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THE PITUITARY GLAND AS A FACTOR IN ACROMEGALY AND GIANTISM.

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(*Continued from vol. lxvii, page 453.*)

WHEN we come to look at the general and constitutional symptoms of giantism, one of the things which most forcibly strike us is the short life in most of the reported cases. Dana, out of sixteen cases in which the age of death was given, found only one beyond the age of fifty, and, as this represents the results of a careful research into all the records of giantism for the past two hundred years, and includes a survey of nearly one hundred cases, I think it may be taken as establishing a fair average of the longevity of these huge, abnormal creatures. The following are the ages at death of such giants as I have been able to get the life records of: Charles Byrne, twenty-two years; Cornelius McGrath, twenty years; Winckelmeyer, twenty-two years; James Toller, twenty-four years; the Tall Girl of Basle, "in childhood"; Thomas Hasler, twenty-five years; the "Kentucky Giant," twenty-two years; Lady Aama, eighteen years. From these eight, which are not by any means selected cases, but represent all of simple giantism in which I have been able to get the exact age at death, we should get the average longevity, counting the Girl of Basle at eighteen, which was probably above her real age, of 21.3 years as the average duration of giantism. And when we remember that in several of these cases the abnormal stature did not begin to manifest itself until from the eighth to the twelfth year, we are justified, I think, in the somewhat surprising conclusion that we are actually dealing with a condition, call it disease or not, as we like, which is almost as rapidly fatal on an average as is acromegaly itself, which, as we have seen, may last anywhere from three to twenty-five years.

The next thing which would probably strike us is the decided impairment of the sexual functions in the majority of these huge creatures. So far as I have been able to gather, not more than two or three out of thirty-odd giantesses on record ever married at all, and of the giants only a small percentage. As Dana sums up his conclusion, "giants marry and even have children," but the number who do so appears to be extremely small. None of the giants in the lists given above, with the possible exception of Winckelmeyer, left any children, and, in fact, only one of them was married. And when we consider this fact, with the remembrance that exhibitors and owners of giants, from Frederick the Great down, have been most anxious that these monsters should marry, in the hope that their progeny would inherit the gigantic size of their parents (all of which experiments, I need hardly say, were entire failures, such children as were produced being of normal stature), the fact of this extraordinary indisposition to enter into matrimonial ventures, and marked infertility, is of itself a striking comment upon the low ebb of sexual development in most of these cases. In the few cases in which accurate investigations and measurements of the organs of generation have been made, the external organs of generation have been found to be extremely imperfect in their development; and in my own case the uterus was scarcely more than infantile in size; there was a clitoris so large as to give rise to the popular report that she was an "hermaphrodite," and the ovaries were rudimentary. A similar lack of development was present in Dana's Peruvian giant, in whom the penis was barely three inches in length.

As to the mental symptoms of the disease, in spite of such gory records as *Jack the Giant Killer* and *Og, King of Bashan*, all the accounts which we possess of any value show that giants in the vast majority of instances are a weak-minded, feebly amiable, indolent sort of people. For the most part their intelligence seems to develop little beyond the child stage; and as the disease progresses toward the fatal termination, we have the familiar acromegalic symptoms of weakness both bodily and mental, sometimes the weakness being so great that, on being kept on exhibition, they were obliged to hold on to some support when in the standing posture. There is the same failure of memory in many cases, the same headache, and death usually comes from a general failure of all the vital powers, unless the scene is cut short by the appearance of some ordinarily mild intercurrent disease. McGrath is said to have died as the result of a fall upon the stage, from slipping upon a piece of orange peel. Another giant is reported as dying immediately after a paroxysm of coughing, and Lady Aama died in syncope in the course of a very mild attack of *la grippe*.

As to the sex of these monsters, the male decidedly predominates. Dana, from his study of nearly a hundred cases, says that the giants outnumber the giantesses many times, and out of fourteen cases which have been accurately studied and recorded ten were in males. A similar but less marked preponderance appears to prevail in acromegaly. Out of fifty-seven successive cases, thirty-seven were in males.

To sum up briefly the result of our study of the phenomena of giantism, we find:

1. That the greater part of the overgrowth is found at or near the tips of the segment-crescents, as in acromegaly, differing from the latter mainly in that it is not exclusively confined to the tip of the segment or last division of the limb.

2. That the facial part of the skull is enlarged out of all proportion to the cranial, particularly in the region of the lower jaw.

3. That the condition, whether it be regarded as normal or morbid, is one that distinctly tends to shortness of life, and would appear to have an average duration of scarcely more than twenty years.

4. That the mental and physical vigor of the giant is distinctly below par, and his death usually comes either from a steady progressive increase of this weakness, or from some trifling accident, or usually mild, intercurrent disease.

5. That the sexual powers appear in the great majority of cases to be far below normal.

6. That there is a decided preponderance of males among the victims of this condition; in all of which statements there is a decided parallelism with acromegaly.

Last of all, and from the point of view of this essay of greatest interest, is the fact that the one morbid condition which is peculiar to both these disturbances of nutrition, the enlargement of the pituitary body, is found to be present in a large majority of cases of both.

Hitherto we have been dealing with conditions which can only be regarded as symptomatic indications of some deeper-seated dystrophy or disturbance of nutrition; but the fact of the totally different position of this body from any of the other parts affected, the extraordinary degree of the enlargement which it undergoes, and the constancy of its involvement in all cases in which autopsies have been made, have directed attention to it as the possible causal condition from the very first, more than any other change which is found to be present. The constancy of this change may be judged from the following: We have been able to secure reports from the time of Souza-Leite's essay to the present date of writing of in all forty-eight cases of acromegaly, pure and simple, in which autopsies were held, and in no fewer than forty-four of these the pituitary body was found markedly hypertrophied. In one of the four, in which it was reported as normal, the case of Waldo, the whole base of the cerebrum was found to be the site of cystic degeneration, and from the rapid course of the case and the atypical character of the symptoms presented, several writers have seriously doubted as to whether it is to be regarded as a case of acromegaly at all. In the other three cases, those of Bonardi, Packard, and Frantzel, the pituitary body is reported as "apparently normal," but no microscopic examination was made in any case. But even including this doubtful case, we have this symptom occurring in no less than ninety-two per cent. of all the cases reported in which autopsies were held. On the other hand, it is only fair to say that we have now on record two cases, reported by Packard and Wills, in which there was marked apparently normal hypertrophy of the pituitary body, without any of the characteristic symptoms of acromegaly.

So far we have been considering those cases which were originally regarded and reported as cases of simple giantism, and only a part of which were afterward suspected to be victims of acromegaly. I now wish to call your attention to a series of cases which would be acknowledged by even the most confirmed "dualist" to be, as he would express it, a "combination" of acromegaly and giantism. First of all we may mention those cases of giant skeletons preserved in museums which, after the publication of Marie's paper, were investigated with a view to determining the possibility of their presenting acromegalic features. The first of these was the magnificent memoir of Cunningham, from which we have already extensively

Fig. 3.

quoted, in which he produced conclusive evidence that the Dublin "Irish giant," Cornelius McGrath, was unquestionably a victim of this disorder, and believed that he had strong ground for coming to the same conclusion in reference to the London Irish giant, Charles Byrne, very shortly after. The second was a skeleton described by Taruffi, in 1892, that of a man dying in 1808, and preserved in the museum simply on account of its giant size. Upon investigation the pituitary fossa was found enormously enlarged, the lower jaw markedly increased in size, the hands and feet out of proportion to the rest of the skeleton, and, in fact, Taruffi felt justified in declaring it to have been an unquestioned case of acromegaly in a giant. About the same date Tamburini reported a similar case, which was followed in the autumn of 1893

by the almost simultaneous report by C. L. Dana and the writer of a case of this disease in a giant and giantess respectively, in both of which an autopsy was fortunately secured. Dr. Dana's case was one of such interest that I venture to give a brief *résumé* of it from his account published in the *Journal of Nervous and Mental Diseases*, November, 1893. The subject was a Bolivian Indian, Santos Mamai, thirty years of age, who was exhibited in a "dime museum" in New York, under the name of the "Peruvian giant." He was one of a troupe of Indians who had come for the purpose of exhibiting themselves, but, being unsuccessful, drifted to New York in a bankrupt condition, where Santos

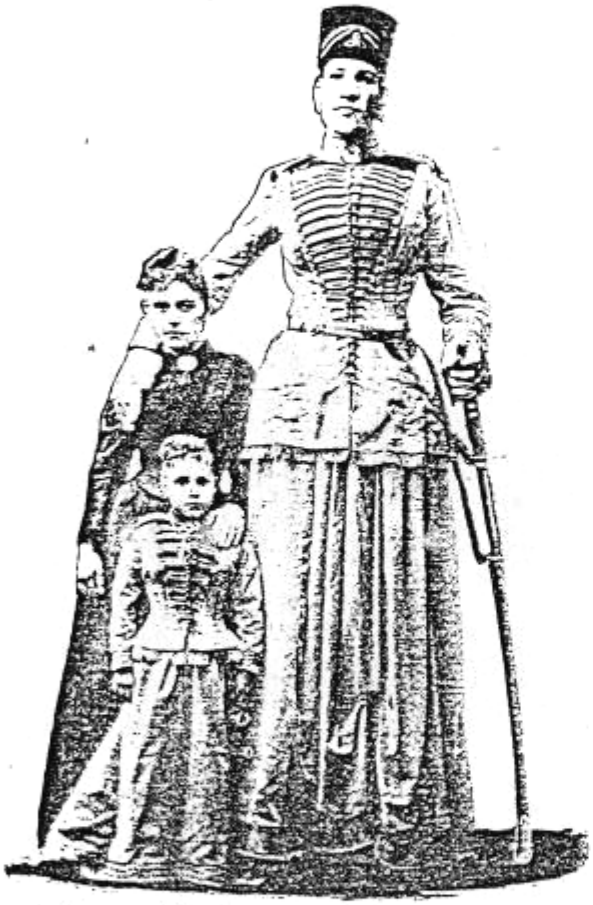

FIG. 4.—Lady Aama and her sisters. Height, six feet seven and three quarter inches. Age, eighteen years.

was taken ill. The principal symptoms presented by him were excessive weakness, mind dull and irresponsive, pulse feeble and rapid, some signs of slight bronchial trouble, but no elevation of temperature. Dana says "he was apparently suffering from no pain, and presented no evidence of paralysis or any manifestly acute disease; he simply seemed to be in a state of collapse. In spite of stimulants, this collapse increased, and he, in the course of four or five hours, passed into a state of coma and remained so until death, about twelve hours after admission." Upon examination after death, his height was found to be six feet seven inches, his weight three hundred pounds. His first appearance instantly suggested to Dr. Dana the possibility of acromegaly, and upon careful measurements of all parts of the body he was found to present a hypertypical case of the disease—huge jaw, immense hands and feet, very prominent malar bones, enormous enlargement of thorax,

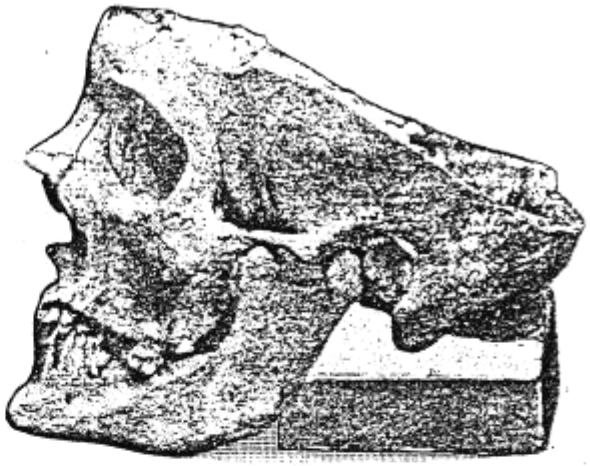

FIG. 5.—Skull of Lady Aama, showing enlarged nasal bone (outlines accentuated by crayon).

kyphosis of the dorsal spine, etc. The pituitary body was found enormously enlarged, and a microscopic study of it will be presented further on in this article.

The case of the writer was in a French giantess, known as Lady Aama, a full report of whose case was published in the *American Journal of the Medical Sciences*, August, 1895. She was eighteen years of age, six feet seven inches and three quarters in height, and died in what appeared to be a mild attack of *la grippe*, after gradually failing in strength for some four or five years previously. Here also the first glance at the face suggested the possibility of this disease, and a

FIG. 6.—Skull of Lady Aama, showing large pituitary fossa and huge frontal sinuses.

series of measurements, as included in the report, corroborated this impression, and showed the characteristic developments in almost every particular. The only unusual or specially characteristic feature was the ex-

tremely imperfect development of the sexual organs. The pituitary body was found to be greatly enlarged, but, owing to the fact that the body was not secured until some days after death, it was so degenerated that

Fig. 7.—The giant Constantine. Born in Germany. Acromegalic in jaw, nose, ears, eyes (divergent strabismus), hands, and feet. Height (alleged), eight feet one inch. The other individual is his father. Mother is also of medium height. Three brothers, all of normal proportions.

it was torn across in removal, and could not be preserved for purposes of study. It appeared to be of about the size of a pigeon's egg, and could be pretty closely estimated from the dimensions of the fossa, which measured an inch and a quarter from before backward, and an inch and a half from side to side (31 mm. × 37 mm.).

Later in the same year, Klebs reported a case of a man exhibited under the title of the "German giant," with the singular history that his overgrowth did not begin until about the thirty-sixth year, after which he rapidly attained sufficiently gigantic stature to make him available for exhibition purposes. The case was found upon examination to be a typical one of acromegaly.

In July, 1894, Sirena, of Palermo, reported a case of fairly well-marked acromegaly in a giant from Cairo.

In January, 1895, Brissaud and Meige reported a singularly interesting case which will be dealt with in greater detail in another connection, that of a man, aged forty-seven years, seven feet high, weighing three hundred and forty-six pounds, who had been exhibiting as a giant for a number of years, and who presented well-marked symptoms of the disease.

Sternberg has unearthed a case of acromegaly in the description of a giantess by J. Wier as far back as 1567, which he not unnaturally is inclined to regard as the oldest case of acromegaly on record.

To these I am prepared to add four new cases, in two of which, however, the study has been so imperfect, and the details to be obtained so meagre, that I must apologize for presenting them at all, my only excuse being their extreme interest in this connection. The first of these is that of the "Kentucky giant," whose skeleton is preserved in the Mütter Museum, College of Physicians and Surgeons, Philadelphia. There was absolutely no history of the case to be had during life, as the body was secured by the museum authorities only upon the condition that no questions should be asked. It was merely known that the body came from Kentucky, and was that of a man supposed to be about

Fig. 8.—Giant Hassan Ali. Probably acromegalic. Age, twenty-three. Alleged height, seven feet eleven inches; real height about seven feet four inches. Length of palm, twelve inches; length of foot, twenty-six inches.

twenty-two years of age. An examination of the epiphyses confirmed the tradition as to his age, the degree of their union indicating the age of twenty-two to twenty-four. Nothing, of course, was known as to the

cause of death, and the body was in such poor condition when received that no investigation or measurements of it appear to have been made. The height of the skeleton from a plane passing through the tuberosity of the os calcis to the under surface of the head of the first metatarsal to the vertex was seven feet six inches and a half. The measurements of the entire skeleton are appended, and we think will be found to show abundantly sufficient evidence to justify us in regarding the case as one of acromegaly. First of all, the pituitary fossa is greatly enlarged, measuring twenty-seven millimetres in antero-posterior diameter and no less than forty-two millimetres in transverse, with a depth of thirteen millimetres (this being more than double the diameters of the fossa, which ordinarily measures about twelve millimetres from before backward, and eighteen millimetres from side to side). Next the lower jaw measures thirteen centimetres from angle to symphysis as compared with the normal male measurement of 9.3 centimetres, a preponderance of 3.7 centimetres, an excess of nearly forty-two per cent., while the excess of the entire stature above the normal

FIG. 9.—Miss Ella Ewing. Height (c), seven feet six inches; age, twenty-three; weight, two hundred and fifty-six pounds.

is barely eighteen per cent. The size of the frontal sinuses, again, is most strikingly increased, as shown by their transverse diameter of 7.5 centimetres, and their antero-posterior of 2.4 centimetres, which is between two and three times the normal size. On the other hand, while the proportional length of the lower limb is slightly greater than that of the normal, yet it is

FIG. 10.

scarcely more than ten per cent., and the size of the hands and feet is a little below the normal proportion to the stature. These last dimensions, however, as pointed out by Cunningham, can not always be relied upon in judging of the actual size of the hands and feet during life, as in some cases of acromegaly the overgrowth appears to confine itself largely to the soft parts, although, as a rule, the bones also participate.

The next case is that of a giantess from Missouri, named Ella Ewing, whom I discovered on exhibition at a Western State Fair. I regret extremely my inability to give accurate measurements in this case, which proved impossible, partly from the natural modesty of the young lady in question, and partly from the well-known reluctance of exhibits of this description to submit to accurate measurements. Her height was given at eight feet two inches, her age as twenty-three, and her weight as two hundred and fifty-six pounds; and as Dr. Dana has declared as a result of his experience with this class of cases that an approximately accurate result may be obtained by deducting from three to five inches from the advertised height of these individuals, this would give her a probable height of about seven feet nine inches. My own estimate of her

height, from such crude methods as I was permitted to adopt by standing beside her and comparing her height with that of normal individuals of known stature in the room, was that she was in the neighborhood of seven feet six inches. Although declining to permit any measurements other than those appended to be taken, I was given the privilege of quite an extensive conversation with Miss Ewing, and she seemed to be perfectly willing to give me any information which was in her power. According to her own statement, she had not begun to grow beyond the normal rate until about nine years of age, when she rapidly shot up to nearly her present level, although she had not yet apparently reached the limit of her growth, as she had gained an inch during the past year. In both the photographs here given I think that the disproportionate enlargement of both upper and lower limbs is so striking as to be in need of no verification by actual measurements. In fact, so apparent was the tremendous elongation of her lower limbs that I was inclined to suspect that her height had been added to by means of some form of stilt. Direct investigation on this suspicion was, of course, out of the question, in view of her sex; but after careful watching I succeeded in getting a good view of her feet, which at once dispelled any suspicions which I had entertained as to the possible use of stilts or artificial feet. They were of such enormous size and clumsy shape that no woman of any age, giantess or otherwise, would have dreamed of counterfeiting them, and her refusal to permit me to measure them was extremely emphatic. It will be noticed, however, that the hand in the second picture descends to apparently below the normal level of the mid line of the femur, but this is probably due to the fact that this member is also greatly increased in length, as is shown by the statement that the spread of her arms was no less than ten feet two inches, a disproportionate development even relative to the stature which reminds one of the anthropoid apes. The length of the hand from the bend of the wrist to the tip of the middle finger was ten inches, an excess of nearly an inch above the normal proportion of her "estimated" stature. But it is in its other proportions that it becomes most characteristic, as it has a circumference of no less than ten inches, and the fingers, though not strikingly thickened, have the peculiar sausagelike appearance of a mild form of acromegaly. No measurements were permitted of the jaw or other parts of the face, but the impression given upon inspection was that both the lower jaw, the nose, and the malar bones were distinctly excessive in their development in comparison with the forehead and cranium; and we think that this shows sufficiently, even in the photograph presented, to justify the statement of this disproportion. Miss Ewing was born in Missouri, and was the only child of her parents, who are represented in the first photograph standing upon either side of her, whose heights are given as six feet two inches and five feet one inch and a half respectively, and who appear to be normal in every particular. She gave no history of any illness other than the ordinary diseases of childhood, her growth having started shortly after an attack of the measles; and the only thing of interest in her previous life was the fact that she had broken one of her tibiæ (her "ankle," as she expressed it) some two years before, simply by jumping down carelessly from the top of a stump about two feet high. She stated that the broken bone had healed without any deformity, but declined to permit me to examine the part. Although no examination of her mouth was permitted, her speech had a distinctly thickened and almost lisping character, which strongly suggested an enlarged tongue. Her intelligence, while normal, appeared to be about that of the ordinary country girl of thirteen or fourteen. She had no disturbance of vision, and denied the existence of headaches, although admitting that she was rather easily tired. There were no symptoms which could be elicited pointing to any marked enlargement of the pituitary body. No kyphosis could be detected, and the girl declared herself to be in every way in perfect health.

While it would be impossible to make any definite statement upon such meagre data, yet in view of the decided impression made by the appearance of the girl, of the excessive development of both upper and lower extremities, the shape of her hands, the disproportionate size of both jaws, as also of the nose, and the lisping speech, I should be inclined to regard the case as an early stage of acromegaly. I shall endeavor to keep watch of the further developments in her case.

There is one other case which I can hardly refrain from mentioning in this connection, although I must admit that for purposes of scientific record it is of the very slightest value. The case was that of a giant who was traveling with a troupe of dwarfs known as the Lilliputians, under the name of "the Giant Caleb," and whom I incidentally saw while attending one of their entertainments two years ago. He was said to be eight feet three inches in height, and he looked every inch of it. His appearance even upon the stage was instantly suggestive to my mind of acromegaly, and when, at the close of the first act, to my great delight, he came out by one of the side doors and proceeded to walk down the aisle for the purpose of allowing the audience to assure themselves that he was a genuine giant, and not a "fake" on stilts, I saw that he was in face, hands, and feet an unmistakably typical case of the disease. The first impression that his face made upon me was a rather singular one, for although large and massive, and with the peculiarly "horselike" expression characteristic of the disease, it at first sight appeared as if the lower part of the face was not developed out of proportion to the upper or cranial portion. But upon closer inspection this apparent symmetry was found to be produced by an enormous overgrowth of the fore-

head, giving it a positively overhanging, prominent, bulging appearance, under which his small, beady eyes twinkled in a positively repulsive fashion. I have no doubt whatever that this was due to an enormous expansion of the frontal sinuses which is characteristic of this disease, inasmuch as the central and posterior parts of the cranium were not in any way proportionate to the apparent overdevelopment of the frontal part. His lower jaw was huge and massive, and his articulation thick and indistinct. His hands were enormous and of the characteristic spadelike shape; while as to the size of his fingers, this was illustrated in a most singular manner by his taking off one of his rings and allowing any one who wished to slip a half-dollar through it, which could be done with ease. His feet also were of enormous size, and he walked with a stoop and shuffle. In an evil moment for myself, I postponed calling upon him, for the purpose of securing, if possible, measurements and a photograph, until the following morning, only to find, to my great disappointment, on going to his hotel, that the company had left on a midnight train, and I have never since secured any trace of him. As I said, the case is simply presented as a naked-eye observation, for what it is worth, and not as a positive addition to the scientific literature of the subject.

This, then, brings the number of cases reported up to thirteen, forming a considerable portion of all the giants which have been reported and investigated during the past ten years, and, in fact, we are not surprised to find it generally admitted even by the "dualists" that a considerable proportion of giants become acromegalic in later life. Sternberg, who has made an elaborate *résumé* of all the cases of both conditions reported up to 1895, although still keeping up a distinction between acromegaly on the one hand and giantism on the other, admits that twenty per cent. of all acromegalic cases are giants, and forty per cent. of all giants are acromegalic and die of acromegaly.

In this connection there are still three other cases to be presented, which to my mind are of peculiar interest as furnishing, if anything further was needed, the essential "missing link" between these two morbid conditions. The first is that of a case reported by Virchow as early as 1889. The patient was a man who could barely be described as of gigantic stature, but was especially distinguished for his enormous strength, and for a number of years was on exhibition as a champion "strong man." Later, however, his strength began to fail, his mind followed suit, and the characteristic symptoms of acromegaly developed. The veteran pathologist includes with this case two others in which, though no gigantic growth occurs, yet a marked increase of muscular development and power appears, rapidly followed by acromegalic decline; and with that wonderful insight which has always distinguished him he announced even then that in his opinion acromegaly was a "secondary stage of degeneration after overgrowth."

The next was the celebrated case of Brissaud and Meige, reported in the *Journal de médecine*, January, 1895. The patient was a man of forty-seven, who up to the age of sixteen had presented nothing unusual in his stature or development. At this age, however, he began to grow rapidly until he reached the height of seven feet. He also developed muscular strength in proportion, and weighed three hundred and forty-six pounds. At the age of thirty-seven, twenty-one years after the first symptoms of overgrowth, he is said to have "strained his back" by lifting heavy weights in some of his exhibition feats of strength. Kyphosis rapidly developed, accompanied by general failure of strength, and in a short time the poor fellow's height was so markedly diminished that he was no longer available for exhibition purposes as a giant, and his strength left him as rapidly as Samson's. His height at the time he came under the observation of the writers was only six feet two inches. He was so bowed that his hands hung below the level of his knees. He suffered extremely from thirst and had night sweats. Both jaws were hugely developed, the cheek bones extremely prominent, and the supraorbital ridges projecting to such a degree as to, in the language of the authors, "resemble those of an anthropoid ape." His tongue was enlarged and the skeletal muscles were generally atrophied.

Last of all, by singularly good fortune I have been able to get a tantalizing although most suggestive glimpse and sketch almost parallel to the preceding, the interest of which, and the circumstances under which it was seen and attempted to be investigated, must serve as its own apology and defense for here presenting it. Two years ago I was in a train on my way to the meeting of the Iowa State Medical Society with a group of medical friends. The party was joined at one of the smaller stations by a local practitioner who, knowing that I was interested in the subject, hastened to inform me that the station agent at the next station was, or, more accurately, had been, a giant, and presented such curious symptoms that he thought it well worth my while to get a sight of him while the train went by, with a view to further study of his case in the future. I accordingly went out on the front platform of the car and, as the train slowed up at the depot, gazed around for the individual in question, but to my great disappointment he was nowhere to be seen, either in his office or anywhere about the platform. However, as the train moved on and brought us opposite the end of the little ticket office, we discovered the poor fellow evidently endeavoring to hide from the curiosity of the passengers behind the end of the building. On seeing us looking at him he promptly stepped forward and made demonstrations with both features and fists, in evident resentment of our perhaps

somewhat inconsiderate curiosity. The train was moving very slowly, and, although the time that he was under observation was very short, yet the impression he made was a most striking one. He was a young man apparently considerably above the average height (as he stood there I should say six feet seven inches), with an extraordinarily elongated countenance and projecting jaw, and of a dirty yellowish or earthy complexion. He stooped tremendously, so that evidently his original height had been much greater than it then was. His eyes were small and sunken, his brows projected; his arms were long and ungainly, and hung down in front of him in the most simian fashion; his hands were huge and misshapen, and his feet perfectly enormous. In fact, the entire impression was positively a repulsive one, and the poor fellow bore a most striking resemblance to one of the great anthropoid apes, a likeness which his threatening gestures and grimaces in no way diminished. We afterward learned that the man had become a local wonder to such a degree that nearly every train which passed his station would bear one or more curious gazers, and he had hence been gradually goaded into this childish but pardonable method of screening himself from such unwelcome curiosity. We were told that he had been persuaded to come and have himself examined by the members of the State Society in the hope that some one might be able to suggest some method of relief for his trouble, but this proved to be an error. Shortly after my return home I wrote to one of my fellow practitioners in the nearest town, asking him if he would kindly call upon the patient and elicit his history, and, if possble, have a photograph taken and make some measurements, intending, if the opportunity seemed favorable, to go down and make a careful study of the case myself. My friend kindly called upon the station agent, but was instantly met by a flat refusal to communiciate any information whatevr or allow any measurements, and least of all any photographs, to be taken. The poor fellow had grown so sensitive over the curious remarks and inquisitive looks to which he was so constantly subjected that the mere mention of his defects or request for their study produced in him a perfectly uncontrollable irritation. All that my friend, Dr. Bell, to whose kindness I am much indebted, was able to elicit was his name (of which, out of consideration for his feelings, the initials only will be given), his age, and a few of the details of his history. Mr. K. H. was thirty-two years ago and born in Missouri. In boyhood he began to show signs of great stature and strength, and as early as thirteen years of age was a local celebrity on account of his remarkable muscular development. At eighteen years of age, nearly fourteen years ago, he believed that he had "overstrained" himself in pulling against a team of horses, which was one of his exhibition feats. Only a short time after that, curvature of the dorsal spine began; although this had not interfered sufficiently with his height and strength to prevent his exhibition as a giant at the World's Fair in 1893, yet since that time its progress has been so rapid that he had lost so much of his height as to be entirely disqualified for exhibition purposes, and he had accordingly accepted the position which was offered him by the railroad company as station agent. His strength, however, began to fail much earlier, so that within three or four years from the time of his strain he was no longer capable of exhibition feats of strength. His height was stated to have been originally seven feet four inches, but his present stature certainly did not exceed six feet five inches or six feet six inches, although his stoop was so enormous that one could readily believe that he might at one time have attained the former alleged height. No measurements, of course, being permitted, we are obliged to simply depend upon the statements or impressions made upon the eye at the time of this conversation. As to his hands

Fig. 11.—Minnesota giant with partial (hemifacial) acromegaly. (Dana.)

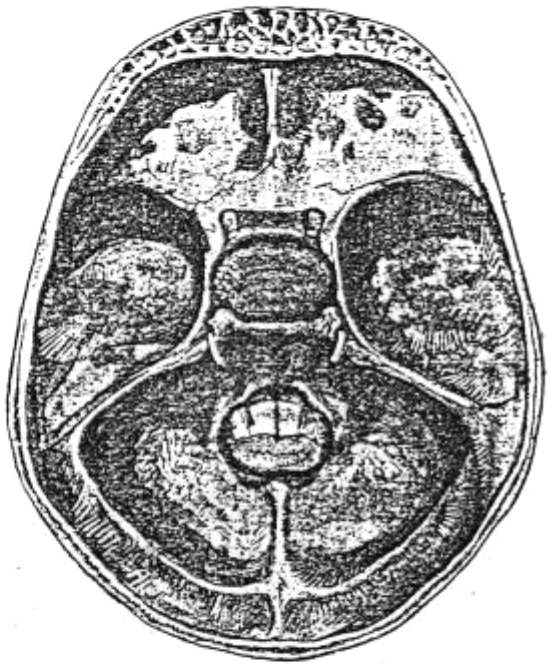

Fig. 12.—Base of skull of Minnesota giant, showing huge pituitary fossa and enlarged frontal sinuses. For account of autopsy see appendix.

and feet, the enlargement of these was so striking as to need no measurements in support of the fact that they were immensely hypertrophied. His hand, for instance, was so large that he could readily grasp an ordinary dinner plate and lift it with his right hand directly from a flat surface, which must have involved an expansion from thumb to middle finger of at least fifteen inches. This had been one of his exhibition feats. The hands were also of the characteristic spade shape, and the fingers thickened and bolsterlike. As to his feet, they were the principal source of suffering to his sensitive nature, as they were the facile butt of the delicately personal shafts of wit of the country neighborhood in which he lived. The most widely

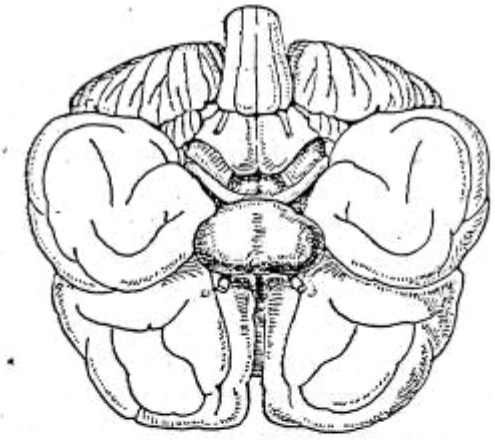

FIG. 13.—Base of brain of Minnesota giant, showing pituitary tumor.

admired of the *jeux d'esprit* of which they formed the subject was the declaration of a local satirist that whenever he had new shoes made, each one had to be brought from Chicago in a separate box car.

His general health appeared to be fairly good, except, of course, that he was not as capable of sustained exertion as a man of average proportions and development, and his mental condition seemed to be about the average, and was said to be quite equal to the clerical and other duties of his position. There, however, seemed to be little question that he was developing a degree of irritability and childishness in his methods of showing resentment at exhibitions of curiosity which was perhaps even more than could be normally accounted for by the many really trying attentions to which he was subjected.

Another attempt was made later to obtain measurements and a photograph, but was again met with an angry refusal, Mr. K. H. declaring that he was not going to have "them there doctor fellers" make an exhibition of his peculiarities before the public as long as he could prevent it. Probably a photograph might have been obtained by means of a concealed kodak, and a few measurements by the adoption of a little modern journalistic "enterprise." But the poor young fellow's sensitiveness was evidently so genuine, and his mortification so bitter over the coarse though not unkindly meant ridicule to which his deformities had subjected him, that I did not feel that even the demands of scientific investigation would justify me in such a procedure. I am, however, still keeping watch of the case, and shall hope at some future time to be more successful in overcoming his reluctance, or, if the worst comes, as his evidently rapidly weakening condition would seem to render quite probable, to be able to obtain measurements and photographs after death.

The impression made by the appearance of Mr. K. H. was so striking that I have no hesitation in declaring my opinion that he was a typical case of acromegaly beginning in early life, and producing first of all those manifestations of that stage of the disease which we call gigantism, and later revealing itself in its usually accepted form.

Last of all, since the publication of this paper was begun, I have secured the photograph and history of another acromegalic giant from Minnesota. For these I am indebted to the great kindness of Dr. C. O. Cooley, of Madelia. The person, James McIndoo, is a boy of eighteen years, the second son in a family of eight children, all of whom, together with the parents, are normal and healthy. His weight at birth was nine pounds, and his size and development attracted no special attention till he was about thirteen years of age, when he began to grow very rapidly, and he has now reached the height of seven feet one inch and the weight of three hundred and eight pounds.

His intelligence is about that of a boy of ten and, though his muscular strength is great, his movements are slow and imperfectly coordinated. His appetite is enormous, and he sleeps from fifteen to twenty hours at a stretch. His chest is huge, measuring forty-nine inches and a half on full inspiration, with an expansion of ten inches and a half. His sexual development is backward.

The acromegalic characters are: 1. The disproportionate size of both hands and feet, which is well seen in the photograph. His foot is sixteen inches long, or two inches above the normal one sixth of his stature. His hand has a span of fourteen inches, or forty per cent. above the normal, while his stature is only twenty-five per cent. above normal. 2. The thick, cushionlike shape of his feet, though his hands are comparatively well shaped. 3. The great size of the facial portion of his skull as compared with the cranial. He can wear a No. 9 hat and his cranial circumference is only twenty-six inches, or three inches above the average, and much of this is probably due to enlarged frontal sinuses. 4. The huge size of the orbit compared with that of the palpebral aperture, probably due to enlarged malars and frontal sinuses.

These figures and descriptions are, of course, in the nature of the case and from the rarity of the disease, few in number as yet, and not such as to justify us in any very positive statements in regard to the identity or

difference of acromegaly and gigantism; and yet, so far as they go, they point so constantly in one direction that we are, in my mind, justified at least in the tentative conclusion, until some evidence to the contrary can be adduced, that acromegaly and gigantism are simply different expressions of one and the same morbid condition; in other words, that acromegaly is a general overgrowth tendency which does not, for some reason, begin to express itself until after adult stature has been reached, and which consequently expends itself upon those points in the body at which growth last ceased—the extremities of the segment crescents and the distal extremities of the appendages. Second, that gigantism in a large majority of cases is this same condition manifesting itself in childhood or before complete stature has been reached, and the growth in consequence is more symmetrical and less strictly confined to the last segment of the arches and appendages. In most cases, however, the tendency appears to be for these last segments to grow in an unsymmetrical and excessive manner. Third, that in view of the short-livedness, the sterility, the feeble mentality, and weak, clumsy bodily development of giants, we are justified in regarding both acromegaly and gigantism as distinctly morbid conditions of very nearly the same course-history and degree of fatality. Last of all, that in the remarkably large percentage of all carefully studied cases of both diseases in which hypertrophy of the pituitary body is found, we have what appears to be the common pathological basis of both these morbid conditions.

We will now proceed to study somewhat in detail first the frequency and extent of this interesting hypertrophy and, second, the apparent nature of the overgrowth so far as it can be judged from the cases in which microscopic examinations have been made. As I have already stated, we have now on record forty-eight cases of acromegaly in which autopsies have been held. Out of these forty-eight cases the pituitary body was found enlarged in no less than forty-four, giving a percentage of nearly ninety-two. This list includes only two of the cases already mentioned in which the subjects were giants or giantesses also; and in the so-called pure giants outside of this we have nine cases recorded, in no less than eight of which, either from the state of the pituitary fossa after death or from the local pressure symptoms during life, an enlargement of this body may be affirmed, making a total of fifty-four autopsies, in only five of which pituitary hypertrophy was not found. This preponderance in this list which I have collected, and which I believe is the most extensive hitherto published, is also confirmed by the experience of almost all other observers who have reported upon this phenomenon. For instance, Dana, in his paper already referred to, reports this condition in nine out of the eleven autopsies which he had been able to collect up to that date. Tamburini, in a recent article in the *Rivista sperimentale di freniatria*, reports twenty-four cases of acromegaly in which an autopsy was held, in which the pituitary body was found hypertrophied in seventeen; but, as no less than five of the cases in which it was not so found are rejected by him as extremely doubtful, and probably not cases of acromegaly at all, and in the other two the examination was made within six months after the first appearance of the symptoms of the disease, we are, I think, justified in excluding at least half of these seven for purposes of this comparison, which would give us seventeen out of twenty-one cases. In November, 1897, Percy Furnwall reported in the *British Medical Journal* thirty-four autopsies, in only three of which enlargement of the pituitary was not found.

The amount of this enlargement varies very considerably, but is always both striking and out of all proportion to the enlargements which take place in any other part of the body. The normal weight of the glands varies quite considerably in healthy individuals, but within comparatively narrow limits as compared with its enlargement in this disease. For instance, Dr. Boyce, in a careful study of the gland, based upon an examination and weighing of over a hundred cases, finds its normal weight to vary from 0.3 to 0.6 of a gramme, the average weight being 0.5 gramme. The smallest case of enlargement in which the weight is given is three grammes, and the largest reaches to no less than thirty-one grammes, so that the hypertrophy is an evident and striking one. In the great majority of cases, however, weight measurements are not given, and our estimate must be based upon either the measurements of the gland itself or upon those of the pituitary fossa. The normal size of this appears to vary more than that of the gland on account of the irregularity and indefiniteness of its anterior and lateral borders, the former being formed simply by the olivary body or roll, and the lateral boundaries by the anterior clinoid processes, which may vary somewhat in the degree of their divergence without any necessary relation to the size of the body which lies between them. Indeed, in some perfectly normal skulls these processes are so short and so divergent that there can hardly be said to be any bony lateral boundaries to the brim of the fossa at all. On the other hand, in other cases so great will be the forward projection of the dorsum sellæ and posterior clinoids that the fossa will assume the proportions of a transverse slit rather than its usually comparatively circular outline. However, this range is, like that of the pituitary body, within comparatively narrow limits, certainly as contrasted with its size in acromegalic skulls. It would vary from ten to fifteen millimetres in its antero-posterior, and from twelve to twenty millimetres in its transverse diameters, while its enlargement in the cases in which measurements are given would reach an average antero-posterior diameter of about twenty-five milli-

metres, and a transverse of about thirty-five. For instance, in Holsti's case, the measurement was 25 × 30 millimetres; in Hensot's, 30 × 42 millimetres; in Brigidi's 28 × 38 millimetres; in Heron's, 32 × 38 millimetres; in Dana's, 30 × 31 millimetres; in Lady Aama, 31 × 37.5 millimetres. These measurements will represent a fair average of all cases in which accurate measurements were given, those of Byrne, McGrath, and the "Kentucky giant" all coming within a few millimetres of these measurements. On the other hand, the cases in which the measurements are not given appear to have been considerably above this size, one of Marie's cases being described as "large enough to contain a tangerine orange," another of the size of a "hen's egg." In Taruffi's it was the size of a "small apple," so that it will readily be seen that in no case was the enlargement of the fossa much below double the normal average development, and in some cases its diameter appears to have been three and four times the normal. Thus it is obvious that not only is the situation of this enlargement as far removed as anything could be from the characteristic "acro" situation of the other overgrowths, but it is also utterly beyond all proportion to either the general body growth or any one of the other enlargements, which, as has been shown, are seldom more than, in the case of the stature, from fifteen to twenty per cent., and in the case of the local overgrowths from ten to forty per cent. above the normal size.

As to the occurrence of this enlargement in those cases in which autopsies were not held, nothing can, of course, positively be said, but we have strong corroborative evidence of it in the fact that in more than sixty per cent. of all these cases which had reached any distinct degree of development there were disturbances of vision or other pressure symptoms pointing to an enlargement in this neighborhood, and in practically all cases more or less "vertical" headache and sense of pressure.

Before proceeding to consider the somewhat more difficult question of the nature of the overgrowth in these cases, I would like briefly to call your attention to such scanty information as I have been able to gather together in regard to the condition of this body in the opposite body condition—namely, in that of dwarfism. Strange as it may seem, the number of dwarf skeletons preserved in museums in this country appears to be even smaller than that of giants, and a tolerably exhaustive study of the principal museums of our larger cities has only resulted in the discovery of four skeletons of dwarfs, three of whom were obviously and confessedly rhachitic, and one was a dwarf from the purely mechanical reason of a frightful spinal curvature, evidently due to tubercular caries. My attempt to study living dwarfs has been almost equally peculiar in its results, as out of a total of six specimens, upon only two of which I had any opportunities at all for a careful study, two were obviously rhachitic, three the victims of hereditary syphilis, as plainly shown in their teeth, noses, and cornea, and one a cretin. So that from my own altogether too limited personal experience, I am decidedly impelled to doubt whether the "normal dwarf" exists any more frequently than the "normal giant." A professional friend of mine, who has made some study of this same subject in the European collections, has come to nearly the same conclusion, and informs me that the vast majority of dwarfs whose skeletons are preserved are either rhachitic or cretinous, and that he has never yet succeeded in discovering a skeleton of a dwarf which could be in any sense regarded as normal. I append the measurements which I was kindly permitted to make of two dwarfs, one of them preserved in the Mütter Museum in Philadelphia, and the other in that of the Medical Department of the University of Pennsylvania. In both of these the proportions of the lower part of the face are distinctly diminished in comparison with the cranial development. The proportion of the lower limb in No. 1 is barely forty per cent. of the entire height instead of over fifty per cent., as it should be. In the second case it is about forty-two per cent., while the length of the trunk in both cases is, considering the extremely short stature, extraordinarily near to that of the average individual. Not only this, but, as will be instantly noted upon examination of the inclosed print (kindly given me by the curator, Dr. Hinsdale, to

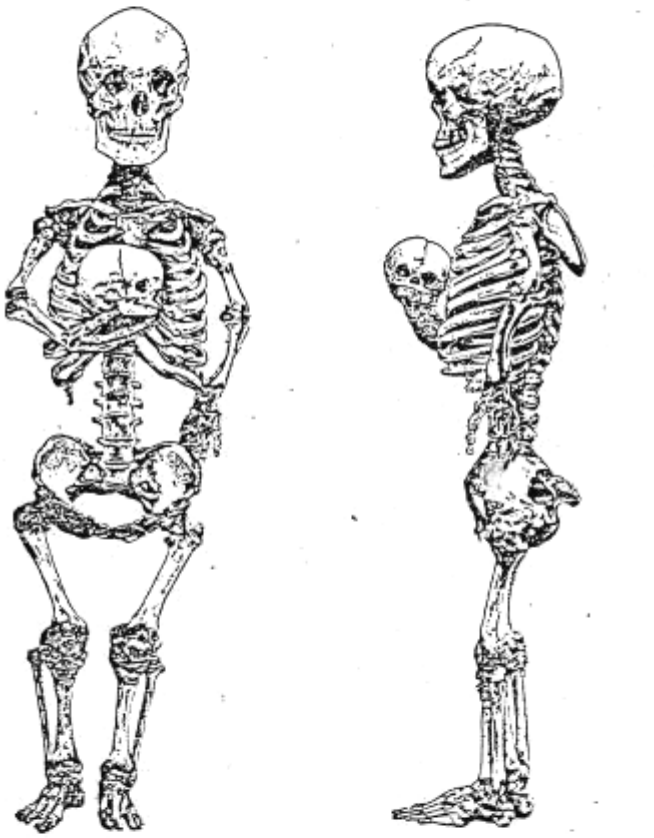

FIG. 14.—Skeleton of rhachitic dwarf, with skull of infant whose attempted parturition caused her death (Mütter Museum).

whose courtesy I am indebted for many valued privileges) of the skeleton of one of these, the positions of the greatest shortening in this skeleton are precisely those of the greatest amount of enlargement in the acromegalic skeletons—in the hands and feet, and at the growth lines of the bones of the extremities. In fact, the more carefully one compares the skeleton of the rhachitic dwarf with that of the acromegalic giant, the more forcibly is one impressed with the truth of Klebs's statement that giantism and dwarfism are both diseases arising from similar disturbances in growth, and analogous to acromegaly; in fact, that the giant is the result of an excess of growth processes in certain special situations, while the dwarf is the result of a diminution even of the normal degree of this growth-tendency, expressing itself in precisely similar situations. I have also had the opportunity of examining the skulls of three cretins in the celebrated Hyrtl Collection in the Mütter Museum, the measurements of which I append; and although, unfortunately, we have no record of their stature, yet in two out of the three there was a most striking diminution in the size of the pituitary fossa, although, as will be seen, the cranial development of the skull was quite close to the average. In the one case its dimensions were only four millimetres from before backward, by eleven from side to side—a mere transverse slit. In the other, its dimensions were eight millimetres from before backward, by nine from side to side, which must be compared with the average diameters of twelve by fifteen millimetres. In the third skull the proportions were more nearly normal, though distinctly below the average measurements, being nine millimetres from before backward, by twelve from side to side. The arches of the maxillæ, however, appeared upon measurement to be nearly normal, although the decided impression made upon the eye by a profile view of the skull was that they were not developed in the same proportion as the cranial part of the skull.

In this connection it is of great interest that Virchow, nearly forty years ago, in his classic work upon *Die Entwickelung des Schädelgrundes* figures the longitudinal section of three cretin skulls, in two of which the pituitary fossa is reduced to little more than a deep, narrow, transverse slit, in the one case overhung by the forward-curving posterior wall (dorsum sellæ), and he speaks of a singular shortening (*Verkrümmung*) of the skull base, attended by what he terms "sphenoidal kyphosis," as characteristic of the cretin skull.

We are now prepared to study the nature of the overgrowth in those cases of acromegaly in which a microscopic examination was made of the gland. In the first place, the almost universal testimony of all who have made even naked-eye examination of the gland is that the hypertrophy is chiefly confined to the anterior or buccal lobe of the body, the true glandular portion. In most of the cases in which any statement as to the nature of this growth is made which is not followed by microscopic examination, the assertion is that it appears to be a "genuine hypertrophy" of the gland substance proper, with a somewhat thickened capsule. This hypertrophy usually maintains a shape and formation quite similar to that of the normal gland, although it is frequently lobulated, usually in transverse folds in its lower and anterior portions. As we shall see, the reports of the microscopic findings vary somewhat in the terms which they apply to the growth, but we think that with the assistance of the specimens which we are prepared to present, nearly all of these can be grouped under one heading. The first question which of course suggested itself to investigators of this subject was as to whether the pituitary body might not simply be the site of some morbid neoplastic formation, either tuberculous, gummatous, or malignant. But this question may be practically regarded as set at rest, inasmuch as in no case of accredited acromegaly has the overgrowth presented any of the distinctive features of any of these formations, with the exception, as we shall see, of sarcoma. Further than this, we have now upon record no less than five cases of carcinoma of the gland reported by various observers, in which no acromegalic symptoms whatever were present, unless headache, disturbances of vision, and other local pressure symptoms could be so regarded. Woollcombe has also reported (*British Medical Journal*, June, 1894) a case of Virchow's psammoma of this body, in which only the local pressure symptoms were present. Cecil Beadles (in the same journal, December, 1896) has reported three cases of enlargement of this body, one tubercular and two gummatous, no one of which presented any acromegalic symptoms whatever. Bury has also reported three cases of apparent fibroma of this body with again no characteristic symptoms. So we have already a total of twelve cases of tumor formation in this body without the production of a single true acromegalic symptom, and, on the other hand, we have only two cases of even apparently normal or true hypertrophy of this body (those of Packard and Wills) in which no such symptoms resulted.

(To be concluded.)