

occurred where medical aid was not sought. By the second table it will be seen that cases of the disease have occurred in seventeen States, in the District of Columbia and in Canada. The State from which the largest number of cases has been reported is New York, which also heads the list in regard to the number of reports. On the other hand the largest definitely estimated epidemic occurred in Massachusetts. The greatest number of cases reported in one year occurred in 1892, when there is seen to have been more than fifty-one cases. The reason for this can not be given and there is no evidence of any growing frequency of the disease before or after that year. There occurred in that year three outbreaks of considerable size, two in Massachusetts (15 and 21+) and one in Mississippi (19).

Occurrence by States.	Total.	Number of reports.	Largest number at one time.
New York	80	11	12
Massachusetts	56+	6	21+
Pennsylvania	45+	9	14
Mississippi	20	2	19
Indiana	19	4	10
Michigan	16	4	5
Iowa	15	2	9
Oregon	15	1	15
Illinois	14	4	5
Texas	14	2	9
California	14	2	10
Minnesota	13	1	13
New Jersey	11	1	11
*Canada	9	1	9
West Virginia	5	1	5
Ohio	2	1	2
Louisiana	1	1	1
Maryland	1	1	1
District of Columbia	1	1	1

*Canada was inserted for comparison with the various States.

Year.	Number of cases.	Year.	Number of cases.
1864	7	1880	9
1866	11	1881	7
1867	2	1882	2
1868	6	1884	14
1869	24	1885	35
1870	23	1887	27
1871	11	1888	12
1872	6	1889	1
1873	9	1891	15
1874	3	1892	51+
1875	20	1895	1
1878	23	1897	2
1879	15		

In conclusion, I report this isolated case in order to again draw attention to a disease that I believe may be of greater present importance than is usually thought, and also to draw particular attention to a symptom that did much to guide me to a correct diagnosis—the great rapidity of respiration without other evident cause. I mention this symptom especially for the reason that, while many state that symptom was present in their cases, I do not believe that sufficient importance has been attached to rapid respiration as a prominent symptom of this affection. Finally I would urge the importance of certainly excluding trichinosis before making the much abused diagnosis of muscular rheumatism.

A REPORT OF TWO CASES OF MYXEDEMA WITH REMARKS ON AN ANOMALOUS TYPE.

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Myxedema is a general disorder of metabolism, dependent upon diminished or lost thyroid function. Among various morbid processes affecting the gland and which have been observed to give rise to myxedema are the following: atrophy, atrophy associated with calcareous degeneration, atrophy with enlargement of

the pituitary body, actinomycosis, syphilitic degeneration of the organ, and the presence of neoplasms. It is to be recollected, however, that disease of the thyroid is not followed by cachexia strumipriva, provided even a small portion of the gland remains functional. The truth of this dictum was shown by the postmortem findings in the case contributed by Sieveking,¹ in which sarcoma had invaded the thyroid. This fact is also fully confirmed by the results of experimental extirpation of the thyroid in animals; total removal of the gland is regularly followed by myxedema (except functional accessory thyroids be present), while if even one-tenth of it is allowed to remain, the animal escapes the disease.

Of intense interest are recorded cases in which myxedema is either associated with or occurs in persons who have previously suffered from exophthalmic goiter. Baldwin² reports four cases belonging to this category. The first occurred in a boy of ten, four years after Graves' disease; the second affected a girl of fourteen, two years after the exophthalmic goiter was cured; the third, a girl of fifteen first showed signs of myxedema five years after improvement from Grave's disease; and the fourth, a woman of forty-four, four years later.³ It is an almost universally accepted belief that exophthalmic goiter is dependent upon excessive thyroid secretion the direct antithesis of myxedema. Like cachexia strumipriva, exophthalmic goiter is held by the weight of authority to be caused primarily by thyroid changes that bring about "thyroidation." Accepting this view it is quite conceivable that morbid processes first causing over-stimulation of the gland, may, in their future progress, lead to abnormally feeble or an entire absence of glandular secretion, and thus the former condition may predispose to the latter. The tendency to myxedema may be observed in several members of the same family, but I believe this to be rare.

The complex symptom-group of typical cases of myxedema is at present writing well known, and the literature bearing on this aspect of the subject is so extensive as to be much beyond the compass of this article. The following cases are reported: 1. For the reason that one of them manifested certain features of unusual significance. 2. To confirm the well-deserved professional favor gained by thyroid extract in the therapy of this disease. 3. To discuss a few of the main questions which have been raised in connection with the subject of treatment; and lastly, to direct attention to an anomalous or a rudimentary type that yields easily to sheep's thyroid.

Case 1.—M. R., age 50, female, fell ill about fifteen years ago, showing symptoms that were of slow and gradual development, becoming eventually typical of this affection. When I first saw the patient, the neck and supraclavicular regions were observed to be bloated; also the face, giving rise to a peculiar physiognomy. The features were bulky and expressionless, the face broadened, and the lineaments were practically obliterated; the lips were greatly thickened and the tongue markedly swollen. The general bulk of the body was obviously increased. The pressing finger showed an absence of pitting, even over the face, where stiff edema was most marked. A circumscribed red patch was noticeable on the cheek. The skin, particularly the backs of the hands, was dry, rough, somewhat scaly and inelastic; the nails were quite brittle, the hair was coarse and constantly shed.

The mental symptoms were not striking, except that thought and speech were slow, and the tone of the voice, was characteristically leathery. Hallucinations and impairment of memory were not observed. Occipital headaches and neuralgic pains

¹ Gould's Year-book of Medicine and Surgery, 1897, p. 963.

² Centralbl. f. innere Med., January, 1894.

³ Gould's Year-book of Medicine and Surgery, 1896.

were frequently complained of, as was also muscular weakness. The temperature was slightly subnormal (98 degrees), but cold hands and feet were not experienced.

There was slight though decisive albuminuria, and this symptom I learned had been present for four or five years at least, with hyaline and granular tube-casts at intervals.

On account of the presence of persistent albuminuria, her former physicians, two in number, had diagnosed chronic nephritis. Temporary albuminuria with casts, is frequently met with in this disease, but the persistent characteristic features of chronic Bright's are not seen. After treatment with extract of thyroid for six weeks, the urine presented no abnormalities; neither has albumin or casts reappeared since then (as shown by repeated testing). Believing herself to be a sufferer from renal affection, and being possessed of superior intelligence, I was unable for a long time to induce the patient to make a trial of thyroid extract.

The interesting features were limited to the urinary phenomena. The relation of mere albuminuria or actual nephritis to myxedema is not definitely known. On the other hand, it should be pointed out that the symptoms of Bright's have been observed to appear after the accomplishment of a cure by thyroid feeding, in cases in which no urinary phenomena had been present during the course of myxedema.

Case 2.—Mrs. Rebecca Coates, aged 50, a patient under the care of Dr. A. E. Roussel at the dispensary service of the Howard Hospital.⁴ Mother died of phthisis, father killed in an accident. Patient has been in the best of health until three years ago, when menstruation ceased. Has had several attacks of rheumatism, and recently, the body in general has been getting more and more bulky. The face at present is puffy and edematous-looking, but does not pit on pressure. The skin is rough and dry and the lips blue. The hair is dry and falling out. The nails are clubbed and brittle. Her expression is heavy and stupid; the speech is slow and hesitating and the voice rough. The memory is impaired and she frequently suffers from headaches. Mental aberrations occur frequently, she talks incoherently and believes she sees objects. There is a certain stiffness and clumsiness in the gait. The respiration is slow. Her temperature is 98 degrees and she complains of feeling cold. She is easily fatigued, complains of a bitter taste in the mouth, has a poor appetite, and her bowels are irregular. The urine is normal (specific gravity 1020, no sugar, albumin nor casts present).

Treatment was commenced on March 20; the patient was asked to lead a quiet life and was put on the extract of thyroid, grs. iii, three times a day. On March 23 the patient returned and stated that since taking the remedy, she suffered greatly from pain in the stomach and bowels, and at night from aggravated nervous symptoms, such as mental wandering and the apparent sight of different objects. The dose of the remedy was then reduced to 1 gr., three times a day, and on March 27 the patient came back complaining that the medicine still disagreed with her and produced profuse sweats.

On April 1, the desiccated thyroid powder was ordered, grs. 3, three times a day. On April 6, the dose, which had been well-borne in the meanwhile, was increased to grs. 5, thrice daily. On April 10, she presented herself again and reported that she had been troubled with copious sweats, and had noticed that her weight (found to be 168 pounds at this time), was decreasing. On April 13, the thyroid gland powder was increased to 7 grs., three times a day, and on April 17, she complained of severe pains in the limb particularly the legs, and a burning sensation in the stomach. After the use of small doses of hydrochloric acid, internally and of chloroform liniment, locally for the leg pains, relief came. The patient did not return for eleven days (May 1), or about six weeks from the date of the commencement of the treatment. At this time the bloating of the hands and face had largely disappeared; the voice was less harsh and leathery in tone, and her weight 160 pounds. On April 18 she presented herself again apparently in excellent health, and expressing herself as being free from gastric or other symptoms. Her weight was now 143 pounds, a loss of 25 pounds while under treatment with thyroid gland powder.

⁴ The notes of this case have been kindly prepared by Dr. Mishkin.

As the result of wide experience, to which a mite has been contributed by many different clinicians, the specific virtues of sheep's thyroid in the treatment of pure myxedema have been conclusively established. It is also the unanimous opinion of writers, that certain precautions must be taken during the administration of this remedy. The commencing dose must be small, since many individuals are remarkably susceptible to the action of this agent. Thus in case No. 1, not more than one grain daily of the thyroid gland powder could be tolerated at first. The dose was very gradually increased, until at the end of the fourth week, five grains daily were well borne, and the myxedematous condition rapidly disappeared under this small dose. This patient took three doses of 3 grains each on the same day, and after the last, symptoms of hyperthyroidism developed. There were intense headache and syncope, with a feeling of powerlessness in the legs. Rest in bed for a short period, and the use of cardiac tonics soon caused these symptoms to disappear. Subsequently, I combined with each dose of thyroid extract, gr. 1-36 of strychnin sulph., and after that no toxic effects were observed. There can be no question but that the evidences of cardiac failure constitute a really serious defect, and perhaps, the only one in the thyroid treatment. Murray⁵, who first used thyroid extract in the treatment of myxedema, lost two of his early cases from cardiac failure, brought on by over-exertion. This observer strongly recommends rest in bed for a time after treatment has been instituted, with a view to avoiding cardiac and arterial strain. This may be necessary in long-standing cases, and in those in which "cardiac or vascular degeneration" are present. Ordinarily, the administration of strychnin will be found to avert any dangerous degree of cardiac failure, and this should not be omitted until a cure is effected. Only the gentlest exercise is permissible during the same period.

Case No. 2 manifested toxic symptoms (gastro-intestinal pains, profound sweats, etc.,) from the administration of small doses (gr. 1, t. i. d.) of the glycerin extract of thyroid. It is worthy of repetition that the desiccated thyroid gland could be taken by this patient in doses three times as large as the glycerin extract, and without unpleasant or toxic effects.

Not all of the symptoms that follow the administration of thyroid are due to over-dosing. As pointed out by Murray, an increase in the pulse-rate amounting to ten or twenty beats per minute simply indicates that the dose is quite large enough. In case No. 1, a most intense itching over different parts of the skin-surface occurred at intervals, and caused intolerable distress; a diminution in the size of the dose did not seem to influence the course of this symptom. The phenomena to be watched for and to be regarded as adequate reasons for stopping the remedy, are numerous, and are not sufficiently emphasized in our textbooks. They are tachycardia (over 100 beats per minute), elevation of the temperature (amounting to one or more degrees), syncope, vertigo, suffusion of the face, profound prostration, intense headache, profuse sweats and gastro-intestinal disturbance. Granting that exophthalmic goiter is attributable to hyperthyroidism, if during the administration of thyroid glands symptoms of this disease, such as slight tachycardia, fine tremor, exophthalmos, heat and sweat, insomnia, restlessness, polyuria, glycosuria, or albuminuria and the like appear, the dose should be

⁵ British Medical Journal, April 13, 1891.

reduced, but the remedy need not be discontinued. It is well understood, that after total disappearance of the myxedematous infiltration, the treatment may have to be continued off and on; if not continually; this is due to the fact that the thyroid is no longer functional, being as a rule atrophied.

Examples of what may be regarded as an anomalous type, that do not seem to progress to the fully developed disease with its characteristic clinical picture, are, I am certain, not infrequent. They are not to be regarded as instances of cretinism, since they develop after the age of 15 years, and few of the characteristic symptoms of myxedema are present. The face is rather flat, the skin somewhat swollen, dry, firm and inelastic. The features also lack mobility, but are not so coarse or bulky as in true myxedema. The physiognomy is dull, uninteresting and phlegmatic. There is a slight increase in the general bulk of the body, but the lips, nose and tongue are chiefly implicated. The lower jaw may be prognathic. The gait is somewhat uncertain, owing to trivial disturbance of coördination. There is some alteration of the voice with a tendency to occasional nasal explosions during speech. Thought is somewhat slow and the memory lags. Other mental phenomena are irritability of temper and an unnatural degree of suspiciousness though not so pronounced as in typical cases. Such patients are often apathetic or even melancholic and if constipation or gastric disturbance be present, a supposed chronic dyspepsia is liable to be mistaken for this complaint. There is also danger of confounding these cases with neurasthenia. Even in the presence of the above symptom-group it is not possible to make an absolute diagnosis, but the therapeutic test (improvement under thyroid feeding), if properly made, clears the doubt with reasonable certainty. I have recently observed the disappearance of a group of symptoms such as I have described in two cases as the result of the administration of sheep's thyroid. One of these patients had been treated for nervous dyspepsia and constipation for a long period of time.

THE TREATMENT OF EXOPHTHALMIC GOITER AND OTHER VASOMOTOR ATAXIAS WITH PREPARATIONS OF THE THYMUS GLAND AND OF THE ADRENALS.

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I desire to make a brief report of a number of cases of exophthalmic goiter, and of conditions more or less closely resembling exophthalmic goiter, treated by means of extract of the thymus gland and of the suprarenal capsule. It is not my purpose in this paper to discuss at length the vexed questions of the etiology and pathology of Graves' disease, and of those conditions to which I have in a previous paper given the name of vasomotor ataxia. Nevertheless, some slight allusion to these subjects is necessary to make myself fully understood. I hold that there are almost innumerable varieties of disturbances of the cardio-vascular balance, ranging from the merest departure from the normal, to the most pronounced case of Graves' disease on the one hand, and of Raynaud's disease upon the other. The principal clinical

phenomena of these conditions are disturbances of the heart's action, and central or peripheral phenomena indicative of abnormal contraction or dilatation of the vessels. The essential element is incoördination or ataxia of the circulatory mechanism, and among more or less prominent secondary symptoms are murmurs in the heart and vessels; blood losses which may range from severe pulmonary, uterine or renal hemorrhages, to slight epistaxis, hematemesis or hemoptysis, or perhaps merely petechiæ upon the skin, or the presence of blood cells revealed only to microscopic search in the urine; headache or vertigo; syncope with flushed or with pale face; local heat and redness of ears or face, usually unilateral; numbness and tingling of the extremities; discoloration of the hands and feet; subjective pulsations and "flashes" of heat and cold; excessive sweating, polyuria, and the like. These phenomena in their milder or in their severer forms are more common in women and are often associated with disturbances of menstruation; the familiar symptoms of the "change of life" belong in this category.

Among other associations having an etiologic suggestiveness are abnormality of the thyroid gland, gastric and intestinal disturbances, gout and lithemia, rheumatism and rheumatoid arthritis, hay fever, neurasthenia, hysteria and cutaneous pigmentation. The phenomena may be intermittent and capable of artificial reproduction, and we thus find as their principal exciting causes, toxins (both autogenetic and heterogenetic), temperature changes, and emotional disturbances. In most cases, of whatever origin, a distinct temperature relation can be made out, the patient feeling better or worse in summer or winter, respectively.

As a whole the phenomena are merely exaggerations, in duration and degree, of the effects of the same kinds of exciting influences upon normal individuals, or to put it another way, the same phenomena which in the cases under consideration are interpreted as evidences of disease, may occur transiently in normal individuals under similar exciting causes of greater magnitude. Thus severe cold may cause in a healthy person phenomena much like those which, excited by a minor cause, we call Raynaud's disease; and intense heat, anger, fright, sexual excitement, produce many of the phenomena we find among the symptoms of Graves' disease. Familiar illustrations of the minor varieties are the attacks of urticaria, which in some individuals result from the ingestion of foods that most persons can take with impunity, and the eruptions and edemas that mark so-called idiosyncrasies to drugs. Here, too, we find an interesting connection with angio-neurotic edema, which in some of my cases can be produced at will, in certain localities, by moderate trauma, for example as a slap on the lips; and in this as in other phases of the general subject the influence of family and of heredity is marked. In some cases the phenomena of irregular and excessive dilatation, in others those of irregular and excessive contraction of vessels predominate; in all some phenomena of both kinds are found; in all there are paroxysmal exacerbations; in some normality apparently prevailed during the interval. Whether the group of affections thus included would or would not form in rigorous nosologic classification and order, whatever the exact mechanism of the symptoms or the immediate exciting influence, the fundamental cause is apparently a