19. FLECHSIG.—*Loc. cit.*, and *Journal of Mental Science*, January, 1899.
20. MOREL.—*Traité des Degenerescences Humaines*, 1859.
21. MAUDSLEY.—*Pathology of Mind*, 1896.

Acromegaly with Insanity. By DAVID BLAIR, M.B., County Asylum, Lancaster. ([1])

ALTHOUGH the condition of acromegaly existed and was described many years ago, its recognition as a morbid entity practically dates from the year 1886, when Dr. Pierre Marie, of Paris, named and defined it as a disease characterised by great overgrowth of the hands, feet, face, and head. Since then the disease, though rare, has been universally recognised, and more than 200 cases have been reported. Of these some have been typical, some atypical, and some have not been acromegaly at all.

The following case, which has been under my observation for more than two years, besides being typical, has the additional interest of being associated with a well-recognised form of insanity.

J. S—, a tailoress, was admitted to the Lancaster County Asylum on the 1st of May, 1891. Three months before admission some of her teeth had been extracted under nitrous oxide gas, which was the assigned cause of her insanity, and one month later she began to exhibit delusions.

She persistently complained of a gas which pervaded the house and suffocated her. She charged certain people with maliciously causing it to enter. She maintained that she talked to people at a distance. She would walk about in front of her house with only her nightdress and boots on, and had to be brought in by the police. Four weeks before admission her delusions became so troublesome that she was constantly out of bed at night to search for the source of the gas.

The patient was married and had four children. Only the youngest of these had survived, and was, at the date of admission, nine years old. She had had no miscarriages, nor was there anything peculiar about any of her children. There was no hereditary predisposition to insanity, so far as known.

Though usually sober, quiet, and industrious, she had at times been intemperate. For six years menstruation had been irregular, and for some time she had been subject to headaches.

At the time of admission she was an unsightly woman with low forehead and coarse hair. Her nose, hands, and feet were very large. Her speech was slow, and she said that she could not use her needle so dexterously as formerly. Her bodily health was good: pulse 72, respiration 16. At night she usually curled herself up in a blanket and insisted on sitting on the floor.

For several months after admission she worked well in the kitchens, but could often be seen with her head hidden behind her apron, or any other convenient article, to ward off the gas. She continued to complain of increasing and severe headache, and began to perspire heavily. She would weep, groan, wipe the perspiration from her face, and say "See what they are doing with the gas!"

Antipyrin had no effect on the headache, but large doses of potassium bromide had some quieting influence by day.

Her face became puffy, the hands and feet soft, spade-like, and swollen, as if myxœdematous. For a long period, therefore, thyroid extract was given in beef tea.

During the past summer I noted the following symptoms:—All the tissues of the hands are enlarged except the bones. A skiagram represents the bones as, if anything, less than normal. The result is a general hypertrophy in width and thickness, but the length from the wrist to the end of the middle finger is not increased. The feet are similarly affected. There is no pitting on pressure. The arms and forearms are of large size, but do not correspond in dimensions to the hands. The cranium is elongated in the antero-posterior diameter, and presents some hyperostosis along the margins of the interparietal suture.

The face is elongated and oval, while the hypertrophy, of the nose and lower jaw especially, is slightly greater on the right side than on the left. The forehead is low, and supported on well-developed orbits. The eyes are relatively small and out of proportion to the size of the orbits. The lids are long and thicker than normal. The nose is the most hypertrophied part of the face. The alæ are especially thickened, and en-

larged at their lower part. The upper lip is less hypertrophied than the lower, which is very prominent. The mouth is usually open, and the tongue, tonsils, and pillars of the fauces are hypertrophied. The voice is guttural and metallic. All the teeth which were not extracted have fallen out; they are very small.

There is kyphosis of the spine in the cervical region, and the patient can hardly hold her head straight. Her favourite position is sitting with her arm on a table, and her forehead resting on her arm. All the tissues around the neck are much hypertrophied. The clavicles, ribs, and sternum are similarly affected. The abdomen is pendulous, while there is some lordosis in the lumbar region. There is profuse perspiration of a disagreeable odour.

On an average she passes eighty ounces of urine in twenty-four hours. It is usually neutral or slightly acid in reaction. The specific gravity is usually as low as 1012, although on one occasion it was 1024. The urea is on an average ·009 grammes per c.c. but 20·5 grammes per diem; in other words, the percentage of urea is below normal, but the total amount passed in twenty-four hours approaches the normal. On the other hand, she takes more than the average quantity of nitrogenous food, so that practically less urea is excreted than under normal conditions. Occasionally there is a little albumen, but I have never detected peptones nor sugar.

The most noteworthy feature about her urine is an excessive and persistent deposit of phosphates. As this deposit ceased when the patient was fed exclusively on milk, it is undoubtedly evidence of imperfect assimilation, and not of softening of the bones.

The headache, though persistent, is more so at one time than another, and there are intermittent pains in the limbs and joints.

The menstruation seems to have entirely ceased, but at irregular intervals of many months there are severe attacks of metrorrhagia. The patient is much given to masturbation. Intra-ocular pains are present, but the sight and field of vision are remarkably intact. There is also at times a complaint of pain in the right ear.

In association with this physical condition her mental symptoms are most interesting. Her sense of humour is very

highly developed ; but her spirits are dejected and her temper irritable. There is a constant feeling of lassitude and a strong desire to recline ; but though heavy and drowsy in appearance, sleep is disturbed. Until a few months ago she insisted on sleeping on the floor, as she said her bed was charged with electricity. She ascribes her headache, which of course we should refer to the pathological condition of the pituitary gland, to the presence of an electric battery in her head ; and to the electricity produced therefrom she attributes her intra-ocular and intra-auricular pains. She accounts for the pains in her limbs and joints by the spread of the electricity through her body. She indignantly denies she has a husband, and if any reference is made to him, flies into a fury. Her husband is alive, writes regularly concerning her, and says jealousy of him was a very early symptom in the case. When we reflect on the bitterness with which a woman once comely sees herself slowly degenerating into a hideous creature, we can appreciate these early suspicions which culminate in delusions. Her outstanding ugliness never fails to attract attention. As a result she is very distrustful with strangers, declines to converse with them, and is especially afraid of medical examination. At one time she heard voices at a distance, now she hears them underneath the floor. She asks me to go down and I shall see for myself the gang of ruffians who are plotting to murder her, and have introduced this electricity into her system. These auditory hallucinations arrive not only through her ears but also through her body by means of the electric wires, and are most intense by night, although they are also heard by day. The original delusions regarding gas have been replaced by delusions regarding electricity. The perversions of general sensibility cause the patient great distress. She has pains all over, feels as if people were constantly pricking her with needles.

She imagines every one is quite aware of her condition, and when asked about her hallucinations says testily, " I am sure you know well enough without asking me."

Finally, she has pronounced delusions of grandeur. She asserts that the asylum and the land around it belong to her ; that she has been left large estates in Ireland, and that she is possessed of great wealth. When the slightest doubt is cast on these assertions, she replies, " you'll see by-and-by." There is no

dementia. Her intelligence and mental acuteness are above the average of her class.

In this description of mental symptoms I think there is to be read a typical case of persecutory mania. And it is interesting to note that while the hallucinations are the insane interpretations of pains in the head, ears, and limbs, and alterations of general sensibility due to the acromegaly, that these are the identical hallucinations with which we are most familiar in cases of persecutory mania, of which the pathological basis is purely problematical. And still further it is to be observed that in this case there are in operation all those physical causes to which persecutory mania is by most recent writers referred. Mental causes are now believed to play an unimportant part in its production; they act only indirectly by lowering the vitality.

The physical causes of persecutory mania are divided by Ritti into three classes. (1) Causes which act on the brain and nervous system. Of these we have here the implication and perversion of function of the pituitary gland, the exact significance of which we shall see later.

(2) Those causes which have their origin in the reproductive organs or in sexual life. In this case we have the early appearance of amenorrhœa with the subsequent attacks of metrorrhagia and masturbation.

(3) General causes of physical debility, such as insufficient nutrition. Acromegaly is essentially a disease of malnutrition. In short, this is a case of persecutory mania in which we may point to the direct physical causes.

Of the ætiology of acromegaly itself we are practically ignorant. In these cases, where an exciting cause has been suggested, alcoholism seems to be the most frequent. It attacks every race, males and females, nearly equally, and it may occur at any age; but the majority are seized from twenty to forty years of age, although it most probably begins to develop shortly after puberty.

Of the diseases with which acromegaly has been confused, the two most common are myxœdema and hypertrophic osteo-arthropathy. This confusion is increased by the fact that acromegaly has been described in connection with both.

From the former it is differentiated by the fact that in acromegaly the bones are always implicated, while in myxœdema

there is no enlargement of the bones. In addition to this salient distinction, other points of difference are so numerous that a well-established case of acromegaly could now-a-days hardly be confused with myxœdema.

From hypertrophic osteo-arthropathy acromegaly is distinguished by the fact that in the former only the bony tissue is enlarged, and that especially at the articular ends of long bones, whereas in acromegaly both the bony and soft tissues are increased. Again, in hypertrophic osteo-arthropathy the symmetry of the hands is destroyed by enlargement, principally at the joints and ends of the fingers, whereas in acromegaly the hands and fingers are enlarged universally and symmetrically.

Both Marie and Souza-Leite point out that acromegalics are far from being giants. Yet the disease is frequently confused with gigantism. While there is no reason why acromegaly should not occur in a giant, it has nothing to do with the height of the individual. The majority of acromegalics are not above middle height—the case under discussion is only five feet one inch—while a perceptible diminution in size has been observed in some after the onset of the disease.

In the latest issue of the *Journal of Mental Science*, Professor Joffroy is said to have described a case of acromegaly, and to have considered gigantism to be the same disease as acromegaly, only occurring before adult life—that is, during the period of growth. I do not know Professor Joffroy's reasons for this contention, but I fail to see how the proportions of the limbs and face would preserve their relationships to each other before adult life any more than after. Some cases of acromegaly have been described before adult life. The appearance of gigantism is never that of acromegaly. Gigantism is only an exaggeration of a normal process; acromegaly is a true disease.

Dr. Middleton, of Glasgow, has described a case with trophic lesions of the joints, like Charcot's joint lesions in locomotor ataxy. In the same case Raynaud's phenomena occurred in a minor form, and there was a tendency to erysipelas. And in the forty-seven autopsies collected by Sternberg, of Vienna, in his recent monograph, and quoted by Furnivall, there was degeneration of the spinal cord in four, in Goll's column especially in two, in Burdach's column in one, and of the peripheral

nerves in one. Such are further indications of the profound trophic disturbance which must be at the root of the disease.

The structures to which most importance is attached in the pathology of the disease are the pituitary body, the thyroid and thymus glands, and the sympathetic nerve ganglia.

In the table of forty-nine cases compiled by Furnivall, chiefly from the collection of Sternberg, the sympathetic ganglia were observed in thirteen. Of these six were normal, six were hypertrophied, and one was hypertrophied with degeneration.

The thyroid gland was observed in twenty-nine cases. Of these only five were normal, thirteen were hypertrophied, while the others showed various forms of degeneration.

The thymus gland was observed in nineteen cases. It was found to be absent in seven, hypertrophied in three, persistent in eight, left lobe hypertrophied in one.

Cases of acromegaly have been described in which it is said that no change in the pituitary gland occurred. This is very doubtful.

In 1895 Professor Tamburini described a case of acromegaly, and discussed the pathology of the disease. Up till then, so far as he knew, only twenty-four cases were described in which post-mortems had been made. In seventeen of these, all of which were typical cases, a tumour of the pituitary was found. Out of the other seven he disposed of five as not having been cases of acromegaly at all. In the remaining two the disease had only been of brief duration, while the absence of structural changes was not established by microscopical examination.

In the whole of the forty-nine cases quoted by Furnivall, the pituitary gland was hypertrophied or the seat of a lesion. We may therefore conclude that the most constant organ to show disease in acromegaly is the pituitary gland. This lesion may take the form of hypertrophy, tumour, cyst, or other degeneration, and it is generally believed to be the most important ætiological factor. This constant lesion of the pituitary gland as a concomitant of acromegaly has brought that body into special prominence. It was, of course, known that it consisted of two lobes, of which the anterior is the larger, and concave behind where it embraces the posterior smaller lobe. It was likewise known that the two lobes are entirely different both in structure and development, yet their functions were practically unknown. Of late years some light has been thrown on this subject.

At the Annual Meeting of the British Medical Association in 1893, Andriezen read a paper giving results of researches on the morphology and evolution of function of the pituitary body. He showed that the subneural gland in larval Amphioxus is the analogue of the pituitary gland in higher animals and in man. He believes it to be a complex organ composed of three parts: (*a*) an anterior secreting glandular organ; (*b*) a water-vascular tube lined with ciliated epithelium and connecting the buccal cavities with the ventricles and the rest of the neural cavities; and (*c*) a posterior sensitive nervous lobe. The last two are well developed and functionate in ancestral vertebrata, but become obliterated and atrophied in function and structure in all forms above larval acraniates and Ammocœtes. The anterior lobe—the glandular secreting portion—is the type of a secreting structure of epithelial cells arranged in lobules and acini with many ducts opening into one principal duct. Its secretion is carried with the water-vascular stream through the central nervous system. The function of that secretion must be either trophic, acting on the nervous tissues, or destructive and neutralising waste products of nervous tissues.

In man the water-vascular system has given place to a blood-vascular, and the duct of the pituitary gland is closed. But the secretion of the pituitary is needed just as much after the closure of the pituitary duct and the cessation of the water-vascular system. The only difference is that the oxygen which was provided for the nervous system by the water-vascular system is now provided by the blood-vascular system. Hence the pituitary gland continues its secretion after the duct is obliterated and after it becomes ductless. The secretion is internal and absorbed by the lymphatics.

But it is not on the grounds of evolution alone that the function of the pituitary is believed to be that of internal secretion. In its microscopical structure the anterior lobe of the pituitary bears a resemblance to another internal secreting gland—the thyroid body, and a colloid substance like that in the thyroid vesicles is found sometimes in the alveoli of the anterior lobe of the hypophysis. Rogowitsch observed that the blood-vessels of the pituitary contain something besides blood, which he assumed to be colloid; Pisenti and Viola showed that it is colloid matter. Extirpation of the thyroid causes structural alteration of the hypophysis, and pathological

alteration of the latter has been found in cases of lesion of the thyroid. Louis Compte, the most recent writer on the relationship between the functions of the pituitary and thyroid glands, concludes from the examination of 100 miscellaneous cases that these organs act vicariously. Drs. Boyce and Beadles, in the *Journal of Pathology* for March, 1892, describe two cases of myxœdema with hypertrophy of the pituitary body, and in one of these there was a striking increase of pituitary colloid. Dr. Beadles reports three fatal cases of myxœdema in the *Journal of Pathology* for 1898, in all of which the pituitary body was above the normal size and weight.

In a case of myxœdema at present under my care in which the symptoms have only been kept in abeyance by the almost constant administration of thyroid extract, I have obtained the same result with pituitary extract.

Still further, experimental destruction of the gland has been followed by notable results. The organ has been successfully removed both in dogs and cats. In all cases of complete removal death results, usually within a fortnight of the operation. The symptoms observed are (1) a diminution of the body temperature; (2) anorexia and lassitude; (3) muscular twitchings and tremors developing into spasms; (4) dyspnœa. Many of the symptoms show abatement after the injection of pituitary extract. The investigators Vassale and Sacchi conclude that the pituitary must furnish an internal secretion which is useful in maintaining the nutrition of the nervous and muscular systems.

But although the pituitary and the thyroid glands are to some extent vicarious, they are certainly not identical. For just as the disease associated with perversion or suppression of function of the pituitary differs in its clinical features from myxœdema, so do the effects of experimental injection of the extracts of pituitary and thyroid materially differ.

Thyroid extract causes dilatation of arteries and consequent fall of blood pressure without diminishing the heart's beat. Pituitary extract increases the contraction of the arteries and the heart, giving rise to marked increase of blood pressure. Moreover, in myxœdema thyroid extract is of the greatest benefit; in acromegaly it is of little value.

According to Shattock there is considerable ground for believing that both glands have more than one function, but

that they have at least one in common, namely, their colloid-producing capacity.

The two glands are vicarious only as to what they have in common, and thyroid and pituitary extracts can be of service in disease of the converse gland only *pro tanto*.

Virchow suggested that in acromegaly we have described only half a disease—the latter and degenerative half. This does not seem improbable. For although in a case recorded by Duchesneau progressive muscular atrophy preceded the development of the acromegaly, some cases in the beginning seem to have an increase of muscular power.

Such a state of matters might possibly mean that there is an increase of secreting cells in the pituitary with consequent increase of function during the period preceding degeneration. And so in the treatment of the disease there would be a period when pituitary extract was contra-indicated as well as a time for its administration. Just as in the treatment of Graves' disease, which is believed to be due to a hypersecretion on the part of the thyroid gland, the thyroid treatment has been found to aggravate rather than to allay the morbid phenomena, as opposed to its great value in myxœdema, in which the thyroid is shrivelled or completely atrophied.

The treatment of acromegaly has been so far chiefly symptomatic. Pituitary and thyroid extracts have been tried in many cases, but with very doubtful results.

Thyroid extract is not entirely useless. Its most constant effect is to reduce the body weight, and it may produce slight physical and mental improvement, as in the case reported by Dr. Neal.

Treatment by pituitary extract seems to have been rarely tried. In a few cases negative results have been reported.

Cyon, however, on the 28th November, 1898, communicated to the Paris Académie de Médecine a contribution to the treatment of acromegaly by hypophysin. He reported the case of an obese acromegalic in whom seven weeks' treatment diminished the weight by nine kilogrammes, and the circumference of the abdomen by 35 cm. The pulse became regular, and the headache, nystagmus, and intellectual apathy were improved.

Last September I began giving the case under my care pituitary extract. During the first month 7½ gr. per diem were

distributed in three doses. The amount was then increased to 15 gr., and after a fortnight to 19¼ gr.

The first pronounced effect was a severe onset of metrorrhagia accompanied by hæmorrhage from the bowel. This passed off in a few days, and a marked improvement in the patient's condition set in. Her irritability and drowsiness almost vanished. She went to bed willingly and slept all night. She became very amiable and useful in the hospital, while she developed great ingenuity and activity in making and dressing dolls. She was induced to go to entertainments, and began to read solid literature.

The month before treatment was commenced she weighed 12 st. 3 lbs.; one month after treatment was begun, 11 st. 11 lbs.; two months after treatment was begun, 10 st. 7 lbs. At the end of two months the extract was withheld, and she began to increase again in weight.

A few weeks after treatment was begun her urine was found to be reduced in quantity from an average of eighty ounces per diem to fifty-nine. There has been no diminution in her appetite, and she has menstruated about once a month since treatment was begun—a condition which has not existed since her disease began many years ago.

Encouraged by these results, I have tried the effect of pituitary extract on two cases of myxœdema. In one severe headache and sickness occurred, so it was promptly stopped. In this case, too, thyroid extract appeared to have no effect. In the other, which has been previously referred to, the patient said she derived great benefit, and it certainly appeared to act as a physical and mental tonic. I have tried the effect of pituitary extract on several cases of insanity, but as a rule with negative results. In one case at least, in whom insanity was associated with irregular and scanty menstruation, mentalisation became less sluggish, dirty habits ceased, the patient began to read and play on the piano, her menstruation became re-established, and her general improvement was marked.

Acromegaly appears to be extremely rare in asylums; in fact, the only other undoubted case I know to have been in a British asylum died at Colney Hatch in 1885. It was under the care of Dr. Robert Jones, who was medical officer there, and, although the disease had not then a name, yet Dr. Jones's

clinical and post-mortem notes at the time leave no doubt of its nature. It has been reported by Dr. Beadles.

From the Continent two cases have been recorded, to both of which casual reference has already been made. One of these occurred in an Italian asylum under Professor Tamburini, another in a French asylum under Professor Joffroy.

The problem of acromegaly is still unsolved. But, despite its rarity in asylums, its future physiological developments will be fraught with interest as great for the mental physician as for any other class of medical men.

Discussion

At General Meeting, Chester, 1899.

Dr. Robert Jones said he had charge of a case in 1884, just a year before M. Marie described the malady. There was then much uncertainty as to the exact diagnosis. He got several of his colleagues from St. Bartholomew's to see the patient. The woman was distinctly ugly. She had thickened lips, a large lower jaw, a very dull look, and frequently complained of rheumatic pains. She passed large quantities of urine. No one was able to give the disease a name. The patient eventually died from gastric hæmorrhage, and a very marked tumour was found replacing the pituitary body. Since then two hundred cases had been reported. The last he saw was a man in the Isle of Wight, at Ryde, who he believed was still at his occupation in a bicycle shop. As Dr. Blair said, there were probably more cases outside than inside asylums. He thought it was borne out by experience that the most constant change was observed in the pituitary body.

Dr. Wigglesworth said it was somewhat doubtful whether the insanity was in this case dependent on the acromegaly or on previous alcoholic intemperance, which last was a very much more common cause. As far as he knew there had been hardly any similar cases recorded. There was no doubt that the pituitary body had been found diseased in a large number of cases, and the conclusion had been reached that that was the cause of the disease. He thought the proof of that was not yet complete. They had negative cases as well as positive. He remembered a case in which the pituitary body was extensively destroyed by a tumour of slow growth, yet there was no acromegaly.

Dr. Mercier said it might be true that the pituitary body might be diseased without acromegaly, yet for all that acromegaly might be the result of a particular pathological affection of that body. They knew that defects in the supra-renal bodies might occur without the ordinary appearances of Addison's disease; but they knew that Addison's disease was invariably associated with and dependent upon a defect of the supra-renal bodies. He should be glad to give the members of the Association an opportunity of seeing a typical case of acromegaly at no great distance from Dartford.

Dr. Nicolson said that he would be most interested to know whether the condition that gave rise to the enlargements arose from the existence of some specific detrimental material supplied to the tissues, or from the want of some corrective material in the nutriment of those particular tissues. By getting at the commencement of the destructive changes of the pituitary body, and by investigating the peripheral portions where the enlargement took place, they might be able to find out cause and effect.

Dr. Campbell said that he had seen two cases of tumour of the pituitary body. In neither were there acromegalic changes, but he had no desire to criticise the views expressed.

Dr. Whitcombe said a case came under his notice lately: a young man 28 years of age, who was an epileptic, and whose disease was diagnosed before admission to

the asylum. He certainly was in the early stage of this disease, as his appearance entirely concurred with that which they had heard from Dr. Blair. He regretted that post-mortem examination could not be obtained.

Dr. BLAIR, in reply to Dr. Wigglesworth, said it was very difficult to find out exactly whether the woman drank to excess or not. They had information that at times she was a little intemperate; but he did not think her insanity was due to alcoholism. Acromegalics nearly always in the end became demented; but he did not know of any other case in which there had been an acute form of insanity.

A Degenerative Form of Syphilitic Insanity, with Clinical Types. By G. A. WELSH, M.D., Assistant Physician, Crichton Royal Institution, Dumfries.

AS an introduction to this paper I have detailed three cases as clinical pictures. My conclusions are based on an examination of sixteen cases, six of which proved recoverable. Case No. 1 is an example of recovery and illustrates the condition found; but it presented no congestive attacks, which sometimes occur during the course of such a case. Cases Nos. 2 and 3 show in addition confirmed muscular and degenerative lesions precluding any chance of recovery; in both, however, there were distinct remissions.

Before passing to general considerations I have formulated in a few sentences the points to be considered. This malady is a degenerative condition of the nervous system primarily attacking the nerve-cells. It closely resembles general paralysis in its clinical manifestations. The progress, however, shows that in some cases the disease is curable; in others, which do not permit of cure, alleviation in the form of remissions can be obtained by antisyphilitic treatment. These cases which progress follow closely that progressive degeneration known as general paralysis.

In studying this form of nervous degeneration the first question to be considered is, "How does the virus act in producing the nervous disorder?" The clinical phenomena give evidence of a degenerative process, and point to the presence of an irritative lesion of nerve-cells (mental and motor). What then is the irritant, and what is the *modus operandi?* The irritant, I believe, is a toxine produced by syphilis; and in using this term toxine I have done so in its widest significance. The evidence