

The administration of thymus in exophthalmic goitre / by R.H. Cunningham.

Contributors

Cunningham, R.H.
Maude, Arthur
Royal College of Surgeons of England

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mesorchium, so that it hangs freely on a pedicle, which, at any rate, is not fixed for some distance. This explains in itself the necessary anatomical conditions under which the twisting can be complete. Nicoladoni lays special stress upon this point, the absence of a short fixation, by a short mesorchium. The origin of this abnormal condition, which shows itself either as a too slender or too long, or as a complete absence of fixation, is to be traced back to early disturbances in the development of the processus vaginalis, and the shortening of the gubernaculum, which takes place at the same time.¹ As the abnormal formation of the mesorchium allows great movement to the testicle, it can, hence, make difficult the entrance of the testicle into the inguinal canal, and in this way be the cause of late or incomplete descent. Kocher has shown two examples of this kind.² In fact, the majority of cases have been with incomplete descent, and in many of them this abnormal condition has been mentioned. Nicoladoni says, "The expressions 'absence of a mesorchium' and 'too long a mesorchium' do not refer to opposite conditions, although apparently we might think so. In no case is there an 'absence' of the mesorchium, for as the testicle already has a peritoneal covering before its descent, while in the posterior part of the abdominal cavity, the mesorchium cannot possibly be absent after it has descended. Hence, the cases described as 'absence of the mesorchium' mean only that the testicle is deprived of its normal fixation, while a 'too long mesorchium' relates as well to the cord as to the peritoneal covering both of itself and testicle."

Besides this, according to Lexer, we have another important predisposing factor, as well for the occurrence of the torsion as for the impossibility of its untwisting itself, especially when the testis is in the canal, and that is, its flattened shape, to which attention was drawn in several of the cases. With this condition present it can be understood how certain, perhaps unusual, movements of the body and lower extremities can become the direct cause of the torsion, and, if having once taken place, how difficult it would be for the testicle to resume its normal position. So, during heavy work, as in Nicoladoni's second case, and in Lauenstein's, after lifting a heavy piece of wood.

It has been impossible, however, in all cases to discover a direct cause, for although, besides these two, we find Whipple's coming on after a strain, von Meyer's after sneezing, Johnson's while blowing on a cornet, Nash's after boxing, Barker's after straining at stool, and Owen's after bowling at cricket, yet there are a number where nothing whatever unusual had happened, as in those of Keen, Davies-Colley, Page, Anders, Lexer, and in my own; in fact, in several, the first symptoms appeared while the patients were asleep. In several, where the pain came on only some time after the accidents which were supposed to have caused them, it looks as if the torsion had perhaps commenced at the time of the accident, and had afterward been completed by subsequent bodily movements; that is, completed sufficiently far to cause a disturbance in the circulation of the cord and testicle. For testes which lie in the scrotum the conditions would be different from those where they lie horizontally in the inguinal canal, and in this connection Meinhardt Schmidt has drawn attention to the fact that we have an analogue in the torsion of ovarian tumors, which certainly finds some causation in mechanical acts, such as changes in position from movements of the body and intestines. We naturally get more torsion with a long mesorchium than with a short one, but violence *per se* is not necessary. Any slight movement may complete the amount necessary to interfere with the circulation, which varies in the individual cases.

Pathology.—As we have seen, in all cases where the vaginal process was opened there was a greater or less

quantity of bloody serum and clots. The testis and epididymis were congested and swollen, of a dark or bluish-black color, and sometimes in a more or less advanced state of necrosis. Sections of testis showed it filled with blood and clots, with sometimes no trace of tissue structure, as in Lauenstein's case, while microscopically there was a true hemorrhagic infarction, a high grade of hemorrhage, or overflowing with blood of the entire organ, both of the lobules themselves and of the interlobular tissue. The necrosis, when present, was especially marked at the periphery. This condition of hemorrhagic infarction is well explained by Miflet's important work,¹ in which is found the foundation for a complete understanding of the consequences of torsion, as far as is possible, by experiments upon animals.

He used eighteen dogs, as follows: In seven he made artificial emboli; in four he ligated the internal spermatic artery; while in five he ligated both the internal spermatic artery and veins; and in two the veins alone. In two of the first seven the deferential artery was also stopped. These are his general conclusions and results:

1. The internal spermatic artery has, for the testis, the significance of a terminal artery.
2. Interruption of the flow of blood through the internal spermatic artery, either by ligation or by embolus, is quickly followed by the formation of a hemorrhagic infarction, and these infarctions involve especially the superficial layers of the testis.
3. The glandular structure of the testis is especially sensitive to any disturbance in the circulation of the cord, not only when both the arteries and veins are interfered with, but also when the circulation through the veins is interrupted. The glandular tissue always disappears rapidly, which change takes place with more or less tissue proliferation.
4. The epididymis, which is supplied by the deferential artery, is not at all affected by ligature, and very little by embolus.
5. If at the same time the circulation is disturbed in both the spermatic and deferential arteries, then the secreting tissue of the epididymis is also destroyed.

As to the torsions themselves; where stated, the accident happened twelve times upon the right side, and nine times upon the left; the greater length of the left cord, therefore, not having increased its liability, but, on the other hand, the twisted cord has always been abnormally short, the testis either lying within the inguinal canal or high up in the scrotum. The direction of the twist, however, when mentioned, has been nine times from without inward, and but three times from within outward. Lauenstein mentions this point, as resembling the idea brought forward by Küstner, as regards the torsion of ovarian tumors, that the pedicle of the tumors of the right side had a left twist, and those upon the left side had a right twist. The degree of torsion sufficient to cause strangulation has varied greatly, from a half-turn in Keen's and Nash's cases, to two full turns in Defontaine's and my own; for, as we have seen, a long mesorchium would permit more twisting to take place, before the circulation would be interfered with, than a short one.

Symptoms and Diagnosis.—In most cases there have been more or less well-developed symptoms of inflammation, such as pain, local swelling, and, in some instances, œdema, redness, and fever; and when we find these conditions associated sometimes with constipation and vomiting, together with absence of impulse in an irreducible swelling, developing suddenly, after perhaps some strain or exertion, we are naturally led to suspect a strangulated hernia. There are, however, some distinctions. With torsion of the cord the constipation may not be absolute. The vomiting, which is not apt to become stercoraceous, is not so persistent.

¹ Ueber die pathologischen Veränderungen des Hodens, welche durch Störungen der lokalen Blutcirculation veranlasst werden. Langenbeck's Archiv, Bd. xxiv., 23.

² Bramann: Archiv für Chir., Bd. xl., S. 136.

³ Deutsche Chirurgie, 1887, p. 578.

The shock is less, and there is not so much abdominal distention nor pain at the umbilicus. In fact, these latter may not be present at all. Again, the tumor, especially if outside the external ring, is apt to be harder and more solid to the touch, and if the seat of torsion is below the ring, the swelling would not extend into the canal, and the finger passed through the ring would, in this case, be able to clear up any doubts. Still, as we have seen, a correct diagnosis may at times be extremely difficult and impossible before making an exploratory incision, especially where we also have a hernia present. Abscess from an inflamed appendix, as also gonorrhœal and traumatic inflammation of the testis and epididymis, should not be forgotten.

Treatment.—If left alone there would probably be either one of two results—atrophy or gangrene. In this connection Chaveau's experiments on goats are interesting. He found that after a subcutaneous torsion of the cord the testis would atrophy, and that gangrene only occurred in cases where he had previously introduced substances into the circulatory system which had undergone putrefactive changes. Atrophy is not a very infrequent result following the subcutaneous operation for varicocele, and it is well known that the surgeon Delpuch was killed by a patient on whom he had operated for double varix, and who afterward had atrophy of both testes. As Nash says, "It will probably not happen very often that surgeons will be fortunate enough to see cases at their commencement, but now that the accident and its causes are becoming generally known, they will at least be prepared for it, and some will undoubtedly be recognized in time to be untwisted." In all cases where castration has been performed there has been a good recovery, and this would be much earlier resorted to where we have a testis in the inguinal canal, as it is well known that they are apt to become sarcomatous if left in this situation. In eight cases the testis was not removed. Two of these were untwisted without operation, followed by atrophy in one. In three the testis sloughed away during healing. In two, there was subsequent atrophy; and in one, five months after operation, there was no change except that it was harder than normal, and fixed by adhesions at the root of the penis.

I record still four cases* which, without doubt, were results of this accident, but where the torsion was not discovered; and I am especially indebted to the papers on the subject by Lauenstein and Lexer.

36 WEST THIRTY-NINTH STREET.

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THE ADMINISTRATION OF THYMUS IN EXOPHTHALMIC GOITRE.

By R. H. CUNNINGHAM, M.D.,

ASSISTANT DEMONSTRATOR OF PHYSIOLOGY, COLUMBIA COLLEGE, NEW YORK.

APROPOS of a report by David Owen, in the *British Medical Journal* of February 16, 1895, of a case of exophthalmic goitre that was successfully treated by the accidental administration of the thymus gland, a survey of the benefits derived from the administration of minced thymus in the following cases of that disease will additionally tend to show that in certain cases, at least, of exophthalmic goitre a diet of thymus may be followed by results that are surprising, gratifying, and very suggestive.

The first of these cases, whose history I give in full detail from my private case-book, was under my personal observation for eighteen days only. She has,

however, reported her progress to me by letter a number of times since I saw her. Since treating her, several other cases have come under my observation, two* in the Department for Nervous Diseases at the Vanderbilt Clinic, and the others in private practice, and all have been treated either with the fresh gland or with thymus tabloids. These cases are still under treatment with the thymus; nevertheless from the improvement that has occurred in one or more of the symptoms, even in a few weeks' time, I feel justified in adding them to this report.

CASE I.—Miss B—, aged twenty, consulted me, October 2, 1894, stating that several physicians whom she had consulted had told her she had Basedow's disease. She consults me now to get something to make her sleep, as she has been unable to sleep for the past two nights, and also because she has felt so extraordinarily weak for the past few days.

Her hereditary history is noteworthy. Her deceased father had prominent eyes, was a sufferer from insomnia, and had died of pneumonia two years ago. Her paternal aunt had prominent eyes, and also a slight swelling in the neck. She had frequently complained of palpitation of the heart and of general weakness. The patient's mother says the doctor who attended her stated that her death was due to "heart trouble." Miss B—'s brother, aged twenty-five, has a tendency to prominent eyes, but is strong and active.

Except for an attack of measles at fourteen years of age, Miss B— had had good health until two years ago. A short time after her father's death, at which she was very deeply grieved, she began to suffer from palpitation of the heart on the least exertion. From that time her eyes have gradually become more prominent, though she has been seriously troubled with insomnia for the past year only. In addition to the above she complains of a loss of energy, mental depression, excessive sweating on the right side at night, sensations of "flushing," trembling of the hands, and occasional headaches, but has had no aural disturbance. Her appetite is poor, and her bowels are usually constipated.

The examination showed a fair amount of exophthalmos, both Von Graefe's and Stellwag's symptoms being present. The inco-ordination on convergence was slight. The apex-beat of the heart was strong, 124 per minute, regular, and was not displaced, nor was there much evidence of hypertrophy. The lungs were apparently normal, and no abnormality could be made out in the region of the thymus. The thyroid was moderately enlarged, soft, and compressible, but no enlarged accessory thyroids or lymph glands were present. A moderate bruit existed over the thyroid. She appeared slightly anæmic, and the result of the examination of the blood was as follows: Red corpuscles, about four million six hundred thousand per cubic millimetre; white corpuscles (not counted); hæmoglobin, sixty per cent. (Von Fleischl's hæmom). Microscopically nothing worthy of remark was noticed. The urine was 1.022 specific gravity, and negative. She was put on the thyroid tablets, one tablet (gr. v.) *t.i.d.*, and, in addition, trional was prescribed for the insomnia.

October 4th.—She states she feels worse and has slept no better than before. The heart-beats had increased to 136 per minute, and were also irregular at times. The respiration was 28. The thyroid tablets were discontinued, and later in the day arrangements were made with a butcher to supply her daily with a fresh thymus from a healthy lamb that had been brought up on milk. This was to be minced fine and taken raw if possible.

October 10th.—She returned and stated she had been unable to take it raw as it made her sick at her stomach and she could not retain it. Therefore she had

* 1. H. H. Johnson: Boston Medical and Surgical Journal, 1888. 2. Bramm: Langenbeck's Archiv, 1890, p. 163. 3. Erichson: 8th edition, vol. i., p. 813. 4. Volkmann: Berliner klinische Wochenschrift, No. 53, 1887.

* For the privilege of referring to these in this report the writer is indebted to Dr. Frederick Peterson, Chief of Clinic, Department of Neurology, at the Vanderbilt Clinic.

taken it broiled very slightly. At this date the heart was 120 and regular, the respirations 20 per minute. She says she has slept a little better, but no change except that noted above is perceptible.

October 20th.—I saw her for the last time, as she and her mother were unexpectedly compelled to return to her home in a neighboring State. She stated she had slept very well for the past few nights (no trional or other hypnotic had been taken since the 10th) and had taken the thymus uncooked for the past three days without nausea. The pulse was 100, the respirations 18.

Since October 20th her mother has written to me a number of times to inform me that her daughter has steadily improved, and in the last letter written by Miss B—, on March 10th, she writes that she feels as well as she ever did, that the swelling in the neck has disappeared, and that she can take a considerable amount of exercise without getting fatigued. Her pulse is about 72 and she sleeps as well as she did before her trouble commenced. Her mother tells her that her eyes are no longer prominent and that the color has returned to her cheeks.

Case II. has, unfortunately, not followed the treatment very regularly; sometimes neglecting to take the glands for several days at a time, but he has nevertheless considerably improved in many respects. Briefly summarized, the most prominent symptoms presented by him were a general diminution of energy, severe insomnia, palpitation of the heart, fatigue and moderate dyspnoea on the least exertion, prominent eyes with lagging of the upper lids on looking downward, and a slight horizontal nystagmus on rapid convergence, a slight increase in the size of the thyroid, pulse from 100 to 110, and a well-marked, fine-waved tremor of the hands. The above symptoms had been becoming progressively more prominent during the past four years. After an irregular administration of slightly cooked lamb's thymus for two weeks the pulse-rate had fallen to 78 per minute and was perfectly regular. He slept very much better, and was feeling stronger. His eyes had become much less prominent, and only after a very searching examination was a slight degree of Von Graefe's symptom found to be still present. When I last saw him his eyes were apparently normal, his pulse was 76, his capacity for hard work had greatly increased, and the tremor of the hands had entirely disappeared.

In a third case that presented the usual symptoms of exophthalmic goitre the thymus gland tabloids of Messrs. Burroughs, Wellcome & Co. have been administered at the rate of twelve to fifteen 5-grain tabloids per day and have been followed by improvement, especially as regards the ocular symptoms. In this case after a week's treatment with the tabloids in the above dose a very considerable decrease in the enlarged thyroid occurred. This diminution still continues to slowly progress. Two and a half weeks after the tabloids were begun, the pulse-rate, which in the beginning averaged about 124 per minute, had become 96, though it would readily mount to 120 after moderate exertion or excitement. She feels, however, much stronger, and has been able to resume her work.

Possibly had a larger number of the tablets been given a more rapid and marked effect would have followed. At present she is taking the fresh thymus gland and the results of this procedure the writer will give in detail in a later paper on this subject.

If the results following the administration of thymus in these cases be compared with those published by Owen,¹ I think one may reasonably exclude the factor of mere coincidence, for though cases of Graves's disease do get well sometimes without any treatment whatsoever, Owen shows the suppressed symptoms began to return when the administration of the thymus was discontinued.

The remarkable and rapid diminution of the increased

heart-action and the progressive abatement of the other symptoms would certainly lead one to believe that by administering the thymus via the gastro-intestinal tract some substance that influences the deranged metabolism in a peculiar and striking way has been added to the blood.

The present state of the knowledge of the physiological chemistry of the thymus gland certainly does not help one to form a definite idea as to what this substance may be. It is true that Schindler has shown that a high percentage of adenine, a base derived from nuclein (Halliburton⁵), exists in the fresh and in the dried thymus of the calf; but whether the extractives or the nuclein (Kossel⁶) or the derivative base, adenine, of the thymus are the chemical bodies or not which act in exophthalmic goitre in a manner analogous to that attributed by Goulay⁷ to the nucleo-albumin of the thyroid body when the latter is given in myxœdema, one has not sufficient evidence for positively stating.

A brief look through some of the scanty literature of the experimental results obtained from depriving young animals of the thymus would lead one to believe that the presence of the thymus gland in the lower animals is not a necessity for the well-being of those animals, provided we are ready to accept the results of those observers as finally conclusive. Though Langenhaus and Saveliew⁸ got negative results in the dogs and rabbits that survived after extirpating the thymus, it is difficult to reconcile such results with the apparent physiological activity of the said gland in certain orders of young animals. The deaths of many of their animals resulted, according to the authors, from gastro-intestinal disturbance consequent to "too much green food" in the case of the rabbits, and in the dog worms were found in the intestine. No definite systematic information, however, is given regarding the character of the diet from first to last, and this, in my opinion, is an important omission when one takes into consideration the difference between the large, well-developed thymus of a calf or of a lamb that has been brought up on milk, and the small, atrophied thymus of a calf of equal age that has been weaned early and fed on grass. Further details on this score will be submitted, however, in another paper.

In 1893 Macalister⁹ called attention to the remarkable metabolic effects that occurred during a diet of thymus in a case of pseudo-hypertrophic paralysis, and his results would tend, to say the least, to substantiate one of the ideas of some of the older writers,¹¹ that the thymus stands in relationship with the state of development of the muscular system. In exophthalmic goitre also many symptoms are manifested by the muscular system that possibly arise from the action of the pathologically altered product of the thyroid which Lemke¹² states is a specific muscle-poison that separates the normal tonus into many small contractions.

But does the thymus add to the blood a special substance that has an "oppositeness" of action to the hypersecretion of the thyroid, or to some poisonous substance occurring in the blood consequent to the qualitative alteration of function of the thyroid? Possibly, as Owen suggests, though I do not unite with him in bringing forward the "oppositeness" of action that is claimed by Zanda,¹⁴ on repeating Bardeleben's (1841) experiments, to exist between the spleen and the thyroid, as a reason to strengthen the probability of this possibility, for Fano¹⁵ was unable to corroborate Zanda's statements, and the writer on repeating Zanda's experiments, using young and middle-aged dogs, finds also that the consequences of total thyroidectomy, after previously extirpating the spleen, are the same as in animals who possess the spleen intact. As Breisacher first pointed out, when thyroidectomized dogs are fed on meat that has been thoroughly extracted by boiling, the appearance of the cachexia is much delayed; if, however, the dogs are fed on the

bouillon from the meat, the cachexia rapidly develops. The writer has, on the other hand, fed thyroidectomized dogs on thymus without apparently hastening or delaying the appearance of the cachexia otherwise than if the animals had been fed on so much ordinary cooked meat. Nor have I ever seen any diminution in the symptoms of exophthalmic goitre follow a diet of underdone meat, provided no other therapeutic means were employed at the same time.

That a functional relationship, at present unknown, does exist between the ductless glands is manifest from the results both of experimental investigation and of clinical observation. Thus the compensatory (?) hypertrophy of the thyroid that occurs after extirpating the spleen is well known. According to Cadéac³⁸ enlargement of the thymus follows thyroidectomy in lambs. Likewise, Rogowitsch¹⁶ has found that after the thyroid has been removed in rabbits, the pituitary body becomes enlarged. Clinically, Boyce and Beadles¹⁷ emphasize the frequency of the same occurrence in myxœdema, sporadic cretinism, and cachexia thyreopriva in man. In acromegaly³⁸ hypertrophy not only of the hypophysis, and either hypertrophy or atrophy of the thyroid occur, but an hypertrophy or a "revival" (Marie¹⁸) of the thymus has often been reported. In myxœdema, and especially in exophthalmic goitre,¹⁸ a similar hypertrophy or revival of the thymus is frequently found, as is evident from the cases of the latter disease reported by Johnston, Hale White, Mosler, Spencer, Marie, Moebius, Lasvenes, Reymond,³¹ and several other observers.

The possibility of the participation of the quantitatively or the qualitatively altered internal secretion (?) of such glands, whether hypertrophied concomitantly with the thyroid or secondarily to the thyroid, as a causal factor of some of the symptoms in certain cases of exophthalmic goitre is therefore worthy of consideration. That the increased secretion of the thyroid is not the sole producing cause of the whole complex of symptoms of exophthalmic goitre many eminent observers concede. A mere glance at the final results of surgical interference with the enlarged thyroid that occur in certain cases of this disease will show that such is correct.

Briefly summarized, these surgical results may be stated to be as follows:

After partial extirpation of the supposed hypersecreting thyroid a complete (?) cessation of the symptoms occurs in one set of cases. In the second set merely a temporary moderation³⁰ of the symptoms has followed, and this moderation has been succeeded in a short time by an increase even in some of the former symptoms.

In other cases no immediate or remote diminution in the symptoms has resulted from the operation.

Lastly, the operation has been followed in a number of instances by fatal results which were accompanied by the symptoms of acute thyreopriva in some cases, while in others the cause of death was attributed to the "inundation"¹⁹ of the system by the large amount of thyroid juice that was unavoidably introduced into the circulation by the necessary manipulations of the operation.

Equally suggestive are the results of the observations both of clinicians and of recent experimenters. Among the clinical reports of sundry diseases treated by the administration of the thyroid extract the most striking in this connection is by Bécclère.²³ According to this observer, after a myxœdematous patient had taken 92 gm. of thyroid extract in eleven hours, the symptoms of the myxœdema disappeared and were replaced by the symptoms of "intoxication," which consisted of tachycardia, instability of the action of the heart, fever, insomnia, agitation, incomplete paraplegia, increased respiration, exophthalmos, and fixedness of look.

A practically similar though less marked effect has been noted by a number of writers to follow the ad-

ministration of large and repeated doses of the thyroid extract, but nothing definite as regards the artificial production thereby of a goitre is mentioned except by Ballet and Enriques.²⁴ These investigators state that after injecting the thyroid extract into dogs they succeeded in producing fever, tachycardia, tremor, and in addition a goitre; all of which disappeared when the thyroid was discontinued, but reappeared when it was readministered. It is true such injection experiments are complicated, as Horsley²⁵ pointed out some years ago, by the presence of toxic tissue fibrinogens, and due allowance must be made therefor. The writer has, however, fed dogs with enormous quantities (50 gm. per day) of commercial thyroid extract, also with 100 to 200 gm. of fresh thyroid daily for fifteen days, but so far with a negative result.

On the other hand, cases of exophthalmic goitre that have been treated with the thyroid extract have improved²⁶ instead of becoming worse. Such improvement results, according to Kocher,¹⁹ from the "thyroidin" causing a retrograde metamorphosis of the hypertrophied thyroid, and as the thyroid disease is not always primary, it is in this way beneficial. The most natural way, and the one more in accord with the evidence above, is that a sufficient quantity of a proper quality of the so-called "thyroidin" is added to the altered blood, and by this addition some of the symptoms of exophthalmic goitre are caused to disappear, while others are moderated only, or even unaffected, and in some instances slightly, or even greatly, increased. In this connection those cases³⁰ which present at the outset the symptoms of exophthalmic goitre, later the symptoms of a combination of exophthalmic goitre and of myxœdema, and finally of myxœdema alone, are very interesting; likewise the case of Jansselme²⁷ in which exophthalmic goitre and scleroderma coexisted. Similarly acromegaly and myxœdema, or cretinism and acromegaly, are well known to occur in combination.

Lastly, we are confronted with the fact that cases of exophthalmic goitre exist in which the administration of thymus is followed by a disappearance of the symptoms and by a recurrence of them, as in Dr. Owens's case, if the thymus is discontinued. This latter factor, as I stated above, certainly negatives the idea of the mere coincidence of spontaneous improvement. Likewise no variation of the ordinary diet except the addition of the thymus was resorted to in the cases under my observation, and though a moderate improvement, which disappeared when a meat-diet was resumed, has been observed to follow the employment of a milk-diet,³⁶ either with or without special attention to the correction by drugs of the disturbed digestion, the effects possibly resulting from this source are reduced to a minimum.

It will be noticed from the description of the cases reported by myself that they, as well as Owens's case, are evidently not of the type that is secondary to an ordinary hypertrophied thyroid and what the ultimate effects of the thymus administration will be on the symptoms exhibited by this latter class of cases, the writer is unable at present to state definitely; but judging from the apparent absence so far of any effect in several such cases that have lately come under his observation, probably no very great improvement will ultimately result.

A consideration of the above evidence and a careful comparative study^{4,10} of the similar and of the opposite objective and subjective symptoms that are met with in exophthalmic goitre, acromegaly, and myxœdema, or in the combinations of these diseases, will lead one reasonably to conclude that the alteration that frequently occurs in one or more of the ductless glands besides the thyroid possibly plays a more or less prominent part in the causation of some of the symptoms of the disease (or possibly diseases?) to which the terms exophthalmic goitre, Graves's disease, and Basedow's

disease are applied. But whether the alteration of these glands, for instance of the thymus, is primary, concomitant, or secondary to a primary derangement of the nervous system (Marie), or to a toxic blood state induced by the functionally altered thyroid (Moebius), or by various "toxins" of gastro-intestinal origin, are questions which possibly may be explicitly answered in the future when a more definite knowledge of all of the functions and of the effects of disordered function of the individual ductless glands has been obtained from clinical observation and from further experimental investigation.

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REPORT OF AN EXPERIENCE WITH ANTI-TOXIN AT THE NURSERY AND CHILD'S HOSPITAL.¹

By ALLEN M. THOMAS, M.D.,

ATTENDING PHYSICIAN, NURSERY AND CHILD'S HOSPITAL, NEW YORK.

SINCE the date of an epidemic of diphtheria in the hospital in the fall of 1893, there has been from time to time an occasional outbreak in the wards. In January of this year, with the aid of fresh invoices from without, another epidemic was started associated with more or less of measles and broncho-pneumonia. These conditions so complicate the histories, and a close personal knowledge of the cases being impossible on account of my obstetrical obligations, I regretfully refrain from any attempt at reporting them. Dr. J. J. Mapes, the house physician, who has given to all this work his intelligent and close personal attention, may be able to do so at some future time.

The following report is consequently limited to an account of the antitoxin immunization in regard to which the facts at hand came under my personal observation, are uncomplicated, and surely simple enough to be beyond the likelihood of misstatement or misconstruction. I present them without further comment as follows:

Total number of cases in the hospital from January 18th, the time of outbreak, to April 18th, the date of immunizing, 46. In all these cases cultures of the Klebs-Loeffler bacilli were obtained, and observations of them doubly verified in most cases by the separate examinations of the Board of Health and Dr. Mapes. In 30 of these 46 cases abundant local clinical aspects existed, there being well-marked pseudo-membrane in the throat, nose, or larynx; the remaining 16 cases had only sero-purulent or sero-sanious nasal discharges as a local manifestation. Of the entire number of 46 cases 15 occurred between April 1st and April 18th, and 7 between April 11th and April 18th, plainly showing the epidemic to be gradually on the increase in the hospital up to the day of immunizing. On April 18th 30,000 units of antitoxin were obtained from the Board of Health, and 110 children immunized. On April 20th 26 more children were immunized, and the 32 remaining children in the hospital that had previously had throat or nose lesions containing Klebs-Loeffler bacilli were not immunized. Of these cases immunized the following table shows the age, number, and antitoxin units:

Age.	Number.	Antitoxin Units.
3 to 4 weeks.....	7	50
2 months.....	12	50 to 75
3 to 6 months.....	36	100
7 months to 1 year.....	22	150
2 to 4 years.....	59	200

Careful examinations were made individually for albumin, variations of temperature, and skin lesions, in connection with the general observation of the children as a whole. A few (4) showed faint traces of albumin in the urine, but this in no case (where the urine could be regularly obtained) persisted more than three to four days, nor was there in any case any rational symptoms pointing to any special disturbance of the kidneys. Three cases, eight days after the injections, and 4 cases, nine days after the injections, had an eruption, more or less profuse, of erythematous patches of the size of a silver dollar, in some isolated, in others running together about the head, trunk, and extremities; but in no case were they associated with any appreciable fever; in this respect markedly differing from cases that have been reported of erythematous eruptions occurring with rather startling elevations of temperature. Red, pea-sized, shotty papules appeared rather profusely on the face, in one case on the eighth day, and in another on the ninth, and the same kind of papules appeared on the face and both arms in a third case, also on the

¹ Read at a meeting of the New York Clinical Society.

ninth day; these likewise were associated with no rise of temperature.

The only temperature which occurred following the injections that could be accredited to antitoxin (one case with persistent high fever proved to be measles) happened within the twelve hours immediately succeeding the injections, and stood as follows:

In from six to twelve hours after the giving of the antitoxin the temperature rose, in the cases of children who had been previously normal, to

100°	plus in 17 cases
101°	" " 32 "
102°	" " 16 "
103°	" " 4 "

That is, in 69 cases out of a total of 136 children immunized the temperature rose within twelve hours from 100 to 103° F., but within the next twenty-four hours it had in all these cases virtually fallen to the normal. The amount of reaction, as manifested by rise of temperature, crying, restlessness, and sleeplessness, seemed to be directly proportionate to the youth of the infants, and to their general debilitated condition; while the stronger and older ones showed little reaction, scarcely being disturbed at all, many of the younger infants, especially the marasmic ones, cried all night, going almost entirely without food or sleep for twelve to fifteen hours.

No new case has broken out in the hospital since April 18th, the day of immunizing, with the exception of the assistant physician on the resident staff, who about three weeks after the children were immunized, and one of the ward nurses, who five weeks after, developed well-marked cases of tonsillar and pharyngeal pseudo-membrane, with both clinical and bacteriological evidences of true diphtheria. Neither had been previously immunized. This would seem to show very conclusively the continued presence of diphtheria bacilli in the hospital, and will make subsequent observation of the children still more interesting and instructive.

The conclusions, which seem not only justifiable, but fairly inevitable, to be drawn from this report are as follows: 1. The evident value of antitoxin in affording a certain period of immunity against the infection of diphtheria. 2. The apparent harmlessness of its use in this way with children even of tender age and condition.

May 28, 1895.

NOTE.—During the epidemic four nursing babies went to the diphtheria ward with their mothers who were suffering with diphtheria. These babies were all injected and then stayed from two to three weeks constantly exposed to diphtheria without contracting it.

An Ingenious Medical Man.—One of the most novel methods which has come under our notice for bringing one's name "under the notice of the public" was recently adopted, as we learn from a French contemporary, by a medical man in Montpellier. Desiring to practise in the town, he set himself to work to conjure up a scheme for informing the inhabitants that he was quite prepared to attend to their ailments. After mature consideration he decided upon the following ingenious plan: He engaged the services of the town-crier, and instructed him to announce throughout the town that Dr. So-and-so, giving his address and full qualifications, had lost a valuable dog, and that anyone finding and returning the same to the owner would receive a reward of £25. It soon happened that the subject of the lost dog became widely discussed, as well as the owner who had incurred the loss. The conclusion was arrived at that he must be wealthy, owing to the large reward offered, and the latest information is that the dog has not been found, but the ingenious practitioner has now plenty of patients.—*Medical Press.*

Progress of Medical Science.

The Permanent Results of Symphyseotomy.—Sufficient time has now elapsed since the wide adoption of symphyseotomy by antiseptic methods to furnish data which will assist in estimating the permanent results of the operation. As most of the patients requiring the operation are dependent on their work for a livelihood, it becomes a serious matter to ascertain the condition of health as regards ability to work which can be promised to these patients in selecting this operation. The reports from Schauta's and Gustav Braun's clinics by Von Woerz and Richard Braun (*American Journal of the Medical Sciences*) afford data of value upon this question. Von Woerz reports ten symphyseotomies performed some time previously, most of the patients being still available for observation. Of the 10 patients, 1 died of sepsis after the operation; 6 are in good condition, abundantly able to work without inconvenience; 1 could not be followed after leaving hospital care; 1 cannot stoop to work on her hands and knees without pain in the sacro-iliac joints; 1 suffered from incontinence of urine, which was cured by taking cold baths. Braun reports 8 symphyseotomies, and of these none died; 6 are now in good condition, working without inconvenience; 1 suffers from incontinence of urine and sacro-iliac pain on heavy lifting; 1 has incontinence of urine on straining and lifting. In Von Woerz's cases 5 were treated by drilling the symphysis and wiring with silver wire; in 4 the wire suture could not be successfully applied, and 1 had no suture. While good union is possible without suture, yet suture is preferable. Braun treated his cases with drilling and wiring, 3; with suture of the periosteum, 4; and without suture, 1. There seemed to be no difference in the result in these cases. From these cases the conclusion may be fairly drawn that symphyseotomy under good surgical care is an operation undoubtedly saving foetal life at no serious risk of death or permanent disability to the mother. In view of the excellent results obtained without drilling and wiring the symphysis, the procedure is unnecessary.

Acute Perimeningitis.—Acute perimeningitis is an inflammation of the cellular fatty tissue around the cerebral dura (*The New York Medical Journal*). Its evolution is sometimes acute, spontaneous, with no appreciable pathogenic cause, and sometimes secondary, with cellulose-muscular inflammation near the spinal column. The symptoms resemble those of inflammation of the medullary meninges. It begins with sharp pains, with alternate remissions and exacerbations, in the legs and along the spine, and they are accompanied by stiffness of the limbs or of the neck. At the same time there is febrile movement with constipation. Subsequently there are pains in the abdomen and in the lumbar region, also in the legs. During the suppurating period, when the spinal canal is invaded with pus, the disease becomes infectious; sometimes paralysis sets in, and death takes place in a short time. In this evolution the meningitic symptoms may fail to show themselves, and the diagnosis is consequently rendered more difficult. The idea of cerebral meningitis, however, may be dismissed in the absence of the meningitic tripod, of ocular complications, and of the typical course of the temperature. Cerebro-spinal meningitis is epidemic and associated with infectious localizations in the lungs and in the heart, and its characteristics are distinct from those of acute perimeningitis. In the diagnosis of spinal meningitis great difficulties often arise, although in the beginning the early development of paralysis is a symptom of the disease. If it appears later on, there is reason to believe that it is a question of acute perimeningitis. Perimeningitis may be confounded with typhoid fever, osteomyelitis, and rheumatism. For this