject of thymic physiology.

ACUTE SYMPTOMS

Suffocating Spasms.—The child, during the feeding or otherwise, becomes suddenly cyanotic; he chokes and for a while appears in an alarming condition.

Breath-Holding Spasms.—The child in the excess of temper or in a crying spell suddenly holds his breath, becomes blue and may become unconscious. These spasms are not infrequently confused with petit mal.

Fainting Spells.—Fainting spells without apparent cause should draw the attention of the physician to the possibility of thymic disorders.

Asphyxia of the New-Born.—Asphyxia of the new-born is occasionally an acute expression of thymic pressure. The cyanosis and dyspnea are marked and death may result.

CHRONIC SYMPTOMS

Dyspnea.—Dyspnea, of greater or lesser degree, may be a prominent symptom. Dyspnea, not otherwise accounted for, should draw attention to the thymus. The dyspnea may be very slight, but, nevertheless, recognizable by a peculiar crowing inspiration as the baby cries.

Cough.—A chronic, hoarse cough, refractory to ordinary treatment, is an occasional symptom. This symptom as a rule is not recognized as being of thymic origin. A chronic, hoarse cough in a child, in the absence of lung findings, should indicate an x-ray study of the thymic region.

Asthma.—Thymic asthma has not received sufficient attention. Its recognition is particularly important owing to the fact that x-ray treatment of the thymus gives prompt relief. The writer has seen over a dozen cases treated unavailingly for long periods of time, which cleared up promptly after judicious x-ray exposure.

Cyanosis.—Cyanosis, of greater or lesser degree, may be present. It may be persistent, becoming worse after a spasm or choking spell, but never completely clearing up. It is, however, usually paroxysmal.

Thymic Stridor.—The dyspnea may be accentuated to the point of stridor. This stridor is most marked during inspiration and may only be noted in the presence of a bronchitis or other respiratory infection. Children with enlarged thymus seem to have excessive mucus in the bronchii and this excessive mucus is, perhaps, a factor in the production of the stridor.

We should hesitate, however, to classify every tracheal noise as thymic stridor even in the presence of an enlarged thymus, as indicated by the roentgenogram. Slight colds, bronchitis, and similar conditions may cause a stridor that has no reference to the thymus. Stridor is usually absent during sleep and is aggravated or provoked by exertion.

Systemic Disturbance.—Disturbance of the nervous system, excessive crying and irritability, restlessness and insomnia are occasionally noted. Eczema has been reported in a number of cases. In our experience, however, it has had no particular significance.

The baby may be well nourished, may, however, be malnourished, puny, and pasty in color. He may be subject to colds and "sniffle" a good deal. Disturbed and noisy nasal breathing is somewhat characteristic.

Thymus and Thyroid.—Most of the cases of Graves' disease associated with hyperplastic thymus do not display symptoms definitely characteristic of the latter condition. Occasionally, in addition to the thyrotoxicosis, the patient may suffer from severe choking spells. The dyspnea in some cases may be greater than the degree of thyrotoxicosis would lead us to expect. Furthermore, muscular relaxation and weakness of severe degree is somewhat suggestive of a complicating thymus hyperplasia.

DIAGNOSIS

Light percussion may show an area of dulness on either side of the sternum, frequently more marked to the right. It is suggestive if the dulness as outlined by a light percussion is continuous with the cardic dulness. The dulness due to enlarged thymus may disappear when the head is flexed. Occasionally the thymus may be felt in the midsternal notch. Physical examination and the x-ray will often clear up the diagnosis. The symptomatology already outlined should furnish the clew to the diagnosis in children. In adults, however, the difficulties are greater. The history is of utmost importance. It may be of interest to note a few of the clinical findings, interesting from the diagnosis viewpoint, that were present in our series. It was frequently noted that the patients with tumors of the thymus suffered from obstruction to the respiration when relaxed under general anesthesia. Another indication we noted frequently was the inability of the patient to breathe when the head is thrown backward. The stridor, when present, is not in the nature of a crowing sound like that from pressure of the thyroid gland. The patient sometimes describes a sensation of weight in the chest at about the location of the thymus.

Posture.—It is, of course, far fetched to say that patients suffering with tumor of the thymus present a characteristic posture. However, the following observation is significant: A sustained posture with the head held slightly forward, the shoulders slightly raised, the chest slightly expanded, and almost entire abdominal breathing, was noted in many instances.

Cyanosis.—Cyanosis of varying degrees, generally slight, was noticeable in forty-two of our cases; it was especially noticeable in the finger nails and was to a degree intermittent.

Extreme pallor and weak spells were present in eighty-four of a series of 127 cases; flabbiness in 100 of these cases; dyspnea or choking when going to sleep was noted in forty-two instances.

Epileptic Attacks.—Fourteen out of the above 127 cases were subject to epileptic attacks. Two of the fourteen had had no return of the epileptic seizure two years after operation. In six of the fourteen the attacks were much lighter and rarer. In the six other cases no effects were noted.

Dysphagia.—Of the 127 patients, nine could not eat solid food comfortably; two of the nine claimed that swallowing solid food caused coughing; four stated that swallowing of food "shut off their wind"; three claimed that the food just would not go down, that they could not swallow. The dysphagia disappeared in all nine cases after operation.

Anemia.—The hemoglobin index in no case was over 85. In thirty-six instances the hemoglobin was below 50. It was our observation that all these patients with pathological thymus were definitely anemic.

Additional Symptoms Noted in Our Series

Twenty-three of our patients suffered from chronic eczema; four of these had a peculiar thickening of the skin suggestive of fish skin. In about half the cases, one of the noticeable symptoms was a definitely accentuated abdominal breathing and fourteen gave a history of asthma. A slight cough was present in sixty-four cases; the cough was rather peculiar in character. There was apparently a definite desire to cough which was suppressed and kept under voluntary control as much as possible.

X-Ray Findings

The x-ray is an important help in the diagnosis of thymic enlargement. It is not, however, omniscient or infallible. The thymus enlarged longitudinally and hidden throughout its length behind the sternum, may not give us the characteristic shadow. A picture taken during diastole may not show a broad thymic shadow. The same patient, if pictured when the heart is in systole and during inspiration when the mediastinal tissues are broadened out may show the characteristic shadow.

The shadow of the normal thymus should not be recognizable upon the x-ray film. It is hidden behind the sternum and does not extend laterally to sufficient degree. When there is definite enlargement the shadow may be seen on either side of the sternum encroaching on the lung shadow. The density may be more pronounced on one side than on the other and below the shadow merges with the heart shadow. The shadow is, in a considerable number of cases, triangular in shape.

The x-ray shadow of enlarged thymus is wider transversely where it merges with the heart shadow. The bilateral symmetry is usually lacking in other conditions that might be roentgenologically confused with thymic enlargement.

A characteristic feature of the enlarged thymus shadow in children is that it increases or decreases, depending upon whether the child is crying or at rest. This fact should be borne in mind, as in the first place moderate enlargement often may be seen only if the baby cries; in the

second place, an erroneous idea may be given as to the actual size of the thymus if only one plate is taken, and that during the crying spasm. The convulsive effort of crying brings the diaphragm to a higher level shortening the vertical diameter of the chest and in so doing causing the mediastinal structures to flatten or broaden out. Naturally, under such circumstances the thymus shadow appears larger.

According to Gertsenberger (192), the shadow is wider during expiration than during inspiration. This observation seems well founded and is dependent upon factors already discussed.

For similar reasons we may assume that the shadow will vary with the degree of intra-abdominal tension. Any degree of intra-abdominal tension that is sufficient to raise the diaphragm and shorten the vertical diameter of the thoracic cavity should have the effect of broadening out.

Some writers compare the thymus shadow to a cap superimposed and fitting over the base of the heart. We have found this simile true in a fair percentage of cases.

Mosher, MacMillan and Motley (193), in an article in the *Laryngoscope* (St. Louis, January, 1926), find that crying during the taking of an x-ray plate does not enlarge the size of the thymus. The contrary in our experience is true.

Fluoroscopy

In the adult, the enlarged thymus may readily be seen by fluoroscopy in nearly all cases if a careful technique is followed. At least thirty minutes in an absolutely dark room should be allowed for the observer's eyes to become adjusted before he attempts to see a thymus under the fluoroscope. Longer time may be required if the observer is over forty years of age. The observation should be made in an absolutely dark room.

Starting with a moderate amount of voltage and milliamperes, the outlines of the bones, heart and heavier structures of the thorax should be viewed in a short exposure. Then the amount of current should be cut down with each short exposure until the outlines of the shadow of the thymus are visible. If the shadow is not clearly visible the voltage should be increased or decreased until just sufficient penetration for best results is determined. Then by varying the amount of milliamperes the maximum visibility is attained. This procedure requires patience and is obviously impossible with children.

Plates should be made in an attempt to provide a permanent record. In children plates are more often successful than in adults and we must depend upon them for diagnosis. Positive results can be shown in adults by plates in about 50 per cent of the cases where the thymus is clearly visible by fluoroscopy. The child is restless and difficult to handle; the plate is much more satisfactory and picture should be taken even if fluoroscopy is done. As a further word of caution, it may be stated that sometimes, when an enlarged thymus is not evident by fluoroscopy or on the film taken by the usual routine, an enlargement of the thymus sufficient to cause symptoms may be found by a lateral exposure.

The differential diagnosis between an intrathoracic prolongation from a hyperplastic thyroid and an enlarged thymus frequently depends

upon an x-ray plate taken, lateral view; in x-rays taken antero-posteriorly the shadows of a large goiter, the enlarged vessels, and an enlarged heart blend so closely that they cannot be differentiated from the shadow of a thymus. The matter is of considerable importance if thymic hyperplasia is preoperatively diagnosed; a brief preoperative course of treatment over the thymic areas, in such cases, would seem to be rational. This procedure we have followed in some instances with good results.

Kocher advocated, at one time, routine prophylactic treatment of the thymus previous to the thyroidectomy (194). Some surgeons still follow this routine. It has been our practice to submit all suspected cases of thymic enlargement to x-ray treatment previous to thyroidectomy.

DIFFERENTIAL DIAGNOSIS

Clinical Differentiation

(a) **Thymic Death** must be differentiated from: suffocation from overlying, poisoning, asphyxia, from aspiration of food into the larynx, congenital heart disease, chronic heart disease, etc.

(b) **Stridor.**—Thymic stridor must be differentiated from: stridor due to bronchial asthma; laryngospasm; obstructed mediastinal gland; retropharyngeal abscess; acute laryngitis; etc.

(c) **Cyanosis** due to hyperplastic thymus must be differentiated from cyanosis due to congenital heart disease; fibril conditions; chronic heart conditions; drug cyanotic sepsis.

(d) **Cough** due to hyperplastic thymus must be differentiated from cough due to aortic aneurysm, mediastinal tumor, etc.

Briefly, from the clinical standpoint, we should consider hyperplastic thymus last rather than first. We should, in the first place, attempt clinically to rule out those other conditions which, it may be said in a broad way, are more common. We should again bear in mind in this connection that the chase after the rara avis is not profitable.

X-Ray Differentiation

If the x-ray shows a decided increase in the lateral diameter of the gland there will, usually, be no difficulty in establishing a diagnosis of thymic hyperplasia. Where the lateral widening, however, is moderate or slight the so-called "thickened hilus" due to tuberculosis may cause confusion; increase in size of the tracheo-bronchial or paratracheal glands may throw shadows which simulate thymic hyperplasia.

The shadows due, however, to tuberculous adenopathy are usually more marked on one side and more irregular in distribution. Furthermore, they may possibly be associated with signs of constitutional tuberculosis as loss of weight; night sweats, etc. In adults an intrathoracic prolongation of the thyroid or an aneurysm may cause confusion.

It may also be necessary to differentiate hyperplastic thymus from the various types of cardiac hypertrophy; the clinical findings and the analysis of the types of shadow will usually make the differentiation sufficiently clear.

In adults thoracic aneurysm may have to be distinguished from enlarged thymus. The aneurysm shadow is clear-cut, and regular in outline.

TREATMENT OF THYMIC HYPERPLASIA

Opotherapy

It must be considered difficult to satisfactorily use gland products or extracts in the case of glands the physiological function of which is up to the present time extremely problematic. Extracts of the thymus have been given with apparent good results in cases of psoriasis and one or two other constitutional dyscrasias. To date it has not been shown that the administration of thymus extracts have any influence on thymic hyperplasia or on symptoms that may be referred to the thymus.

X-Ray and Radium

Surgery of the thymus nowadays is limited to thymectomy done in association with thyroidectomy; some years ago, before the effect of x-ray of the thymus was fully recognized, thymectomy for symptoms of thymic hyperplasia (generally in children) was not unusual. Rehn (195) in 1896 and Burniker in 1899 did partial thymectomies with good results. Friedlander (196) may be regarded as the pioneer in the roentgenological treatment of thymic enlargement. In 1904 he treated with good success an infant suffering from a severe form of thymic asthma. Since then the pendulum has swung back and forth between ultra-conservatism and misguided enthusiasm. A note of warning has occasionally been sounded concerning the danger of excessive dosage of infants. It has been held by some that complete involution of the thymus at a very early age is liable to lead to arrest of mental and physical development and even idiocy. Experimental and clinical evidence seem, to some extent, to support this stand.

The treatment of thymic hyperplasia in children by the x-ray was, in this country, really initiated by Lange (197) in 1911. Lange definitely established the fact that x-ray treatment of the thymus brings about involution of the gland.

Indication for Radium and X-Ray Treatment

1. All cases in children which present definite symptoms of thymic hyperplasia as thymic asthma, stridor, etc.

2. All children of the so-called "thymic-lymphatic" type in whom the x-ray shows increased thymus shadow and who are to be subjected to an operative procedure of any kind.

3. According to some authorities all children, irrespective of symptoms, who show increased thymus shadow on the x-ray should be subjected to carefully regulated roentgenological treatment.

4. According to some writers, children of retarded physical or mental development should, in certain instances receive trial x-ray exposures.

Shall we use radium or the x-ray? Some prefer one method, some another, while still others use both radium and x-ray, resorting to radium in cases which do not respond readily to the x-ray. De Buvs (198), Sam-

uel and Bowie advise the use of 100 mg. of radium element in 2 mm. of brass filter, separated from the skin by a distance of 5 cm. firmly fixed in place by adhesive plaster reinforced by a binder. The writers give duration of treatment as from eight to twelve hours, depending on the urgency of case, size of thymus, age and size of child; they advise, usually, anterior applications or in case three applications are given, that first an anterior, then a posterior and finally another anterior application be given. The interval between applications according to their technic is from ten days to two weeks. They state that three applications according to this plan is the limit as they feel that if results are not then discernible the case is not amenable to radium irradiation. Brayton (199) and Hueblein have advocated the following technic:

> One hundred milligrams of radium element, still in its 0.3 millimeter silver capsule, is wrapped in sufficient gauze so that when strapped to the chest by a strip of adhesive, it will lie half an inch from the skin surface. Four marks are made in the form of a rectangle over the thymic area, and the nurse is instructed to allow the package to remain two hours over each mark. This makes a total exposure of 800 milligram-hours.

Those who use radium claim that the application can be made with less discomfort and fright than is the case with the x-ray. They claim that struggling and crying paroxysms are avoided. Furthermore they feel that it is difficult to keep a baby accurately placed with relation to the x-ray tube, that it has to be held by others and that these others run some risk from exposure to high voltage currents and the rays.

X-Ray Treatment of Hyperplastic Thymus

X-ray treatment has a valuable place in the treatment of hyperplastic thymus in children. It also has a place in the treatment in adults if the conditions can be diagnosed. A case in point may be interesting: A man aged fifty was operated on in our clinic for removal of an old adenomatous thyroid of long standing. After the goiter was removed it was noted that he had a degenerate hyperplastic thymus. Owing, however, to his critical condition the operation was discontinued. Later the operation of thymectomy was suggested but firmly and finally refused by that patient. X-ray treatment was resorted to and the condition of the patient is gradually improving. His chief symptoms, at the time of operation and afterward, were difficulty of breathing which the thyroidectomy had not improved.

Regarding the technic of x-ray application, there is considerable difference of opinion. Some authorities advise one exposure; others advise daily exposure if symptoms are urgent; weekly exposure once a week for three weeks is advocated by some; this procedure to be followed by a second series if satisfactory results are not obtained. Pfahler (200) advised one treatment in four weeks and found that three to five treatments were sufficient.

Perhaps we might generalize by saying that the number of treatments should depend on the urgency of the clinical symptoms and on the degree of hyperplasia demonstrated in the x-ray.

For the actual treatment, the child is laid on his back with the limbs straight out, so that the vertebral column is kept in midline; the head is retracted and the arms held by the side. Some find it advisable to use a sandbag to keep the feet in position.

As regards the actual technical procedure—there seems to be considerable variation. Some radiologists get better results with one method, some another. The variation in technic, as a rule, comes within the following limits:

> 1 to 4 mm. of aluminum filter, ten inch distance; from 5 in. to 9 in. spark gap; 5 milliamperes and one to 5 minutes exposure.

Personal Observations

In a series of approximately 14,000 thyroidectomies it was found essential to perform a partial or total thymectomy in 127 cases. It is of interest to note that in three of these 127 cases there was no pathological change noted in the thyroid gland. The tumor mass, which was supposed prior to operation to have been thyroid was hyperplastic thymus present in the cervical region. Out of the 127 cases twenty-seven were patients in whom thyroidectomies with unsatisfactory results had been previously done. Pressure symptoms remained and a secondary operation, thymectomy, with practically entire relief was done. Twenty-three of our series of hyperplastic thymuses were discovered in the course of operation for toxic adenoma of the hyperplastic type. The remaining 104 were discovered in the course of operation for removal of long standing adenoma. In our series of cases we have not had a case of Graves' disease complicated with hyperplastic thymus of such a degree as to appear to need thymectomy. Neither have we encountered intrathoracic goiter associated with enlargement of the thymus.

In none of our cases were the symptoms present sufficiently distinctive to enable us to make a preoperative diagnosis. Weakness, out of proportion to the increased metabolic rate and disturbance of the respiratory function was the only symptom that could be considered, even in a mild degree, characteristic. In 19 instances, hoarseness of the voice (that had been attributed to stretching of the recurrent nerve) was noted; this symptom disappeared completely after operation in fourteen of the nineteen cases.

Pathologic Findings

The literature does not seem to have much of value concerning the pathological findings in hyperplastic thymus associated with goiter. It must be remembered that the hyperplastic thymus is subjected to considerable pressure. Evidence of this pressure was present in about two-thirds of our cases in the form of degenerative change. In about two-thirds of the cases, the growth removed was in the form of yellow, greasy, adenomatous tissue. The adenomata were definite and shelled out fairly easily leaving cavities that did not bleed. The specimens submitted to the pathologists were reported to contain typical thymus tissue and in addition degenerated areas.

In contra-distinction to these localized adenomas, in about one-third of the cases the tumor mass was composed of thin-walled, rather grape-like formations of follicles, each follicle whitish in color, having the appearance of a small cyst attached to the body of the mass by a thin connective tissue pedicle.

The freedom of the capsule seems characteristic. In this latter type, the capsule of the mass is freely movable and may be drawn up through the thoracic aperture and can be removed quite completely.

The capsule, on the other hand, of the type first discussed, the degenerative thymic adenoma, was in almost all cases, firmly attached to surrounding structures and was left in situ.

Relative Position of Thyroid and Thymus

The writer has observed that in the cases in which the thymus was presented at the upper thoracic aperture, the thyroid was situated at a higher level in the neck than usual.

Has this relative position of the thyroid and thymus any specific relationship to the length of the thyro-thymic duct? It has been already noted that the thymus is in itself a soft structure and deep in the thorax, and even when enlarged is not liable to cause serious pressure symptoms. It seems to us it is only when it is drawn up into the bony ring of the aperture that it causes serious disturbance.

Microscopic Pathology

As regards microscopic pathology we had section of both types of thymic hyperplasia examined by pathologists; in the reports of degenerated thymic adenomata the pathologists frequently included evidences of inflammatory change. In five instances the report read "Studded with numerous small abscesses." We were, however, inclined to doubt the existence of actual pus. We have never seen an abscess of the thymus; then again in these five cases there were no evidences of infection either during or following the operation. Only a small rubber drain was left in each instance and no evidence of suppuration was subsequently noted. These various considerations incline us to the belief that the pathologists mistook degenerated areas of tissues for actual pus.

TECHNIC OF THYMECTOMY

A short transverse or curved collar incision is usually made. As a rule, it is immediately above the manubrium sterni. We sometimes make an incision as for thyroidectomy. Burns' space is opened by vertical incision in midline. The anastomosing branch of the anterior jugulars in Burns' space is cut and ligated. The anterior jugulars are ligated or cut and ligated. The posterior wall of Burns' space is opened in midline from low behind the manubrium sterni to three inches above. The anterior plane of cleavage is exposed and the prethyroid muscles retracted.

We find that exposure and identification of the thyrothymic tract facilitates further operative procedure; this tract is usually found to originate from the lower border of the isthmus, but sometimes from the inner

margin of the lower pole of a lateral lobe or at the inferior junction of the lateral lobe and isthmus it is a thin, usually almost cord-like structure and is usually accompanied by the inferior thyroid veins. The sternohyoid and the sternothyroid should be separated well posterior to, and below the edge of, the manubrium sterni as well as above. After proper exposure has been made, traction of the ligament and blunt dissection with the finger will bring the mass up toward the thoracic aperture.

When the thymus is intrathoracic, at times, the hyperplastic thymus will reach high in the neck, even to the lower poles of the thyroid. In such instances identification of the thymus structure may easily be made.

With continued traction upon the ligament, the thymus, a more or globular mass, will be seen to appear in the wound on expiration and disappear again on inspiration.

What is the next step? Shall the operation be completed through the extracapsular or the intracapsular route? Shall the thymus be removed in toto, capsule and all, or shall it be drawn up as far as possible into the wound, the capsule perforated, the contents evacuated, and as much of the capsule removed as is deemed advisable? If the thymus lies high in the cervical region or if it is small and the capsule easily freed, removal by the extracapsular route may be easily and safely accomplished.

In certain instances the capsule of the thymus is adherent to surrounding structures and an attempt to dislodge it in toto may result in considerable hemorrhage in a situation where hemorrhage is difficult to control. The intracapsular route to us seems preferable. The anterior plane of cleavage is followed downward with the finger anterior to the thyrothymus tract until the capsule of the thymus is encountered. By blunt dissection with the finger, the capsule is freed in every direction by following the plane of cleavage surrounding it until attachments are encountered. Then the finger is passed downward posterior to the thyreo thymus tract and anterior to the pretracheal fascia and as much separation of the capsule from surrounding structures made as can be done with safety.

By traction on the thyreo thymus tract, the superior pole of the gland can usually be brought up above the sternum. Sometimes by continued traction and careful blunt dissection, the entire gland with its capsule can be brought up into a location that makes it possible to pass a ligature around a small pedicle that is the only remaining attachment of the gland. This pedicle contains some arteries and veins and should be ligated before it is cut. It should never be grasped with forceps as it is so friable that forceps will usually cut through it and hemorrhage, that can only be controlled by packing, result. Usually it will be found that the capsule can be freed to only a limited extent. The gland may easily be drawn upward until the upper pole presents at the thoracic aperture but no further. Sometimes an inferior thyroid artery presents an obstruction and should be ligated and cut. After all efforts at freeing the capsule, deemed safe, have been made, if the gland is still fixed in the thorax, the capsule over the upper pole is opened by blunt dissection and the gland is enucleated carefully with the finger, intracapsularly. Usually the gland is

broken up, especially if adenomatous, and brought out in pieces. After the contents of the capsule have been enucleated, the capsule can be drawn further out.

In many instances almost the entire capsule can be easily freed and only one or two points require ligation. In other cases the plane of cleavage seems to have been obliterated by adhesions to surrounding structures and only a portion of the capsule can be brought up into a position that it can be ligated and amputated. With this method we have never experienced a hemorrhage of any importance. Furthermore, it seems to us that this technic entails a minimum of pain and discomfort to the patient. Closure is made along the usual line. Drainage is always instituted with a strip of rubber tissue that is removed on the third day.

CASE I.—Mrs. H. G. ———. This patient had been diagnosed as a case of multiple adenoma of the thyroid. At operation it was found that the thyroid was small and apparently normal in every respect and was left undisturbed. The tumors were found in the thymus. Thymectomy was done with little difficulty. The respiratory trouble was greatly relieved. Her pulse rate increased after operation from 62 to 88. Her blood pressure rose from 105 systolic to 118. These improvements and clinical findings were established by a marked improvement in general health. In a period of five months she gained twenty-six pounds in weight.

CASE II.—Mr. ———. This patient was operated for a large adenomatous goiter accompanied with severe pressure symptoms. Great difficulty was experienced due to obstruction of the respiration. At operation definite tumors of the thymus were palpated. It was our intention to remove them; the condition of the patient, however, became so critical that any attempt at further interference was contra-indicated. The patient was allowed to come out of the anesthetic. He promptly recovered from the thyroidectomy; and his general condition improved but he obtained no relief from the marked interference with the respiratory functions; he has been urged to submit to a thymectomy but has consistently refused. His condition is gradually improving with the exception of the severe respiratory trouble, which continues unabated.

CASE III.—Mrs. J. F. ———, a doctor's wife, had been operated on seven years previously for goiter and a subtotal thyroidectomy performed. She continued to have respiratory and asthenic symptoms; with the aid of the x-ray, tumors of the thymus were diagnosed and operation was advised. At the operation it was found that the tumor mass was quite distinct from the thyroid. A large nodular thymic tumor was drawn up out of the chest; the tumor held 22 oz. of the soft, white nodular tissue already described. After the nodules were evacuated the entire capsule of the thymus was drawn through the aperture and removed.

CASE IV.—Mrs. C. J. T. ———, eleven years previous to our seeing her, had been operated for goiter and a subtotal thyroidectomy done. Previous to the operation she had had considerable respiratory symptoms, following the subtotal thyroidectomy, for a period of six years, no relief was experienced from the obstruction to respiration. At the end of six years a tumor, soft in character, appeared in the midsterno notch and in the midline of the neck; co-incident with the appearance of this tumor her respiratory trouble was much improved, after a period of about three years this tumor had almost entirely disappeared; a feeling of weight in the chest, however, and inability to sleep soundly caused her to seek relief. Tumor of the thymus was diagnosed and operation was advised. At operation a tumor was discovered, brought up and enucleated without much difficulty. Its blood supply and attachment were found to be continuous with the thyreo-thymus tract. After removal of the first tumor slight traction on the thyreo-thymus tract brought up two more tumors, all about the same size, from the chest; these were also removed. Finally the capsule of the thymus in almost its entirety was brought up and its attachment ligated and severed. Relief was immediate and recovery prompt and complete.

CASE V.—Mrs. Post. age 46 years, was seen seven years after previous thyroidectomy. A small tumor was palpable in the neck; the pulse rate and the metabolism were within normal limits. Marked obstruction of the respiration was evident and the patient's chief subjective complaint was that she could not breathe deeply. At operation, the grape-like type of thymus tumor was found. The tumor mass was pulled up toward the thoracic aperture and masses of this whitish tissue removed. The amount of adenomatous tissue brought out through the perforated capsule was amazing—two pints in full being removed. Finally the capsule was drawn up and removed in toto.

Case Report of Carcinoma of the Thymus

Our experience has been limited to two cases of malignancy of the thymus in children:

J. C. ———, boy, seven years old. Prior to operation, on clinical examination, a large hard tumor was found extending from the suprasternal notch to about the level of the cricoid cartilage. The tumor was

apparently fixed to all the surrounding structures. Great difficulty in swallowing and marked obstruction of respiration were present. X-ray and radium treatment had been employed to no avail. At operation the mass was found to be hard, dense, almost fibrous mass in character, dissection was impossible, and large portions of the mass were destroyed with the actual cautery. Considerable temporary relief of the respiratory trouble followed the operation. The patient could, however, swallow no better than before and died on the sixteenth day following operation, apparently from starvation and exhaustion.

Baby F. J. Infant, four months old. Clinically an enormous tumor was found extending from the suprasternal notch upward and backward on both sides behind the ear on the left and as far as the lobe of the ear on the right. At operation the tumor was found to be an extension from a tumor in the thorax and only lightly adherent to a thyroid of normal size and appearance. This entire tumor mass in the cervical region was removed by dissection and by the cautery. The intrathoracic mass was densely adherent and could not be removed. The child recovered from the operation and improved considerably for a period of three or four weeks. The pathological report was sarcoma of the thymus. After the fourth week the tumor mass returned and by the seventh week after operation was almost as large as before. Large doses of x-ray failed to check its growth and the baby died.

CHAPTER XIX

HISTORICAL

From our present knowledge of thyroid function it is evident that the thyroid gland has always been a necessary unit of human anatomic structure, and that thyroid disfunction has been a scourge of mankind since the beginning of time.

Pre-Christian Era

No definite description of goiter as a distinct clinical condition; no written record of goiter as a disease—has been given us by the pre-Christian era. It must be borne in mind that only a few fragments of ancient literature have come down to us, and that even these are not always susceptible to clear interpretation. Some passages in the **Hippocratic** writings seem to refer to goiter, but there is quite evident confusion between this disease, scrofula, and other tumor conditions in the neck.

Aristotle, though he describes well the trachea and the structures surrounding it, makes no mention of the thyroid gland. **Asclepiades** was acquainted with tracheotomy, but makes no reference to thyroid tumor. While the Greeks of the Hippocratic age seemed unable to differentiate goiter from other tumors, in some way they stumbled on to the curative properties of iodin without realizing the nature of the curative agent, and they were accustomed to the use of sea water and seaweed products for treating certain tumors and swellings.

Early Christian Era

First Century

One might expect a vast amount of medical literature from this period. Rome, the center of the world, was in a phase of intense intellectual activity. Horace was alive at the dawn of the century; Ovid was writing; it seemed that Virgil had passed on but yesterday. It was the golden age of song and story, the peak of Latin culture.

That medicine had a share in the intellectual activity of the age, we know from the writings of Celsus (205). Medicine and surgery reached a rather high standard of development for the time. The physicians, mostly Greeks, were acquainted with herniotomy and plastic surgery. **Celsus** gives us one of the first accounts of the use of the ligature. The surgical instruments, over two hundred in number, found in the ruins of Pompeii are a testimonial to the surgical ingenuity of the age.

It is from this age and from the pen of the erudite Celsus that we draw our first definition of bronchocele. "To Celsus, bronchocele was a tumor 'under the skin between the skin and the larynx, which is fleshy only or may contain a sort of honey-like substance, sometimes even containing

* For general information on the history of the thyroid and its diseases the reader is referred to Garrison (201), Brown (202), Halstead (203), and Dock (204). For important classical contributions to thyroid disease, see Major (204A).

small bones and hairs mixed together'." He too recommended, in the way of operative measures, a midline incision, evacuation of fluid, if there were any, or, if the tumor were solid, he advised that it be drawn out of the wound and treated with liniments. "But," he says, "it is easier to remove it with the scalpel." Thus this would seem to indicate that the surgeons of that day had some success with goiter extirpations, which, if true, is more than can be said of any age again until the nineteenth century.

From another source we have a sidelight on the medical treatment of goiter. **Dioscorides,** the father of materia medica, an army surgeon in the service of Nero, is our authority. His array of remedies, for instance, distillations of the feces of various animals and reptiles, brine, seashell and seaweed preparations, and vegetable decoctions of various kinds, will not have the sympathy of the modern therapeutist. Dioscorides assures us that "the root of Oxalis hanged about the neck of them that suffer with goiter will prove a perfect cure."

It is interesting to note that goiter was recognized and its prevalence realized by some of the lay writers of this century. **Vitruvius,** architect to the great Augustus, speaks of it in writing of aqueducts and of water supply. He mentions that nitre-containing waters have a tendency to diminish the size of struma or goiter. We have one line from **Juvenal,** the great satirist of the first century, that says all there is to say of the prevalence of goiter in his day: *"Quis tumidum gutter miratur in Alpibus?"* Freely, "who wonders at a swollen neck in the Alps?" Goiter must have been indeed common and its prevalence realized by the public when the satirist could use the fact to point one of his jibes.

The Second Century

The Second Century brought **Galen,** (206) the peripatetic Greek: wanderlust and the desire to acquire and inculcate knowledge seem the motives of his career. With all his extraordinary knowledge of anatomy and physiology, sometimes right, often wrong, Galen is a disappointment, at least in so far as goiter is concerned. In his book on tumors, he does not definitely refer to goiter; he does, however, speak of tumors pressing on the windpipe and causing aphonia; he shows familiarity with the recurrent laryngeal nerve and warns of the danger of injury to the nerve in operative procedures. It is of interest to speculate as to whether this oversight of Galen's in regard to thyroid swellings has any reference to the lack of interest in goiter during the succeeding centuries. Galen was the master. After him, for centuries, there was no initiative or originality. As Galen had not found goiter worthy of mention, his disciples could not find goiter worthy of study, observation, or comment.

The contemporaries of Galen—**Heliodorus, Soranus, Antyllus**—have written nothing that can be construed as being directly pertinent to goiter.

Sixth Century

With the decline of Greco-Roman civilization in the west went culture and cultural aspirations. For several centuries we find little of

importance in medical literature and practically nothing pertaining to goiter. In the sixth century, we find that **Aetius,** the royal physician to Justinian, has a chapter on goiter. He defines bronchocele as a definite form of tumor involving the gland in front of the trachea, and advises operation as well as applications and liniments.

Seventh Century

In this century lived **Paul of Aegina,** one of the last of the Greek compilers and an ardent disciple of tradition and the old order. Though a capable surgeon for his time, he prostrates himself before the ancients; they know all, have said all that is to be said, and he fancies himself in the rôle of a humble scribe. Paul's attitude is typical of his time and an indication of the low level of medical thought and initiative of that period.

An operation which he describes comes very close to our conception of thyroidectomy. He describes the skin incision, retraction of the superficial tissues, removal of small tumors, and continues, "The bigger strumae being lifted out with hooks and suspended, the membranes everywhere surrounding them are to be separated, and the tumor removed. With the utmost care we should see to it that neither the arteries, which are called 'the carotids' nor the recurrent nerves are injured. And if some vessel interferes with the work, it is to be bound about with a cord or cut through the middle, unless it be too large. Now when we have reached the narrow base of the struma, the one to the right is first to be cut off."

Arabian and Mohammedan Influence

For our next record, we must look toward the east. The oriental mind of this age was not keenly interested in surgery. The Arab, Mohammedan, and Hebrew genius tended rather in the direction of polypharmacy and intricate therapeutic formulas.

In spite of this racial antipathy to surgery we find that the three great exponents of the medical art in the Bagdad Caliphate, **Rhazes, Haly ben Abbas,** and **Avicenna,** showed interest in the subject of goiter.

Rhazes (860–932) of measles and smallpox fame, one of the great clinicians in medical history, was acquainted with goiter, and is perhaps the first to discuss intelligently both the surgical and medical treatment of the disease.

Haly ben Abbas, who was at the height of his renown about the year 994, described goiter, but showed some tendency to confuse it with other cervical tumors.

Avicenna (980–1036) was an extraordinary character who may be pictured as a Galen reincarnated in Bagdad of the eleventh century. He was brilliant, versatile, a positivist, and somewhat of an egoist. He was court physician to several succeeding caliphs, and wielded an immense influence on sane medical progress. Though he considered surgery an inferior art and not worthy of his best attention, he discussed goiter and described what may be taken to be a goiter operation. In his description he reiterated the already age-old warning concerning the danger to the recurrent laryngeal nerve during the operative procedure.

Albucasis was a prolific writer of the eleventh century, and is responsible for a medicochirurgical treatise entitled the "Collection." He is interesting chiefly from the fact that he was the first of whom we have definite record that undertook the "genuine extirpation of a goiter"(207).

Europe and the Middle Ages

The story of surgery in medieval Europe is drama, tinctured with burlesque. The élite of the profession were the monks and ecclesiastics; next in order of merit and degree of dignity, the apothecaries; next the lowly barber who played the despised rôle of surgeon as a sideline; and on the heels of the barber a motley and zealous army of faith-healers, psalm-singers, bone-setters, cuppers, blood-letters, itinerant fanatics, philter-sellers, magicians, wisewomen, and mountebanks. The sins committed in the name of surgery were so appalling and the abuses so grievous that the Church made an attempt to control the situation in the famous Edict of the Council of Tours, *Ecclesia abhorret a sanguine*, "The Church frowns upon the shedding of blood."

Gautier in his "History of Medicine at Geneva" throws an interesting side-light on the situation. In searching through the city annals of Geneva and investigating all available sources for the names of those who had practiced the healing art in Geneva in the fifteenth century, he found the names of ten apothecaries, three barbers, and no physicians (208).

Another factor that undoubtedly tended to retard the progress of surgical development in those days was the intense anti-Semitism that animated many of the European nations. The Jew and his genius were debarred from the practice of medicine as shown by the following edict of the city council of Geneva: *Fiat conclusum quod Judeo Medico interdictum officium medicandi, et ipse omnes expellantur a civitate.* Progress was inacceptable, the Jew representing progress was inacceptable, and both were shut out.

It is not surprising, then, that the net of interrogation which we throw into this maelstrom of feudalism, supersitition, and ignorance of the Middle Ages, comes back empty of any valuable information on the subject of goiter. **Mundinus,** the medieval anatomist, does not identify the thyroid gland; **Arnoldus de Villanova** of the Salerno School advises against operation and advocates "dissolving and resolving remedies." Most of the writers of this period are equally vague and show no scintilla of a new idea in the field of surgery. There is one exception, one figure that stands out as a giant among pigmies.

Guy de Chauliac (1300–1370) was one of the comparatively few licentiates in medicine of the fourteenth century. From peasant boy to the most prominent place in his profession, and to the rank of physician to several successive popes at Avignon is the story of his life. He possessed originality and vision and may be said to have inaugurated the Renaissance in surgery. He was interested in thyroidectomy as well as in several other surgical procedures, and in 1363 advocated extirpation of the goiter in preference to expectant measures (209).

Renaissance Period

Vesalius' (1514–1564) works contain illustrations of the trachea and larynx, but his conception of the thyroid, as drawn, is quite inaccurate. [Brown was unable to find even a fair illustration of the thyroid or laryngeal gland up to the time of Bartholin (1616–1680).]

Paracelsus (1493–1541) (210).—This ingenious quack seems almost to have stumbled on to a fact of definite importance. Under the heading *De generatione stultorum*, he establishes a coincidence between cretinism and goiter, but does not hint at a causal relationship.

Wharton (1610–1673).—The first really accurate description of the thyroid gland we owe to Wharton (211). He described it as consisting of two lobes and an isthmus, but was completely at sea in regard to its function. To it he gave the name thyroid from the Greek *Thureaos*, signifying shield. Wharton's reports stimulated the interest of other investigators and caused great difference of opinion among scientists for a century or more. **Morgagni** said, almost a hundred years later, "It is certain that the thyroid is a single gland, but as to whether it possesses a duct or not is doubtful" (212).

Dawn of Scientific Medicine

The seventeenth century may be termed the dawn of exact science in the domains of physiology and histology. **William Harvey** with King Charles looking over his shoulder, was working on the circulation of the blood. **Malpighi** (1628–1694), the father of microscopy, completed Harvey's picture and gave the story of the capillary circulation. **Morgagni** and Malpighi studied the thyroid and devoted much thought to its possible function. Their opinion, which was shared by Bartholin, was that the gland exuded a secretion into the larynx for purposes of lubrication.

Further Knowledge of the Thyroid

Vater in the first quarter of the eighteenth century was inclined to the hypothesis that the thyroid was a gland of external secretion, but was unable to locate definitely an outlet.

Haller, towards the end of the eighteenth century, was perhaps the first to decide that the thyroid was a gland of internal secretion. After careful search for a duct had failed, he classed the gland with the spleen, and assumed that the secretion was taken up directly by the circulatory current.

Cruveilhier.—It was not until the middle of the nineteenth century that the conception of the thyroid as a ductless gland was placed on a firm basis. The prolonged investigations and minute dissections of Cruveilhier demonstrated beyond doubt that there was no duct, and led investigation toward more profitable objectives. From this point great strides were made in the histologic and physiologic knowledge of the gland. **Schwager-Bardellen** described in detail the vesicles of the thyroid in 1841. Streif and others, a little later, demonstrated that the gland was composed of closed vesicles.

It is to the two great physiologists of this period, **Claude Bernard** and **Brown-Séquard,** that we owe our first definite conceptions of the internal secretions. Claude Bernard (1813–1878) was making his epochal studies of glycogenic and pancreatic functions. Brown-Séquard (213) (1817–1894) was busy with his adrenal investigations, and chronicled interesting sequences due to the removal of the adrenals in animals.

Schiff (214) of Geneva contributed some of the first experimental work on the thyroid secretion, and demonstrated the importance of the secretion to body function. **Curling** (215) who first noted myxedema in 1850 connected the absence of thyroid with "symmetric swellings of fat tissues of the sides of the neck connected with defective cerebral development."

Recognition of Dysfunction of the Thyroid

Hypothyroidism

The deficiency of thyroid secretion as a clinical condition was recognized partly by clinical observations, partly by animal experimentation, and partly as a result of operative procedures on the human.

In 1873, **Gull** of London described the syndrome of myxedema (216). In 1877, **Ord** made further observations and proposed the name of myxedema (217). In 1882 **Reverdin** of the University of Geneva confirmed the findings of Gull and Ord by showing a case of myxedema which had followed complete extirpation of the thyroid (218). In 1883, **Theodor Kocher,** already a prominent figure in goiter surgery, made a master demonstration of the results of thyroid privation and proposed the term of cachexia strumipriva (219).

Cachexia Strumipriva

Kocher, like Billroth, in his first series of thyroidectomies had done total excisions, and in his paper in 1883 he recounted that eighteen patients, out of thirty-four with total excision, returned for examination, and only two were free from symptoms of cachexia strumipriva.

Schiff, (214) in 1884, by means of animal experimentation, laid the foundation of organotherapy as far as the thyroid was concerned. He proved that the reimplantation of gland tissue corrected the condition of thyroid deficiency, and this discovery opened up the wonderful possibilities of thyroid extract in myxedema and cretinism.

In 1884, also, **Horsley** (220) proved that cretinism, myxedema, and cachexia strumipriva were identical as regards causation, were all due to thyroid deficiency and were all susceptible to the same remedial agent, thyroid extract. In 1892, **Murray** (221) was using thryoid extract routinely in thyroid deficiency cases.

Hyperthyroidism

Investigations of hyperthyroid conditions did not proceed as well.

Isolated observations were made, even by the ancient writers, tying together one or more of the symptoms of hyperthyroidism with the presence of goiter. Not even a remote approach to our conception of thyrotoxicosis was made until towards the end of the eighteenth century. About

the year 1788, **Flajani,** an Italian, observed the coexistence of goiter, exophthalmos, and palpitation (222). It was observed and nothing more.

In 1835 **Robert Graves** of Dublin gives us our first clear impression of hyperthyroidism as a distinct disease. In 1843, in his *System of Clinical Medicine*, he goes into further detail. He says, in describing Graves' disease, "The enlargement of the thyroid seems to be essentially different from goiter in not attaining a size at all equal to that of the latter disease, and seldom attains serious deformity" (223).

Basedow (224) had been pursuing independent investigations for years, and in 1840 gave an account of the cardinal symptoms, but considered the condition to be due to a masked scrofula.

Even in comparatively recent years, the significance of the cardinal triad, in connection with goiter, has not been fully grasped. This is especially true of the cardiac condition, and the significance of goiter heart is even at present not sufficiently impressed on the medical mind. The writer recalls an interesting incident in Theodor Kocher's clinic in 1904. Kocher was discussing a case he had operated upon a week previously and marveled at the wonderful postoperative improvement in the cardiac condition. "Had I anticipated this improvement," he said, "I would have postponed the operation for a week or two." He did not realize that the improvement in the cardiac condition was due to the operation.

Two years later the writer was visiting one of the early goiter clinics of America when the operating surgeon, in discussing a case similar to Kocher's eight days after operation, seemed surprised by the marked improvement in the cardiac condition and pulse rate. He observed that rest alone could not account for the improvement; that these cases sometimes have periods of decided improvement rather unexpectedly. In other words, even in 1904 and 1906 leading surgeons were operating cases of toxic goiter for deformity rather than for goiter hearts.

Surgery of the Thyroid in Recent Years

Resuming the history of thyroid surgery, we find that in the early part of the nineteenth century the extirpation of a goiter was still a formidable task. The early years of this century saw the birth of four individuals who were to raise the science of surgery in general, and the surgery of the thyroid in particular, to a plane undreamed of heretofore. The four future benefactors of the race were **Louis Pasteur** (1822–1895), **Lord Lister** (1827–1912), **James Simpson** (1811–1870), and **Billroth** (1829–1894). **Kocher,** born twenty years later, was to raise thyroidectomy to a plane near perfection.

Preantiseptic Era

Today we have little conception of the conditions that confronted the surgeon in the preantiseptic and preanesthetic era. Infection and hemorrhage made every operation a major hazard; goiter operations particularly were dreaded owing to the extremely vascular field, the important structures involved, and the great dangers of infection. Those brave enough to undertake thyroidectomy had to face a mortality of about 50 per cent.

Billroth (225) showed a mortality of 40 per cent in the first twenty thyroidectomies prior to 1869, and a slightly lower mortality in his thirty-six operations, 1869 to 1876. According to Süskind the mortality up to 1850 amounted to 40.9 per cent (226). **Bruberger** reports eighty-two operations prior to the antiseptic period with a mortality of 34 per cent (227).

Introduction of Antisepsis

In 1865, **Lister** commenced his immortal work on antisepsis. In 1876 Listerism was accepted in Germany, in 1878 in Italy, in 1880 in France and Britain, but not until 1890 was it generally accepted in America.

Introduction of Anesthesia

Nitrous oxid was discovered by **Humphry Davy** in 1799, but its benefits were not pursued. The first use of nitrous oxid or anesthesia was made by **Doctor Horace Wells,** a dentist of Hartford, Connecticut, in 1844. Ether was first exhibited for anesthetic purposes in 1846. There are two aspirants for the honor of its introduction, Doctor L. Charlton Morton and Doctor Charles T. Jackson, both of Boston. The great impetus, however, to the cause of anesthesia was given by **Sir James Young Simpson** when on November 4, 1847, he administered the first chloroform anesthetic in the amphitheatre of the Royal Free Hospital in Edinburgh.

The immediate results of the combined factors of antisepsis and anesthesia were a greatly increased number of operations and a greatly decreased mortality. Prior to 1861 **Halsted** was able to collect only one hundred and six authentic goiter operations from the literature of all times (203). In Kocher's clinic alone, from about 1880 to the time of his death in 1917, over five thousand cases were operated for goiter, and the mortality in his last two or three thousand cases was considerably less than 1 per cent (228).

Pathfinders

Some of the pathfinders have already been discussed, the men who cut through the undergrowth of obstruction and ignorance and cleared the way for the brilliant accomplishments of the last fifty years. The list of these great men includes Billroth, Kocher, and Mikulicz; Pasteur, and, treading on his heels, Lister; Humphry Davy, and, half a century later, Simpson. One worthy name is usually absent from the rôle of honor: **Semmelweiss,** who in the obstetric wards in the General Hospital in Vienna in 1846, preached and fought for the principles that were Listerism twenty years later. The forest of ignorance, conservatism, and professional obstruction was too much for Semmelweiss. He was unable to crash through as did Simpson, Lister, and Pasteur. He died in a madhouse and never knew his greatness.

It is of interest to try to ascertain, in tracing the evolution of the technic of thyroidectomy, the originators of the different steps in the perfection of the operation.

We are indebted to Halsted (203) for his collection of historical data: **Sir William Blizard** (229) was the first (1811) to ligate a thyroid artery

for the cure of goiter. **Luigi Porta** (230) (1850) made the first ligations of superior and inferior thyroid arteries. **Green** (231) is usually credited with the first goiter operation in Great Britain. **N. R. Smith** (232) is credited with the first operation in America. **Kocher** (219) is responsible for the midribbon muscle splint. **Boeckel** (233) (not Kocher as commonly supposed) is responsible for the "collar incision." **Mikulicz** originated the bilateral resection of the gland (234).

Thyroid surgery was promoted, in the middle of the nineteenth century, against the force of a tremendous wave of pessimism. There were few surgeons anywhere, prior to 1850, who were brave enough to undertake or advocate thyroid extirpation. The attitude of the profession in France is evident from the fact that in 1850 goiter operations were prohibited by the French Academy of Medicine. In England, with the exception of Watson, goiter surgery found little support. The great **Liston,** of whom it was said that the flash of his knife and the crunch of the saw through the bone (in an amputation) were almost simultaneous, found himself helpless in the face of thyroid vascularity, and acknowledged it. He said, in 1846, "You could not cut the thyroid gland out of the living body in its sound condition without risking the death of the patient from hemorrhage" (235).

In 1866 in America, **Samuel D. Gross** pictures the disgraceful path of the goiter surgeon. "Every step he takes will be environed with difficulty, every stroke of his knife will be followed by a torrent of blood, and lucky will it be for him if his patient lives long enough to enable him to finish the horrid butchery" (236).

There are dozens of such protests in the literature, but these two excerpts will demonstrate that the men who undertook surgery of the thyroid in those days were men of courage and resource, pioneers in the full sense of the word.

The attitude of the German medical profession is apparent from **Dieffenbach's** article in 1848. "The operation for goiter is one of the most thankless, most perilous undertakings, which, if not altogether prohibitive, should at least be restricted to certain varieties of the malady" (237).

Pioneers

Billroth (225) (1829–1912).—Billroth's first series of cases after the introduction of antisepsis showed a marked drop in the mortality rate. In the period from 1877 to 1881 he operated forty-eight cases with a mortality of 8.3 per cent. Consider this as against his mortality in the preantiseptic days when he operated on the thirty-six cases in the period between 1869 and 1876 with thirteen deaths, or a mortality of 36.1 per cent. In eight of his cases previous to 1883, tetany developed. Halsted indulges in interesting speculation on this incident. He compares the results of the Billroth and Kocher clinics, and finds that Billroth's cases were liable to tetany and that Kocher's cases were very liable (before 1883) to cachexia strumipriva. From observation of the technic of the two surgeons, he explains the conflicting results in this way: Billroth was a hurried operator, and pushed on regardless of hemorrhage and of a clear oper-

ative field; in many cases he probably removed the parathyroids and left part of the thyroid. This hypothesis is borne out by his rather high percentage of injury to the recurrent nerves. Kocher, on the other hand, was a neat, precise operator with hemostasis as perfect as he could make it. He did a thorough enucleation of the gland, but spared the posterior surface of the capsule and thus protected the parathyroids and the recurrent nerves.

Billroth later modified his method and did a unilateral lobectomy instead of a complete extirpation. In early days, like most of the other surgeons, Billroth had recourse to some procedures current at the time for the palliative treatment of goiter, among which were the use of hair seton, incision, through drainage, iodin injections, chlorid of iron injections, caustics, and actual cautery, debridement and morcellement.

Billroth is more famous for his school than for any other personal contribution. Among the many distinguished men who studied with him at Zurich are Wölfler and von Mikulicz, the latter of whom gave us bilateral resection in lieu of lobectomy.

As regards the cause of mortality in Billroth's preantiseptic days, it may be interesting to note that of the eight deaths, seven were due to infection and one to hemorrhage.

Watson (1792–1882).—Watson, a Scotchman, may be counted as the pioneer in thyroid surgery of Great Britain. He was one of the first to connect in a vague way the postoperative improvement, in cases of toxic goiter, with the operation. In a series of cases reported in 1874, he notes that three showed exophthalmos and that in one case the exophthalmos and anemia had subsided greatly after operation (238).

In order to give some idea of pioneer operations it may be interesting to give a brief report of Watson's operation. According to Bruberger (227), after the preliminary measures of gland exposure, Watson carried a threaded aneurysm-needle beneath the gland from the middle of the upper to the middle of the lateral edge. When this thread was tied about one-fourth of the vessels leading into the gland were shut off. In the same way the needle was passed three times beneath the remaining quarters of the gland, and after all the threads were tied, the tumor was severed from its connection by means of the curved scissors.

Desault. (1744–1795).—Desault is easily the leading figure in the early days of thyroid surgery in France. Halsted states that the operation devised by Desault in 1791 had not been improved on in France or America up to 1883 (239).

He was the first to dissect the firmly adherent gland from the trachea. Lücke, Kocher, and surgeons everywhere up to about 1874 found it necessary to ligate the tumor *en masse* when it was firmly bound to the trachea.

Desault was the first surgeon, of whom we have record, who performed an excision for struma. His operation featured a fixation ligation of the pedicle. In his operation he understood the technic of isolation and ligation of the superior and inferior thyroid arteries.

J. A. W. Hedenus.—Hedenus was prominent in the early part of the nineteenth century. In 1821 (240) he published an account of

six thyroid extirpations without a mishap. In all six the goiter was huge and almost suffocating the patient. This record is unsurpassed in the days of preantisepsis.

As the method devised by Hedenus remained in use for about eight years afterwards, a description of it may be of interest. Under vertical midline incision, liberating the tumor sufficiently to expose the superior and inferior thyroid arteries, sixty-four arteries were tied. The thyroid vessels were then tied. Difficulties were encountered as the operation progressed because new arteries always had to be ligated in the depth of the wound. Since arteries as large as the radial continued to present themselves, the pedicle of the tumor was transfixed with a double ligature and tied off. The goiter was then cut away without further bleeding.

In the United States and Canada up to 1883, we have record of forty-five operations and five deaths, one of which was due to pneumonia. Excluding the pneumonia case, we have a mortality of 9 per cent. This compares very favorably indeed with European statistics. The operators among others were **Nathan R. Smith** (232), **William Warren Greene** (241), **E. L. Marshall** (242), and **F. F. Maury** (232).

The mortality statistics may be cited with some satisfaction considering Süskind's attitude that operative work on the thyroid up to 1877 was chiefly promoted by German surgeons. Bruberger (227) is inclined to be more generous than Süskind (226). In 1876 he writes: "There are several surgeons who have very recently rendered conspicuous service in matters pertaining to the technic of goiter extirpation. These are the American, Greene; the Englishman, Watson; our German fellow-countryman, Kocher; and the Frenchman, Michel."

Successors to the Pioneers

Von Mikulicz is one of the most brilliant exponents in the second generation of thyroid surgeons. A pupil of Billroth's, he adhered for a time to Billroth's technic. Later, in an effort to lessen the incidence of tetany and injury to the recurrent nerves, and at the same time remove enough of the thyroid tissue to prevent recurrences, von Mikulicz devised the bilateral excision on which much of the present day technic is based (234).

Paul Sick.—To Paul Sick, perhaps, we owe the first report on the condition that Kocher was to describe in 1883 under the name of cachexia strumipriva. In 1867, he reported what amounted to a total bilateral lobectomy, followed by the symptoms of cachexia strumipriva (244).

The period from 1878 to 1883 may be termed the golden age in the development of thyroid surgery. In Kocher's clinic, in fact, everywhere throughout Germany, Switzerland, and Austria, great interest was manifested in this branch of surgery. Operations were more frequent and the mortality less disturbing. At this period Kocher had developed his technic and had reached the first place in thyroid work.

Kocher.—In 1872, at the age of thirty-one, Kocher was appointed successor to Lücke as director of the surgical clinic in Bern.

Kocher, in the early days, did a complete bilateral lobectomy as did Billroth. In 1883, however he was much disturbed by the frequency of an

unusual syndrome in his postoperative cases. Kocher for the first time employed the term cachexia strumipriva to define this condition (219). **Reverdin** (218) in 1882 had already called attention to postoperative myxedema.

As early as 1882, it is interesting to note that Kocher's attitude toward thyroid surgery was the acme of optimism. He writes, "The timely excision of ordinary goiter is an operation free from danger."

After his discovery of cachexia strumipriva in 1883, Kocher radically changed his technic and for the remainder of his life usually confined himself to enucleation of tumors and unilateral lobectomy. He was never an exponent of bilateral resection. The paper he published gives the detail, technic, and standardization of the operation of lobectomy (219).

When he died, July 27, 1917, five thousand cases of goiter had been operated upon in his clinic at Bern.

Halsted, who esteemed him as a teacher and revered him as a friend, says, "For nearly half a century Professor Kocher had been in surgical harness at Bern, toiling vigorously and triumphantly to the end" (203).

Kocher's achievements are listed by Halsted:

1. Discovery of the condition "cachexia strumipriva."
2. Studies of malignant tumors of the thyroid.
3. Perfection of operation of thyroidectomy.
4. Stimulus which he gave to the operative treatment of Graves' disease and to the study of the milder forms of hyperthyroidism.
5. Recognition of ingrafted forms of Graves' disease.
6. Demonstration of the value of the ligature of the arteries as a preliminary step to lobectomy in highly toxic cases.
7. Demonstration of the danger of indiscriminate administration of iodin to patients with goiter.

American Surgeons

In America, from 1900 to 1910, the surgeons especially prominent in thyroid work were Halsted, Rogers, A. J. Ochsner, Crile, Crotti, and Charles Mayo.

Halsted (245), as already stated, did much work on the parathyroid glands. His *History of Operative Goiter* (203) is an interesting and instructive work, and those interested in this subject are referred to it for a complete compilation of the facts for both ancient and modern times. The procedures devised by him have added much to the technical development of the operation in this country. Halsted also made valuable contributions to the progress in local anesthesia.

John Rogers (246) of New York was the outstanding early advocate of ligation of the inferior thyroid artery in the treatment of exophthalmic goiter. The technic developed by him in 1909 for the ligation of the trunk of the thyroid artery near its origin has not been improved upon to this day.

A. J. Ochsner did not claim to have contributed much of an original nature to the development of goiter surgery. He freely admitted that he tried the methods of others and retained for his own use those which he liked. As a teacher and writer of medical literature he has contributed much to the subject of goiter.

Crile (247) has emphasized the value of combined anesthesia in certain cases. He has done much in improving preoperative routine and has contributed largely to thyroid literature.

In 1918 **Crotti** (248) published the first comprehensive treatise upon the diseases of the thyroid gland. The effect of this book upon the development of the modern conception and treatment of thyroid disease is hard to evaluate. In this classical treatise he brought together all the worthwhile thought and all the investigations which had been done up to that time and by making this knowledge accessible the appreciation of the importance of the goiter problem was enhanced.

It is hard to do full justice to the rôle that has been played in the development of goiter work in America by the **Mayo Clinic** (249). The clinic is entitled to credit not only for treatment of the largest group of goiter cases in history, but also for the brilliant, successful, original investigations conducted, the conclusions made possible, and notable participation in the development of the technic of thyroid surgery.

They also deserve credit for being, perhaps, the first physicians fully to appreciate the value of group efforts in the study and treatment of disease. In no other field of medicine is the advantage of the clinical group so apparent.

One outstanding scientific attainment and one of epoch-making importance was the discovery by E. C. Kendall (250), at the Mayo Clinic, of thyroxin as the active substance in thyroid secretion.

Thyroid Surgery of Today

The advance in goiter surgery in the last twenty years is perhaps the most outstanding development of medicine in all times. If a word of reminiscence may be pardoned, the writer recalls the days in the early part of this century when thyroid surgery was in its infancy in this country. Medical treatment, x-ray treatment and such procedures as the injection of hot water, carbolic acid, potassium iodid or tincture of iodin solutions into the gland were the only therapeutic agents then in general use. Marked temporary improvement was often noted. The results, however, were too indefinite and so seldom of any permanent benefit that these procedures were gradually abandoned by the majority of the members of the medical profession.

Previous to the year 1910 the general medical profession gave little attention to diseases of the thyroid gland. Thyroid conditions were rarely discussed at medical meetings and seldom considered in diagnosis. Usually the only goiter cases that received consideration were those with extreme enlargement of the gland or with obvious pressure symptoms.

In the period from 1910 to 1920 physicians in all parts of the country, working independently, advanced quite diverse views. The majority were antagonistic to surgical intervention and enthusiastic over some medical, x-ray, or injection treatment.

An idea may be gained of the diverse opinions held at that time from the discussion of a paper entitled, "A Brief Study of Goiter; Based upon One Thousand Goiter Operations" which was presented by the writer

before the Tri-State Medical Association in Madison, Wisconsin, in 1915. This paper stressed the fact that relief from cardiac conditions followed operation in a large proportion of cases, pointed out the favorable results obtained by the early removal of atoxic adenomas and the extremely satisfactory results obtained in exophthalmic goiter cases by radical removal of the diseased thyroid tissue. In this paper the author insisted that by utilizing flexion, rotation, and extension—a technic which the called "goiter obstetrics"—the gland could be removed without cutting the prethyroid muscles.

In the discussion that ensued at that convention in 1915, prominent men from various parts of the country declared that "entirely too many goiter operations are being done"; that "the majority of goiter operations are unnecessary" and that "these patients cannot live many years deprived of so much of such an important organ"; that "the idea that heart disease can be cured by cutting out a piece of the thyroid gland is ridiculous and not worthy of consideration"; that "the only reason that anyone can give for advocating the removal of a non-toxic adenoma that is not causing pressure symptoms is the fact that a fee for the operation can be obtained."

Several surgeons severely attacked the author for stating that "favorable results in the operative treatment of exophthalmic goiter depend upon almost complete removal of the abnormal thyroid tissue." Opinions differed widely regarding the amount of thyroid tissue that should be left. Some stated that at least one-third or one-fourth of the entire gland present should be left. Two surgeons who had recently returned from Europe stated that in European practice it was considered safe to remove the major portion of one lobe and one-half of the other, but not more.

The author's statement that in all cases thyroidectomy could be performed without cutting the prethyroid muscles was seriously condemned. The majority of those who spoke were strongly antagonistic to the use of local or gas anesthesia and were enthusiastic advocates of ether anesthesia.

The opposition to the statements made by the essayist was so pronounced that editors of several journals declined to publish the paper in its entirety on the grounds that it would merely arouse controversy.

In the period from 1920 to 1930 progress was marked by a great increase in the number of investigators interested in the goiter question and the notable amount of scientific research done. Many confusing problems were solved and an understanding and recognition of thyroid diseases became general among the profession. Although differences of opinion remained among the individual workers, interest in the problem became widespread and intensified. In 1923 a group of men calling themselves the Sloan Clinic Goiter Club, who for several years had been meeting in Bloomington, Illinois, twice a year for a general exchange of views, decided to make these meetings accessible to a larger group of men. In response to the first invitation to attend a conference on the subject of goiter, two hundred and eighty-nine physicians, representing twenty-three states, met in Bloomington, Illinois, in January, 1924. Three days of surgical clinics were presented and two days were devoted exclusively to diagnostic

clinics, presentation of papers, and open forum discussion in which every man present was encouraged to express his opinion. Out of this first gathering a permanent organization developed, having as its prime object "to bring together each year men who will present the best that has been thought, said and done in the study of goiter and its associated problems."

Annual conferences held in a different city each year have served to disseminate knowledge concerning goiter problems and to insure better cooperation between clinicians, surgeons and pathologists in dealing with these problems. An honorarium has been offered for several years by one of the members for the best contribution, on any goiter problem, presented at the annual conference.

This Association has had its part in a wider field, being represented by fourteen delegates, including the author, at the First International Congress of Goiter, held in Bern, Switzerland, in 1927 (251). The publication of the report of this conference in English was made possible by the delegates and other interested members.

We have progressed far along the road of scientific thyroid surgery in the last quarter of a century. Have we reached the end of the road?

The minimal mortality of goiter surgery, a mortality of less than 1 per cent, seems to us not an ultimate achievement. The future may place simple thyroidectomy and tonsillectomy on the same plane as regards operative risk.

Thyroid Prophylaxis

Before closing this chapter, mention perhaps should also be made of the work of **Marine** and **Kimball** (252) of Akron, Ohio, along the lines of prophylaxis. Their methods of prophylaxis in the schools by means of iodin preparations will undoubtedly add emphasis to public health activities in the prevention of goiter. The history of goiter up to the time of Marine and Kimball was really the history of an already existing disease, and of the progress in its treatment. We knew little of prevention.

Over 80 per cent of our first one thousand cases of goiter were operated upon because of the tumor in the neck. We did not realize the rôle that goiter played in the development of heart conditions. We were not awake at that time to the fact that a campaign for goiter prevention would, of necessity, be followed by a considerable drop in the mortality from heart disease.

Marine and Kimball were the first to start the great movement, the objective of which is prevention rather than treatment. The keynote for the future must be prevention. The surgeon can only reach a few individuals. Prophylaxis, on the basis of a nutritional campaign, will reach millions; will reach schools, institutions and homes, and repeat once again the story of smallpox and yellow fever. We know much of the principles of goiter prevention; all we need is the appreciation of these principles.

When the story of this century's medical history is finally told, prophylaxis of goiter with the consequent prevention of heart disease will be found the outstanding achievement.

CHAPTER XX

NOMENCLATURE AND CLASSIFICATION

For the proper development of any branch of medicine a standard nomenclature would seem to be one of the essentials. In the matter of goiter, however, there are special considerations which render a uniform classification difficult or, in the state of our present knowledge, even impossible.

Authorities are not agreed on many, perhaps most, of the goiter questions. The pathologists do not agree among themselves nor is there agreement in the co-relation of pathological findings with the clinical picture of goiter. The pathological picture is extremely diversified; in the same gland may be found a variety of pathological changes ranging from normal gland tissue to an extreme grade of hyperplastic or degenerative change. In one section, the pathologist may find typical colloid goiter, in another the papillary formations suggestive of exophthalmic goiter and in a third area definite evidence of fetal adenoma.

Among the clinicians also there is considerable confusion as to terminology, and lack of uniformity as to classification. On the part of some clinicians there is apparent effort to compress all goiter symptomatology into a few inelastic types; others, on the contrary, have a tendency to erudite and detail classification that is confusing to the average reader.

The general practitioner, who reviews the literature in an effort to classify his cases is apt to be discouraged by the diversity of opinion and varying terminology among the authorities on this subject. He finds that almost every man giving special attention to goiter has his own nomenclature, classifications and definitions. The surgeons, pathologists, internists and Public Health agencies, whether municipal, State or Federal, seem to be working independently and show a tendency toward individual terminology and classification. The authorities speak in different tongues and the student looks in vain for a universal language which will clarify for him the evolutional phases of goiter pathology and the clinical sequence of goiter symptomatology.

In a disease as protein in its development as goiter—exhibiting in its evolution, both clinically and pathologically, such an infinitude of gradations from the normal to advanced disease—it doubtless will never be possible or even essential to elaborate a classification that will fit every type of the disease. It should be possible, however, and it is assuredly desirable, to devise a nomenclature and classification that will have the merit of uniformity and form the basis of a common language for the students and the workers in this field.

This universal language will undoubtedly come in time; the amount of research being done on thyroid problems indicates its necessity, and

the need of closer cooperation and better understanding on the part of the workers will bring about its development.

In view of the confusion in terminology, it is necessary to define the terms used in this book and to review in a brief way some of the current ideas on classification.

GOITER (Struma, bronchocele, big neck) was originally defined as an enlargement of the neck. Later, as knowledge of the condition developed, it was more properly defined as an enlargement of the thyroid gland. In recent years this definition has, in turn, become inadequate and somewhat misleading. We have come to recognize the fact that in certain instances the thyroid gland may be seriously diseased and yet show no appreciable evidence of enlargement. In order to meet this situation, and in an effort to make the definition more comprehensive, we have come to define goiter as **"the abnormal portion of the thyroid gland, from disease or dysfunction—usually, but not necessarily, producing enlargement of the gland." The term goiter should be limited to the portion of the gland that is actually diseased**. For a brief definition, it may be said that goiter is **"the abnormal portion of the thyroid gland."**

COLLOID GOITER signifies thyroid enlargement characterized clinically by a smooth, soft globular, symmetrical enlargement of the thyroid, and characterized pathologically by increased storage of colloid, due either to increased production or decreased absorption.

SIMPLE COLLOID GOITER is a term used to designate all colloid goiters in their early stages prior to the onset of proliferative or degenerative change.

ENDEMIC GOITER is the term applied to designate the occurrence of thyroid disease, usually colloid in character, in a large proportion of the inhabitants of certain restricted geographical areas.

SPORADIC GOITER is applied to goiter occurring generally but intermittently in localized areas.

GOITERS OF PREGNANCY, PUBERTY, ADOLESCENCE (sometimes wrongly termed "physiological goiter") are simple colloid goiters due to greatly decreased glandular function in the presence of mineral deficiency, and are subject to spontaneous recovery as the "functional call" on the thyroid decreases.

NODULAR COLLOID GOITER (Nodose Goiter) is colloid goiter in which adenomatous nodules have developed. The term is commonly used, however, to denote those colloid goiters in which the adenomatous nodules **are comparatively small in size.** When the nodules or adenomata have attained considerable size, and form the principal feature in the pathologic picture, the condition is usually termed **MULTIPLE COLLOID ADENOMA.**

ADENOMA OF THE THYROID is the term used to embrace all forms of thyroid tumor in which proliferation of the glandular elements is the predominant lesion. Adenomas may be classified as:

Primary Adenoma
Multiple Adenoma
Multiple Colloid Adenoma
Fetal Adenoma

Primary Adenoma presupposes the occurrence of an adenoma in a gland previously normal.

Multiple Adenoma indicates several adenomata in the gland.

Multiple Colloid Adenoma refers to colloid goiter in which the nodules or adenomata have attained considerable size.

Fetal Adenoma is a well defined, definitely encapsulated tumor of embryonic origin, single or multiple.

TOXIC NODULAR COLLOID (Secondary toxic goiter, secondary Basedow, Basedowified goiter) signifies nodular colloid goiter with symptoms of thyrotoxicosis.

TOXIC ADENOMA is thyroid adenoma of long standing which has undergone secondary degenerative or proliferative changes, and is characterized clinically by symptoms of thyrotoxicosis.

TOXIC PRIMARY ADENOMA differs from the preceding group in that as a result of infection, **it becomes toxic in its early stages.**

EXOPHTHALMIC GOITER (Graves' disease, Parry's disease, primary toxic goiter, Basedow's disease, Flagani's disease, Hyperplastic goiter) is a chronic (rarely an acute) systemic intoxication due to dysfunction or hyperfunction of the thyroid gland, characterized pathologically by epithelial proliferation and papillary formation, and characterized clinically by thyroid enlargement (in the majority of cases), cardiovascular symptoms, nervous instability and tremor, sometimes exophthalmos, **and always increased basal metabolism.**

Graves' Disease is the term used to designate the mild exophthalmic goiter that runs a slow course with a rather mild degree of toxemia and with only a slight degree of exophthalmos.

Basedow's Disease is the term used to designate the fulminating type of exophthalmic goiter as described by Basedow.

HYPERTHYROIDISM is a condition of general systemic intoxication induced by the presence in the system of excessive amounts of **normal** thyroid secretion due to hyperfunction of a practically normal gland.

Thyrotoxicosis (thyrotoxemia) is often used synonymously with hyperthyroidism, but a more accurate definition would read:

Thyrotoxicosis is a condition of general systemic intoxication due to the presence in the system of normal or excessive amounts of a **qualitatively changed** secretion elaborated by pathological or dysfunctioning thyroid tissue.

FORME FRUSTE is an elastic term which is made to include the extremely mild, atypical, undeveloped and abortive types of Graves' disease. The condition is characterized clinically by slight or no enlargement of the thyroid, nervous instability, mild cardiovascular symptoms as compared with typical Graves' disease, the presence of one or more of the cardinal symptoms of Graves' disease to a mild degree, a good prognosis (as regards life) with or without surgical treatment and an unchanged or only slightly elevated metabolism.

LATENT GOITER is a term used by the writer to cover a group of cases which are often unrecognized and are usually turned over to the cardiologist. The nerve and eye symptoms are in abeyance, and the heart condition (goiter heart) is the predominant consideration. The thyroid condition is always of long standing and the prognosis without surgical interference is grave. The writer has repeatedly based his decision to operate upon the presence of a "goiter heart." In all such cases to date, the excellent results of the operation confirmed the diagnosis.

HYPOTHYROIDISM is a clinical syndrome due to deficiency—not a total suppression—of thyroid secretion, characterized clinically by trophic changes, intellectual impairment and lowered metabolic rate. This term includes all degrees of gland deficiency, and consequently includes a great variety of types, ranging from the case that is slightly hypothyroid, and that usually eludes diagnosis to the case that borders on infantilism or myxedema.

ATHYROIDISM is a condition of complete absence (thyroaplasia) of thyroid secretions due to congenital defect, operation, or complete degeneration of thyroid tissue and is revealed clinically by nanism and idiocy in the congenital case, by the development of skeletal change, trophic disturbance, and intellectual impairment in the infantile case and by the development of myxedema in the adult.

MYXEDEMA (Cachexia strumipriva, cachexia thyropriva, pachydermic cachexia) is a clinical syndrome induced by total suppression of thyroid secretion due either to operation or degeneration, characterized clinically by gain in weight, marked trophic changes, nervous disturbance, myxedematous infiltration of the skin, intellectual and emotional impairment, lowered metabolic rate, and a remarkable tendency to recovery on the exhibition of thyroid extract.

CRETINISM, which may be endemic or sporadic, is a congenital condition of nanism, idiocy and genital hypoplasis due to absence of thyroid secretion.

THYROIDITIS signifies inflammation of the thyroid gland, and may be acute or chronic, purulent or non-purulent.

STRUMITIS signifies inflammation in a pre-existent goiter.

GOITER HEART is a distinct clinical entity, characterized by tachycardia and distinctive heart sounds, and by the presence of murmurs only in the most advanced cases. The following clinical sequence is observed in the majority of cases: tachycardia, arhythmia from pre-ventricular contractions, auricular flutter, auricular fibrillation.

CLASSIFICATIONS

The subject of classification is one that presents very great difficulties. The literature contains dozens of classification schemes: many are very similar in general outline, others present some novel plant of arrangement which happened to appeal to the ingenuity of the writer.

Two of the more popular classifications are included, with the writer's, for the convenience of the reader.

PLUMMER'S CLASSIFICATION (253)

1. Diffuse colloid goiter.
2. Adenomatous goiter with hyperthyroidism.
3. Adenomatous goiter without hyperthyroidism.
4. Exophthalmic goiter.
5. Myxedema.
6. Cretinism.
7. Childhood myxedema.
8. Thyroiditis.
9. Malignant disease of the thyroid.

DE QUERVAIN'S CLASSIFICATION (254)

I. Diffuse goiter.
   A. Forms deficient in colloid.
      1. Parenchymatous goiter in the new-born.
      2. Parenchymatous goiter in childhood.
      3. Parenchymatous goiter in puberty.
      4. Graves' disease.

B. Normal amount of colloid.
   1. Hyperplasia of the gland with normal structure.
C. Forms rich in colloid.
   1. Diffuse colloid goiter without symptoms of hyperthyroidism.
   2. The same with symptoms of hyperthyroidism.

II. Nodular goiter.

A. Forms deficient in colloid material.
   1. Adenoma with flat cells, small vesicles or narrow tubules, practically free from colloid.
   2. Adenoma with cylindrical cells, formation or papillae, vesicles or tubules of very irregular shape, reminiscent of Graves' disease.
   3. Adenoma with tubules or solid columns of cells.
B. Forms containing a normal amount of colloid (practically non-existent).
C. Forms rich in colloid.

During twenty-five years experience in goiter surgery, the writer has evolved several schemes of classification which seemed to him satisfactory at the time. Usually, as time went on and the attempt was made to classify the cases, one classification after the other proved inadequate **and failed to offer selective pigeon-holes for the different types of the disease.**

The classifications looked well on paper, but did not measure up to the practical demands of clinical work.

The scheme which the writer has used for several years past, has proved more satisfactory than any other in his hands, and has proved extremely useful for purposes of record and reference.

THE WRITER'S CLASSIFICATION

Group I. Non-Toxic

1. Diffuse Colloid Goiter.
   - A. Simple Goiter
   - B. Endemic Goiter
   - C. Goiter of Puberty } Syn.
   - D. Adolescent Goiter }
   - E. Goiter of Pregnancy
2. Diffuse Nodular Colloid
   - A. Diffuse Multiple Adenomata
3. Multiple Adenomata
4. Primary Adenoma
5. Fetal Adenoma

Group II. Toxic Adenoma

1. Nodular Colloid (Diffuse multiple adenomata)
2. Multiple Adenomata
3. Primary Adenoma
4. Fetal Adenoma

Group III. Exophthalmic Goiter

(Basedow's Disease)
(Graves' Disease)
(Forme Fruste)

Group IV. Miscellaneous

1. Misplaced Goiters
   - A. Intrathoracic
   - B. Substernal
   - C. Sublingual (Intralaryngeal)
   - D. Goiters in accessory thyroid
2. Inflammations (Thyroiditis. Strumitis)
   - A. Acute—Purulent. Non-purulent
   - B. Chronic—Reidel's Disease
     Woody Thyroiditis
     Syphilitic Goiter
     Tubercular Goiter

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