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SURGERY OF THE THYMUS GLAND. THYMECTOMY. REPORT OF FIFTY OPERATED CASES

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Most of the surgery of the thymus gland up to the present has been concerned with the direct operative relief of tracheal and esophageal obstruction due to hypertrophy of the gland, the not infrequent cause of sudden death in infants. As this particular condition is practically limited to the period of infancy and early childhood, it follows that most of the operative work on this organ has been done during this early stage of growth; in fact, I am able to find the report of but one thymectomy performed on an adult. This one case will be considered more in detail in discussing the relation of the enlarged thymus to Graves' disease. The major portion of this paper will, therefore, be devoted to the thymus in infancy.

My attention as an operating surgeon was first called to this restricted but none the less promising field of recent surgical endeavor by seeing an infant in a ward of the Children's Memorial Hospital in this city in April, 1911, which was suffering from recurrent convulsive attacks, with cyanosis. The child was entered on the service of Dr. Frank S. Churchill, who called me in consultation and suggested the operative treatment.

REPORT OF CASE

Roger S., male child, born May 1, 1910, entered service of Dr. F. S. Churchill, Children's Memorial Hospital, Chicago, April 28, 1911. The child had been in the hospital during the previous November and December for digestive disturbances and was discharged in good condition Jan. 1, 1911. It was brought to the hospital the second time, April 28, 1911, on the advice of Dr. Grace Meigs, with the complaint of convulsions the last two evenings, coming on irregularly and lasting five to ten minutes.

Physical Examination (by Dr. Churchill).—A well nourished child, head large, fontanel open, skin of face, chest, back, and to a slighter extent of the anal region, is red and covered with a fine maculo-papular eruption. Chest: Area of dulness over upper end of sternum, upper limit at first interspace, extends 1 cm. to right of median line and 3 cm. to left of median line and to lower limit of fourth interspace on left side. X-ray plates show a shadow which corresponds to the area of dulness over the thymus. (Fig. 1.)

May 24. Since admission child has averaged two to three convulsions a day. These convulsions vary in severity from slight rigidity lasting a few seconds to rigidity of the whole body lasting from five to ten minutes. Child very cyanotic during attacks. Attacks are apparently brought on by any disturbance of the child which causes him to cry; e. g., a bath or changing of linen. When not disturbed the child is free from symptoms. Child has a marked stridor, which is heard in practically all his crying spells.

I had been consulted during this time on the feasibility of removing a part or all of the thymus, as Dr. Churchill believed the condition of the child demanded it, not only on account of its present distress but for its future welfare. It was fully as much for the latter as for the former that I consented to operate, as he had not appeared in very serious straits at the times of quiescence when I had happened to see him.

Fig. 1.—Radiograph taken before operation showing shadow of the thymus extending up from heart. Viewed from behind.

Operation.—May 25, under ether anesthesia, which caused no untoward symptoms, I removed a portion of the thymus about 5 cm. by 3 cm. wide and 1.5 cm. thick, weighing 9 gm. about a half hour later after having dried some in the air. At 10 p. m. the child had a convulsion lasting four minutes.

The plan of operation was that of Veau,¹ who has operated in more cases than any other surgeon. A median incision four to five cm. long was made in the middle line of the neck with its lower end just below the upper border of the sternum, and extending down to the deep fascia. (Fig. 4.) The sternal portions of the sternomastoid muscles appeared in the field. An incision of the deep cervical fascia exposed the sternothyroid muscles which were separated by incision and blunt dissection. This exposed the pretracheal tissues and in the lower part of

1. Veau and Oliver; *Presse méd.*, 1910, xviii, 257.

the wound could be seen, rising and falling with each respiration, the upper portion of the thymus, resembling very closely in color and structure the omentum seen through a thin hernial sac. (Figs. 5, 6 and 7.) The gland when first seen was inside its capsule, which was lifted up with dissecting forceps and incised. Further resembling the omentum, the gland showed a tendency to herniate through the capsule at each expiration, when it was seized with forceps and gradually stripped of its investing sheath until the larger portion was extra thoracic, when it was tied off at its more fixed portion under the sterno-clavicular junction, where it is joined by the nutritive branches from the internal mammary artery. (Fig. 8.) Veau believes this precaution against hemorrhage unnecessary as it is sometimes impossible to apply the ligature on account of rupture of the gland, these cases having done just as well as others in which the ligature was applied. The wound was closed with deep sutures of catgut in the cervical structures and skin stitches of horse hair.

Fig. 2.—Radiograph taken after operation, showing smaller shadow above the heart in the region of the extirpated thymus. Viewed from behind.

Subsequent History.—The temperature, which was normal before the operation, became 102 F. a few hours afterward, and 105 the next day and the day following, when it gradually went down to normal at the end of the week. Two slight convulsions were also recorded during the week.

At the end of the week the lower part of the wound was found infected, but it drained well and caused no rise in temperature. The early and rapid rise I believe occurred too soon to be entirely due to infection.

June 9. The wound in the neck is practically healed. The child has had no convulsions for several days and has had no stridor since the operation, is bright and contented, eczema all cleared up, and appears like any perfectly normal, bright baby.

The photograph (Fig. 3) was taken June 9, two weeks after operation. The x-ray picture taken June 20 (Fig. 2), shows a decided change of lessened density in the region from which the thymus was removed.

PATHOLOGIST'S REPORT

Operation, Thymectomy (Pathologist, Dr. J. H. Hewitt).—The specimen consists of a grayish-white mass of tissue weighing about 9 grams, and measuring 4 by 6 by 1 cm. It is soft in consistency. It is divided into two lobes. The lobes are held together by connective tissue along one border. One of the lobes is further divided into two parts which are likewise held together by connective tissue bands along their lower border. The capsule is thin and transparent.

Sections show the tissue to be made up chiefly of lymphoid cells, which are divided by bands of connective tissue running in from the capsule into areas of various sizes but which show in general a regular arrangement of the elements. Along the outer border of these areas the lymphoid cells are densely packed. In the central portion of these areas the lymphoid cells are fewer in number and more loosely arranged. Here may also be seen blood-vessels whose walls are thick-

Fig. 3.—Photograph of child taken June 9, after operation, showing scar.

ened. There are also in these areas a certain number of corpuscles of epithelial cells. A certain number of these corpuscles show an infiltration with a variable number of leukocytes and lymphocytes. Some of these corpuscles (Hassall's) show deposits apparently of lime salts.

Diagnosis.—Normal thymus.

Figure 9 shows the patient October 31, five months after the operation. At this time Dr. Churchill examined the patient and reported him in excellent condition as the picture would suggest.

As the gland lies in front of all the important structures in the neck and thorax, the trachea, innominate artery and veins, as well as the heart and pericardium, these deeper structures were not interfered with in the enucleation, and indeed were not seen.

The child when seen a year after the operation was in excellent condition, although he had just passed through a severe siege of whooping-cough.

ANATOMY

The thymus gland is originally a bilaterally symmetrical organ derived embryologically as an evagination from the third visceral pouches, with the region of which it may in some cases remain permanently connected.² It attains its greatest development during the first two or three

Fig. 4.—Modified from Veau. Showing the inner borders of the two sternomastoid muscles covered with the cervical fascia.

Fig. 5.—Modified from Veau. The deep cervical fascia is retracted showing the sternomastoid, the depressors of the hyoid, and the upper border of the manubrium sterni.

2. Biedl, A., in his recent work, "Innere Sekretionen, ihre physiologischen Grundlagen und ihre Bedeutung für die Pathologie," Wien, 1910, states that it is developed from the third, fourth and perhaps the second visceral clefts.

Fig. 6.—Modified from Veau. The depressors of the hyoid are retracted exposing the pretracheal fascia, in the lower portion of which appears the thymus in its capsule. This moves with the respiration.

Fig. 7.—Modified from Veau. The capsule of the thymus has been seized and opened. The gland tends to herniate through this opening.

Fig. 8.—Modified from Veau. The gland has been pulled out of its sheath and a ligature applied about its base near the sternoclavicular articulation.

Fig. 9.—Photograph of patient taken Oct. 31, 1911, five months after the operation.

years of life, when its weight varies, according to different authors, from 6 to 15 grams, 2 to 7 grams being the average at birth. At puberty it begins to diminish in size, and is usually very small and more or less completely degenerated by the twenty-fifth year. Friedleben³ states that it reaches complete development at birth, remains in this condition with some increase in size until the second year, and then gradually atrophies, the retrograde process being well advanced at puberty. Important exceptions to this course of growth at times occur. It is a ductless gland of a grayish-red color. In the new-born the gland extends from near the thyroid gland in the neck to the fourth costal cartilage below, lying directly behind the sternum and internal mammary arteries, whence it derives the

Fig. 10.—The thymus gland in a child one month old. From Olivier.

most of its blood-supply, and in front of the pericardium, large vessels and trachea. Laterally it is bordered by the two pleurae between which it lies. It is composed of two lobes, the right and left, lying together and rarely separated in the median line, being united by a thin tissue. The upper extremities, or poles, lie in the loose tissue immediately in front of the trachea, just above the sternal notch, and resemble two cords of fat 2 to 3 mm. in diameter, lying side by side and extending upward toward the thyroid isthmus. They move up and down with the respiration and

3. Friedleben, *Die Physiologie d. Thymusdrüse in Gesundheit und Krankheit*, 1858.

are the important parts to recognize in the operation for their removal. The gland is contained within its proper capsule, to which it is very loosely attached, allowing its easy removal in the living subject. The capsule itself is closely united with the surrounding structures. Its removal is not surgically feasible.

Besides the internal mammary artery, the superior and inferior thyroid arteries supply it with blood, the latter going principally to the upper poles. A pericardiac branch and possibly a phrenic branch reach it from below. The veins empty into the internal mammary, the innominate and the thyroid veins. The lymphatics go to the anterior mediastinal glands, and by some are said to terminate directly in the internal jugular vein. The nerves are said to be from the vagus and the sympathetic, though Olivier gives only a branch from the left phrenic. Histologically, the gland is composed principally of lymphoid tissue, within which are groups of cells, the corpuscles of Hassall, referring by their epithelial structure to the seat of their embryonic origin.⁴ (Fig. 10.)

PHYSIOLOGY

The function of the gland is none too well understood, although the recent extensive researches of Klose and Vogt, to be referred to later, furnish very strong evidence of its particular physiologic function and the absolute necessity of this function to normal development. Its occurrence throughout all the vertebrates and its maximum development and comparative large size during the early period of development naturally suggest some important relation to the phenomenon of the growth in this large division of the animal kingdom. That this function or relation is lost or is absent very soon after birth, at least in the higher animals, is well attested by numerous experiments on lower animals, as well as by several observations on infants from which it has been removed surgically for local disturbances of respiration. Possibly it is especially important during intra-uterine development before respiratory and alimentary functions have been established. Complete absence of the gland in infancy has been observed without serious disturbance of the health being attributed to this cause. However, it is difficult to be sure that some aberrant portion of the gland may not be present elsewhere and carry on its functions.

Friedleben (published in 1858) removed the thymus from twenty dogs and three goats, and observed very little influence on the general health of the animals operated on, although his technic for complete removal was not entirely free from criticism. His results refuted those

4. Biedl says that while it appears like a lymph-node, Stoehr and others consider these lymphoid cells as transformed epithelial elements and that it should no longer be considered a lymphoid structure or the site of origin of leukocytes, as held by some.

of Restelli in 1845 (the first one to remove the gland experimentally), the dogs, sheep and calves on which he operated all having died after a short period of fever. Friedleben did, however, among various changes observe in some cases increased flexibility, accompanied by slow growth of the bones. Thirty-five years later, in 1893, this line of investigation was resumed, and since that time many experiments have been made with observations and counterobservations offsetting each other about equally. However, with the constant improvement in technic and interpretation, certain negative and positive findings have been and are still being gradually evolved from the records of many experiments and observations. In 1898, Calzolari, quoted by Biedl, observed that removal of the testicles in rabbits led to increase in size of the thymus. Henderson, in 1904, quoted by the same author, reported that in a large number of cattle observed, castration produced a continued growth of the thymus and delay in its atrophy. Paton, quoted by Biedl, observed no enlargement if the thymus was removed before puberty.

U. Soli, quoted by Biedl in 1907, reported the thymus of capons to be more than double the size of the gland in non-castrated fowls, though removal of the thymus led to a lessening of testicular weight in his experience. The later experiments, quoted by Biedl, Basch (1903-1908) and Ranzi and Tandler (1909), bring out some positive phases that at present appear quite convincing. These investigators removed the thymus completely by splitting the sternum of dogs, as they believed it was not always completely removed by other experimenters. Basch removed the gland from twenty suckling puppies, seventeen of which he followed with controls. Most of these animals died in two months after the operation. In the second or third week after operation it was noticed that the bones were more easily bent than those of the controls, that the dogs spread their legs out more and were more unsteady in their gait. The posterior part of the body was smaller and the hind legs turned out more than normal. The dogs were less lively. Later the fore legs became more bent and weaker and the feet came down flatter than normal. There was a general lack of growth. It took less force to break leg bones in the operated animals. In fifteen to seventeen days the callus was larger in the controls. The difference could also be observed in the x-ray. The difference was most noticeable when the fracture occurred three to four weeks after extirpation. The bones were smaller and weaker. Microscopically, there was evidence of delayed ossification, not a rachitic type, but a general disturbance of bone development, especially in the lime content, which was lessened. He believes this may be the ground for rachitic changes. Double the normal quantity of lime was excreted from the animals. Svelha found that injection of extracts of thymus into dogs produced a fall of blood-pressure and acceleration of the pulse, the ani-

mals ultimately dying with symptoms of suffocation, but other observers have not obtained these results, and it is well known that extracts of many organs cause a fall in blood-pressure. Biedl does not believe in hyperthymism as a cause of death, and, in conclusion, says: "The pathologic relation of the thymus to *mors thymica* is not cleared up, nor is its relation to so-called status lymphaticus."

The work of Klose and Vogt,⁵ previously referred to, is the most conclusive yet published on this subject and merits especial consideration. These authors observed that the thymus in dog increases in size until the fourteenth day and then rapidly degenerates. They believed the thymectomy should be done between the tenth and twentieth days after birth. Most of theirs were done the tenth day. Complete removal was absolutely necessary, as a small portion of the gland allowed to remain quickly reproduced itself and carried on its function. (In the case reported by the author, in which the larger parts of both lobes were removed, an examination by Dr. Joseph L. Miller over a year later showed an area of dulness corresponding to the gland fully as large as the normal area in a child of the age at which this one was examined.) The sternum of the animals had to be split to allow a complete removal of the gland. They studied fifty-four dogs operated on in this manner. Each dog had a control from the same litter. All the thymectomized dogs passed through four well-defined stages before succumbing to invariably fatal effects of the operation. In the first, or latent stage, the dogs resemble the controls, but on account of ravenous appetites and indiscriminate eating, they soon pass into the second, or adipose stage, in which they may be even heavier than their controls. These stages last two to three months or possibly longer. Their general appearance, even at this time, is one of physical weakness or flabbiness of the tissues, with definite mental apathy. Then follows the cachectic stage, in which they rapidly degenerate and become veritable runts. They become clumsy and stupid and walk with wide-spread legs, frequently falling. The condition well befits the name "*idiotia thymica*." Coma follows this—"*coma thymica*"—in which the animals may lie several days before death supervenes. The life of these animals varies from three to seventeen months. The bones are smaller than normal and contain about one-half the normal percentage of lime salts. Taking this with the diminished size of the skeleton, the total lime content is only about one-fourth that of a normal skeleton. Summed up, the bones show the changes of osteoporosis, osteomalacia and rachitis. Their theory is that these changes are due to the

5. Klose and Vogt: Klinik und Biologie der Thymusdrüse, Beitr. z. klin. Chir., 1910, lxi, 1-200; Klose: Arch. f. Kinderh., 1910, lv. The first article gives a very complete bibliography of the clinical and biological literature with special reference to its surgical and neurological relations. The second article gives a very complete bibliography of the literature relating to pediatrics.

action on the bones of an unneutralized excess of nucleinic acid consequent on the absent detoxicating action of the thymus. They believe the lymphocytes bring the nucleins to the thymus rather than that the thymus is the origin of the lymphocytes. In short, a form of acid intoxication diminishing the deposition of lime salts in the bones or dissolving out some already deposited and at the same time causing edema of the brain and other tissues, in accordance with the theory of Martin Fisher, producing profound disturbances of the nervous system and various organs, accounts for the whole clinical picture.

The function of the thymus in older animals is probably taken up by the thyroid gland, spleen, pancreas and possibly other organs. It cannot be wholly removed surgically in man, and some thymus tissue is said to be present in every normal human thyroid.

It is suggested that destruction of its elements by faults of development or disease, or disturbance of its function in hypertrophy may produce in man metabolic changes proportionate in extent and character to the amount of interference with the normal physiology of the gland.

Thymus feeding is not efficient where there is deficient thymus function, as the ingested material does not have the detoxicating action of the normally functioning gland. The ingested gland contains but the metabolic products of its former activity which are really toxic in their action. Transplantation of thymus from other species of animals has not been effective as the tissue is soon destroyed or absorbed; but the transplantation from the same species into the peritoneum or spleen has been suggested by Klose and Vogt as worthy of the further investigation they intend to give it. The use of alkalies to overcome the supposed excess of nucleinic acid they claim should also be carefully studied. Several cases of *idiotia thymica* in children are reported and illustrated in a recent volume of the *Neue Deutsche Chirurgie*,* devoted entirely to the surgery of the thymus. No definite plan of therapy is suggested in the text and the prognosis is discouraging. Thyroid feeding was useless.

PATHOLOGY

The rôle of the thymus in causing disturbances of respiration is mentioned in the literature of the seventeenth, eighteenth and nineteenth centuries, but the beginning of our more definite knowledge of the gland dates from Kopp's description of "thymic asthma" in the years 1829 and 1830. He believed it was a mechanical or compression disturbance exercised by the gland on the trachea. Friedleben, in 1858, denied the existence of "thymic asthma." Renewed interest in the gland was awakened by Grawitz's⁶ article in 1888, on cases of sudden death in babies. He

* Klose, Heinrich: *Chirurgie der Thymusdrüse*, *Neue Deutsche Chirurgie*, 1912, iii.

6. Grawitz, P., Griefswald: *Ueber plötzliche Todesfälle im Säuglingsalter*, *Deutsch med. Wchnschr.*, Leipzig and Berlin, May 31, 1888, No. 22, 429.

mentions two cases of sudden death from suffocation in previously healthy children and considers the importance of the subject from the medico-legal standpoint. The first case was that of an 8-months-old child that came to his notice four years before writing his article, when he was in Berlin. The child, which had previously been healthy, was found dead in its own bed one morning with the feather coverlet over its face, and the nurse, whose bed was next to the child, was blamed for neglect and brought before the court for punishment. An autopsy showed the only pathologic condition to be a greatly enlarged thymus which the author believed to be the direct cause of death by suffocation, as further evidence showed that the covering of the child's head as on the night of its death was not an unusual occurrence. The nurse was freed, but more on account of lack of proof of guilt than the judge's agreement with his professional opinion. After that he was on the lookout for a similar case and it was not until four years later, shortly before he published his article, that he met his second one. This was a 6-months-old child that had been in apparently perfect health. The father had been holding the child in his arms, showing it off to his friends when it suddenly had an attack of suffocation, became cyanotic and quickly died. The autopsy showed some rachitic changes at the chondrocostal junction and a greatly enlarged thymus that extended from the thyroid over the front of the pericardium and measured 7.5 cm. long by 6 cm. wide and 1.5 cm. thick, although the latter figure was somewhat uncertain on account of its shape. The antero-posterior diameter of the thoracic outlet at the upper part of the manubrium measured 1.8 cm. Diagnosis, suffocation from hyperplasia of the thymus. As his experience was in direct contrast to that of Friedleben's teaching that "enlargement of the thymus is not to be considered as a cause of sudden death," he believed his two cases "go to fill a certain place in legal medicine previously left vacant."

In 1614 F. Plater recorded the death of a child 5 months old that had died suddenly from respiratory obstruction. Two sons had previously died in a similar manner. Plater found at autopsy an enlarged thymus. Morgagni, in 1762, reported a similar case.

Hedinger, quoted from Zesas,⁷ reported eighteen cases of thymus death in the new-born from flattening of the trachea by pressure of the thymus on the innominate artery. The children died from suffocation. Serious circulatory disturbances have been reported by pressure on the pulmonary artery and the superior vena cava. Farret mentions that abnormally the vena cava may lie between the gland and the sternum. Pressure on the trachea direct and interference with swallowing have occurred. Pressure on the vagi and left recurrens may possibly cause spasm of the glottis and disturbance of the heart.

7. Zesas: *Deutsch. Gesellsch. f. Chir.*, May, 1910, p. 125.

In the years 1889 to 1891, soon after the appearance of Grawitz's paper, Arnold Paltauf⁸ formulated his well-known hypothesis which soon became quite generally accepted. In his opinion it was not proved that "thymus death" was ever due to pressure of the enlarged thymus on the trachea, blood-vessels, or nerves; and he attributed it to the patient's having a peculiar "lymphatico-chlorotic" constitution, which he called "Status lymphaticus."

This rather uncertain nosological entity is described as a "condition of bodily debility which is characterized by hyperplasia of the thymus and of the lymphoid tissues generally throughout the body; and also, especially in adult cases, by hypoplasia of the heart and of the arterial system. It is accompanied by a great lowering of the patient's power of resistance, and is believed to account for a large number of otherwise unexplained causes of sudden death." He believed the enlarged thymus to be but one of the manifestations along with the general increase of lymphoid tissue elsewhere. In all cases the thymus is said to be above normal in size and often the enlargement is very great. The enlargement is a general hyperplasia of the lymphoid elements.

Escherich suggested that the symptoms were due to a hyperthymization of the blood. The sudden death of Professor Langerhans' boy after a prophylactic dose of antidiphtheritic serum was attributed at the time to this condition.

Death in or following narcosis has frequently been shown to occur in persons with a persistent thymus, the death supposed to be due to some irritation of an abnormally susceptible heart. Deaths from cocaine poisoning have been considered in the same category. Audebert and Lenormant, quoted from Zesas, report from literature forty cases of narcosis death in which a more or less enlarged or persistent thymus was present—20 to 25 gms. Twenty-nine were under 20 years of age. The following anesthetics were blamed for the deaths.

Chloroform	22	Laughing gas	1
Ether	7	Ethyl Chlorid	1
Billroth's mixture	5		

Two patients had previously taken chloroform safely.

Besides the conditions in which enlargements or persistence of the gland play the principal rôle, the gland is subject to various other pathologic changes such as might be expected to occur in an organ of its dual origin. Its vascular changes are similar to those occurring in other organs. Acute pyogenic affections with abscess and sudden death have been reported. Syphilitic and tuberculous infections also occur. Lym-

8. Paltauf, A.: *Wien. klin. Wehnschr.*, 1889, No. 46; 1890, No. 9.

phoid infiltration with enlargement may take place in leukemia and pseudoleukemia. Primary tumors, both mesoplastic and epiblastic, develop from its tissues, lymphosarcoma being the more frequent representative from the former, and dermoid cysts and carcinoma the more frequent from the latter elements.

Portions of the thymus may be inclosed within the thyroid and give rise to tumors, the "*epitheliome thymique intrathyroïdien*," of Achard and Paisseau.

THE THYMUS IN GRAVES' DISEASE

Astley Cooper first directed attention to the persistence or hyperplasia of the gland in association with Graves' disease. Bonnet, quoted by Zesas, reported twenty-eight cases of persistent thymus with Graves' disease, six of which ended in sudden death. The persistent thymus was considered to be in direct relation to the death in four of these.

Hauseman, in 1905, reported four cases of persistent thymus in eight autopsies on Graves' disease subjects. Thorbecke, quoted by Zesas, in thirty-five cases of Graves' disease, found twenty-one with persistent thymus or hyperplasia. Twelve of these died of heart paralysis shortly after the operation (ligature, strumectomy and excision), and two during the operation. The weight of the thymus varied from 250 gm. to 690 gm. Capelle (Zesas), in sixty reported autopsies on cases of Graves' disease, found 79 per cent. had enlarged thymi. Of twenty-two operative deaths, twenty-one, or 95 per cent., had enlarged thymi. In Allbutt's second edition, Hector McKenzie says, "The thymus was enlarged in all fatal cases of Graves' disease observed by the author that came to autopsy," and he suggests that "possibly every case in which there is a thymus persisting into adult life is one of potential or latent Graves' disease."

Gebele,⁹ of München, in an elaborate article, reports his observations on and conclusions derived from a series of experiments made to determine the interrelation of the thymus and thyroid glands. At the beginning he states: "Status lymphaticus is relatively frequent with Basedow's disease and is considered to-day as the most common cause of death in this disease." He experimented with forty-nine dogs 4 to 8 weeks old, and four kittens 3 to 4 weeks old. The experiments included feeding with sheep's thyroid both before and after extirpation and implantation of thyroid and thymus, thyroid implantations in bone, spleen, abdominal and thoracic walls, thymus implantations in the abdominal wall, and two cases of implantation of human goiter material from cases of Graves' disease. Total extirpation of the thymus led to results similar to those reported by Basch. He believes that the thymus plays a detoxicating rôle and that its increase in Graves' disease is com-

9. Gebele: Ueber the Thymus persistens beim Morbus Basedowii; Klinisch-experimentelle Studie, Beitr. z. klin. Chir., Tübingen, 1910, lxx, 20.

pensatory and the death a heart death from the thyroid secretion. He further states that when enlargement of the thymus is present operation on the thyroid should not be attempted as it shows a late stage of the goiter, and death is likely to ensue, not as a result of the enlarged thymus, but as a result of heart weakness.

Zesas, in 1910, suggested removal of the thymus with the thyroid in severe cases of Graves' disease with enlarged thymus, but at that time knew of no such attempts having been made. In June, 1910, a removal of the thymus was done by Garré in the case of Capelle and Bayer,¹⁰ to be referred to later, with much improvement of the general condition, although removal of a portion of the thyroid became necessary later. These authors believe that the thymus unfavorably affects the course of Graves' disease, and that it has an independent action separate from the hyperplasia of the lymphatic system. It adds the depressing effect of its secretion on the action of the heart. They quote Svelha's observations, previously mentioned, on the influence of the thymus secretion in lowering blood-pressure and diminishing heart-action. They believe "the greater the size of the thymus the greater the danger from Graves' disease." They believe the improvement with return to normal of the previously typical struma blood-findings six weeks after thymectomy supports their contention. This is the first reported case of thymectomy in this condition so that from the practical standpoint we have much yet to learn of the interrelation of these organs in diseased conditions.

As stated in the introduction, the surgery of the thymus gland up to the present time has been almost entirely limited to its operative removal—thymectomy—for the relief of urgent symptoms of tracheal or esophageal obstruction.

A careful study of these symptoms is therefore necessary to determine their origin, as other factors than the thymus may be responsible for them. It seems advisable, however, to take up the operative measures first and the indications for operation later on.

OPERATIVE TREATMENT. THYMECTOMY

The accumulating evidence against the thymus as a mechanical agent in causing severe respiratory distress and sudden death led to the first operative treatment of the gland in man by Rehn, in 1896. König also reported an operation on the gland the same year, and Purrüker an operation in 1899. In the sixteen years since these pioneers first ventured into this new domain of operative surgery, something over fifty operations for removal of the thymus have now been performed. A study of these cases lays a good foundation for operative technic and furnishes a modest

10. Capelle and Bayer, Bonn: Thymektomie bei Morbus Basedowii. Beitr. z. klin. Chir., Tübingen, 1911, lxxii, 214.

basis for determining indications for operation. The immediate results of the operation have also been determined; the remote results are yet to be learned. Three types of operation have been performed, exothymopexy, resection of the manubrium and thymectomy.

Exothymopexy was the operation performed by Rehn and consisted in elevating the thymus out of the thorax and fastening it to the tissues of the neck or top of the sternum, as he feared the consequences of a complete removal of the gland. In a later case Rehn removed a small portion of the gland prior to its fixation, as did also König in his first case. Three cases have been treated in this manner with no fatalities.

RESECTION OF THE MANUBRIUM

This has never been practiced alone, but always in connection with other measures, as exothymopexy or partial thymectomy. Three operations of this type have been reported by König, Morse-Murphy and D'Oelsnitz and Pratt, respectively. Two of these patients died, one of mediastinitis. Schwinn split the manubrium in one case as an accessory measure to a thymectomy. The patient recovered.

THYMECTOMY

This is practically the only operation performed now. The gland is enucleated from within its capsule. Owing to the normal fixation of certain parts of the gland within the capsule the entire gland is probably never removed. On account of these conditions, the French authors, to whom we are greatly indebted for much of our knowledge in this branch of surgery, designate the operation as "*thymectomie subtotale sous-capsulaire*."

ANESTHETIC TO BE USED

This is an especially interesting problem when we consider that deaths from anesthesia are so frequently attributed to the influence of the thymus on which we are now contemplating operating. Veau and Olivier, in their work, used chloroform in most of their cases. In thirteen cases chloroform is mentioned as the anesthetic, and in five ether was given. Chloroform and ether were given once. Thus a general anesthetic was used in at least nineteen, or about two-fifths of the cases, and in none of them was there any evidence that it influenced unfavorably the course of the operation. It was not used in some cases in which the condition of the child was such that an anesthetic was contra-indicated on general principles. Ether will naturally be the anesthetic of choice to American surgeons, although Jackson and Schwinn, in this country, both operated under chloroform anesthesia. Cocain has been advocated by some, but there is no record of its employment, and its uncertain action makes it a particularly dangerous drug to use in children.

TECHNIC OF OPERATION

The plan of operation is that worked out by Veau and presented with illustrations by Veau and Olivier.¹¹ Several of the cuts accompanying this article are modified from those of Veau. An incision 4 to 5 cm. long is made in the middle line of the neck with its lower end terminating just below the upper border of the sternum and extending down to the deep fascia (Fig. 4). The sternal portions of the sternomastoid muscles appear in the field. An incision of the deep cervical fascia now exposes the sternothyroid muscles, which are separated by blunt dissection. This exposes the pretracheal tissues and in the lower part of the wound can be seen rising and falling with each respiration, the upper portion of the thymus resembling very closely in color and structure the omentum seen through a thin hernial sac (Figs. 5, 6, 7).

The gland when first seen is usually inside its capsule, which must be lifted up with dissecting forceps and incised. Further resembling the omentum, the gland now shows a tendency to herniate through the capsule at each expiration when it is seized with forceps and gradually withdrawn from its investing sheath until the larger portion is extrathoracic, when it may be tied off at its more fixed portion near the sternoclavicular junction where it is joined by the nutritive branches of the internal mammary arteries (Fig. 8). Veau believes this precaution against hemorrhage unnecessary, as it is sometimes impossible to apply a ligature on account of rupture of the gland during removal, these cases having done just as well as others in which the ligature was applied. Some have used blunt instruments for separating the gland from its capsule when it did not herniate readily. At times one lobe may be removed in its entirety before the other is accessible, or both lobes may come out together. Such was the case in my single experience. The wound is closed with deep stitches of catgut in the cervical structures and the skin with silk or horsehair. The vertical skin incision has been employed by nearly all operators. Buford reports two cases in which he used a low curved transverse incision, and Chas. Mayo reports one case in which the transverse incision was used. Garré used it once in operating on an adult.

As the gland lies in front of all the important structures in the neck and thorax, the trachea, innominate artery and veins, as well as the heart and pericardium, these deeper structures are not interfered with in the enucleation, and, indeed, usually are not seen. The intrathoracic pressure and the viscosity of the tissues thus enable the surgeon to accomplish with ease and comparative safety in the living child what is difficult or impossible through a similar incision in the cadaver. The pleurae are in no way interfered with, as they are attached to the capsule of the gland which is carefully and easily left, except at the point of the original incision

11. Veau and Olivier: *Presse méd.*, 1910, xviii, 257.

for liberation of the contents. A little study of the upper poles of the gland in the infant cadaver will familiarize one with their appearance and relations, although, as I have said, it is only in the living child that one can appreciate the real condition with which one has to deal and the facility with which the enucleation can be carried out. It is certainly very much easier and simpler than a thyroidectomy. The tissue removed has almost invariably been normal thymus with simple hyperplasia, although Veau has several times removed broken down lymph-glands as incidents of the operation. In fifteen cases in which the weight removed was mentioned, it varied from 2 gm. to 21.5 gm., with an average of 8.6 gm. The real efficacy of the operation, however, does not always depend on the total amount of gland removed, for the removal of a small portion directly concerned in producing symptoms of obstruction has produced quite as striking relief as the removal of considerably larger portions less directly concerned in the compression. The youngest child operated on was 23 days old, and the oldest, with the exception of a single adult, 5 years; the average age being about 14 months. One-half of the patients of whom the age was given was under 12 months.

The x-ray has been used with apparently good results, particularly where the constitutional symptoms were the more urgent, but it is not to be recommended in place of the so generally successful operative measures in the cases imminently threatening death by suffocation.

OPERATION IN THE ADULT

In the adult case, a woman 22 years old, reported by Capelle and Bayer, and operated on by Garré, the patient was suffering from Graves' disease. A curved incision was made across the lower part of the neck, exposing the thyroid, and lower down the thymus. The capsule of the thymus was opened and the gland bulged out. It was seized with the forceps and several portions removed. A suspected pleural injury caused the operator to desist and the wound was closed and prompt healing followed. The thymus removed weighed 15 gm. All symptoms improved and the blood picture returned to normal in six weeks. Several months later the symptoms increased again and the right lobe of the thyroid was removed.

This is the only case of thymectomy in the adult I was able to find. It appears that the same tendency for the enlarged gland to herniate obtains here as it does in the infant. He mentions, however, his fear of pleural injury. Possibly the extra organic respiratory sounds frequently heard in the empty space after removal of the thymus or thyroid were heard in this case. If the indications suggest the necessity of removal of the hypertrophied thymus in the adult it appears from Garré's experience to be entirely feasible.

INDICATIONS FOR OPERATION

Olivier,¹² in his recent work on the surgery of the thymus, which is the most complete exposition of the subject yet published, groups the clinical symptoms of hypertrophy demanding surgical interference in two general classes. In the first class are included all cases characterized by permanent dyspnea. This he terms the continuous form. In the second class he includes those cases characterized by irregular suffocative attacks while free from dyspnea in the intervals. This he terms the intermittent or discontinuous form. Several clinical varieties are included in these two general types, and occasionally aberrant forms occur.

THE CONTINUOUS FORM

This form is generally seen in very young infants—4 to 6 months—that have had difficult respiration since birth or shortly after. This difficulty gradually increases until the child has a suffocative attack lasting ten to fifteen minutes, accompanied at first by rapid respiration and followed by complete apnea and cyanosis with eventual resumption of breathing and amelioration of distressing symptoms. A similar attack may occur the next day or even in a few hours. Between the suffocative attacks the dyspnea is continuous and there is commonly heard a distinct stridor day and night. This stridor is usually more intense on inspiration and may resemble a coarse moist râle. There is commonly present suprasternal retraction in connection with the dyspnea and both are increased by hyperextension of the head, the recumbent position or examining the throat with a tongue depressor. These symptoms should suggest an enlarged thymus and lead to a systematic examination of the patient.

Several observers have called attention to an arching forward of the manubrium sterni seen by them in several instances and believed to be due to the presence immediately behind of the enlarged gland. Rehn called attention to a soft tumor to be felt in the suprasternal space during expiration only. This is referred to as "Rehn's sign." Several observers claim to have seen and palpated such a tumor in their examinations, while a not inconsiderable number of equally careful diagnosticians have been unwilling to commit themselves on this point. It certainly is very difficult to determine just what is under the examining finger when the jugulum fills out in a strenuous expiratory effort in a dyspneic child.

Percussion may furnish definite evidence of hypertrophy of the thymus, but its value in children depends greatly on the skill of the examiner. According to Blumenreich the normal area of dulness is

12. Olivier: *Anatomie topographique et chirurgie du thymus*, G. Steinheil, Paris, 1911.

triangular, with its base above, corresponding with the sternoclavicular articulations and the apex below at the level of the second rib, the right border corresponding with the right border of the sternum and the left border 6 mm. to the left of the sternum. He further states that it is always separated from the heart dulness by a resonant area one or two fingers wide corresponding to the interposition of lung tissue. In hypertrophy this area passes the normal limits usually more to the left and is continuous with the heart area below without the interposed pulmonary resonance (Fig. 11). Boggs¹³ noticed that the area of dulness varied in height with the flexed and extended neck, sometimes at the lower border as much as an interspace. This has since been called "Bogg's sign."

The *x*-ray is another diagnostic help. Hochsinger¹⁴ used it in studying this condition in 1903. In fifty-eight infants under 2 years of age, each presented a distinct thymic shadow going from the manubrium to the heart shadow.

Fig. 11.—Percussion of the thymus after Friedjung-Blumenreich. Heavy line delimits normal thymus dulness.

Malavialle, quoted by Olivier, speaks of a mediastinal shadow extending either to the right or to the left—more frequently the left—beyond the vertebral shadow, and which is always continuous with that of the heart; sometimes blending with it so exactly as to render impossible the separation of the one from the other, and sometimes becoming directly continuous with the heart shadow without disturbing its regular form. While the lateral boundaries of the shadow are not very definite, an observation made by me before and after operating shows a difference of at least 2 cm. in the breadth of the shadow, it being that much narrower after the operation (Figs. 1 and 2).

Where the *x*-ray evidence is positive it is of real value in diagnosis, but when it is negative it is not to be considered as final. The specific gravity of the thymus gland is not much different from that of the blood

13. Boggs: *Arch. Int. Med.*, Nov. 15, 1911.

14. Hochsinger: *Stridor Congenitus und Thymus Hypertrophie (mit Röntgenbildern)*, lxxv *Congres des naturalistes et medicines allemands*, Cassel, September, 1903, ii, 247.

in the great veins and the aorta with whose shadows it must be blended and on whose shadows it must be superimposed. When extending beyond these and separating the lungs its shadows must then become unique and of distinct value.

Chevalier Jackson,¹⁵ of Pittsburgh, first successfully used it as a diagnostic measure previous to operation in a case reported by him.

Jackson was also the first one to observe the tracheal stenosis by means of the bronchoscope in the same patient. Laryngoscopy seldom affords more than negative evidence owing to the inherent difficulties attending its use in young children. Intubation has several times led to the diagnosis of hypertrophy of the thymus; in fact, it has been the previous treatment in a number of cases that have later come to operation. The first reported operative case by Rehn, in 1896, had had a previous intubation without permanent relief, the long tube demonstrating the presence of an obstruction low down in the trachea.

Complete inability to swallow was observed by Flügge in an infant that showed a large thymus on section. Demmer reported orally a similar case that also came to section. Avellis mentioned two cases in which the stridor hindered the swallowing, and Hinrichs adds a case of a female child that soon after birth was observed to drink very slowly, requiring an hour to swallow a feeding. Several weeks later the constant regurgitation of food immediately after swallowing with an increasing respiratory distress led to an operation for removal of the thymus, with immediate improvement in breathing and entire relief of the dysphagia.

A negative diagnostic measure is the absence of all other causes for the existing condition.

Summarizing: The occurrence in a child of constant dyspnea with attacks of suffocation and a more or less continuous stridulous respiration and possibly a suprasternal tumor on expiration may well be considered diagnostic of an enlarged thymus.

The diagnosis being established, the operation in this type is imperative. Death has occurred in the first suffocative attacks as in the two original cases reported by Grawitz. It may occur in any subsequent attack or after longer or shorter periods of dyspnea. The dyspnea has a tendency to augment and the suffocative attacks to increase in number and severity so that such a child is at all times in imminent danger of sudden death.

Four of the operative cases were complicated by the presence of enlarged and necrotic tracheobronchial lymph-nodes. Three were in the practice of Veau and one in that of D'Oelsnitz. Portions of the thymus were removed along with necrotic lymph-nodes. Although these four were thymus operations the enlarged tracheobronchial glands were con-

15. Jackson, C.: *Jour. Am. Med. Assn.*, May 25, 1907.

sidered responsible for the symptoms. All four of these patients died sooner or later from shock, local infections and general tuberculosis. Olivier offers the following suggestions for making a differential diagnosis to guard against operation in a condition fraught with such a high operative mortality.

There is in almost all of these cases a history of a previous pulmonary infection and the dyspnea is of later origin instead of being congenital, or of very early appearance as in the typical condition. The stridor is also acquired and is predominately of the expiratory type. The percussion note may give no abnormal range of dullness in purely tracheobronchial adenopathy. The *x*-ray also gives a different picture, the shadow when broadened being lower down and often to the right.

Three other varieties of the continuous form are mentioned. They are the "*forme dysphagique*," "*forme stridoreuse*" and "*formes reduites*." To the first belongs the case of Hinrichs, previously mentioned, of the child that from birth experienced great difficulty in swallowing and was entirely relieved by thymectomy. The "*forme stridoreuse*" refers rather to an epiphenomenon than to a separate form in which stridor is an accompanying symptom. Thymectomy for stridor alone should never be done, as it may easily be due to other causes than an enlarged thymus, and its presence without dyspnea and suffocative attacks is not an indication for the operation. Under the term "*formes reduites*" are considered two cases with dyspnea and stridor, but without suffocative attacks. As permanent dyspnea is an indication in itself, and the first suffocative attack may be fatal, an operation should be performed in these cases, provided no other cause than the enlarged thymus is found to account for the symptoms.

THE INTERMITTENT FORM

Under this heading Olivier includes six cases. The personal one described by the author belongs to this type as does one of Buford's cases. These would increase the number to eight. These children are usually older than those in the other main group, their ages being 4, 4, 7, 10, 10, 11, 12 and 12 months, respectively. They are generally quite normal during their earlier months, or at least have not shown evidence of respiratory troubles. Suddenly without warning they have a suffocative attack with cyanosis, jerking of the limbs and absolute apnea, followed by gradual resumption of breathing and return after four or five minutes to normal with neither dyspnea nor cyanosis. It may be several months before a recurrence of the attack. The attacks may eventually become much more frequent and even several a day. The children are usually well nourished. A fit of anger or fear or crying will bring on an attack. The physical signs of an enlarged thymus, the increased dullness, the suprasternal bulging with the appearance of a palpable tumor—Rehn's

SYNOPSIS OF FIFTY CASES OPERATED ON FOR HYPERTROPHY OF THE THYMUS GLAND,

No.	Name of Observer	Date of Operation	Reference	Age	Résumé of Symptoms and Pathology	Type of Disorder
1	Rehn	April 16, 1896.	Berlin. klin. Wehnschr., Oct. 5, 1896, p. 887. Article by Siegel.	2½ years	Constant dyspnea with inspiratory stridor and suffocative attacks.	Continuous
2	König	Not given. Probably 1896.	Centralbl. f. Chir., 1896, No. 21, p. 605.	9 weeks	Constant dyspnea, stridor and suffocative attacks; mass felt in jugulum.	Continuous
3	Purrücker	Not given. Probably 1899.	Med. Gesellsch. z. Magdeburg, May 18, 1899.	2½ years	Constant dyspnea, stridor and suffocative attacks.	Continuous
4	Ehrhardt	Sept., 1905.	Archiv. f. klin. Chir., 1906, lxxviii, 599.	2 years	Constant dyspnea with suffocative attacks and stridor, noncongenital. Trachea definitely flattened from before backward.	Continuous
5	Rehn	Not given. Probably 1906.	Archiv. f. klin. Chir., 1906, lxxx, 468.	4 months	Constant dyspnea with suffocative attacks and stridor.	Continuous
6	König	Not given. Probably 1906.	Verhandl. d. Deutsch. Gesellsch., 1906, p. 692.	7 months	Constant dyspnea with stridor.	Continuous
7	Jackson	Oct. 2, 1906.	Jour. Am. Med. Assn., May 25, 1907, p. 825.	4 years	Constant dyspnea with stridor. Compressed trachea seen through bronchoscope.	Continuous
8	Hinrichs-Alsberg	Dec. 5, 1906.	Berlin. klin. Wehnschr., April 27, 1908, p. 825.	10 months	Constant dyspnea with stridor and dysphagia.	Continuous
9	Enderlen	Not given. Probably 1906.	Deutsch. med. Wehnschr., 1906, p. 1976. Reported by Kaufman.	3 years	Constant dyspnea with suffocative attacks.	Continuous. Due to abscess from spondylitis
10	Nicoll	Not given. Probably several years previous to 1908.	Glasgow Med. Jour., 1908, lxx, 107. Article by MacLennan.		Cough and dyspnea.	Continuous
11	Schwinn	March 29, 1908.	Jour. Am. Med. Assn., June 20, 1908, 2059.	23 days	Constant dyspnea with stridor and suffocative attacks. Enlarged thyroid.	Continuous
12	MacLennan	Not given. Probably 1908.	Glasgow Med. Jour. 1908, lxx, 107.		Stridor.	Continuous ?
13						
14	MacLennan	Not given.	Reported by Olivier in Anatomie topographique et chirurgie du thymus, Paris, 1911.		Hypertrophy of the thymus.	Continuous ?
15						
16						
17						
18	Rammstedt	Not given. Probably 1908.	Reported by Klose; Arch. f. Kinderh., lv, Parts 1 and 2.	10 months	Constant dyspnea with suffocative attacks and convulsions.	Continuous

WITH IMMEDIATE AND REMOTE RESULTS. FROM 1896 TO APRIL, 1912

Type of Operation	Anesthetic	Amount of Gland Removed, gms.	Result of Operation on Permanent dyspnea.	Result of Operation on Suffocative Attacks	Result of Operation on Stridor.	General Results and Autopsy Findings
Exothympexy after tracheotomy.			Immediate and complete relief	Immediate and complete relief.		Good recovery.
Tracheotomy, partial thy-mectomy, exo-thympexy.			Relief complete in 1 month.	Immediate and complete relief.		Good recovery in one month. Suffered from rickets for 2 or 3 years. Health good 9 years later.
Thymectomy, intracapsular.			Immediate and complete relief	Immediate and complete relief.	Immediate and complete relief.	Recovery.
Thymectomy, intracapsular.			Immediate and complete relief	Immediate and complete relief.	Complete relief later.	Recovery.
Thymectomy, Exothympexy			Immediate and complete relief	Immediate and complete relief.	Appeared when child cried.	Recovery.
Cracheotomy. Thymectomy with removal portion manubrium sterni.			Improved.		Improved.	Improvement.
racheotomy. Thymectomy, intracapsular.	Chloroform		Eventual complete relief.		Complete relief.	Recovery after slow convalescence.
Thymectomy, intracapsular.		6	Immediate and complete relief.		Immediate and complete relief.	Recovery. Immediate and complete relief of dysphagia.
racheotomy. Thymectomy.			Immediate and complete relief.	Immediate and complete relief.		Death from bronchitis 1 week later. Autopsy: Compression of the trachea by a tubercular abscess from cervical spondylitis.
Thymectomy.			Immediate relief.			Recovery. Condition good two years later.
Thymectomy. Section of sternum. Thyroidectomy.	Chloroform		Immediate and complete relief.	Immediate and complete relief.	Immediate and complete relief.	Recovery.
Thymectomy.					Progressive relief.	
Thymectomy.						Three deaths from spasm of the glottis and progressive heart weakness.
Thymectomy.	Chloroform		Immediate and complete relief.	Immediate and complete relief.		Recovery. Condition good 2 years later.

SYNOPSIS OF FIFTY CASES OPERATED ON FOR HYPERTROPHY OF THE THYMUS GLAND,

No.	Name of Observer	Date of Operation	Reference	Age	Résumé of Symptoms and Pathology	Type of Disorder
19	Morse-Murphy	Not given. Probably 1908.	Arch. Pediat., August, 1908, p. 607, Article by Meyer.	11 weeks	Constant dyspnea with stridor.	Continuous
20	Denecke	Aug. 7, 1908.	Deutsch. Ztschr. f. Chir., 1909, xeviii, 544. Résumé by Olivier, Anat. top. et chir. du thymus, Paris, 1911.	5 years	Enlargement of veins at the base of the neck, stridor, tumefaction in jugulum, loss of consciousness with cyanosis.	Cyanotic form
21	Veau and Olivier	May 19, 1909.	Arch. méd. d. enf., 1909, p. 817.	1 year	Suffocative attacks with stridor and spasm of the glottis.	Intermittent
22	Veau and Olivier	May 29, 1909.	Arch. méd. d. enf., 1909, p. 817.	11 months	Constant dyspnea with stridor and suffocative attacks.	Continuous
23	Veau and Olivier	June 19, 1909.	Arch. méd. d. enf., 1909, p. 817.	22 months	Suffocative attacks with spasm of the glottis.	Intermittent
24	D'Oelsnitz and Prat.	August, 1909.	Bull. Soc. de pédiat. de Paris, 1909, No. 7, 357.	13 months	Suffocative attacks with constant dyspnea and stridor.	Continuous
25	D'Oelsnitz and Boisseau	Nov., 1909.	Bull. Soc. de pédiat. de Paris, Mar. 15, 1910.	4 years	Constant dyspnea with suffocative attacks.	Continuous
26	Vignard and Sargnon	Not given. Probably 1909.	Ann. de méd. et chir. enf. 1910, xiv, 632.	4 months	Suffocative attacks, slight stridor and spasm of glottis.	Intermittent
27	Lexer, Tiling	Not given. Probably 1909.	Königsberg These, 1909. Reported by Olivier in Anat. top. et chir. du thymus, Paris, 1911.	7 months	Constant dyspnea with stridor.	Continuous
28	Veau and Olivier	Feb. 1, 1910. Oct. 17, 1910.	Reported by Olivier in Anat. top. et chir. du thymus, Paris, 1911.	4 mos., 1 yr.	Constant dyspnea with congenital stridor and suffocative attacks.	Continuous
29	Bircher	Not given. Probably 1910.	Schweiz. Rundsch. f. Med. April 9, 1910, No. 14.	2 years	Constant dyspnea.	Continuous
30	Veau and Olivier	May 30, 1910.	Anat. top. et chir. du thymus, Olivier, Paris, 1911.	7 weeks	Constant dyspnea, stridor and dysphagia.	Continuous
31	Tisserand	June 11, 1910.	Lyon chir. February, 1911, p. 145.	1 year	Constant dyspnea and stridor.	Continuous
32	Capelle and Bayer Garre operator	June 26, 1910.	Beitr. z. klin. Chir., Tübingen, 1911, lxxii, p. 214.	22 years	Graves' disease.	Associated with Graves' disease

WITH IMMEDIATE AND REMOTE RESULTS. FROM 1896 TO APRIL, 1912—CONTINUED

Type of Operation	Anesthetic	Amount of Gland Removed, gms.	Result of Operation on Permanent dyspnea.	Result of Operation on Suffocative Attacks	Result of Operation on Stridor.	General Results and Autopsy Findings
Exothymopexy with resection of manubrium sterni.			Improved.			Died 16 days after operation.
Thymectomy.	Chloroform-ether.				Progressive relief.	Gradual diminution of venous distention.
Thymectomy.	Chloroform	2		Immediate and complete relief.	Immediate and complete relief.	Recovery.
Thymectomy.	Chloroform	4.55	Immediate and complete relief.	Immediate and complete relief.	Gradual relief.	Recovery. Stridor practically gone 1 year later.
Thymectomy.	Chloroform			Gradual and final relief.		Complete relief 2 years later.
Thymectomy.	Chloroform		Complete relief in 10 days.	Immediate and complete relief.	Immediate and complete relief.	Recovery. Well 4 months later.
Thymectomy. Tracheotomy and resection of manubrium sterni.			No permanent relief.	No permanent relief.		Died 10 days later from infection.
Thymectomy.		4.25		Complete relief second day.	Immediate disappearance.	Died from infection 6 days later. Autopsy: 14.25 gms. thymus remained. Trachea flattened from sixth to fourteenth ring.
Thymectomy.			Complete relief by fourth day.		Complete relief by fourth day.	Died from diarrhea 1 month later.
Two successive thymectomies.	Chloroform	5	Complete relief.	Relief for six months; then reappearance and final relief by second operation.	Disappeared gradually after second operation.	Recovery.
Thymectomy.			Moderate relief.			
Thymectomy.	Chloroform	21.5	Immediate and complete relief.		Disappeared gradually.	Recovery. Stridor absent 14 months after operation. Complete relief of dysphagia.
Thymectomy.	Chloroform	3.1	Complete relief in 5 months.		Complete disappearance in 5 months.	Recovery. Complete relief in 5 months.
Thymectomy; later thyroidectomy.	Ether	15				Recovery. Symptoms improved, then recurred with complete relief after thyroidectomy 6 months later.

SYNOPSIS OF FIFTY CASES OPERATED ON FOR HYPERTROPHY OF THE THYMUS GLAND,

No.	Name of Observer	Date of Operation	Reference	Age	Résumé of Symptoms and Pathology	Type of Disorder
33	Aviragnet and Veau	Dec. 2, 1910.	Anat. top. et chir. du thymus, Olivier, Paris, 1911.	17 months	Dyspnea and stridor.	Tracheobronchial adenopathies taken for enlarged thymus. Continuous
34	Boissonnas	Not given. Probably 1910.	Congr. pédiatrie, 1910. Quoted by Olivier in Anat. top. et chir. du thymus, Paris, 1911.	2 months	Constant dyspnea and stridor, trachea flattened, tumor felt in suprasternal region.	
35	Gaudier	Not given. Reported 1911.	Soc. chir. Paris, Feb. 14, 1911.	11 months	Suffocative attacks, stridor, spasm of glottis type. Sarcoma of thymus.	Intermittent with spasm of glottis.
36 37 38 39	Gaudier	Not given. Probably 1911.	Anat. top. et chir. du thymus, Olivier, Paris, 1911. Brief personal communication, no details.	Not given		
40	Swyngedauw, Durand and Gaudier	Not given. Reported 1911.	Echo Med. Nord., February, 1911. Quoted by Olivier in Anat. top. et chir. du thymus, Paris, 1911.	1 year	Suffocative attacks, stridor, spasm of glottis type.	Intermittent with spasm of glottis.
41	Veau	Feb. 16, 1911.	Anat. top. et chir. du thymus, by Olivier, Paris, 1911.	7½ months	Suffocative attacks with cyanosis.	Tracheobronchial adenopathy operated for thymus. Continuous
42	Veau and Olivier	March 6, 1911.	Anat. top. et chir. du thymus, by Olivier, Paris, 1911.	23 days	Constant dyspnea with suffocative attacks and stridor.	
43	Veau	March 11, 1911.	Anat. top. et chir. du thymus, Olivier, Paris, 1911.	4 months	Dyspnea, suffocative attacks and cyanosis, dilatation of veins of neck, dysphagia.	Tracheobronchial adenopathy operated for thymus. Continuous
44	Veau, Olivier and Jean Du Bois	March 15, 1911.	Anat. top. et chir. du thymus, Olivier, Paris, 1911.	1 year	Constant dyspnea with suffocative attacks and stridor appearing at 9 months.	
45	Veau and Chatelin	March, 1911.	Thèse Malavialle, Montpellier, 1911.	15 months	Little's disease, suffocative attacks, convulsions, spasm of glottis type.	Intermittent with spasm of glottis.
46	Parker & Churchill	May 25, 1911.	Reported in this article.	13 months	Suffocative attacks with cyanosis and stridor, spasm of glottis type.	Intermittent with spasm of glottis.
47	Chas. Mayo	Aug. 31, 1911.	Ann. Surg., July, 1912.	11 months	Constant dyspnea from birth with convulsions and cyanosis.	Continuous
48	D'Oelsnitz	Not given. Probably 1911.	Bull. Soc. d. Péd. d. Paris, June, 1911. Reported by Olivier in Anat. top. et chir. du thymus, Paris, 1911.	21 months	Suffocative attacks and wheezing respiration.	Tracheobronchial adenopathy operated for thymus. Continuous
49	Buford & Walker	March 26, 1912.	Unpublished. Reported by courtesy of Dr. Buford.	4 months	Constant dyspnea since birth, stridor and cyanosis.	
50	Buford & Soper	April 2, 1912.	Unpublished. Reported by courtesy of Dr. Buford.	1 year	Convulsions, stridor, cyanosis, spasm of glottis type.	Intermittent with spasm of glottis.

WITH IMMEDIATE AND REMOTE RESULTS. FROM 1896 TO APRIL, 1912—CONTINUED

Type of Operation	Anesthetic	Amount of Gland Removed, gms.	Result of Operation on Permanent dyspnea.	Result of Operation on Suffocative Attacks	Result of Operation on Stridor.	General Results and Autopsy Findings
Thymectomy. Intubation.	Chloroform	2				Died 7 days later. Autopsy: Numerous enlarged tracheobronchial lymph-glands.
Thymectomy. Tracheotomy.	Ether	20	Immediate relief with some recurrence from bronchitis.		Disappeared gradually.	Died 18 days after operation from bronchopneumonia.
Thymectomy.	No anesthetic.	5		Immediate and complete relief.	Complete relief.	Died 3 days later, bronchitis and hiccough. Autopsy: large portion of gland remaining in chest. Sarcoma of thymus.
Thymectomy.						Recovery in all.
Thymectomy.		9		Immediate and complete relief.	Immediate and complete relief.	Recovery.
Thymectomy. Removal of lymph-nodes, drainage.	Chloroform					Did well for over a month but died later.
Thymectomy.	Chloroform	15	Immediate and complete relief.	Immediate and complete relief.	Gradual and complete relief.	Recovery. In good health 6 months later.
Thymectomy. Removal of lymph-nodes.	No anesthetic					Died 4 days later. Autopsy: Lungs and spleen filled with tubercles
Thymectomy. Intubation. Tracheotomy.		8	Temporary relief only.	Temporary relief only.		Died 4 days later. Autopsy: Congestion of lung with mucopus in bronchi; 16 gms. of thymus.
Thymectomy.		4		No relief.		Died several days later. Autopsy: 12 gm. of gland remaining. No infection.
Thymectomy.	Ether	9		Relief almost immediate.	Immediate and complete relief.	Recovery. One year later in excellent condition.
Thymectomy.			Immediate relief becoming permanent.			Good recovery. Six mos. later in good condition.
Thymectomy.						Died 3 hours later. Autopsy: Tracheobronchial adenopathy.
Thymectomy.	Ether		Greatly relieved.		Greatly relieved.	Recovery.
Thymectomy. Bronchoscopy	Ether				Relief.	Died 5 days later of lobar pneumonia.

sign—and frequently the increased *x*-ray shadow, with the absence of other known causes, confirm the diagnosis.

Laryngismus stridulus is eliminated by the absence of the peculiar hoarse barking cough. Spasm of the glottis from insufficiency of the parathyroid secretion resembles this condition most closely and it may be impossible to distinguish the one from the other. When the hypertrophy can be established the thymus should be removed, and in doubtful cases, Hutinel believes that even if the thymus cannot be proved the cause, its removal ameliorates the spasm and diminishes greatly the danger of sudden death. Thus in either case the treatment of the intermittent form is essentially surgical.

Olivier speaks of a "*forme cyanotique*" as a separate group that was first described by Marfan. He refers to eight cases in the literature with but one operation. This was Denecke's case. The child was a male 5 years old. When he was a little over a year old the parents noticed that when he cried his face became cyanotic and he lost consciousness. Soon after there appeared a tumefaction in the lower part of the neck that at first appeared only when the infant cried, but later appeared on coughing or even speaking. When first observed by Denecke, at 5 years, at the least agitation the veins of the neck became swollen and the face cyanotic. During this time there was present a slight stridor. In spite of the absence of corroborative physical signs he made a diagnosis of compression of the veins at the root of the neck by an enlarged thymus and performed a thymectomy which greatly diminished the frequency and severity of the attacks, though it did not control them. In this connection it may be mentioned that certain dry forms of eczema in infants have been considered to be of possible thymic origin, and Lesage several years ago proposed in this form, that had hitherto so frequently resulted in sudden death, trying thymectomy. No instance of operation for this condition has been reported, although a rather extensive eczema that was present in the case reported by the writer cleared up very soon after a thymectomy.

A complete list of the cases operated on to date, fifty in all, is shown in the accompanying table.

ANALYSIS OF CASES OPERATED ON

It will now be of interest to consider the results of treatment in the fifty cases of which we have records. First, as to mortality. Of the fifty cases operated on, seventeen died, showing a mortality of $33\frac{1}{3}$ per cent. An analysis of the deaths, however, will show that the operation is much more benign than these figures suggest. In passing it may be observed that all cases are included in a new field of surgery wherein the mortality is likely to be higher than in an older field of established procedure.

The seventeen fatal cases, according to operators (see accompanying table), were as follows: Enderlen, No. 9; MacLennan, Nos. 15, 16, 17; Morse-Murphy, No. 19; D'Oelsnitz, Prat and Boisseau, No. 25; Vignard and Sargnon, No. 27; Aviragnet and Veau, No. 33; Boissonnas, No. 34; Gaudier, No. 35; Veau, Nos. 41, 43; Veau, Olivier and Jean Dubois, No. 44; Veau and Chatelin, No. 45; D'Oelsnitz, No. 48; Buford and Soper, No. 50.

The Morse-Murphy patient died sixteen days after operation; cause not given. But it is known that a resection of the manubrium was made, which increases the severity of the operation greatly. In four operations of this type two patients died. It is no longer practiced. So late a death, however, may not be due to the operative act itself. The same may be said of Lexer's case, reported by Tiling, in which the patient died from diarrhea some time after the operation, after the child had returned home to its parents. MacLennan states that none of the three deaths reported by him was the immediate result of the operation, but they were secondary to a spasm of the glottis and a progressive enfeeblement of the heart. In one case of D'Oelsnitz and Prat the thymectomy was done after several attempts at tubage, which had increased the cyanosis and distress. The child died three hours later.

The patient of Veau and Chatelin was a sufferer from Little's disease with frequent convulsions and permanent contractures and the co-existence of an enlarged thymus. The child died several days after the operation without an infection of the wound or other evidence of its part in the causation of death. In Buford's case a bronchoscopy was done before the thymectomy which led to a pneumonia several days later. In this group of eight cases the operation can only indirectly, if at all, be blamed for the deaths.

Of the nine remaining cases four were in the service of Veau. The first was a child with permanent dyspnea. Forty-eight hours after the operation dyspnea reappeared and a tracheotomy became necessary. This wound extended to the thymus wound and infected it, the child dying three days later from asphyxia, with a temperature of 40 C. The second child died from infection fifty days after a thymectomy with removal of tracheobronchial lymph-nodes. The third child died four days after operation for a condition similar to that existing in the second. The death was due to asphyxia and infection. The fourth child also had tracheobronchial lymph-nodes removed at the operation and did well, but died from syncope the seventh day when an unskilful attempt at intubation was made.

The fifth case was that of D'Oelsnitz, Prat and Boisseau. The child was semi-comatose when operated on. A tracheotomy and a resection of the manubrium complicated conditions. The child died several days

later from asphyxia and infection. The sixth case, that of Boissonnas, died eighteen days later from bronchopneumonia. A tracheotomy had also been performed. Gaudier's patient died forty-eight hours after operation from hiccough and bronchitis. The patient of Vignard and Sargnon died seven days after operation without closure of the cervical wound, from infection. Enderlen's patient had an abscess from spondylitis. A tracheotomy was performed. Death from bronchitis occurred one week later. In four cases where tracheotomy was done the child died; usually from infection with asphyxia. Four cases suffering from tracheo-bronchial adenopathy contribute to the mortality. From this analysis of cases Olivier comes to the following conclusions: "Thymectomy in itself, without drainage or tracheotomy or ablation of septic organs, such as infected lymph-nodes, has no operative mortality. The shock is never sufficient to hasten the death of the child. It is an operation by itself benign."

RESULTS ACCORDING TO TYPES OF CASES AND WITH RESPECT
TO SPECIAL SYMPTOMS

Thirty-two cases belong to the continuous type, if we include the six cases of MacLennan which Olivier includes in his classification. This leaves the four cases of Gaudier unclassified on account of too meager data. Eight cases belong to the intermittent type, one to the cyanotic variety (Denecke's), and one is associated with Graves' disease in an adult (Garre's). In the thirty-two cases belonging to the continuous type there were nine deaths and twenty-three recoveries.

The persistent dyspnea in this type disappeared immediately and completely in fifteen cases. In one of these it reappeared after eight months and gradually disappeared after a second operation. Two died later from bronchitis. In five cases the relief was complete only after the lapse of several days and in one case, five months. One of these died one month after the operation from diarrhea. In four cases the relief from dyspnea was incomplete or moderate, or "improved." One of these died sixteen days after the operation. In one case the relief was temporary with death four days later, and in another there was no permanent relief, death occurring from infection ten days later. In the six cases of MacLennan this symptom was not given in the available histories. Thus in the twenty-six cases in which this symptom was mentioned the dyspnea was eventually completely relieved in twenty, or over 75 per cent. of the cases.

The occurrence of suffocative attacks was mentioned in fifteen of the continuous type of cases. In twelve cases these disappeared immediately and completely after operation, although in one of these it reappeared six months later to permanently disappear after a second operation. One died a week later from bronchitis. In one case the relief was gradual

and in two others it was only temporary or absent, both patients dying a few days after the operation. These attacks were thus suppressed in thirteen out of fifteen cases.

Stridor was mentioned as a symptom seventeen times in the continuous type, six times in the intermittent type and once in the cyanotic variety — twenty-four times in all — or in approximately one-half the cases. It disappeared immediately after operation in ten cases. In eleven others the relief was more gradual though not always complete. In one it was very slight, in another it reappeared when the child cried and in another it gradually disappeared after a second operation. Thus the stridor was suppressed or diminished in nearly every case.

In the intermittent form there were eight thymectomies with four cures or improvement, and four deaths. Suffocative attacks occurred in seven of these. In six there was immediate or remote suppression of the attacks. In one there was no relief. Three of this seven eventually died.

In the single dysphagic case of Hinrichs the dysphagia was immediately relieved and the child swallowed without trouble shortly after the operation. In the cyanotic case of Denecke the relief was great, though the cure was not complete. The improvement in the general health is particularly noticeable in many cases as one might well expect after relief from serious respiratory obstruction.

CONCLUSIONS

Many sudden deaths in infants have been caused by an enlarged thymus producing obstruction of the trachea.

Frequently this is the sole factor responsible for the compression, but at times enlarged tracheobronchial glands or spasm of the glottis are contributing factors in producing the fatal result. Compression of the trachea is shown at autopsy by the presence of a flattened trachea associated with the enlarged thymus, and is revealed *intra vitam* by the bronchoscope showing the narrowed lumen of the organ, the symptoms referable to which being completely relieved by thymectomy. The diminished caliber has also been demonstrated by intubation, only a long tube sufficing to keep the trachea open, and immediate and permanent relief following removal of the gland.

Two general types of cases are observed, the continuous type in which the symptoms usually date from birth or soon after with permanent dyspnea usually present, and the intermittent type, usually of later development, in which there are longer or shorter intervals free from symptoms.

The three most important symptoms in either type are permanent dyspnea, recurring suffocative attacks and stridor. All three of these frequently occur together, when their presence is an imperative indica-

tion for immediate operation. The presence of either one of the first two symptoms is an equally imperative indication for operation. Stridor alone is not an indication for thymectomy.

The treatment is essentially surgical. Operative treatment—thymectomy—is as necessary and effective in tracheal obstruction from the thymus enlargement as tracheotomy or intubation are for obstruction higher up. It is frequently an emergency operation.

Although the accumulating evidence is strongly suggestive that the thymus gland is absolutely necessary to life and normal development in the earlier stages of growth, its operative removal in the young human subject, as far as present evidence has shown, is not fraught with the slightest untoward metabolic disturbances. This is probably due to the fact that it is never completely removed and that the remaining portion quickly reproduces the tissues of the organ. It may also be in man, as in the lower animals, that after a certain period of growth its function is taken up by other organs, as the thyroid and spleen, and its complete removal, if it were possible, would have no baleful influence on the organism.

Of the seventeen recorded deaths that occurred in thymectomized children, four followed a complicating tracheotomy and one an unclosed wound with drainage and infection. Four were due to infection from septic tracheobronchial glands. In one there was a preliminary bronchoscopy and in another there had been several unsuccessful attempts at tubage immediately preceding the operation. In three cases with incomplete histories the operator expressly stated that the deaths were not due to the operation itself. One was in a severe case of Little's disease. And, finally, in two cases the deaths occurred several weeks after operation from causes remote from if not entirely separate from the operative procedure. In no case was the operation immediately fatal.¹⁶

Intracapsular thymectomy is the only type of operation now employed. The vertical median incision terminating about 1 cm. below the upper border of the sternum is the skin incision usually employed. This is the one used in Veau's operation. The low transverse incision has been successfully employed in a few cases.

General anesthesia is usually well borne when competently given.

The operation is easily and safely performed.

7 West Madison Street.

16. Since preparing this paper I have learned that Dr. W. E. Schroeder, of this city, performed a successful thymectomy on a child in February, 1912.