HERRICK (J.B.)

Thyreoid Therapy.

BY

JAMES B. HERRICK, M.D.

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THYREOID THERAPY.[1]

BY JAMES B. HERRICK, M.D., CHICAGO.

During many decades no therapeutic advance has been made at all comparable in importance to the discovery of the antitoxin of diphtheria, and the use of the thyreoid gland in the treatment of myxedema. The antitoxin opens up the wide field of serum-therapy, in which many workers already make more or less favorable reports concerning the serum treatment of other infectious diseases, such as tetanus, typhoid, pneumonia, scarlatina, septicemia, tuberculosis; and the thyreoid opens up the field of organ-therapy, with experiments and observations rapidly multiplying as to the therapeutic value of extracts of the kidney, adrenals, testicle, brain, and other organs. Omitting from consideration all preventive measures, such as vaccination, boiling and filtering of water, etc., it may be said that we have four remedial agents that are truly curative or specific—potassium iodide, quinine, diphtheria antitoxin, thyreoid extract. To the latter I wish to direct your attention for a few moments.

The story of the discovery of the virtues of the thyreoid gland in the treatment of myxedema is as interesting as a romance. You are undoubtedly familiar with it, so that I need merely call to your minds some of the more important facts. You remember that Gull in 1873 made a clinical demonstration "on a cretinoid state supervening in adult life in women." Ord in 1877 reported two cases, with an autopsy where atrophy of the thyreoid gland, and mucin in the subcutaneous tissue were striking post-mortem findings. Charcot and his pupils, and Hadden in England, made still further clinical observations, and a little later the surgeons Reverdin and Kocher declared the changes in many of their patients from whom they had removed thyreoids to be the same as in Ord's myxedema. Independently, too, the physiologists Schiff and Horsley—the one in Switzerland, the other in England—showed that the removal of the thyreoid in the lower animals—the dog and the monkey—was followed by cretinoid symptoms and death. By the implantation of a thyreoid into the abdomen, however, life was prolonged. The conclusion, therefore, was inevitable, that the thyreoid gland had a function necessary to the maintenance of health or even life. In 1888 the report of the Committee of the London Clinical Society was made, declaring that cretinism, idiopathic myxedema and oper-

[1] Read at the meeting of the Illinois State Medical Society, Ottawa, May 19, 1896.

ative myxedema were but different types of one and the same disease, depending upon an anatomical or physiological (functional) absence of the thyreoid gland.

Surgeons and experimenters now noted the good effect of leaving a portion of the gland when it was to be removed, and also the benefit from implanting thyreoids, as of sheep, into the abdomens of human beings suffering from myxedema (Kocher, Horsley, Bircher, Lannelongue). Vassale injected thyreoid juice; and Murray, in England, reported in 1891 the successful subcutaneous employment of a glycerin extract of the thyreoid gland. The next year fresh glands were fed by Horwitz in Copenhagen, and Mackenzie and Fox in London, and a little later the pharmacists had prepared the dried powdered glands or dried extracts in various forms.

It is of interest to note that we owe this great discovery in medicine to no one man, to no one nation. Clinicians, surgeons, experimental physiologists, pharmacists, have each worked, often independently, in their own lines, until fact upon fact has been accumulated, all proving that myxedema, under whatever name it goes, is athyreoidea, and that the disease is curable by supplying through the thyreoid glands of lower animals the chemical substance that is lacking.

Theory of Action.—The older theories as to the purely nervous origin of myxedema are at present discarded. Since Schiff and Horsley experimentally, and many observers clinically, have proven that the thyreoid gland has a function, other theories have been advanced. Schaefer[1] states the two main theories clearly when he says the first is the *auto-intoxication* theory—the thyreoid a gland having for its function the destruction of natural toxins which without this antidotal action lead to the condition we call myxedema; the second the *internal secretion* theory, the thyreoid a secreting gland, its secretion taken up by the lymph-vessels and necessary for the proper metabolism of the body, especially for nervous and connective tissue. According to either one of these theories the administration of thyreoid extract merely supplies the lacking secretion—supplies, in other words, some chemical substance that is necessary to health, or even life, but which the diseased or absent gland fails to supply. To quote Ewald: "The secretion of the gland acts as an antitoxin against certain toxins that appear as the by-products of tissue change."[2]

Just what this substance is, has not been accurately known.

[1] *British Medical Journal*, August 10, 1895.
[2] *Centralblatt für Innere Med.*, No. 17, 1896.

But Baumann has recently eliminated an organic iodine compound from the thyreoids of sheep, to which he gives the name *thyro-iodine*, and investigations are going on to try to prove whether this is the effective chemical agent in thyreoid therapy. The results thus far are in favor of this view.[1] If it is, and if it can be manufactured synthetically in the laboratory, and if its dose can be proven experimentally, we shall have a most valuable therapeutic acquisition. Baumann hopes to be able to explain why glycerin-and-water extracts of the gland are therapeutically active, while thyro-iodine is insoluble in water. There may be other compounds equally as efficacious as thyro-iodine.

It may be added that some of the untoward effects of the thyreoid extract are believed by some to be due to impure or contaminated remedies. Fresh glands produce less of unpleasant thyreoidism than older ones that have undergone decomposition with the formation of undesirable chemical compounds. With a synthetic thyro-iodine any undesirable by-effects would be avoided.[2]

Method of Administering.—The cruder methods of feeding fresh or cooked thyreoids or of injecting subcutaneously a glycerin extract, have given place to the more accurate, pleasanter and easier methods of employing the dried powdered glands or the tablets containing the essential principles. Several firms now furnish good and reliable articles.

Dose.—For an adult, from three to fifteen grains of the powdered gland a day. Burroughs & Wellcome prepare a compressed tablet of dry thyreoid gland. One tablet equals one sheep's gland. The dose is from one-half to four tablets daily. Kraus has given as high as five or six a day.[3] Parke, Davis & Co. have a thyreoidin tablet that I have found reliable in a case of cretinism, the largest dose in one day not exceeding two tablets. They also make in tablet and powder form a preparation they call thyreoids, claiming for it all the virtues of the powdered glands.

Effects on Healthy Individuals.—The effects in health are not constant. Many report no effect. Commonly, however, large doses produce loss in weight. Diuresis, rapid heart's action, headache and insomnia are reported (*vide* Kraus).

[1] Cf. Ewald, Roos, Treupel.

[2] Roos, Treupel and Ewald believe the thyro-iodine contains the specific principle or principles of the thyreoid gland, and that it can be substituted, therefore, for the fresh glands, the extracts, and the dried preparations of the same. One gramme of thyro-iodine contains three-tenths of a milligramme of iodine, and corresponds, so far as amount of iodine is concerned, to one gramme of sheep's thyreoid.

Ewald on the "Therapeutic Use of Thyreoid Gland Preparations." Report of the Proceedings of the Fourteenth Congress of Internal Medicine at Wiesbaden, April, 1896. *Centralblatt für Innere Med.*, April 25, 1896.

[3] *Therapeutische Wochenschrift*, Jan. 26, 1896.

THE THERAPY OF THE THYREOID GLAND.

1. *In myxedema.* It can be put down as a settled fact that thyreoid extract is curative in myxedema. It would be useless to cite the numerous reliable reports of isolated cases and of series of cases that have thus far been published. British journals, particularly, seldom let a week pass without reciting some new case, often with cuts showing the "before and after taking" stages, in which thyreoid extract has wrought the almost miraculous change in some woman's physical and mental condition, or has transformed some stunted, stupid, pigmy-like imbecile — "toad-like caricature of humanity," Osler calls it—into a bright, laughing, growing, wide-awake child.

When the extract is fed to a myxedematous individual in full doses, most remarkable effects are noted. To these phenomena the term "thyreoidism" has been given. One is reminded in this connection of the somewhat analogous effects of our other specifics—cinchonism and iodism.

There is a rapid loss of weight; the fatty masses above the clavicles disappear; the mucin in the subcutaneous tissues vanishes. Not infrequently a sharp rise of temperature occurs in striking contrast to the previously existing subnormal temperature. The pulse rate increases. There are sweats; the skin itches; at times desquamation takes place. There may be diarrhea and vomiting. Pains in the joints, in the back, in the cardiac region, are sometimes noted. The patient may grow nervous, sleepless, anxious, irritable, even delirious—a wonderful change from the former condition of mental hebetude or imbecility. The urine is increased in amount and may contain a little albumin or sugar. Cretins have the hair become soft and the teeth develop naturally; they may grow several inches in height in a single year, whereas for perhaps twenty years before not an inch had been gained. They learn to talk and to walk; the voice loses its harsh character and becomes soft and natural. It is a transformation from *horribile dictu* into *mirabile dictu.*

A very few fatal cases in those already ill of some other organic disease, as of the heart, are reported. Murray lost two under these circumstances. Thomson[1] reports a fatal case, where autopsy showed myocardial degeneration.

If the theory as to the causation of myxedema be true, the artificially fed thyreoid extract merely supplies the chemical sub-

[1] *Edinburgh Medical Journal*, 1893, p. 1014.

stance that is no longer elaborated by the absent or inactive gland. It need excite no surprise, therefore, to learn that in cases of myxedema relapse into the old condition soon follows the stopping of the remedy. Moderate doses have to be continued for indefinite periods. This is the experience up to the present date, at least. Murray reports [1] that the first patient he treated by thyreoid feeding, in 1891, is still alive and well, but that the treatment is still continued. What future trial will disclose, especially in the case of cretins after they have attained full physical and mental development, cannot be foretold. It is probable that in all cases, unless it be where a temporarily inactive gland can be roused to activity, the remedy will have to be continued for years or during life.

In obesity. The rapid loss of weight that occurs in myxedema when the remedy has been employed, suggested its use in obesity, and the results warrant a trial in all cases. Kraus finds thyreoidin of greater value in anemic obesity than in that form accompanied by rosy lips, ruddy cheeks, good appetite, strong muscles. In all cases the action on the heart is to be watched. Diet may or may not be altered. Where great tendency to weakness is shown, a full nourishing diet should be allowed during the treatment. Relapses are common unless moderate doses are continued. Among those who give favorable reports may be mentioned Davies, Leichtenstern, Wendelstadt, Dercum, Barron, Ewald.

Losses in body weight, even up to ten kilogrammes in six weeks, are reported. [2] Ewald finds that the thyro-iodine answers fully as well in the reduction of weight as does the entire gland. Just why some cases are refractory and others amenable, is still not definitely settled.

In struma. The outlook for improvement or cure in cases of simple parenchymatous goitre is good. Cures by the use of the raw glands, the tablets, the extract, and thyro-iodine, are reported by many: Bruns, nine out of twelve cases; Reinhold, five out of six; Ewald, eight out of eight; Leichtenstern, an unsuccessful case treated with the tablets; Stabel, in twenty-five cases four cured, twenty-one improved. Stabel prefers the fresh glands or fresh extract to the tablets, finding—if the glands are not decomposed—fewer unpleasant symptoms develop.

The most elaborate report is that of Bruns, of Tübingen, who for two years has systematically treated goitre by the fresh glands, the tablets, and later by the thyro-iodine. His conclusions, briefly

[1] *British Medical Journal*, Feb. 8, 1896.
[2] Ewald's report.

put, are that the majority of cases of simple hyperplastic struma are amenable to treatment, improvement being seen ordinarily in from two to four weeks. The younger the patient and the younger the goitre, the better the prospect for permanent cure or decided improvement. Relapse should be guarded against by long-continued use of moderate doses of the drug.[1]

In tetany. Following removal of the thyreoid, tetany and other forms of spasm have been observed in man and in the lower animals. The use of the remedy in tetany was therefore tried. Some successes, at least temporary, are reported—*e. g.*, by Breisach, Levy-Dorn. Others, as Jaksch and Gottstein, report no benefit or but slight and temporary improvement. It is probable that if tetany is due to varied causes, those cases only will be benefited that are due to the absence of the thyreoid antitoxin. Further observation on the thyreoid treatment of tetany is needed.

In skin diseases. The remarkable effect upon the subcutaneous tissue of feeding thyreoids in myxedema, the frequent desquamation, the replacing of the dry harsh skin by a softer and more natural integument, the growth and improved quality of the hair, have led to the use of thyreoids in the treatment of skin diseases. Here reports are conflicting. Cases of psoriasis, of lichen, xeroderma, scleroderma, ichthyosis, lupus, etc., have been reported as improved or as having recovered, while negative results in similar cases have been obtained by others. As typical of these reports, and because the number of cases is unusually large, may be cited that report made by P. S. Abraham to the Medical Society of London. Of sixty-five cases of psoriasis, eighteen were improved; of the remainder, some were worse, some unimproved, and in many the symptoms of thyreoidism compelled the observer to stop the treatment. He reported the same uncertain results in other cases of skin disease.[2]

So far is the report of the dermatologists from being unanimous, that we must refuse as yet to accept it, and declare that they must be granted further time before bringing in a final and conclusive report. Thyreoid therapy in skin diseases is still *sub judice.*

In mental disorders, epilepsy, etc. While there is a wonderful transformation in the mental state of the sufferer from myxedema after thyro-iodine has been administered, there is little theoretically or practically, to judge from the published reports, to warrant the hope of relief in psychoses not due to thyreoid inactivity. Perverted

[1] Proceedings of Fourteenth Congress of Internal Medicine, reported in *Centralblatt für Klin. Med.*, April 25, 1896.

[2] *British Medical Journal*, Jan. 13, 1894.

mentality due to disease of the brain and not of the thyreoid will not respond to this treatment.

In exophthalmic goitre. The employment of thyreoid extract in exophthalmic goitre seems contra-indicated on every ground. Symptomatically the two diseases, myxedema and exophthalmic goitre, are antitheses of each other. In the one there is mental dullness, slow heart, lowered temperature, dry, harsh and thick skin, atrophic thyreoid, eyelids drooping over a sunken eyeball. In the other there is mental excitability, irritable and rapid heart, normal or slightly elevated temperature, moist, thin skin, enlarged thyreoid, prominent eyeballs with retracted lids. The most rational theory to-day is that exophthalmic goitre is hyperthyreoidea—too much thyreoid secretion. Overdosing with thyreoid extract produces "thyreoidism," closely akin in its phenomena to exophthalmic goitre, at times even to the presence of exophthalmos. The majority of clinicians who have employed thyreoid extract in Graves's disease have had no good results or have aggravated the symptoms. Starr, in the *Medical News* of April 18, 1896, gives an excellent summary of the reasons why myxedema and exophthalmic goitre are diametrically opposed and cannot, therefore, be treated in the same way. In the one case the aim is to increase thyreoid secretion, in the other to lessen it.

In this brief review of thyreoid therapy I have not aimed to present an array of authorities or of statistics. I have merely tried to present the conclusions one feels justified in drawing from a study of the work already done in the line of the employment of this remedial agent in various diseases. From such a study it seems to me that one may reach the following conclusions concerning thyreoid extract:

1. It is curative in myxedema (idiopathic, cretinism, operative).
2. Many cases of obesity are cured by it.
3. Simple hyperplastic struma, particularly if in the young, is frequently cured or improved.
4. In 1, 2, and 3, the remedy has to be continued for an indefinite time, to prevent relapse.
5. It may prove of value in some cases of tetany.
6. In skin diseases it is of doubtful value, to say the least.
7. The same is true of mental and nervous diseases.
8. In exophthalmic goitre it is contra-indicated.
9. The results are practically the same whether fresh glands, extracts or dried glands are employed.
10. This is probably true also of the thyro-iodine of Baumann.

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...ssical and must, hereafter, be consulted by ever...
...o the best work in this field."

"Medicine"

THE appearance of the first number of the second volume of *Medicine*, the monthly medical journal edited by Harold N. Mayer, M. D., of Chicago, and published by George S. Davis of Detroit, prompts the just comment that no medical journal that we have seen at all approaches it in newness and beauty of typography or, in general, in the quality of the printer's and publisher's work. In contrast with the host of so-called medical journals, printed poorly upon inferior paper, it is a keen pleasure to pick up a number of *Medicine* and realize what an important part the mere mechanical work put upon a journal plays.

It must not be concluded, however, that charm of appearance is the only good quality of *Medicine*. It is well edited and its pages are clean and free from any objectionable feature. It deserves a place among the very foremost of American medical journals and we sincerely wish it a full measure of success. The general quality of medical journals of this country is so low that the success of all the better ones is to be devoutly wished for by all physicians who feel a pride in American medicine.

THE *Journal of Experimental Medicine*, a periodical to appear at ... "l be pub" ... the beg ... e year by D... ic...

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