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PART 1.—ORIGINAL ARTICLES.

*The Mental Symptoms of Myxœdema and the Effect on them of
the Thyroid Treatment.* By T. S. CLOUSTON, M.D.

In Sir William Gull's classical description of "A Cretinoid State," which we now call Myxœdema, in 1873 he thus describes the mental condition of his first patient:—"In the patient whose condition I have given above there had been a distinct change in the mental state. The mind, which had previously been active and inquisitive, assumed a gentle, placid indifference corresponding to the muscular languor, but the intellect was unimpaired." He noticed "changes in the temper," and assumed that the mental changes were pathological and a part of the disease. In Dr. Ord's almost equally classical paper, in which he gave the disease its present name,† he referred to the "slowness of thought," the "long and diffuse letters" of one of the patients. In every full description of any case of myxœdema that I have seen some such morbid mental change has been referred to. In the Report for 1888 of the Committee of the Clinical Society of London on Myxœdema, the mental condition of the patients was inquired into, but there is internal evidence that the reporters did not all understand mental symptoms in the same light. Slowness of mental action was the symptom most common, for its absence was only noted in three of the 109 cases. Delusions and hallucinations are stated to have been present in 15 cases, or 14 per cent., and actual insanity in 24 cases, or 22 per cent. There is very frequent mention of morbid suspicions under the mental heading, and memory is usually stated to be impaired where reported on. In his experiments on

* "Clinical Society's Transactions," Vol. vii, 1874.

† "Med. Chirurgical Trans.," Vol. lxi, p. 52.

monkeys, detailed in the report, Horsley specially refers to mental symptoms that followed extirpation of the thyroid. He says the "mental operations, normal at first, soon diminished in activity, and then follow apathy, lethargy, coma." "Gradually the intellect became duller, the energy of the animal diminished, and apathy alternating with idiotic activity resulted."

In March, 1892, Dr. John Macpherson described the cure of the mental and bodily symptoms of an insane myxœdematous patient by thyroid grafting.* In the "Edinburgh Medical Journal" for May, 1893, Dr. G. H. Melville Dunlop has described a case of typical acute mania cured by thyroid feeding.

When Dr. Ord's description of the disease was published in 1878, so that one began to be on the look-out for it—how few things have been seen in medicine till they have been looked for—I found that I had in the asylum one case of myxœdema, a man, as a patient, whose morbid mental peculiarities I described,† and within the year another case, a woman, was admitted. When the correlation of the insanity and the myxœdema was investigated I found that in both cases the patients had never been insane before, that in both of them the bodily symptoms of the disease preceded by a considerable time the mental, that in both the mental symptoms beginning in a very slight, and, to most people, unobservable form, became more marked as the disease advanced, that in both they had come to a head in a decided way just before coming into the asylum from causes exciting to mental disturbance, and that in certain respects they had some psychical symptoms in common, though in most of their symptoms these first two cases of mine differed widely. During the fifteen years that have elapsed since then I have had other seven cases, all women, sent into the asylum, making nine in all, in whom certifiable insanity was associated with myxœdema, the last two of whom I have discharged cured of their combined mental and bodily ailments within the past three months.

Analysis of Mental Faculties Affected.—It would be tedious and not specially profitable to detail the symptoms in each of these cases of myxœdematous insanity. The mental symptoms in every case of insanity must largely depend on the innate qualities of the brain affected and on the environ-

* "Edinburgh Med. Journ.," May, 1892.

† "Edin. Med. Journ.," Feb., 1861, p. 748.

ments and education of its owner. I have gone carefully over our records of each case, and have endeavoured to recall the outstanding mental symptoms of each. There are few varieties of mental disease where the causation is so absolutely definite. Whatever may be the chemical or organic constituent wanting in the blood when the thyroid gland is atrophied, it must necessarily, from the nature of the case, be only a slight and extraordinarily definite deficiency. We see the changes this deficiency produces in the other tissues of the body. Little irritation is caused, and no sign of any inflammatory process. The various tissue-cells seem to be separated more or less by a deposit of mucin. Especially the heart's action and the rest of the vascular system, as well as the heat-forming processes, are depressed. In the great clinical and pathological features of the disease, and in the changes undergone by the various organs, a wonderful similarity exists between one case and another. Had we to do in the brain and other nerve-centres with cells as simple in function as those of other organs, no doubt the results of myxœdema on motion, heat, sensation, and mind would be practically the same in each case. It is as we ascend from the lower to the higher nervous functions that we realize that the same cause of disease may produce quite different effects in different cases, because the reactive qualities of the cell of higher function are so very different in different individuals. All myxœdematous patients have a lowered vaso-motor tone; they all have a lowered temperature; they all have slow voluntary movements in speech, walking, writing, and other motor processes; the reaction time is prolonged in all of them. The amount of this diminution of nervous function is different, of course, in different cases, according to the stage and duration of the disease. It is when we come to the function of sensation that we begin to find marked differences in different cases. Not according to the stage of the disease, but according to the original qualities of the sensory centres is the individual affected. The personal equation evidently comes in noticeably. I found that my only male case of myxœdema was so insensible to pricking and to heat and cold as to amount to marked anæsthesia and analgesia. The other cases varied so much in this respect that two of them were almost normally sensitive, and the others ran all the way between these two extremes.

When the mental functions of the nine cases were analyzed

I found extreme differences, not only in the degree in which each faculty was affected, but in the kind of mental symptoms present. A simple analysis of the mental symptoms put on record in our case books, and as I remember them, brings out this very vividly. The memory was affected by general loss in eight cases; by special loss of power of recalling recent events in certainly eight of the cases; by loss in regard to special points in seven cases; and by a paræsthesia of memory in seven cases. One lady described in detail conversations that never could have taken place. She was not able to distinguish between the remembrance of fancies and the recollection of real events. The general power of attention was diminished in all the cases, but this was accompanied by an accentuation of attention on disagreeable things and delusional beliefs and impressions in at least six of the cases. Curiosity was sluggish in all the cases.

The functions of sight, hearing, taste, and smell were unfortunately not scientifically tested, but there were hallucinations of sight and hearing in at least four cases. My impression is that in all the cases the senses were somewhat blunted. In the male case that went on to death here this was very marked towards the end. His sense of smell was quite lost for a year before his death. In the same case there were pains, evidently of neurotic origin, but called "rheumatic," in the back and wrists for two months before death, this being at a time when sensation was much dulled. One of the women, for a year before admission, imagined that everything smelt of gunpowder, and another imagined that she was continually made to "breathe gas." The affective faculty was in every case more or less abnormal. In every case there could be no doubt that the power of intense emotion was diminished. The patients were less sensitive, cared less for their husbands—all the women were married—and their children than they had done in health, some of them being strikingly indifferent. There was depression of spirits amounting to a melancholic state in five cases; there was exaltation of feeling in abnormal ways in three cases. This was best brought out by the fact that seven cases were classified as mania and two of them as melancholia in our case books on their first admissions, but on the readmission of two of them who had been classified as mania they were put down as melancholia. I would say that in most of the cases the subject consciousness was more diminished than the object consciousness.

The intellectual power was characterized by more or less marked slowness of effort in all the cases. In the more advanced cases this was most marked. The male case seemed for a few months before his death scarcely to be thinking at all, and when an act of judgment was performed it was only as the result of a strong stimulus from without. Dr. Ord noticed this slowness of thinking, and ascribed it to the want of peripheral stimulus through the endings of the sensory nerves being over-padded and so not sending up impressions to the sensory and mental cortex. I think this explanation is not sufficient and it does not account for all the other mental changes. In seven of the cases there were marked insane delusions. These were chiefly of suspicion. No doubt in any brain cortex that is anæmic or ill-nourished delusions of suspicion are apt to arise. The perpetual acts of sound judgment which are needed to prevent misinterpretations of the actions of others, with regard to self, cannot be performed in such cases. Two of the women showed marked jealousy of their husbands. I had an opportunity of seeing the course of two of the cases up till death here, and one in another asylum; and the tendency in each was to become more generally enfeebled intellectually as time went on. But complete and typical dementia was never reached in any case. A strong mental stimulus had always the effect of rousing more mental power than appeared to be present.

Volition was impaired in every case, either in the direction of slowness of putting the will power into action, or of loss of mental inhibition, shown by irritability and anger for inadequate cause. The male case at the last seemed to have small and slow volitional power, no obstinacy, no initiative, and action of every kind seemed to be impossible of origination. He was content to lie in bed all day and not act or speak at all. To exercise that amount of volition implied in setting his articulatory apparatus in action seemed to be impossible except on great and repeated stimulus. The general loss of volitional power was well seen by the inability to control the drink craving in one of the cases; by the excitability in most of them in the early stage; by the tempers they were apt to get into on very slight, real, or quite imaginary causes; by the acts of violence and destructiveness that were seen in two of them.

General Course of the Cases.—Taking a general view of the mental symptoms in all the cases as seen in their clinical

histories from the beginning of the attacks to the end, so far as I had the means of observing them, they differed greatly in the way the symptoms came on, and in the course taken by them within the first year after they assumed such a decided form that they amounted to technical insanity. I have no doubt whatever that in every case a reasonably close analysis of their condition for a year before admission, as compared with their normal states, would have shown that mental changes had taken place of a morbid character during that period at least. Slowness of mental action, morbid suspicion, and some depression of mind were the common early symptoms.

Immediately before admission, and causing the sending of the patient to the asylum, there was in one case an attempt at suicide by poisoning done in a calm, "rational" manner, the reason assigned being misery from a horribly drunken wife. In seven cases there were maniacal outbursts, four of these being of great intensity, with violence, noise, sleeplessness, and an attempt to jump out of the window in one case. In three cases there were delusions of grandeur, one of the women fancying herself "the Duchess of Albany." In one case in the early stages there was absolute delirious incoherence of speech and incapacity to understand what was said to her. All the acute symptoms subsided in every case under the treatment, the discipline, and the regulated life in the asylum within a month after admission. In four of the cases the mental symptoms became so modified that they were discharged as technically "recovered" in periods of from five weeks to six months from admission. These occurred before the thyroid treatment was discovered, but the recoveries were really not complete. In three of them there were relapses and readmissions. In one case the symptoms got so modified that her husband took her home, where she remained. In two of the cases they died here insane and demented. In the last two cases they were cured by thyroid feeding.

In tracing the course of the symptoms to their "natural termination" before the thyroid treatment was adopted the case of the man was the most instructive. He had been the asylum plumber, and when discharged "recovered" as an insane patient he was kept on as a pensioner, living in the place under observation till his death, 15 years after the commencement of his disease. His mental faculties got slower and more languid in their working until his reflexes,

bodily and mental, nearly disappeared. He got inarticulate in speech, his temperature for ten hours before death was only 92° in the axilla, and he was helpless as an infant, but not comatose. He seemed to die from loss of the power of keeping up his animal heat.

The general course of the mental disease in all the cases was, therefore, first, slowness of mental action; secondly, emotional depression; next, irritability, morbid suspicion, non-resistiveness to outward causes of disturbance and general loss of control or maniacal outbursts; then enfeeblement with some exaltation in some cases, and, lastly, lassitude, hebetude, ending in a condition of mental negation just before death.

Heredity.—In only two of the nine cases could I ascertain a neurotic heredity; and in only one was there a distinct mental heredity, viz., a father and brother having been insane.

Exciting Causes of the Mental Attacks.—In three of the cases there had been mental or moral causes in existence sufficient to stand as the immediate “exciting causes.” In two cases an excessive use of alcohol might fairly be put down as an exciting cause, though the previous loss of mental inhibition from the myxœdema had in both probably aggravated any tendency to excess. In the other four cases there seemed to be no exciting cause whatever, the mental symptoms coming on and slowly advancing till they reached the stage of insanity.

Effects of Thyroid Treatment.—We began by using the solid raw thyroid, but soon took to the use of an extract made by our own dispenser, which answered admirably in all respects. We began with large doses, but very soon found their dangers, and latterly never gave more than what was equal to one-sixteenth of a whole thyroid once a day with frequent intermissions. In each of the two cases put under thyroid treatment the disease had existed for over five years, and the mental symptoms in so decided a form as to constitute insanity for over three years in one case and over a year in the other. Both women presented all the typical bodily symptoms of the disease. One weighed 14st. 2lbs. and the other 13st. 9lbs. Both were mentally enfeebled in a mild way; both were irritable and suspicious, had lost their affection for their husbands, and were jealous of them, while their maternal affection was also very much diminished.

Both had insane delusions referring to events at home that had occurred during the early and more acute period of their mental illness. Both were coherent in speech, but with mild impairment of memory and some general confusion and enfeeblement of mind. Both were in a sort of negative state in regard to enjoyment of life.

They were both placed under treatment by half a raw thyroid on the 16th January, 1893. The temperature rose in both at once, and the weight began to diminish. In one there was much sickness, furred tongue, a tendency to fainting, and a distinct intolerance of the drug except in the small doses I have mentioned, viz., $\frac{1}{16}$ of a thyroid, and that only given twice a week. There was a distinct mental improvement in both within the first month of treatment. The irritability and morbid suspiciousness were the first symptoms to become modified; then there was an improved cheerfulness and an increasing sense of *bien être*; then there came increased intellectual activity, greater power of attention, more legitimate curiosity, a greater tendency to dress smartly and to dress their hair better, and towards feminine adornment. It was at least two months before either of them fully believed in the treatment or went into it heartily. The patient who was made sick by the treatment had several times to be compelled by me to go on with it. No amount of argument, no appeal to duty, and no painting in the most vivid colours of the marvellous cure that was to be effected would induce her to take it. This obstinacy and want of imagination I looked on as symptoms of the mental enfeeblement. Both women steadily "brightened up," until the first case, who had been insane for a year, was discharged recovered on May 17th, that is after four months of treatment. She was sane, and had lost 22lbs. in weight. She would stay in the asylum no longer, and her relatives would not allow her to do so. She was wonderfully changed mentally since admission. Her relatives said after she got home that she had not been so well mentally for many years. She took pleasure in her work and her family. She took only one dose of thyroid ($\frac{1}{8}$ of a gland) four days after leaving the asylum. She walked about a great deal seeing her friends, who were a drinking set, having a festive time, with a good deal of drink and excitement, all of which was quite contrary to the advice I had given her. On the tenth day after discharge she felt ill, and her daughter gave her some

whisky. She went to bed, slept, had an attack of vomiting in the morning, the vomit being a dark fluid; she complained of pain in her throat and of breathlessness, but took a hearty breakfast, eating two ducks' eggs. Soon afterwards she fell back dead when talking with her husband. I have no doubt whatever that she died of syncope from over exertion and whisky while her heart was still in a weakened condition from the effects of the myxœdema.

The other case, who had been ill for three years, remained in the asylum for six months after treatment had begun, and she improved mentally and bodily all the time. She was absolutely changed in facial expression. She became a cheerful, dimple-cheeked, attractive woman, in most marked contrast to her forbidding appearance on admission. When she had been home for three weeks her husband wrote she was still improving every day, taking walks, seeing her family, enjoying indoor games and the companionship of old friends, resuming her old habits and ways, with her affection for husband and children revived after many years of estrangement and dormancy. Instead of refusing she insisted on getting a dose of the thyroid every week. Since then I hear she is "perfectly well in all respects," and her friends think her cure "a miracle."

I am strongly impressed by two considerations in the treatment of myxœdema by the thyroid feeding. The first is that it should be very slow and prolonged. The second is that after the heart and brain tissues have been set free from the perilous stuff that has impaired their working, the danger is not past and the cure not fully complete for a long time after apparent recovery and technical sanity have been established. The damage of years to the tissues of such infinitely delicate and all important organs it would be quite unreasonable to expect to be fully repaired in a few months.

Two pathological facts that have lately come under my observation in regard to the cerebral cortex have impressed me deeply with the possible recuperative capacity of the cortical structure.

One was a puerperal case of a few weeks' standing, a curable case by every clinical standard, who died in a few days of maniacal exhaustion, and whose cortical cells Dr. Middlemass found in a state of marked and advanced degeneration, with spider cells and proliferated nuclei round the vessels and the

neuroglia. If such degeneration is really curable, then we need not despair of recovery in many advanced cases of mental disease. The second fact is the actual cure of the prolonged mental enfeeblement of myxœdematous insanity by the thyroid treatment.

The following is a note of the appearances as seen by Dr. Middlemass in one of our myxœdematous cases:—

The fresh method of examination was adopted in the cortex in one of the cases who died. The patient was 60 years of age, had been myxœdematous for about five years, and insane for more than three years. "There was slight thickening of the pia mater and increase in the number of spider cells in the superficial layer of the cortex. The nerve cells showed decided pigmentary change. The most characteristic appearance, however, was an increased fibrillation of the neuroglia, and in the white matter the small round cells were much more numerous than usual, and here and there these were collected in small groups of three or four or even more. There was also an increase in the nuclei of the walls of the vessels in the white matter which made them stand out very prominently."

The real difficulty in regard to the sections of the cortex in this patient is to distinguish between changes that may be due to senility and those that may be due to the myxœdema. But both Dr. Middlemass and I, after careful examination, have come to the conclusion that the excessive fibrillation of the neuroglia and the marked degeneration of the cells cannot be accounted for by the effects of advanced age alone. If this be so, and if the use of thyroid extract has the effect of clearing up such a diseased condition of the neuroglia, and of reintegrating the normal material of these degenerated cells, then I am convinced that we need not be hopeless of some day discovering remedies that will cure some of our cases of chronic melancholia, chronic mania, and mild dementia, the pathological changes in whose brain cortex I have often seen very similar to those in this myxœdematous patient.

As to the exact pathology of the cortex in myxœdema, and how the changes are caused, and what elements of the cortex are chiefly affected, we are as yet largely ignorant. We know that a wonderfully small amount of a neurine poison circulating in the blood makes all the difference between delirium and sanity, between coma and consciousness. We

have every reason to believe that a very slight pathological change indeed in almost any of the elements of the cortex, whether cellular, fibrous, vascular, lymphatic, or neuroglia, will change the mental condition from that of sanity to insanity. In no other organ or tissue do such slight changes make so great a difference. A constitutional or dynamic change there whose equivalent elsewhere would only cause a moderate pain or a stiffness, may abolish normal consciousness and send the patient to an asylum.

If one might venture a hypothesis, it would be that the neuroglia of the cortex becomes to a slight degree waterlogged by mucin, which causes lowered anabolism and katabolism of the cells, whose reactivity is thereby impaired. An early stage of the process is sometimes characterised by irritability, and the later stages by torpidity of reaction.

No theory of explanation of how myxœdema affects the mental action of the brain cortex can be complete that does not take account of the marvellous acceleration of mental and trophic development that takes place in certain cases of cretinism under the use of thyroid extract, but as I have had no sufficient personal experience of such cases I have refrained from referring to them.

On Melancholia: An Analysis of 730 Consecutive Cases. By
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I proceed at once to the analysis of the cases that have come under treatment in this asylum. The 730 cases under consideration comprise all the cases of melancholia admitted into the Cumberland and Westmorland Asylum during the twenty-seven years from the beginning of 1865 to the beginning of 1892.

Proportion of Cases of Melancholia in the Admissions of the Three Great Classes of Insanity—Mania, Melancholia, and Dementia.—During this period the total admissions, grouped in these three classes, and altogether excluding all cases of