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INCOMPLETE MYXEDEMA (HYPOTHYROIDEA).

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In recent medical literature frequent reference is made to irregular or atypical forms of thyroid disease, the so-called "*formes frustes*" of French authorities. Discussions on this interesting subject have hitherto been mainly confined to that aspect of thyroid disease which is constituted by morbid hyperfunction of the gland; so-called "incomplete Graves' disease" or "hyperthyroïdeia."

The object of this communication is to draw attention to a condition of early thyroid disease characterized by morbid hypofunction or insufficiency of the gland secretion, the direct antithesis of hyperthyroïdeia and which may be designated "hypothyroïdeia." This is an aspect of thyroid perversion which is still less perfectly understood than hyperthyroïdeia.

Clinical enlightenment is much needed in this direction as it seems probable that the condition is by no means infrequent although usually overlooked or misinterpreted. These cases are probably early or incipient myxedema; *myxedema fruste*, "incomplete myxedema." They differ from myxedema not in kind but merely in degree. The symptoms are not yet sufficiently pronounced or typical to be recognized easily and consequently they are apt to be attributed to some other cause or to be overlooked altogether. The symptoms are the same as in fully developed myxedema only less intense and not typically grouped. They disappear under thyroid feeding as does the fully-developed disease.

CHRONIC ATROPHIC THYROIDITIS.

Myxedema is not a proper name for that disease inasmuch as myxoid or solid edema is merely a symptom of an underlying atrophic thyroiditis. Murray insists that there is no more warrant for calling a thyroid cirrhosis "myxedema" than there would be for similar use of the term "dropsy" to designate Bright's disease, or "ascites" to characterize hepatic cirrhosis.

What is known in clinical medicine as myxedema is chronic atrophic thyroiditis; a cirrhosis of the thyroid gland resulting in more or less complete destruction of its secreting structure. It is usually marked by shrinking of the thyroid so that the gland can not be palpated and even is identified with difficulty at autopsy. It is not essential to the development of the disease that the gland undergo reduction in size. In rare cases the gland may even be enlarged but histologically it will be found that its true secreting structure has been destroyed by colloid degeneration. Goitrous cretinism is an example

of enlargement of the thyroid with loss of function. Paradoxical coexistence of myxedema and Graves' disease in the same subject probably constitutes another instance in point.

We have been taught to regard myxedema as a disease possessing marked and characteristic symptoms and as with other diseases having cardinal symptoms this has placed us off guard when we come in contact with imperfectly developed examples. Moreover, myxedema in its full development is not a frequent disease in America and our very unfamiliarity with it renders us indifferent to the many transitional forms which undoubtedly must occur.

Chronic atrophic lesions no matter what gland or structure is involved are invariably slow in their development and progress. Witness the gradual evolution of contracting kidney and hepatic cirrhosis. There is no apparent reason why we should constitute atrophic thyroiditis an exception to this rule. Myxedema does not spring into existence fully developed, but follows the rule of slow development. At what point in its progress symptoms of thyroid insufficiency appear it would be difficult to say, but it is probable that they exist for a long period before the cardinal symptoms of fully developed myxedema become manifest and that we fail to interpret them is no proof to the contrary but merely evidence of our inability to appreciate their true significance.

DIAGNOSIS.

The diagnosis of a well marked, fully developed case of myxedema is readily made owing to the striking character of the symptoms. The appearance of the patient is so peculiar that the disease can be recognized at a glance. It is quite otherwise when the disease is encountered in its early stages or in atypical form. Slight evidences of the condition may readily be overlooked. The profound nutritional changes, which are so striking in cases of more complete development, are absent, or present only in modified degree. Most of the cases of hypothyroïdeia are encountered in woman at, or approaching, the climacteric and the symptoms are usually ascribed to the menopause. The predominance of myxedematous states in the female is well attested by statistics, the ratio being 7 to 1. This undoubtedly is due in great measure to the repeated hyperfunction and irritation of the thyroid resulting from the vicissitudes of woman's reproductive life.

ETIOLOGY.

A history of hyperthyroïdeia in earlier life is not without value from the etiologic standpoint. Hun and Prudden point out that the great majority of women who suffer from myxedema have borne children and only a small proportion are unmarried. This may point to secondary atrophy following puerperal hyperthyroïdeia. In no other way can the great disproportion in fre-

quency between the two sexes be explained than by interpreting many of the cases in the female as due to secondary atrophy induced by the thyroid hyperfunction of pregnancy and lactation.

A few cases both of the fully developed and modified forms of myxedema have been reported in which the apparent starting point was an acute infection, as in a case presently to be reported (Case 1). It is very doubtful whether such cases are true instances of postinfective myxedema although such a possibility can not be denied. It is more probable that the disease had previously existed in a latent form and that the acute infective toxemia provoked an exacerbation. In my own case there exists distinct evidence pointing to previous latent hypothyroidism. Hypothyroidism and myxedema may develop following Graves' disease, sometimes years afterward. Glandular hyperemia and hyperfunction have here passed over into a state of secondary atrophy with hypofunction. Case 2 constitutes a striking example of this transition.

SYMPTOMATOLOGY.

The symptoms which may be present in cases of incomplete myxedema are neither very definite nor characteristic, but taken as a whole they form a symptom group which, to say the least, is very suggestive. Some of these subjects have for years had slight indications of impaired nutrition such as transient edemas, bagging of the eyelids, dry scaly conditions of the skin, thin hair, joint pains, muscular pains and aches, neuralgias, paresthesias, etc. Their chief complaint is often a great susceptibility to cold so that they become chilled on the slightest exposure and one finds them laden down with heavy woolen clothing. One of the most characteristic developments is dryness of the skin so that effort even in hot weather causes little or no perspiration. The scalp is scaly, the hair poorly nourished, dry and thin, and a thinning of the outer half of the eyebrows is often noticed. The fine hair of the nape of the neck may be lost leaving a shiny bald appearance up to the occiput. There may be partial or complete pubic and axillary alopecia. On removing the stockings a fine powdery exfoliation from the skin may adhere to the inner surface of the garments, and there are frequently dry scaly patches over the knees and elbows.

A yellow tinging of the skin is very characteristic. This has none of the saffron tint of true jaundice but is of a pale lemon color. Swelling of the eyelids of a peculiar translucent watery appearance, is among the most constant symptoms and associated with it there may be defective lachrymal drainage resulting in more or less constant weeping. The puffiness of the upper eyelids compels a compensatory elevation of the eyebrows to widen the palpebral fissure and deep furrows form across the brow in consequence. A distinct disposition to obesity exists in these patients. A slow and progressive gain in weight is pretty generally observed and this may stand in marked contrast to the patient's former physical habit. Fat pads may form above the clavicles and not infrequently a similar accumulation may appear over the upper dorsal vertebra. Thickening of the subcutaneous tissues across the lower ribs and above the elbows and knees, and a bib-like roll over the upper sternum have been noted.

The increase of body weight and bulk is not attended by any improvement in strength, but on the contrary by a marked diminution of vigor and resistance. Disinclination to exertion and early fatigue following effort whether bodily or mental and a notable diminution in

resistance to infections so that colds and anginas are easily contracted furnish evidence of the altered nutritive state. Pains in the knees and ankles and occasional "giving way" of the legs are pretty constant symptoms. Loss of memory and impairment of mental alertness characterize the cerebral function. These patients are usually stolid or on the other hand they may display irritability of temper and be sensitive regarding their altered personal appearance. Loss of visual and aural acuity are common accompaniments and the voice has often a peculiar husky quality. The deep reflexes are impaired, there is constipation and the action of the kidneys is sluggish. The thyroid may or may not be diminished in size and occasionally it is even enlarged.

NOT ALL CASES ARE TYPICAL.

It goes without saying, that in a condition so relative and of such transitional character as hypothyroidism, not all nor even the majority of the symptoms above detailed may exist in any given case. The most frequent and suggestive of the symptoms is the yellowish subicteroid tinging of the skin. When encountered in individuals of middle age without indications of hepatic or blood disease this symptom may well suggest the possibility of thyroid insufficiency. The face may not be swollen and "moon-shaped" as in fully developed myxedema, but is yellowish, with watering of the eyes and slight swelling of the loose orbital tissues and a peculiar reddish flush over the malar prominences is often observed. The subcutaneous swelling may be only slight or intermittent, coming and going without apparent cause, and it is often confined to the tissues of the eyelids. The facial appearance and edemas are not unlike those observed in certain cases of nephritis, but the urinary and cardiovascular indications of the latter disease are lacking.

The temperature may be normal or only occasionally subnormal. The skin may be still soft and moist and at times there may be free perspiration. There is usually slight symptomatic anemia. Diagnosis in such cases as these can be but tentative, but acting on the suspicion formed as to their thyroid nature the careful administration of thyroid extract will serve as a simple test to prove the correctness of one's conclusions inasmuch as a gradual clearing of the various symptoms may be confidently expected as in fully developed myxedema.

That the type of case thus briefly described is really myxedema in the earlier stages of its development there seems little room for doubt, and if left untreated there is strong probability of development into the typical fully-formed disease. There appear to be cases where this transition fails to take place, but such an arrest can not be anticipated in any given case. Owing to the essentially chronic nature of the underlying thyroid lesion the advance will be slow. Once the potency of thyroid extract to control the symptoms has been demonstrated it should be continued in such minimal doses as suffice to hold in check the nutritional disturbance.

The following two cases will serve as clinical illustrations of the points noted in this brief sketch:

CASE 1.—Patient.—Male, American, aged 39, average weight 165, weight at time of first consultation 175, married, one child.

Family History.—This is unimportant; his parents are living and in good health and there is no consanguinity.

Personal History.—Scarlet fever at the age of 12. Has had numerous attacks of abdominal colic, the last one ten years ago. No lues, habits good. It had been observed by the patient's wife during the past two years that his face would swell, particularly about the eyes, for a few days; no impor-

tance was attributed to this symptom, which always disappeared without treatment. In April, 1907, he had a severe infection of the throat with a retrotonsillar abscess and a good deal of inflammatory edema of the glottis so that his breathing was considerably embarrassed until the abscess discharged, which it did spontaneously. Cultures from the throat showed the infective agent to be the streptococcus. Opsonic vaccine therapy was employed, four inoculations being given. The opsonic index rose from 0.875 to 2. About June 25 there appeared a general subicteric tinging of the skin, the eyelids became swollen and there was malleolar edema with stiffness and swelling of the hands. Beyond a considerable degree of physical languor and excessive fatigue following exertion, there were no subjective symptoms. Shortly after the appearance of these developments the case came under my observation through the courtesy of the attending physician.

Examination.—Patient appeared to be a man of good physique with moderately thick but prematurely gray hair. The most striking thing about his personal appearance was the peculiar color of the skin, which was pale yellow, distinctly different from the saffron of true jaundice. This coloration was most noticeable on the face and palms of the hands; there was no tinging of the conjunctiva. The eyeballs were unusually prominent, and the loose orbital tissues were the seat of a translucent swelling which narrowed, somewhat, the palpebral fissure; there was a moderate amount of lachrymation. Patient's wife stated that he had for some years shown a tendency to puffiness about the eyes and lachrymation. No other edema was to be detected, although during the previous week it had been noted that there was some swelling about the ankles. The hands were not swollen, although the patient stated that they felt stiff and clumsy, especially when he wrote or essayed fine movements. There was no elevation of the eyebrows or frontal furrow. The scalp was dry and scaly and there had been some loss of hair. The skin was drier than normal, but the patient had remarked no change from his normal in regard to perspiration. Physical examination showed the chest and abdomen to be normal. Deep reflexes, sluggish. Pulse, 96, regular, soft and compressible. Blood pressure, 95 mm. (Stanton). Urine, 1800 c.c.; sp. gr., 1.010; urea 26 gms.; sugar, albumin indican, bile pigments, and casts absent. Blood examination: Erythrocytes, 4,387,000; whites, 9,800; hemoglobin, 78 per cent.; color index, 0.88. Two blood cultures on bouillon incubated at temperature of 37 C. for seventy-two hours showed no growth of organisms. Ophthalmoscopic examination revealed a few pinpoint chorioidal degenerative markings. Throat examination negative, hearing impaired (right, watch 3 inches; left, 12 inches). Rectal temperature, 99.6 F.

Some uncertainty was felt as to the diagnosis. A ferruginous tonic was ordered and the patient advised to spend the summer in the open air. This he did by taking a long yachting trip, and he returned in September stating that he felt very much improved. The blood count now was: Reds, 4,960,000; whites, 8,500; hemoglobin, 92 per cent. Body weight, 172 pounds. Blood pressure, 105 mm.; pulse, 84. The face was still yellowish, although less so than formerly; there was still some swelling about the eyes. It is interesting to note that the patient suffered severely from the cold all summer, no matter how comfortable the temperature was to others he was always less than warm. He also recorded the facts that he felt a very pronounced degree of weakness in the legs and observed that his finger nails were very brittle and grew slowly. His voice was frequently husky. One month after his return home the former languor, depression of spirits and somnolence returned and the icterus and swelling about the eyes became worse than at any previous time.

Treatment.—Acting on the theory that the edema and icterus were due to thyroid insufficiency (hypothyroidia) the administration of thyroid extract was now begun. Improvement in all the symptoms was soon apparent. The loss in weight during the first ten days of treatment was eight pounds. The edema gradually disappeared and with it the icterus, so that in one month after starting the thyroid extract the patient's normal appearance was restored and his weight fell from 175 to 163. Accompanying this effect there was a

great improvement in physical and mental tone. The maximum amount of thyroid extract taken was 15 grs. daily, but this was for a few days only, the average dose being 9 grs. daily.

Subsequent History.—March 28, 1908, the patient reported that he felt perfectly well; his appearance was normal. For four months he had taken 2 grs. of thyroid extract daily, which was the dosage at this date. Acting under instructions he discontinued the drug for ten days, the effect being to cause the reappearance of the former languor and depression, a sense of oppression about the throat and huskiness. These symptoms promptly disappeared when thyroid administration was resumed. It is interesting to note the fact that the patient's wife had become pregnant since thyroid medication was started; last pregnancy four years prior.

The foregoing case furnishes an admirable example of how obscure hypothyroidia may be in its clinical manifestations and how real the difficulties are in arriving at a diagnosis. The rôle played by the infection in this case was in all probability a secondary one, there being evidence that the thyroid disturbance had existed in latent form for some time previous and that the infective toxemia served merely to accentuate a condition already existent but latent. Without the administration of thyroid extract the disease would undoubtedly develop and eventually become complete myxedema.

CASE 2.—*Patient.*—N. O., female, married, nullipara, aged 45.

History.—No definite family history could be secured. Patient stated that she had had "heart disease" since childhood. There was no history of rheumatism. At the age of 33 she developed exophthalmic goiter, her state being characterized by well-marked goiter, exophthalmos, emaciation, extreme nervousness, tremor, sweatings, palpitations, etc. This condition continued for six years with varying severity when the symptoms gradually diminished in severity. The goiter slowly receded until as an appreciable tumor it had disappeared three years ago. It was only recently that her normal weight had been regained. She had always remained very nervous and the exophthalmos persisted when she was seen. During the past year she had been very short of breath and had much cough, which was paroxysmal in nature and apt to cause palpitation and precordial discomfort. Menses regular but scant. The patient stated that she had frequent sinking spells to relieve which she was often compelled to resort to stimulants; she was often dizzy and was much troubled with pains in the knees and ankles. Her legs would often give out suddenly while walking, compelling her to seek the nearest support. She complained much of muscular weakness, with excessive fatigue following exertion. Notwithstanding this progressive weakness she was gaining constantly in weight, having added fifteen pounds during the year past. The bowels were regular, although the movements were small in size; there was much flatulency. She had observed the fact that whereas she formerly was subject to excessive sweating on the least exertion she now had a very dry skin, effort no longer causing her to sweat, and only excessive nervousness bringing moisture to the skin. The hair had gradually thinned out until now it was noticeably scant. During the past three years she had lost all of her teeth. There was marked failure of memory. She complained much of her sensitiveness to cold, the slightest exposure causing chills; so much was this the case that she had been unable during the past year to work with her sleeves rolled up and her arms bare, even this slight exposure of the surface causing repeated chills. At the time she first consulted me, although the temperature was 60 F., she wore, beside heavy outside wraps, two thick woolen petticoats and woolen stockings and underwear. Notwithstanding these heavy coverings the skin was dry.

Examination.—The facies was very striking, the eyes were prominent and staring, but the ocular signs of exophthalmic goiter were lacking. A translucent, baggy swelling surrounded the eyes and a moderate degree of lachrymation existed, the eyebrows were elevated, and a deep furrow ran

transversely across the forehead. The cheeks were somewhat pendulous and there was a pronounced bronze-red malar flush.

There was no edema or swelling elsewhere, although the legs had a peculiar stiff-rubber feel when palpated. The neck had lost its normal roundness anteriorly and the thyroid could not be palpated. The deep reflexes were absent. Pulse, 78; irregular. Blood pressure, 210 mm. (Stanton). Apex beat diffuse and heaving and displaced almost to the anterior axillary line. There was a systolic murmur to be heard all over the heart, and the second aortic sound was markedly accented. The urine was very abundant, of low specific gravity and free from albumin. A few short hyaline casts were to be found in the urine sediment.

Treatment.—A diagnosis of chronic myocarditis and high arterial tension due to atheroma was made and the opinion was expressed that there was probably an incomplete myxedema (hypothyroidism) developing on the soil of an old Graves' disease.

The medication consisted of sodium nitrite and strophanthus for the cardiovascular condition and thyroid extract one grain three times a day, was begun one week after the vascular tonics. The result of thyroid feeding was prompt and beneficial. Within a fortnight there was a noticeable improvement in strength, a return of perspiration, and an entire disappearance of muscular and joint pains. Although the dose of thyroid extract has not been increased the improvement above noted has continued and there has been a slight loss in body weight.

103 State Street.

AN ANALYSIS OF FIVE HUNDRED CASES OF SPINAL INFANTILE PARALYSIS.

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The epidemic occurrence of anterior poliomyelitis is firmly established. The dependence of the disease on infection may therefore be legitimately assumed. The epidemic that prevailed in New York in the summer and autumn of 1907 afforded us unusual opportunity to study the disease, and we herewith present in tabulated form the analysis of 327 cases from that epidemic and 173 cases observed previous to that time. We have previously written¹ of some of the more striking features of the epidemic in New York, so we shall confine ourselves here to comments on the facts set forth by the tabulated matter presented, reserving for a future occasion detailed consideration.

STATISTICS OF 500 CASES OF POLIOMYELITIS.

327 epidemic cases occurring in 1907.

173 sporadic cases previous to 1907.

SEX.												Males.	Females.
1907.....												200	127
1906.....												97	76
Total.....												297	203
Ratio of Males to Females 3 to 2.													
MONTH OF ONSET.													
	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sep.	Oct.	Nov.	Dec.	
1907..	1	1	1	0	0	16	68	81	102	25	4	0	
1906..	1	0	0	0	1	6	9	28	23	10	6	0	
Total.	2	1	1	0	1	22	77	109	125	35	10	0	
Period of epidemic, June to November, maximum number of cases in September.													

1. Med. Rec., Nov. 2, 1907.

		AGE.										
		(Under 1)	1	2	3	4	5	6	7	8	9	10*
1907.....		36	101	88	32	22	12	6	3	0	1	1*
1906.....		26	57	46	13	10	2	2	1	0	2	0†
Total.....		62	158	134	45	32	14	8	4	0	3	1‡

Most occur between ages of 1 and 3 years.

*In 1907, other ages, not tabulated, were: 4 days, 5 weeks.

†In 1906, other ages, not tabulated, were: 11, 12, 15 and 15 years.

‡The extremes were 4 days and 32 years (perhaps one case was intrauterine).

		FEVER.		
		"No Fever."	"Slight"	"High."
1907.....		15	148	109
1906.....		14	43	36
Total.....		29	191	145

The following table indicates maximum temperature in those "high" fevers in which the degree was ascertainable. They are not included in table above.

		103°	104°	105°	106°
1907.....		17	20	5	1
1906.....		0	4	3	0
Total.....		17	24	8	1

		DURATION OF FEVER.	
		1 to 4 days.	5 or more days.
1907.....		191	74
1906.....		70	26
Total.....		261	100

Duration of fever in majority of cases 1 to 4 days.

Not often longer than 1 week.

Cases without fever doubtful, although many instances with slight fever.

GASTROENTERIC SYMPTOMS, DEFECTION, URINATION.

		Vomiting. Anorexia. Diarrhea. Constipation. Retention.			
1907.....		120	77	33	76
1906.....		31	1	16	12
Total....		151	78	49	88

		Incontinence of Urine and Bowels.	Diarrhea followed by Constipation.	Diarrhea previous to illness.
1907.....		4	3	3
1906.....		1	1	1
Total ..		5	4	4

PSYCHOMOTOR (MENINGEAL) SYMPTOMS.

		Somnolence, Stupor, Unconsciousness.		Rigidity & Retraction.	Insomnia. Restlessness.
1907 ..		78	31	6	39
1906 ..		9	9	4	17
Total ..		87	40	10	56

		Twitch. Convulsions.	Delirium.	Scream.	Cry.	Immotility.
1907		58	10	16	28	40
1906		8	8	2	4	19
Total ..		66	18	18	32	59

PARALYSIS.

		Leg	Both	Arm	Both	Triplegia	Quadriplegia	Hemiplegia	Crossed	Other*	Cranial†
1907		137	87	18	2	22	24	11	9	127	23
1906		79	47	18	3	5	8	9	4	29	12
Total		216	134	36	5	27	32	20	13	156	35

* DISTRIBUTION OF OTHER PARALYSIS IN TABLE ABOVE.

		Abdomen & Diaphragm.	Lumbar & Gluteal.	Back.	Chest.	Neck.	Sphincters.
1907		20	53	15	8	27	5
1906		9	12	5	1	2	1
Total ...		29	65	20	9	29	6

† DISTRIBUTION OF CRANIAL (NUCLEAR) PARALYSIS IN TABLE ABOVE.

		Rectus oculi.	Facial.	Larynx and Tongue. (Aphonia & Anarthria.)	Pharynx.
1907		11	4	12	2
1906		4	5	2	1
Total		15	9	14	3

The following order indicates frequency of parts paralyzed: 1. Leg. 2. Legs only. 3. Arm. 4. Quadriplegia. 5. Triplegia. 6. Hemiplegia. 7. Contralateral. 8. Both arms only.

The figures relative to the age are very striking; 95 per cent. of the patients were under 5 years, 70 per cent. were between 1 and 3 years, and 33 per cent. during the