ACROMEGALY.

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Translated from the French original MS. by William Dudley, M.B.

THE disease, the clinical description of which forms the subject of this article, is by no means unknown in England, where it has already been the subject of reports and discussions before the Clinical and the Pathological Societies of London. Among the names of physicians and surgeons who have studied it, we find those of Wilks, Hadden, Godlee, and other able observers. I hope, however, that for the majority of the members of the profession, a formal description may yet prove acceptable, and I have to thank the editor of 'BRAIN' very sincerely, for having kindly furnished me with the means and opportunity of coming forward with such a contribution to medical literature under such particularly favourable conditions.

The first author, to my knowledge, who seems to have observed and described a case of this affection is the surgeon Sancerotti, in 1772; since then, a certain number of observations of the same kind have been published in different countries by various authors, and under the most diverse names—exophthalmic goitre, myxœdema, hypertrophy of the tongue, &c., &c., . . . and "gigantism;" this last designation having been the one most commonly employed, in consequence of the confusion made between this anomaly of development and acromegaly. In 1885 when chief assistant to Professor Charcot, I was able to observe in his ward two cases of this kind, presenting in a high degree the characteristic symptom to be described farther on. Thus I was led to make a special study of this affection, and to en-

deavour to describe it, bringing into prominence the typical phenomena which characterise it. I became convinced that I had before me a distinct *morbid entity*. I did my best to define it in its sharp outlines. In order to complete my task, I selected one of the most prominent symptoms, viz., *a striking non-congenital hypertrophy of the extremities* (hands, feet, cephalic extremity); I proposed for it the name of *acromegaly* (from *ακρον*, extremity, and *μεγας*, large.)

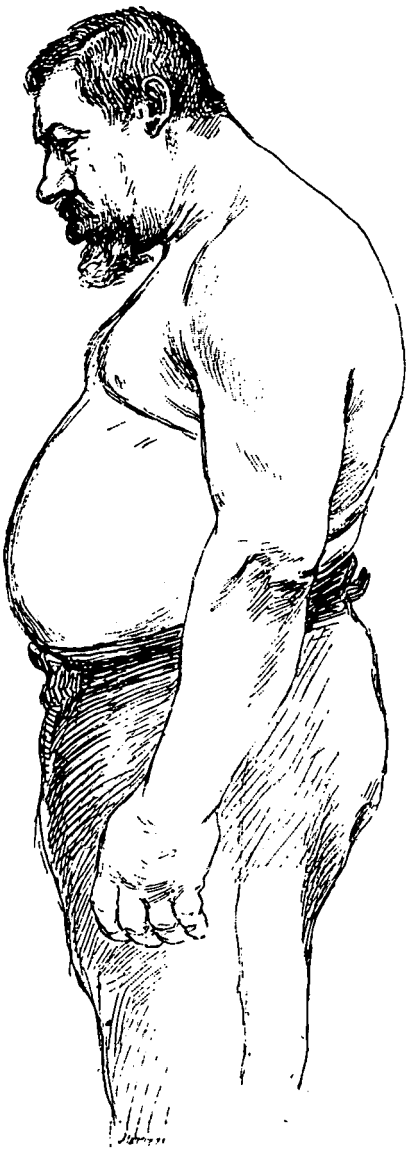
Since this period a certain number of new confirmatory observations have been published and some others which had escaped my first researches have been brought forward; for my own part I have had the opportunity of making an autopsy on one of my first patients, and of studying two new cases; it is one of these last cases, hitherto unreported, that I am now publishing in 'BRAIN.'

CASE.—Baud., age forty-nine, employed in a printing-house. No member of his family (father, mother, brother) has presented any enlargements of the limbs. His father, who is yet living (age seventy-three), is in very good health. The patient himself was very puny at birth (weighed one-and-a-half kilogrammes). At the age of fifteen he had severe typhoid fever. Served his term in the army; has never had any venereal affection (is quite certain on this point). In 1881 had in the scalp over the occiput a very confluent, pustular, very painful eruption; the acute and inflammatory period was of four or five days' duration, he could not sleep it pained him so much, then the pimples dried up.

The patient cannot say exactly since when the limbs have been increasing in size (since he had not attached any importance to it, and had hardly noticed it). This, however, is what he remembers: being a soldier, up to the age of twenty-seven he never wore large shoes, "he was even fitted with shoes rather small than large for his height." Till 1878 no one had ever remarked on the size of his hands; it was only at this time that that began. It seems therefore certain to him that the first symptoms made their appearance between the year 1867 (the date when the patient was discharged from the army) and the year 1878.

At thirty years of age the weight of the patient had already increased a little; he was 80 kilogrammes instead of 64 at 27. But it is especially from 1878 that his weight and size have more manifestly increased; in December, 1887, his weight was 113 kilogrammes; in December, 1888, 106 kilogrammes.

His height (measured barefoot) when the patient was in the regiment, was 1670 mm. At the present time, measured in shoes, (about 2 to 3 cm. in depth of heel), it is 1690 mm.



Present Condition, Jan., 1889. — The appearance of the patient is quite charcteristic (the diagnosis was made in the street); the hands and feet are enormous; the hands present the character stumpy (camard), as well as the fingers; the hypertrophy of the soft parts is such that the patient cannot close his hand in the form of a fist (flexion of the first, second, and third phalanges); all he can do is to flex the first and second phalanges. The tips of the fingers cannot therefore be applied to the middle part of the palm of the hand, but only to the upper part of the latter. The left index finger has had a whitlow (from a splinter of wood), in February, 1888; since then the patient has often experienced at this level the feeling of deadness of the finger. The wrist is thick, but relatively smaller than the hand; the forearm and the arm are equally bulky, without however their dimensions giving rise—as do those of the hand—to the idea of monstrosity; the arm and the forearm are moreover as regards size, in perfect relationship one to the other;

the muscles show very notable development without any hypertrophy; the strength of the patient is great, as a soldier he was the strongest man of his company; since then he has not noticed that he has become weaker out of proportion to his advancing age.

The face is equally characteristic; the nose is large and somewhat pug-nosed. The lower lip is enormous, everted and looks like a hanging pad; the upper lip is rather thick, but is not in this respect comparable to the lower. The lower jaw is very much hypertrophied, the chin forms a marked projection; prognathism is such that the incisors below reach beyond those above from 7 to 8 mm., they are, moreover, neither large nor projecting.

The tongue is very large, very long, rather thick. Articulation of words has become, not difficult, but somewhat confused, probably in consequence of hypertrophy of the tongue and of the soft parts of the mouth.

Neither the eyelids nor the ears are of abnormal dimensions; hair well preserved, rather thick, but has always been so, he says; the beard is rather abundant, slightly curly. The neck is thick and short; there is well-pronounced cervico-dorsal kyphosis, and consequently marked inclination of the head forwards. The larynx is rather large, but it cannot be certainly said to be hypertrophied; the thyroid body cannot be felt sufficiently distinctly for it to be said whether it is normal or not. The voice is strong, the tone of it is not abnormally deep; it is besides very discordant, and it is impossible to make the patient sing the scale so as to measure the limits of it.

The thorax is bulky; the sternum very oblique; the xiphoid appendix very prominent and hypertrophied, makes a very appreciable projection under the skin. The lateral walls of the thorax are a little flattened; the lower part of the thorax moves prominently forward during inspiration. The retro-sternal dulness of Erb has not been able to be determined. The heart is perhaps a little hypertrophied but otherwise seems normal. The pulse is rather small and compressible.

The genital organs present nothing unusual. The penis is rather large, but all the others are of ordinary dimensions. The sexual appetite has never been great and has become lessened during the last few years (it must not be forgotten that the patient is a diabetic). The skin, while not being of a very clear tint, has not however that brown olive colour presented by some patients. Nowhere are vergetures observed, but there is a single growth of molluscum fibrosum on the right shoulder.

Cutaneous sensibility presents nothing to remark; the knee reflexes are present.

Nothing particular as regards the special senses; sight however may have become a little less acute for small print. No ophthalmoscopic examination.

There is very evident dilatation of the veins of the leg, especially in the neighbourhood of the internal malleolus, but only slight varicosity.

The mental faculties are good; the patient has intelligence above his station in life, and he has been self-taught.

He has never suffered from headache—of this fact he is perfectly sure.

The patient's appetite has been excessive, especially for two or three years; likewise his thirst (5 litres on the average, of which 2 litres of wine); to quench his thirst he has to drink much at a time.

Examination of the urine has revealed a very notable amount of sugar. We have before us, therefore, a diabetic, and henceforth it becomes impossible to say if the polyphagia, polydipsia, and polyuria have any relation at all with the acromegaly, or if they do not depend entirely on the diabetes.

Additional Note, May 15th, 1889.—Treatment was instituted in January to combat the diabetes (alkalies, arsenic, diet); the sugar diminished pretty rapidly; now, no trace of it can be shewn with potash-copper solution. At the same time, thirst has diminished, the patient is now much more active, he no longer experiences either lassitude or a tendency to sleep, of which he formerly complained.

	mm.
Length of the hand from the lower fold of the wrist to the end of the middle finger	195
Length of the middle finger, starting from the palmar fold at its base	83
Length of the middle finger on the dorsal aspect, starting from the base of its first phalanx	100
Length of the little finger, palmar aspect	66
Circumference of the hand, without the thumb, at the head of the metacarpal bones	234
Width	95
Greatest circumference of the "obstetric hand"	280
Greatest thickness of the hand (with callipers) at the level of the thenar eminence	57
Circumference of the middle finger	85
Circumference of the thumb	90

	mm.
Circumference of the little finger	75
Circumference of the wrist, immediately below the extremities of the ulna and radius	200
Circumference of the wrist at the level of the styloid process of the ulna	198
Circumference of the forearm (at the middle)	278
Circumference of the arm (at the middle)	315
Length of the nail of middle finger	14
Length of the nail of the thumb	16
Breadth of the nail of middle finger	16
Breadth of the nail of the thumb	23
Length from the iliac crest to the summit of the head of the fibula, (the patient was in bed)	540
Length from the summit of the head of the fibula to the tip of external malleolus...	370
Vertical diameter of the patella	66
Transverse	75
Circumference of thigh (at the middle)	515
Greatest circumference of the calf	400
Circumference immediately above the tip of the internal malleolus	287
Greatest length of foot	280
Circumference over heel and instep	395
Greatest circumference of the foot	265
Greatest width of foot...	104
Circumference of the great toe	110
Circumference of the little toe	70
Length of the nail of great toe	19
Width of the nail of great toe	20
Length from top of forehead to tip of chin (with callipers)	280
Length from top of the forehead to the upper part of nasal bones	79
Length from the upper part of nasal bones to tip of nose ...	63
Greatest width of olæ nasi	35
Distance from the tip of the nose to the point of junction of the latter with the upper lip	28
Length from septum of the nose to the point of the chin ...	80
Greatest distance between outer surfaces of cheek bones ...	136
Width of mouth	55
Vertical measurement of lower lip	16
Transverse measurement of tongue at the middle	90
Thickness of tongue (at the middle)...	190

	mm.
Length of one of the borders of the tongue, drawn out of the mouth, from the tip to the point where this border meets the upper lip	70
Lower jaw, vertical measurement from the free border of the gums to the lower part of the symphysis (with callipers)	44
Distance (with callipers) from the temporo-malar articulation to the lower part of the symphysis of chin ...	145
Distance between the two angles of the lower jaw (with callipers)	116
Ditto (with tape measure along the body of the bone passing in front of the symphysis)	240
Ears, greatest length	62
Ears, greatest breadth...	32
Circumference of the thorax over nipple	1110
Circumference of neck between hyoid bone and upper part of thyroid cartilage	450

Symptomatology.

The description of this patient gives a very correct idea of the usual appearance in acromegaly, and most of the morbid phenomena are sufficiently marked for this case to be regarded as nearly typical.

It will however be useful to trace a general sketch of the disease, insisting on those symptoms, the study of which present special interest, and to point out its course, its different nosographical and etiological characters, and the difficulties which may arise when it has to be distinguished from a certain number of affections.

What characterises it clinically and allows us to make its diagnosis at the first glance, is, as I have shown, the *truly remarkable hypertrophy of the extremities* (hands, feet, cephalic extremity). Certainly there are many other deformities of the most different organs in acromegaly, but from the semiological point of view none seems to me to have the value of this hypertrophy of the extremities. The *hands* are enormous, like battledores; however their general form is almost regular but stumpy (camard), their width being rather out of proportion to their length.

The fingers present the form called "sausage shaped;"

often there is manifest swelling of the articulation of the first and second phalanges (somewhat analogous to the nodosities of Bouchard), with a certain flattening of the finger in the antero-posterior direction. The palmar lines are extremely marked and bordered by enormous folds. The hypertrophy affects not only the skeleton, but in a very marked degree the soft parts also; this hypertrophy of the soft parts is especially developed at the level of the upper part of the hand and at the ulnar border of the latter; there is there, towards the internal part of the hypothenar eminence, a large mass of flesh, which is easily isolated from the fifth metacarpal bone. The nails are flattened, rather widened but short; often they seem too small in consequence of the increased size of the fingers; they are distinctly striated longitudinally, their lateral borders are sometimes curved upwards when the hand is examined with the palm resting on the table.

The wrist itself is generally a little increased in size, but to a less degree than the hand; it is more rarely that the forearm participates in the hypertrophy, and only quite in its lower part; the arm maintains its usual size—sometimes indeed it appears less large in consequence of the flaccidity of the tissues.

On the part of the lower limbs the same characters: the feet are enormous; on their external border the mass of tissue forms an enormous pad. The tendo Achillis may appear increased in size (Saucerotte). The malleoli are generally more or less increased in size; likewise, but to a smaller extent, the head of the fibula and the upper extremity of the tibia. Otherwise the size of the leg is not found much increased. The knees often appear prominent in consequence of the increase in size of the patella, and of the condyles of the femur. The diameter of the thigh is unchanged.

The cephalic extremity presents, too, an increase in bulk, especially marked in the prominent parts of the face. The cranium is but little altered in shape and size, or at least its alterations are not obvious; the face however appears elongated vertically. The forehead is usually rather low, with a very marked prominence of the orbital arches (due

especially to the dilatation of the frontal sinuses). The eyelids are often elongated, sometimes thickened; their tarsal cartilages may be hypertrophied. The nose is manifestly increased in all its dimensions, it is enormous, and in several patients I have seen it take very distinctly the form pug-nosed. The cheeks are generally flattened and elongated. The cheek-bones rather prominent and bulky (not from hypertrophy of the malar bones, but from dilatation of the maxillary sinuses; this prominence of cheek-bones is moreover in part masked by the elongation of the face). The increase in size of the lower lip contributes greatly to give to the patients the remarkable physiognomy which enables them to be recognised at a distance and at the first glance; this lip is protuberant and strongly everted. The upper lip too may be a little thickened, but not in a manner comparable to what has occurred in the lower lip. The chin projects markedly downwards and forwards, it is large and massive; moreover, the lower jaw is altogether considerably increased in size, and as the upper jaw does not undergo the same modifications, a very marked degree of prognathism often ensues. In consequence of the exaggeration in size of the lower jaw, the whole face is found to have a considerable vertical measurement, and takes thus the form of an elongated oval. The teeth undergo no modification in size, but in consequence of the enlargement of the lower jaw they are here seen to be separated a little one from another. The tongue is of enormous dimensions, and in some cases its volume may be estimated at double that which it has in the normal condition, but its shape always remains perfectly regular; the increase in size takes place in all directions, less perhaps in length than in width and thickness. These modifications of the lips and the tongue sometimes impede the patient's articulation.

As for the ears, they do not present always the same characters: sometimes their dimensions are quite normal; in other patients on the contrary they are notably increased.

But it would be a grave error to think when these phenomena—remarkable it is true on the part of the extremities—have been pointed out, that a complete picture of

the disease has been presented; far from it. We shall see indeed that almost all the tissues experience, more or less, marked modifications.

The condition of the spine should especially be described with care if one wishes to have an exact idea of the appearance of the patient, for it influences considerably his attitude. However little the affection be pronounced, there is very marked kyphosis of the upper part of the dorsal region; the patient's head is buried in the shoulders, and his "hump-back" is often the occasion of more than one joke.

Pretty often too a certain degree of scoliosis may be determined, but the latter is always much less marked than the kyphosis; indeed, there may be present in the lumbar region a certain amount of lordosis, this appearing to be compensatory. I cannot enter into a detailed description of the vertebræ; suffice it to say that they are very much hypertrophied.

The neck is generally thick; I have already said how short it is, and this shortness of the neck coinciding with length of chin and kyphosis, it is not rare to see the chin of these patients resting on the anterior surface of the sternum.

For the thyroid body, I cannot say definitely what is its condition; all that I can affirm is that if it seems sometimes a little atrophied it is never absent.

The thorax presents equally special characters. Without insisting here on the increase in size of the clavicles, the sternum and the ribs, I may point out the enormous circumferential measurement of the thorax, the obliquity of the ribs, the development of their cartilages, whence arises sometimes an appearance analogous to that of the rachitic rosary; pretty often too the lower ribs are seen to be strongly forced outwards. The form of the thorax is very remarkable when the affection is well-marked; in fact, this part of the skeleton appears flattened laterally, and on the contrary prominent in the antero-posterior direction; the sternal region is very protuberant and very oblique from above down and from behind forwards; the xiphoid appendix is enormous and its free extremity projects above the level of the sternum.

When the patient is told to make a deep inspiration the forward movement of the lower part of the thorax is quite peculiar. In these individuals respiration seems to be especially diaphragmatic. Professor Erb found in a woman affected with acromegaly a zone of retrosternal dulness, not present in two patients whom I have examined since the publication of this author's paper. Professor Vertraeten however has confirmed the existence of this symptom, which tallies with the state of the thymus in the disease.

I do not wish to insist any further on the malformations presented by the skeleton, as they deserve to form by themselves the subject of a special work, and I shall limit myself, in concluding, to recall the somewhat massive appearance of the pelvis.

The joints are as a rule rather large, sometimes nodose; they are often the seat of cracklings, often also of pains which may be rather acute.

With regard to the muscles, although it is true that in the cachectic period of the affection they appear flaccid and shrunken, it may be quite otherwise in the early stages, and I can affirm that two of my patients, whose stature moreover was not above the average, had muscular strength far above the normal. In the man whose case I am now reporting, the muscular system is really very well developed. Erb has found that in these patients muscular excitability by minimum currents was considerably increased.

If we pass in review the different mechanisms, we discover that a certain number present something abnormal.

Among the phenomena of sensibility, the most notable symptom is headache, which is present in the greater number of cases (but not in all); it may be very intense, and two of my patients who had given but little attention to their deformity had come to receive medical treatment simply for their headache. I have spoken above of joint pains which may be observed. It must be added that in one female patient Erb has discovered slight sensory affections of the forearms and hands.

In the domain of the special senses, sight is most often and most manifestly affected; and when the disease is

sufficiently advanced we observe complete blindness in consequence of compression of the optic nerves by the enlargement of the pituitary body; or else, in less-marked cases, there is only slight visual trouble, but it is already possible to find with the ophthalmoscope indications of optic neuritis.

Hearing may be equally affected; as for taste and smell, we know but little with regard to them.

The skin is generally flaccid, sometimes dry, most frequently presenting a yellow-brown discoloration, sometimes slightly olive and especially marked on the eyelids. Sometimes it is the seat of vergetures: two of my patients had a few pendulous growths of molluscum; it is possible that this is only a common lesion, not depending at all on the acromegaly. The hair and the beard, in all the cases which I have observed, were thick and coarse.

The larynx is generally increased in size, and probably as a result of that increased size, the voice is strong and generally very deep; in one of my patients its compass was from mi_0 to ut_3 (E to C_3).

From the point of view of the digestive apparatus, I shall point out the almost insatiable appetite observed in certain patients, and also the no less excessive thirst. These phenomena moreover are not constant. I have observed them several times, and other authors have also recorded them; they exist in the patient I am now describing but he is a diabetic. Must we attribute the polyphagia and polydipsia to the diabetes or to the acromegaly alone? I cannot say. Finally, is diabetes a usual complication of acromegaly? This again is a question which I cannot decide for want of evidence. I must limit myself now to noting these facts.

The same remarks apply to the quantity of urine which in some cases has been very abundant.

For the circulatory organs, I may mention among the modifications they present, the increase in size of the heart, which I believe is frequent, and the tendency to venous dilatations (varicose veins, hæmorrhoids), which are found more or less marked in most of the patients, if not in all.

The genital apparatus is no more exempt; the penis,

which according to the very true remark of Erb, "is also an *ακρον*," has sometimes (Brigidi, Klebs and Fritsche, and my Spanish patient) dimensions above the normal, but not constantly. Most often there is in the man a diminution of desire and power which may reach to complete abolition. In the woman the most important phenomenon, on which moreover I have insisted in my first work, is the *suppression of the menses*, which is almost always an early phenomenon, so much so in most cases, that it may be considered an initial symptom and one from which the commencement of the disease may be dated. From the anatomical point of view, I may point out the increase in thickness of the soft parts of the external organs of generation (Erb), the unusual dimensions of the clitoris, the prepuce of which is thickened, the width of the vagina and of the posterior *cul-de-sac* (Freund). We can equally, in the woman, prove the absence of sexual desire.

The psychical functions are most often well preserved; sometimes indeed the good humour of the patients contrasts with their miserable condition; in other cases they give way to melancholy which may even lead them to suicide.

Such in its principal features is the clinical aspect of acromegaly. Its course is of very long duration—twenty, thirty years, and even more. The onset in the majority of cases seems to occur between the ages of twenty and twenty-six; but hitherto we have failed to obtain definite data on this point. Since the diagnosis is made only when the affection is very advanced, we have to trust entirely for the period of onset to the patient's statements. At the very commencement the symptoms are but little noticed, except the suppression of the menses or the headache. However, the dimensions of the extremities continually increasing, the patient is astonished to perceive that he has to change his fit as well for his shoes as for his gloves; some individuals do not even notice that they have become prognathous. Later on (but perhaps not always) arise affections of vision which sometimes end in complete blindness. Finally, little by little, the patient falls into a condition of progressive cachexia which necessitates his confinement to bed;

this lasts a few years, and then death supervenes in an unexpected way, with the indications of syncope.

Diagnosis.—It seems that an affection presenting such a group of quite special characters should not offer any difficulty from a diagnostic point of view; in reality it is not always so.

The affection described by Virchow[1] under the term *leontiasis ossea*, will hardly give rise to confusion, for here we are concerned with the development of true bony tumours on the face and the cranium, producing great deformity and a truly hideous appearance; in acromegaly, on the contrary, the bones of the face and of the cranium are the seat of a more uniformly distributed hyperostosis (or rather the increase in size is due much more to the dilatation of the frontal sinuses than to a true hyperostosis), without the formation of osseous tumours or definitely circumscribed bosses. Finally, leontiasis ossea is not associated with hypertrophy of the limbs.

I do not think it any more useful to insist at length on the differences which separate acromegaly from *elephantiasis*, the latter affection consisting in hypertrophy with œdema of the skin and of the subcutaneous areolar tissue without involvement of the skeleton; moreover, it is often unilateral and scarcely ever affects the upper limbs and the face. The aspect of the affected limbs is here completely modified, their contours are completely altered, they form only a shapeless mass; in acromegaly, on the contrary, the prominences and the contours of the limbs remain perfectly normal.

Another affection which is associated with an increased development of subcutaneous tissue, deserves to attract more attention—I mean *myxœdema*, and more than one case of acromegaly has been regarded and published as a case of myxœdema. To avoid this error however it is sufficient to remember that in myxœdema the dimensions of the skeleton are in no way changed, that although the extremities may appear swollen, they are not hypertrophied, and that the face has a characteristic form like a full moon

[1] Virchow, 'Pathology of Tumours.'

(Sir William Gull), whilst in acromegaly the face is considerably elongated and of a very well-defined elliptic form.

There is another disease to which at first sight acromegaly may seem closely allied, although in reality it is quite distinct from it; it is that curious disease described for the first time in England, and in a very remarkable way, by Sir James Paget who has given it the name of osteitis deformans. In consequence of the ambiguity to which this name gives rise—having been already applied to other forms of bone changes of chronic course—I proposed, at the time when I was the first in France to make common the description of this affection hitherto unknown amongst us although several times observed, to give it the name of Paget's disease, at the same time noting that it would be necessary to avoid confusion with the other so-called "Paget's disease," that of the nipple. My proposal was well received, and now this affection is usually designated in France under the name of "*maladie osseuse de Paget.*" I think that this designation will be equally accepted in England as an appropriate one.

The points in which at first sight the *maladie osseuse de Paget* approaches acromegaly are, increase in size of the limbs and increase in size of the head. But if we examine the facts with a little more attention we shall soon be convinced that these analogies are only apparent; the distinctions on the contrary are considerable. Indeed in the bone disease of Paget it is especially the cranial bones which by their hyperostosis produce the increased size of the head; if sometimes the facial bones are themselves affected, it is only to a slight and so to speak accessory degree. In acromegaly on the contrary it is more especially the facial bones which undergo hyperostosis; also in the former the face takes on a triangular shape at the lower part, whilst in the latter it has that of an elongated ellipse, and we have seen that in myxœdema it is rounded "like a full moon," as Sir William Gull has very justly observed.

As for the localisation of the hyperostosis in the limbs, it is far from being alike in the two affections. We have seen that the special character presented by our patients is an

enormous hypertrophy of the feet and of the hands, coming on most frequently without notable change in size of the long bones of the limbs, and, at least, long preceding the latter when it exists, whence comes a strange contrast between the width of the extremities and the slenderness of the limb itself. Now in Paget's disease it is quite otherwise ; the long bones especially are affected, the hyperostosis scarcely ever involving the bones of the extremities, or when it does so it is only in a very slight degree.

In Paget's disease we perceive moreover a very marked tendency in the diaphysis of the long bones to undergo quite abnormal curvatures, whence the name " osteitis deformans ; " except in the case of the spine there is nothing of the kind in acromegaly.

The onset also is quite different : the first of these diseases only manifests itself after the age of forty years ; the second, on the contrary, almost always between twenty and thirty. Further, in the second, invasion of the different parts of the skeleton occurs symmetrically, that is to say, the two hands, the two feet at a time, whilst in osteitis deformans invasion occurs in a much more dissociated manner ; one tibia or one femur is first attacked, the corresponding bone of the opposite limb becoming affected only after a certain time ; and throughout the whole course of the disease the bones of the side first affected may be seen to be more hypertrophied and more deformed than those of the opposite side.

In certain forms of *rachitis* we see patients whose faces seem too large for their stature, and notice especially the prominence of the frontal bosses, of the nose and of the chin. The hands and the feet of these individuals are equally of exaggerated size, and up to a certain point the appearance which they present recalls that of acromegaly ; but there the analogy ceases, and when we examine into details we soon meet with fundamental differences ; moreover, in these individuals we find deformities of the diaphysis of the long bones which do not manifest themselves in acromegaly.

With *gigantism*, the diagnosis would perhaps at first not seem to require long discussion but nevertheless it is

under this title or analagous titles (macrosomia), that several cases of acromegaly have been published; this depends on the fact that the individuals attacked by this disease are sometimes of great stature, and then the increased size of the face and of the extremities being associated with this great height give to the eye the impression of a truly supernatural development, whence a tendency to look upon these patients as "giants." whereas still taller people do not produce this impression. Whatever the explanation may be, in order to avoid the error it will suffice to remark that in gigantism the extremities are in proportion to the stature, that the face is not elongated, that the jaw especially presents neither the hypertrophy nor the prognathism so characteristic of acromegaly. Finally, passing in review the different symptoms proper to this latter, we shall see that they are altogether absent in gigantism.

We must speak now of another affection, the diagnosis of which as distinct from acromegaly, is attended by still greater difficulties. This affection bears no name, and that of the physician to whom we owe the description of the two patients attacked by it could be applied only with an additional designation; "Friedreich's disease" having already the right of a place in nosology. I shall therefore describe this affection by the name of the patients themselves, the brothers Hagner. Here is a *résumé* of the facts with which we are concerned. Friedreich had in 1867 the opportunity of studying two patients, the brothers Hagner, whose feet had begun to increase in size towards the age of eighteen; then the legs, as high as the knees, had become thicker and firmer; two years afterwards both hands began also to become more bulky. When seen by Friedreich, the feet and the hands presented an appearance like that of elephantiasis, but even a superficial examination made it apparent that the increase in size of these parts was produced by an increase in size of the bones. Moreover, certain bones of the skeleton participated in this increased size (clavicles, ribs, sternum, malar bones, &c.). We see here a most striking analogy with acromegaly. In my first work (*'Revue de Medecine,'* 1886), after much reflection

I considered the brothers Hagner as belonging certainly to acromegaly. Since then Professor Erb having had the opportunity of again seeing these patients, published in 1888 *(Deutsches Arch. f. Kl. Med.)* the results of this fresh examination, and thus a certain number of facts were stated precisely which had not been sufficiently mentioned in Friedreich's descriptions. Thanks to this further information, I must now reconsider my first opinion. I may say in fact that the brothers Hagner do not appear to me to be cases of acromegaly; at the same time admitting that I cannot say what they are. Perhaps we have here a hitherto undescribed affection and one which should be isolated from the distinct group of hypertrophies of the limbs. The arguments on which I rely to establish this separation are the following:—

(*a*) The lower jaw by no means presents the very characteristic malformation described in the other patients.

(*b*) There is no increase in size either of the nose, the lips, or the tongue.

(*c*) The xiphoid appendix is small.

(*d*) The neck is slender.

(*e*) The kyphosis is seated not in the cervical and upper dorsal regions, but in the lumbar and lower dorsal.

These are indeed very important distinctions. One might strictly maintain that we have to do with an incomplete form of limited acromegaly, localised only in the limbs and the trunk, and not involving the head or the neck. I confess that this explanation would rather tempt me, but on one condition, which is, that in the form of the limbs we should find exactly the same appearance as that invariably proved in all typical cases of acromegaly. Now there is nothing of the kind. Let the description of the hands and fingers of the brothers Hagner be read, let their appearance be examined in the figures given in Erb's work, and it will be seen what differences separate them from the ordinary type. Likewise for the lower limbs, this complete disappearance of all human shape in the legs—this appearance like elephantiasis, in a word—is by no means characteristic of acromegaly; far from it. In this latter, the contours of

the limbs preserve on the contrary, as a rule, a perfect symmetry, as can be verified on the different figures which we have published; in no case does one see the deformity observed in the brothers Hagner. From all these considerations it must be concluded that the latter should not be included among the demonstrated cases of acromegaly, although in them the extremities of the limbs may certainly have undergone considerable hypertrophy. Indeed this condition of hypertrophy of one or more of the limbs should not suffice when the other characters are wanting and for my part I cannot definitely admit a condition of *partial acromegaly*, which according to Professor Virchow could be deduced from the generalised acromegaly. This method, apparently highly philosophical, tends to nothing less than to create regrettable confusion in clinical medicine. The affection which I have endeavoured to isolate and to describe is one disease autonom and of a well-defined type, and I cannot admit that it should be confused with those unilateral hypertrophies of the face or of the limbs from which in my first paper in the '*Revue de Medicine*,' I had carefully separated it. We know that these hypertrophies may manifest themselves after different types—sometimes a unilateral hypertrophy of the face; sometimes hypertrophy of one or several fingers, or of one foot. We may even see unilateral hypertrophy of the whole body, homonymous, or crossed (one side of the face and one arm, and the lower extremity of the opposite side). But in all these there is indeed nothing which resembles acromegaly. Most often we are concerned with a congenital malformation; moreover, nothing suggests the idea of a progressive affection—the hypertrophy is, so to speak, the sole phenomenon. Finally, this hypertrophy, if it is often localised in *one* extremity, does not attack several extremities in a special way simultaneously; for example, in the case of unilateral hypertrophy of the body. Let established terms therefore be preserved —macrodactylia, macropodia, unilateral macrosomia, &c.; but let us avoid comparing what is not clinically comparable by the thoughtless use of the term "partial acromegaly." That would cause a confusion which could not be otherwise

than prejudicial in the study of an affection yet imperfectly known like acromegaly is.

As for the etiology of this disease, we must indeed confess that we have scarcely any precise data on this subject; in several patients however syphilis could be blamed. In every case I think I can affirm that *heredity* does not play any part; acromegaly is not a family disease; it is not hereditarily transmitted.

Its frequency seems to be about the same in the two sexes.

At the end of this article will be found bibliographical references to the different cases of this affection which have come to my knowledge.

I should have wished in conclusion to pass in review the anatomo-pathological characters of acromegaly, but the study of this is very little advanced yet; for my own part I have had the opportunity of making but one single autopsy. The results of the examination of the skeleton of my patient have been published by my friend Dr. Auguste Broca[1]; this investigation has shewn us that it is especially the spongy tissue (short bones, flat bones, epiphyses) which is the seat of the hypertrophic process, so that the following statement may be considered as representing the reality; "in the skeleton of limbs from cases of acromegaly, hypertrophy shews itself in preference in the bones of the extremities, and in the extremities of the bones."

Independently of the bones of the limbs, I may point out the considerable hypertrophy of the vertebræ, the sternum and the clavicles. The frontal sinuses are the seat of a very well-marked dilatation. Finally, amongst the lesions affecting other organs, and which after what has been observed in other autopsies seem to me to be constant in acromegaly, must be mentioned hypertrophy of the pituitary body with enormous dilatation of the Sella turcica, persistence of the thymus, and finally hypertrophy of the cord and ganglia of the sympathetic system. Until proof to the contrary is brought forward I shall cling to the belief that these last three anatomo-pathological characters manifest themselves not

[1] Broca, *Archives générales de Médecine*, Dec., 1888.

only with a remarkable degree of frequency, but may even be looked upon as constant. The autopsies hitherto published in which these lesions have not been seen, were not of patients suffering of true acromegaly. The clinical picture offered by these cases was certainly different from that observed in the instances which I consider to be typical, and I feel absolutely certain that we have to do here with affections quite distinct from acromegalia.

RATIONAL BIBLIOGRAPHICAL INDEX OF OBSERVATIONS ON THIS DISEASE WHICH HAVE SO FAR COME UNDER MY NOTICE.

A.—Cases which may be considered with certainty as belonging to Acromegaly.

V. BRIGIDI.—Studii anatomopatologici Sopra un nomo divenuto stranamente deforme per cronica infernistié (Societa medico-fisica fiorentina.) Communicated 26 Aug. 1877.

W. ERB.—Ueber Akromegalie (Krankhaften Riesenwuchs) Deutsches Archiv. f. Klin. Med. 1888. T. lxii., fasc. iv., p. 296.

FARGE.—This case is still unpublished. It will appear in June or July 1889 in the *Progrès Medical*. The author is very desirous that I should communicate his manuscript and photographs.

W. A. FREUND.—Ueber Akromegalie. Sammlung Klinischer Vorträge von R. von Volkmann, 1889. Nos. 329, 330.

FRITSCHE ET KLEBS.—Ein Beitrag zur Pathologie des Riesenwuchses. Klinische und pathologisch-anatomische Untersuchungen, Leipzig, 1884.

RICKMAN J. GODLEE.—A case of acromegaly. Clinical Society of London, April 13th, 1888.

W. B. HADDEN AND CH. BALLANCE.—A case of hypertrophy of the subcutaneous tissues of the face, hands and feet, exhibited January 23, 1885—*Clinical Society's Transact.*, vol. xviii. A continuation of their observations on the same disease under the title: "A Case of Acromegaly," read April 13, 1888—*Clinical Society's Transact.*, vol. xxi.

H. HENROT.—Notes de Clinique Medicale, Reims, 1877; and Notes de Clinique Medicale, des lesions anatomiques et de la nature du myxœdeme, Reims, 1882.

LANCEREAUX.—Anatomie Pathologique T. III., 1ère partie, p. 29. Treats of a case of Basedow's disease, with deformation of the skull. In reading this description it appeared to me that the case was one, not of exophthalmic goître, but of acromegaly.

I expressed my doubts to M. Lancereaux and that eminent master graciously sent me all the notes he had preserved about the case. These notes which I expect to publish in treating of the pathological anatomy of acromegaly, show very clearly that the case in question is to be referred to that disease.

CES. LOMBROSO.—Caso singulare di macrosomia. Published at first in the Giornale ital. delle mallattie veneree, &c., 1868, translated by M. Fraenkel in Virchow's Archiv. T. xlvi., p. 253. Republished with considerations on partial osseous hypertrophy in Annali Universali di Medicina, T. ccxxvii., p. 505 et seq.

P. MARIE.—Sur deux cas d'acromégalie, Revue de Médecine, Avril, 1886, 2 cas. L'Acromégalie, Nouvelle Iconographie photographique de la Salpetrière. This second work contains only one new case (No. 1). No. 2, which I had considered as an example of this disease does not apparently belong to it. L'Acromégalie, étude clinique, *Progrès Medical*, Mars, 1889.

O. MINKOWSKI.—Ueber einen Fall von Akromegalie. Berliner Klinische Wochenschr, 1887. No. 21.

SAUCEROTTE.—Mélanges de Chirurgie, première partie, 1801, p. 407 et seq. Case read before the Academy of Surgeons in 1772.

CES. TARUFFI. — Della macrosomia. Annali Universali di Medicina, 1879. T. ccxlvii et ccxlix.

A. VERGA.—Caso singolare di prosopectasia in Rendiconti del Reale Istituto di Scienze e Lettere. Adunanza del 28 Aprile, 1864.

VERSTRAETEN. — L'Acromégalie. Revue de Médecine, May, 1889. This work contains two cases, only the second of which however concerns us here. As to the first, it will be referred to under Section C.

WADSWORTH.—A case of myxœdema with atrophy of the optic nerves—*Boston Medical and Surgical Journal*, Jan. 1st, 1885. It is to Messrs. Hadden and Ballance that we owe the recognition of this case of acromegaly, which, considered as myxœdema by the author, had previously passed unnoticed.

WILKS.—Clinical Society of London, April 13, 1888.

B.—Cases of which Details are wanting, but which very probably belong to Acromegaly.

ALIBERT.—Précis théorique et pratique des maladies de la peau. Paris, 1822. T. iii., p. 317.

W. O. CHALK.—Partial dislocation of the lower jaw from an enlarged tongue—*Transact. of the Patholog. Soc. of London*, 1857, T. viii., p. 305. It was M. A. Broca who first made this case

known, and showed that, according to all appearance, it belongs to acromegaly.

FRED. TRESILIAN.—A case of Myxœdema—*British Medical Journal*, March 24, 1888, p. 642. This case was brought to my notice by Professor Verstraeten.

RUD. VIRCHOW.—Ein Fall und ein Skelet von Akromegalie. Lecture delivered before the Berlin Medical Society 16 Jan. 1889. Berliner Klin. Wochenschr., 4 Februar, 1889. No. 5.

C.—Cases in which the Clinical Aspect differs more or less notably from that of the typical cases of Acromegaly. These probably do not come under the head of Acromegaly at all.

AUG. BIER.—Ein Fall von Akromegalie, Mittheilungen aus der chirurgischen Klinik zu Kiel iv., 1888.

O. FRAENTZEL.—Ueber Akromegalie. Read before the Congrès de Médecin Interne—in Deutsche Med. Wochenschr., 9 Aug., 1888.

FRIEDREICH.—Hyperostose des gesammten Skelets. Virchow's Archiv., Bd. 43, p. 83, 1868. Additional details about these two cases are given in the memoir of Erb, quoted above.

P. MARIE.—L'Acromégalie. Nouvelle Iconographie Photographique de la Salpetrière, 1888. I at first believed the second case here described to be acromegaly, but doubts have since arisen about it in my mind, which are far from being dissipated.

SAUNDBY.—This case was published in the *Illustrated Medical News*, 1889. I had no knowledge of it myself, but the author was kind enough to send me some microscopic preparations and a photograph of the patient. From this last I should be inclined to believe that the case was one analagous to that of the brothers Hagner (Friedreich).

VERSTRAETEN.—L'Acromégalie, *Revue de Médicine*, Mai, 1889. It is the first case in this paper that falls to be considered here. In reading it attentively one sees that it differs very notably from the clinical aspect furnished by the typical cases. I am of opinion therefore that it ought to rank in this third category. I must confess that at first, on looking at a photograph of the patient sent to me by Dr. Verstraeten, I did think that it was a true case of acromegaly; but when I read the detailed description of the symptoms in the *Revue de Mèdicine* doubts arose in my mind about the correctness of this diagnosis.