On myxoedema, a term proposed to be applied to an essential condition in the 'cretinoid' affection occasionally observed in middle-aged women / by William M. Ord.

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A TERM PROPOSED TO BE APPLIED TO AN ESSENTIAL CONDITION IN THE

# "CRETINOID" AFFECTION

OCCASIONALLY OBSERVED IN

# MIDDLE-AGED WOMEN.

BY

WILLIAM M. ORD, M.D. LOND., F.R.C.P., PHYSICIAN TO ST. THOMAS'S HOSPITAL.

Read October 23rd, 1877.

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(Received October 16th-Read October 23rd, 1877.)

ON the 24th of October, 1873, Sir William Gull brought before the Clinical Society of London observations on five cases illustrating what he described as "a cretinoid state supervening in adult life in women." The term cretinoid was avowedly used in that communication in a tentative or provisional way, and the cases were brought forward in the hope of directing attention to the state denoted by it, which Sir William Gull regarded as a substantive and definite one.

Having during the last twelve years had under care at least five cases of a similar kind, in one of which I had the opportunity of making a post-mortem examination, I propose to record two of them at some length, to make short reference to the others, and to draw inferences.

1. H. J-, æt. 54, came under my notice as an outpatient at St. Thomas's Hospital in 1871. She was a widow, and had had two children, both then surviving. Her parents had not been subject to any nervous disorder or to any affection like her own. There was no reason to believe that they had suffered from any marked constitutional disorder. The catamenia were regular up to their cessation ten years ago. Her illness had commenced five years before. Up to that time she had been active, and not stouter than the average.

She had, when first taken ill, been very anxious in connection with the fatal illness of her husband. The first signs of illness were fits of shivering during her work. These were followed by the passage of bloody urine, as she believes, on several occasions. Then her hand became "dead," to use her own expression, when she used her needle; a great addition to her trouble, as she had to work very hard to support herself and her helpless husband. Later on she became "weak-headed," would be stupefied by a glass of beer at luncheon, experienced a general loss of muscular power, and was always falling asleep. After that she had constant pain and weakness in the back, so that she began to stoop considerably; her speech became slow and difficult, and a gradual swelling of the skin of the whole body set in; the skin of the face, and particularly of the eyelids, becoming thick, semi-transparent, and waxy. When first seen she exhibited in a very marked form the character of skin described by Sir William Gull. The face was generally pale, but had the delicate blush on the cheeks. The eyelids, the lower in particular, were swollen and ridged, so as almost to hide the eyeball, and at the same time to hang down flaccidly on the cheek ; they were remarkably translucent, and had somewhat the look of the eyelids in acute Bright's disease. But they were wrinkled on the surface instead of being smooth, and did not pit on being squeezed between the thumb and forefinger. The nose was swollen, broadened and flattened, the nostrils being widely expanded; the lips were swollen, expressionless, and pressed together, the mouth being a simple horizontal slit, opening but slightly in the vertical, more freely than usual in the transverse

direction. The skin was again swollen into folds on the sides of the face and below the chin. The hands were swollen, the fingers looking very clumsy, and much limited in range of flexion and extension; very fairly describable as "spade-like."

The skin over the whole body was singularly dry. On the limbs and trunk it was harsh and rough to the touch; the hairs were feebly developed, and no trace of fatty secretion could be found. The skin was everywhere sensitive, but the limit of confusion in tactile discrimination was everywhere wider than the average. The same sort of swelling observed in the skin was visible in the fauces.

Her mode of speaking was very characteristic. The voice was not harsh or hissing, but dull, leaden, and without intonation, reminding one to some extent of the voice in an early stage of quinsey. When about to speak she closed her lips throwing the under one forward, made a movement of swallowing, and then with much widened mouth commenced inhalation, at the same time expelling air explosively through the nose. The swallowing appeared to be necessary to move the soft palate. The speech was slow and measured. It was noticeable that whatever she did was done slowly and after delay. With the exception of some dimness of sight and the slight deficiency of tactile sensation her senses seemed perfect. But there was a marked slowness of perception, and a marked slowness of response of muscles to voluntary or reflex nerve-impulse. She stated that she could not act or think quickly, that her thoughts would only come slowly; that where any operation, such as dressing, took her half an hour formerly, it now took her two hours, so that she was perpetually behindhand with her work. Although her temper was placid, this was a constant source of distress to her. She could walk only very slowly, and the knees often gave way suddenly. She was consequently very nervous when out of doors, and was always expecting that people would run against her, she being unable to get out of the way; in fact, she was subject to a sort of waking nightmare. She very often had headache, and felt always

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tired, so that her life was utterly wretched. For some time she felt a strange taste in her mouth, which seemed to affect all food; it was partly sour, partly like the taste of blood. She often noticed a foul smell (as of bad breath) in her nostrils. The appetite was bad. The tongue was large and clean, not marked by the teeth, although too large for the mouth. The heart was feeble in its action, and not hypertrophied; there were no murmurs, and no important change of accents in the sounds. The breath was short on exertion or excitement, but not at other times, and there was no orthopnœa. The liver and spleen were not decidedly enlarged, but were somewhat tender, and undoubtedly firmer to the touch than normal. There was apparently a good deal of subcutaneous fat in all parts of the body, particularly in the neck, above the clavicles; and the thyroid body could not be felt. The blood examined under the microscope appeared healthy. The urine was examined repeatedly. The specific gravity was rather low, ranging between 1008 and 1017. The quantity was not materially increased. It contained no trace of albumen in the years 1871 and 1872.

In 1875 all the above conditions existed, in conjunction with increase of debility and languor.

At the beginning of 1876, on her appearance after a long absence, the urine was found to be albuminous, and there was true ædema of the hands and legs. In January, 1877, her state had undergone much change.

The complexion was pale yellow, and in the flush on the cheek were many enlarged vessels. With the occurrence of ordinary anasarca there was some abatement of the old nervous symptoms. She put out her tongue, spoke, and moved more quickly. The dryness of the skin was as marked as ever; but under any excitement she broke into excessive though short-lived perspirations. The skin of the body and limbs was shining, and exhibited flat smooth spaces, alternating with wrinkles and furrows. She "had lost that dreadful sinking in her inside," but was easily put out of breath, and could not lie down with comfort. The heart was decidedly enlarged; the first sound at the impulse was

reduplicated, and so was the second sound at the base, between aorta and pulmonary artery. The second sound was greatly accentuated over the aorta. The arteries were everywhere hard and tense, and the right radial was dilated and irregular in form, as though from atheroma. Tracings were taken of the left radial, obtained with difficulty on account of the toughness of the skin, and obscured by irregular respiratory and muscular movements.

Hawksley's surface-thermometers applied to the surface of the body gave  $94.9^{\circ}$  for the temperature below the right mamma, and  $95^{\circ}$  below the left; the temperature of the ward  $60^{\circ}$ ; of the axilla  $97.2^{\circ}$ , and of the mouth  $98.8^{\circ}$ .

She complained of feeling the cold much, of bad sleep, broken by frightful dreams, but less of the bad taste and smell.

The urine was 1004 sp. gr.; was faintly acid, pale, clear, and contained a little albumen; quantity increased. The symptoms attending destruction of the cortex of the kidneys were clearly developed, and had taken the place of many of the older and, as I believe, quite distinct symptoms.

And these late symptoms increasing in severity, ended fatally by breathlessness and exhaustion at the beginning of March, 1877.

Her axillary temperature continued low throughout January, and up to her death, falling many times to  $95^{\circ}$ , and not exceeding  $97.6^{\circ}$  till four days before her death, when it rose to  $99^{\circ}$ .

The full notes of the post-mortem examination are appended to this paper, and I will here mention only one or two important details.

1. There was ædema of the skin generally; but the cut sur faces yielded less fluid than their appearance would promise.

2. There was much serous effusion in the pleuræ, pericardium, and peritoneum.

3. The heart was of large size, weighing sixteen and a half ounces; the left ventricle hypertrophied, the wall being an inch thick; valves practically healthy.

4. The arteries were everywhere thickened, the larger ones atheromatous.

5. The cortical substance of both kidneys was much wasted and granular both on surface and on section. The renal arteries were thickened and atheromatous; and there was thickening of their outer coats.

6. There was a firm, almost solid œdema in many parts, e.g. in heart, soft palate, larynx, stomach, and neck of bladder.

7. The brain showed very considerable degeneration of the larger arteries.

In preparing portions of the organs for microscopic observation it was noticed that the skin in particular retained its ædematous condition even when cut up into small fragments, whereas the skin of dropsical patients collapses when so treated, owing to the ready draining out of the serous fluid. The skin of the feet was removed and examined by my colleague Dr. Cranstoun Charles and Mr. Shaw, with reference to the quantity of mucin to be detected, the first microscopic views giving rise to the idea that the normal mucin-vielding inter-fibrillar cement was here in excess. These portions of skin being subjected to parallel processes yielded equal and considerable quantities of mucin. Equal portions of skin from the foot obtained from non-ædematous bodies, treated in exactly the same way, vielded less than a fiftieth of the quantity obtained from the foot-skin of H. J.\*

The description of the processes used by Dr. Charles and of the microscopic appearances found in various parts are set forth at the end of the paper, together with the full postmortem report.

For the drawings of microscopic appearances I am indebted to the skill and kindness of my colleague Mr. Charles Stewart, of whose accomplishment in histology it is unnecessary to speak. They were made with the aid of the camera lucida, and the nuclei are individually of the exact size and distribution of the nuclei in the stained sections from which the drawings were made.

\* Since the paper was read, the skin of œdematous bodies has been subjected to the same processes, with the result that no increase of mucin was found.

The second case which I shall quote is that of a lady, æt. 36, who came under my notice in 1863, and remained more or less under my care till her death in 1870.

When I first saw her she was extremely stout, puffy in the skin, and unwieldy. Her face had a tranquil expression, but the surface was waxy and transparent, the eyelids were greatly swollen, and she had the delicate blush on the cheeks. At first sight she appeared to be suffering from renal disease, but on examination no evidence whatever of its existence could be found. The swollen transparent state of skin prevailed in all parts of the body; the lips were blubbery, the tongue was swollen and was protruded slowly, the fauces were swollen without congestion, and the neck was creased with gelatinous-looking folds. The hands and feet were bulky and broad in proportion to their length. The vulva and os uteri displayed the same condition to a marked degree, and the rectum and anus owing to the soft swelling of the mucous membrane offered a serious obstacle to defæcation. It may be remarked that the condition of the genital organs did not prevent conception. She was twice pregnant within the seven years, and on each occasion went her full time. Although her weakness caused great anxiety, her labours were not unfavorable, excepting that that there was some excess of hæmorrhage. The skin except on the face was rough and indisposed to perspiration. These conditions which had been slowly developed during the three years preceding my first knowledge of her, were attributed by her to a very rapid succession of pregnancies. Before marriage she had been slight and active. Her parents were both living, and there was no unhealthiness in her collateral relatives. As in the former case there was no history and no indication of syphilis.

Associated with the foregoing were three marked sets of symptoms:—1st. A remarkable slowness of thought and action; 2nd. A distinctively slow articulation; 3rd. A slowness in muscular action, and an incapacity for the maintenance of muscular effort.

1. Under the first head it must be noted that, though

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placid in her manner, and absolutely amiable in her temper, she was acutely conscious of her slowness of thought, and painfully prolix in dilating on it. As the head of the household she endeavoured during her husband's necessary daily absence to fulfil her duties, but although constantly employed scarcely accomplished anything. The mere act of dressing cost her between two and three hours. Her memory was good, her ideas perfectly clear, but she seemed like a bulky mass slow to respond to external forces, and to take on movement. And her momentum when once set in motion was equally noticeable. The current of her thoughts having been set to flow in any one direction went on flowing, and the digressions thus produced were among the causes of her administrative inefficiency. A question edged in at a pause for breath was, so to speak, swept away by the current, but was not lost, being answered when the whole of the thoughts which she wished to express were displayed, sometimes after an interval of two minutes. She wrote well, caligraphically; her letters were long and diffuse, but always accurate.

2. In speaking, she commenced by closing her lips and swallowing; her voice was nasal, with defective intonation; and while articulating, she often made a partial act of swallowing, and ejected air by the nose. There was a perfect resemblance between her way of speaking and that of H. J.

3. Her walking was a very painful process. She was obliged to move very slowly, and at each step a quiver ran through her whole frame as though the muscles were behind hand of her will, and were not in perfect concert with one another. There was no tremor however, and nothing at all like locomotor ataxy. The movements were like the quivering movements of a person pacing slowly while deeply engaged in thought, and the ultimate principle involved, appeared to me to be the same. As it would be under mental abstraction, there was a want of free response on the part of the central nervous system to influence from without. This want of correspondence sometimes went so far as to cause heavy falls, a step being taken by the agency of one set of muscles before

another set were in readiness to carry on the chain of movements. She sustained in this way a fracture of both ligamenta patellæ, one at one time, one at another, the extensors of the thigh waking up just in time to do the mischief.

As time grew on, the expression of her face became very distressing. It was certainly cretinoid, the swollen lower lip protruding and depending, and at times allowing of the escape of saliva. Her head hung down with the chin on the chest, owing to the inability of the muscles of the neck to maintain their action. When the head was raised after several oscillations, by the slow action of the proper muscles, or by the aid of the hands, it often fell helplessly backwards or to one side in such a way as to make bystanders shudder lest the vertebral ligaments should share the fate of the ligamenta patellæ.

There was no affection of the senses or of the viscera, so far as could be made out, till about six months before her death, when the urine, hitherto perfectly normal, began to be albuminous, and the vascular symptoms of renal disease were rapidly developed. She died comatose, and no examination of the body was obtained.

In three other cases I have witnessed a similar combination of symptoms. The patients were all women between forty and sixty years of age. In two of them the urine became at length albuminous, but not till the anasarcous appearance had existed six years in one, and nearly ten years in the other case. All three of these have passed out of my sphere of observation. But in all, the gelatinous appearance, the harshness and the dryness of the skin were well marked; in all there was the slowness of thought and action and the slow, painful enunciation.

The cases agree, in most respects, very closely with those narrated by Sir William Gull; in fact, I am inclined to think that two of them may have come under his observation. It is evident that Sir William Gull has used the word cretinoid, in relation to his cases by way of labelling them, and of putting them aside thus labelled for further comparison and more minute investigation.

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The opportunity which I have enjoyed of recording a postmortem examination of a case of the kind enables me to carry, at least, a suggestion as to the pathology of such cases a step further. The suggestion is to the effect that a jellylike state of the fibrillar or white element of connective tissue is the essential and common condition of these several cases, and that nervous disorder and vascular change are definitely consequent thereon.

The apparent œdema so well marked in the face, and not more marked, indeed, at first less evident, in more dependent parts-an œdema which is undisturbed by pressure or change of attitude, which is exempt from the laws ruling the distribution of fluids in closed vessels-appears to me an indication of the presence in the skin of either a jelly-like interstitial material or of tissue in a jelly-like state. The microscope (see Plate V, figs. 1 and 2) shows that the interstitial spaces of the cutaneous tissues are large, and that the fibrillar element of the connective tissue is everywhere swollen, while the nuclear element is highly developed, and the nuclei larger than the average. The swelling of the fibrillar element is associated with unusual definition, separability, and size of the fibril. This is well seen in the corium generally, but is brought out most clearly in the investments of glands and of hair-sacs, and in the coats of vessels (Plate V, fig. 1).

In the coats of arteries, the adventitia can often be seen swollen to three or four times its proper proportion, with the fibrils unusually well defined, as though separated from each other by a swollen interstitial substance. And the middle coat, also much thickened, has a much greater increase of matter not stained by logwood than of nuclei. There are, perhaps, more transverse nuclei than should belong to an artery of a given calibre, but they are imbedded at much wider intervals than is natural in the unstained surrounding matter. In many sections these two overgrowths appear to have led to the obliteration of arteries, for there are many round areæ which look like arterial structures without a central cavity—areæ which, in size, would correspond to capillary arteries. In the kidneys a similar thickening, growing inwards from the capsules of Malpighian bodies, can be seen encroaching in various degrees up to obliteration upon the contained glomeruli of capillaries (Plate VI, fig. 1).

4. In the liver an enormously disproportionate swollen connective tissue separates the cells from one another, and evidently encroaches on them, and tends to produce atrophy in them (Plate VI, fig. 2).

In the thyroid gland the alveoli are compressed, and mostly annihilated, by a growth of the kind which can here be seen in great perfection around the vessels; and in the muscular tissues, particularly in the heart, the same sort of excess of cement, with induced attenuation of the muscular elements, is clearly to be recognised. A natural condition very closely resembling this is to be seen, as Dr. Harley has reminded me, in the umbilical cord, where the connective tissue has also often a dropsical look, from excessive infiltration with the mucus-yielding material. In conditions of this kind arises, as I infer, the inaction of the skin observed in all the cases. This may be explained in two ways, 1st, by the manifest atrophy of the sweat glands; 2nd, by alterations in the nerve-endings in the skin. Where these nerve-endings can be observed, it is seen that they are enveloped in soft transparent substance, so as to be padded and removed from the ready operation of incident impulses, tactile, thermal, or chemical. They are so placed, therefore, as to receive fewer impulses, and to receive such as reach them more slowly, so that the first stage of a bradæsthesia is set up. Observation in the case of H. J- showed that there was no material loss of accuracy in perception, while there was a remarkable slowness of response to external and volitional impulses. It is possible that a parallel state of things prevailed in the nerves and nervous centres, but, though I have submitted sections of the latter to the microscope, I cannot say positively that they warrant such a conclusion. The existence, however, of a condition of the skin interfering with the natural exposure of nerve-ends to stimuli appears

to me in itself an explanation of most, if not all, the characteristic nervous phenomena above related. One most essential condition of the health of the central nervous system is that it receive its due amount of stimulation through the skin, and receive it regularly. The stimulation is probably complex. Light appears to be one stimulus, variation of temperature another, variation of dryness and moisture another, the chemical quality of air or water another.

Experience demonstrates the evil result of a restricted indoor life, the benefits of out-door exercise, of bracing air, of the exposure in journeyings by sea. Proceeding upon this basis I would argue that, supposing the cutaneous nerveends to be sheathed unnaturally with a coat of jelly, there would result a failure of the natural stimulation of the centres—a failure sufficient to produce lethargy and inertia of the great centres, with slow mobility and slow response as results.

If the skin be alone regarded, the morbid state called sometimes sclerema, sometimes scleroderma, may be held to be allied to the state here described. The microscopic appearances are certainly analogous; but in sclerema the affection is limited, not general; is varying and not progressive; leaves textural changes not observed in myxœdema; and the swelling is hard instead of pulpy. At the same time I may observe that in the most typical case of sclerema adultorum which it has been my fortune to see, there have been nervous symptoms of a decided kind. When the skin was tense, hard, and dry, there was torpor, slow thought, slow action, and a perpetually oppressive sense of inadequacy of power and energy to the needs of daily life. These symptoms passed away when the action of the skin was established, and in a long course of observation were found to vary with the freedom of perspiration.

Again, the result of varnishing the skin of animals, as practised by Becquerel and Breschet, Valentin, Edenhuizen, and others, may be noticed for sake of comparison. When the skin is covered with a gluey insulating material the temperature falls rapidly and death follows. Even if only

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one sixth of the skin of the whole body is thus insulated the fatal result is produced. This, excluding ideas of poisoning by retained secretion, is due either to rapid loss of animal heat through the varnished surface, or to loss of the tonic influence maintained by exposed periphery; to the latter mainly, as from analogy, I believe; and as the failure of the introduction of heat from without to do more than defer death helps to prove.

The want of free cutaneous secretion is to my mind, as much a result of the insulation of nerve ends as of the compression of the glands. A free cutaneous transpiration is generally held to be a condition and sign of health. The "sweating palm" is called by Shakspeare "the precedent of pith and livelihood." And certainly this phenomenon is part of a chain having for its chief link a vigorous health of the central nervous system. A day of fatigue, a night of excess, dry up the sweat and roughen the skin, for all that the glands still exist, and independently of all external agents affecting the surface of the body. Then, moreover, it comes to pass, that the induced condition of the skin is reverberated upon the centres, in feelings of distressing tension, and fulness, and heat, lasting till the internal disorder having passed away, the skin resumes its proper functions, and with the sign of local health the general ease returns.

To proceed, holding in view suggestions of cretinism; the hands, in all the cases noticed, have displayed the very converse of the conditions belonging to local and general health. Sir William Gull has drawn special attention to the swelling, broadening, and shapelessness of these members. He calls them "spade-like," an epithet which is well justified by their shape and by their want of natural movement and expression. I trust that I shall not be taken to task too severely for claiming *expression* as a property of hands. At all events, I have the support of the physiognomist and of the artist in believing that the hands are in their way an index of the character and reflex of the habits of the man. The movements accompanying passion, the strained grip of anger, the clutch of avarice, the hearty grasp of friendship, the soft presssure of entreaty, mould the lines of this feature in proportion as they recur often, or as ideas related with them often arise in the mind; the service to which the hand is put, again declares itself not only in the acquired texture of the surface, but also in the development of special qualities of strength, mobility, sensitiveness, delicacy, &c.,—in the attitudes, which in rest, remain as shadows left by activity.

The hands of the Crétin, as described in the 'Report of the Sardinian Commission of 1848,' not only have the spadelike shape, but are also covered "d'un cuir rude et épais." The report goes on to say, that "Il paraît que pour lui (the crétin) la main est un instrument uniquement destiné à saisir, et non à d'autre chose." A few crétins acquire by long practice a marvellous dexterity in twirling sticks between their fingers, but none arrive at the power of distinguishing by touch a silk from a cotton stuff, or the like. The hands in crétins are, again, but the type of a general indifference of the whole surface to external impressions. Crétins are mostly indifferent to great cold and great heat; they sweat rarely, and do not care to adapt their clothing to variations of climate. In the case of H. J-, a certain indifference of the skin to atmospheric conditions was well seen. It is true that she was always much depressed in winter, and was conscious that cold weather increased all her troubles. It is also however true, that in cold weather, with windows open near her, she commonly lay with the shoulders and upper half of the thorax covered only by a chemise, which was more often open in front than not. There was no sensation of cold which induced her to cover herself well with the bedclothes. It has been pointed out that perspiration was rare in her, and in the other patients here noted, and, what I do not find in the Sardinian Report, a general dryness, harshness, and coarseness of skin prevailed, more notably in the limbs than on trunk or face. The muscular movements again have in the cases described a decidedly crétinoid character. The attitudes and movements described in the second case were chronicled by me before it occurred to me to compare these cases with crétinism. The Sardinian Report paints the walk of the Crétin as follows:—" Ils marchent en se balançant comme des ivrognes, tiennent le corps et les jambes courbés, *la tête penchée*, trainent les pieds mal assurés et se laissent tomber à la rencontre du plus léger obstacle." This is hardly an exaggeration of what I observed in Case No. 2; but was not approached in the remaining cases, where sluggishness of movement and a tendency to slovenly attitude were alone developed.

As regards the class of cases immediately in question, my suggestion is that the whole collection of symptoms are related as effects to jelly-like swelling of the connective tissue, chiefly if not entirely consisting in an overgrowth of the mucus-yielding cement by which the fibrils of the white element are held together. Accordingly I propose to give the name of Myxœdema to the affection.

I would argue that the most important mode of operation by which this condition produces the symptoms associated with it, is the padding of the peripheric termination of sensory nerves, and perhaps too of muscular nerves, with a soft material which hinders their free reception of impressions, in the same way as cotton wool in the external meatus deadens sound on its passage to the auditory nerve. That perception becoming slower than usual, and the central nervous system losing, through the altered state of the skin, its natural and necessary stimulation, a state of intellectual lethargy and a slowness in co-ordination of movements are necessary consequences. In this chain, slow use, partial disuse, and numbness of faculties are links of one kind, and the constant retardation of guiding sensory impulses, a link of another, so that supposing the myxœdema to be constant, the nervous degradation tends to be progressive. The train of symptoms leading to the fatal termination commences in the encroachments of the myxosis upon vessels and upon the secreting elements of glandular structures. Both fatal cases showed at the last, the symptoms associated with renal disease. And in the case of H. J-, the encroachment of the myxosis upon Malpighian -bodies in kidney, and upon hepatic cells

has evidently proceeded to an extent involving very large interference with the functions of the organs in question. The same process can be seen at work in the practical destruction of the thyroid gland, in encroachment in the glandular tissues of the skin, and in a sort of gelatinous embedding of the vessels, more particularly of the arteries.

Many circumstances in the second case indicate that there was weakening of the toughness of tendons. Both ligamenta patellæ were broken in succession, and the ligaments about the head and neck were evidently lax and yielding. The alteration in the elements of connective tissue would explain this.

If this condition be admitted as an explanation in the cases before us, the parallelism between many of the symptoms associated and certain symptoms of cretinism, the parallelism which has led Sir William Gull to call these cases cretinoid, may justify me in suggesting that it may be possible to trace some similar cause in operation as the beginning of cretinism itself.

1. Cretinism is, according to all authorities, a progressive disease. At the time of birth there is, according to many authors, not much difference between a crétin and a noncrétin; so much so that it is not commonly a point which can be decided until the end of five or six months. That is to say, the unequal and irregular development of the head, the coarseness of the features, and the deformities of the body, are far less marked at birth than afterwards. However much this statement may bear qualification, it is abundantly shown that the perfect development of cretinism does not take place till the age of from four to seven years, according to different observers, while at the same time no healthy child becomes a crétin after such an age is passed.

2. Foderé, as quoted by the Sardinian Commission, asserts that those infants which, without presenting a congenital goître, are altogether destined to become crétins, have a body extraordinarily voluminous, and a head and hands of disproportionate size, and are mostly ædematous.

3. A "subcutaneous œdema," to use the expression of the

Sardinian Commission, is of frequent occurrence in adult crétins.

4. While goître is common in the districts where cretinism is common-their association in one individual is not invari-Many goîtrous persons are not crétins; about one able. crétin in three is goîtrous. In the cases under observation there was notable diminution in the size of the thyroid gland, and the practical annihilation of the gland in H. Jhas been described. In respect of this we may be reminded of Mr. Curling's1 cases of absence or atrophy of the thyroid in idiots in association with great deposits of fat in the supraclavicular region on both sides. The relation between goître and cretinism is ably and fully discussed by Dr. Hilton Fagge in a paper in volume liv of the 'Transactions' of this Society, "On Sporadic Cretinism occurring in England." I may remind the Society that this paper brought out more fully the principle which seemed likely to follow from Mr. Curling's observations, namely, that while goître was more or less associated with endemic cretinism, the thyroid gland was actually absent or atrophied in sporadic cretinism occurring in this country; and that Dr. Fagge infers the existence of a direct antagonism between goître and cretinism. It is unnecessary to reproduce his arguments, but it is obvious that the case of H. J- is one more in favour of them.

If Dr. Fagge's hypothesis that the presence of goître is actually a safeguard against cretinism, and that the atrophy of the thyroid is a possible cause of the sporadic cretinism of this country, be true, it may still follow that there is an ultimate cause present in the one case, and not in the other, upon which the growth or degeneration of the thyroid may depend.

In the cases now under consideration nothing is known of the state of the thyroid in early life; the occurrence of the swelling in the skin had certainly not come on till long after adolescence—till long after the intellect and the brain have undergone their complete development. The nervous symptoms here are accordingly such as would be induced by

<sup>1</sup> 'Med. Chir. Trans.,' vol. xxxiii, p. 303.

#### ON MYXCEDEMA.

partial numbing of the senses, by the sleep or torpor of a central nervous system already built up and capable, in proper conditions, of exerting full activity. Supposing, however, the ædema to begin with life, the position of the central nervous system is different. It should, in natural conditions, be built up, be evolved in great part by the agency of impressions from without. As the deaf child is mute, so the child with insensible skin loses the education upon which the establishment of relations with the world of intelligence depends. The uninformed brain, the sensorial system without exercise, remain shapeless. External influences should, as was fabled of the bear with its cubs, lick the shapeless central organ into shape; and when they are hindered from contact, the brain lies like a polype in the water. Life is possible, because the machinery of organic sensation is not entirely wanting, but an organic life and no more; so that year by year during childhood the crétin, on this supposition, would, as the crétin, in fact, does, depart further and further from the type of healthy humanity.

Lastly, in giving a name to the condition observed, I trust that I may be considered to have shown reason for the new coinage; but the name is only intended to represent the condition, and does not profess to involve an explanation of its causes. Whether the mucous ædema be a degeneration, an arrest of development, or an introduction of new material, is not, at present, a question ripe for discussion; and though I should be grateful for suggestions on these points, I do not propose at present to express any opinion of my own.

# Report on Mucin from the Skin by Dr. CRANSTOUN CHARLES.

Specimen of Mucin, No. 1. Mode of preparation.—The skin of both feet of Mrs. J— was cut into pieces, and divided into three nearly equal portions, a,  $\beta$ , and  $\gamma$ .

a was digested with water for several days; the filtrate from this was treated with an excess of acetic acid, let stand some hours, the precipitate separated on a filter and washed first with water acidified with acetic acid, and then with pure water. This washed precipitate was next left for twentyfour hours in lime water, the solution filtered, and the precipitate again thrown down by excess of acetic acid. To purify the precipitate thus obtained it was washed successively with acidified water, pure water, alcohol, and ether, and then dried over a water bath.

The process is that employed by Eichwald for the separation of mucin from *Helix pomatia* and from tendons. ('Ann. Chem. Pharm.,' Bd. 134, s. 177).

 $\beta$  was left in methylated spirit for three days, in lime water for two days, then filtered, and to the filtrate acetic acid added in excess. The precipitate was separated and purified as in a.

 $\gamma$  was digested at once with dilute baryta water, the dissolved mucin precipitated by acetic acid, and purified as before.

The body obtained by the above three methods was sensibly the same in each case in properties and in appearance, and nearly equal in amount; it corresponded in its reactions to the mucin of Scherer, Eichwald, and Staedeler. (See Hoppe Seyler, "Handbuch der Phys. Chem. Anal.," 'Ann. Chem. Pharm.') Bd. iii, s. 14, Gorup-Besanez, ('Handbuch der Phys. Chem. Anal.')

By operating in like manner Hilger obtained similar mucin in small quantities from the skin of Holothuria. ('Arch. f. d. ges. Physiol.,' iv, s. 336.)

Specimen of mucin, No. 2 (from healthy subject).—This was prepared by Mr. Shaw, under my directions, from the skin of the feet of a healthy adult body. The methods employed were the same as the above.—T. CRANSTOUN CHARLES, M.D.

> Report of post-mortem examination. By Dr. W. S. GREENFIELD.

Hannah J-, æt. 58, widow, admitted into Alice Ward,

January 2nd, 1877, under Dr. Ord. Died March 7th, 1.45 a.m. Examined March 7th, 2 p.m.

Body of female of short stature. Rigor mortis well marked. Great toe joints healthy. Considerable anasarca of face and lower limbs, which scarcely pits on pressure; but on cutting into the skin the fat is found to be considerably œdematous; and watery fluid can be squeezed out of it.

Pleuræ.-Right contains a few ounces of fluid; left about the same; (quantity not measured).

*Pericardium* somewhat widely exposed and contains nearly a pint of clear serous fluid. Left lung considerably compressed by the distended pericardium.

Heart.—Weighs  $16\frac{1}{9}$  oz.; of large size. Some general opacity of visceral pericardium, especially about great vessels at base. A patch of milky thickening ("plaque laiteuse") at base of right ventricle; two or three at base of left.

Left ventricle mainly enlarged, globular; apex rounded; cavity somewhat dilated. Wall (in semi-contracted state) measures at centre 1 inch; near base  $\frac{3}{4}$  inch; near apex  $\frac{5}{8}$ inch. Muscular tissue rather pale, tough.

Left auricle slightly dilated, otherwise normal. Left auriculo-ventricular orifice  $3\frac{2}{3}$  inches in circumference; mitral valve competent, and except slight atheroma of anterior segment (in usual position near base) normal; no thickening of edges.

Aortic orifice only  $2\frac{1}{6}$  inches in circumference (normal  $2\frac{5}{6}$  to 3). Aortic valves competent and natural, free from notable thickening.

Aorta.—Arch of aorta somewhat atheromatous, not obviously dilated.

Great vessels.—Left vertebral artery given off separately from arch, between left carotid and subclavian. Great vessels extremely atheromatous, especially the left carotid, the patches of atheroma greatly thickened, prominent, and superficially of somewhat gelatinous appearance.

Right side of heart fairly healthy. Right auriculo-ventricular orifice  $4\frac{2}{3}$  inches; pulmonic  $3\frac{3}{4}$ . Valves normal. Branches of pulmonary artery here and there very slightly atheromatous.

Lungs.—Right 13<sup>1</sup>/<sub>2</sub> oz.; left 9 oz. Both lungs, but especially left very emphysematous; upper lobe of left lung slightly œdematous; lower compressed, free from œdema. Right free from œdema.

Larynx.-Mucous membrane folds at entrance in, and also vocal cords, œdematous.

Liver 31bs. 5 oz.

Gall bladder contains a large quantity of inspissated bile; and some normal bile.

Capsule here and there slightly thickened; with some small points of fibroid thickening, in places invading the surface of the organ, with some resemblance to grey granulations.

Hepatic tissue apparently normal.

Spleen 3 oz., small, firm, tough, congested.

Stomach.—Mucous membrane somewhat thick and opaque. Along both greater and lesser curvatures, and especially near pylorus, are numerous, small, slightly depressed, smooth cicatrices, the edges of which are vascular or slightly pigmented. (Small mucous ulcers.)

Kidneys,  $9\frac{1}{2}$  oz., of fairly normal size; capsule somewhat thick and opaque, but separated pretty easily from cortex, the thickening somewhat irregular, but not obviously laminated.

Surface of kidneys generally fairly even, though minutely granular; but scattered over the surface are numerous small well-defined depressions, smooth at base. These on section are found only to involve the superficial part; they do not extend through the whole thickness as scars.

Substance of organs somewhat firm, slightly tough, and both surface and section granular. Cortex generally but uniformly wasted, and its arrangement not much distorted; it contains a few small cysts.

Minute arteries in kidneys generally considerably thickened.

Renal arteries much thickened, very atheromatous; the outer coat also apparently thickened.

Bladder.—Some slight signs of chronic congestion about outlet, mucous membrane swollen, congested, and slightly pigmented.

Submucous tissue generally œdematous.

Brain.—Arteries at base extremely degenerated and atheromatous; so also all the visible arteries on surface, even to most minute, present extensive atheroma. The vessels at base appear also to present calcification of middle coat. -W. S. G.

# DESCRIPTION OF PLATES V., VI., & VII.

#### Cases of Myxœdema (Dr. Wm. M. Ord.)

## PLATE V.

FIG. 1. Section of Eyelid : cutaneous surface, showing thickening of fibrous walls of hair follicles and irregular bulging of root sheath, either due to budding from its surface or constriction by surrounding fibrous tissue. Hairs in process of shedding. ( $\times$  80.)

FIG. 2. Section of Eyelid; showing meibomian gland, and arterioles with thickened fibrous coat.  $(\times 80.)$ 

## PLATE VI.

FIG. 1. Section of kidney; showing great increase of fibrous tissue around some of the Malpighian capsules, and between the tubules; also solid masses, perhaps obliterated arterioles or Malpighian bodies. ( $\times$  80.)

FIG. 2. Section of thyroid body; showing almost complete replacement of its vesicular structure by connective tissue with cell-crowded patches. Fibrous coat of arterioles thickened.  $(\times 80.)$ 

#### PLATE VII.

Photographs of H-B-, a patient brought for inspection to the Royal Medical and Chirurgical Society on the occasion of the foregoing paper being read.

FIG. 1. Shows the appearance of the patient at the age of 21, before the beginning of the myxœdematous swelling.

FIG. 2. Photograph taken seven years later, shortly before the reading of the paper.











