alcohol, but not in water. It is a compound of acetic acid with the alkaloid benzoyl-aconine, the latter being a compound of benzoic acid with the alkaloid aconine. Both of the two last-named occur to a greater or less extent in aconite, as derivatives of the first. Neither possesses the properties of aconitine, nor are they poisonous. To the incompatibilities of alkaloids in general, aconitine adds that of being decomposed by alkalies, owing to its peculiar composition, as above described.

The properties and uses of the alkaloid are fully stated under the title *Aconite*. Its activity is, however, so intense that it has to be used and handled with the most extreme caution, as will be appreciated when it is considered that there is but a half pound of it in a ton of aconite, yet the safe dose of aconite is limited to about five grains.

Its external use is for the relief of rheumatic and neuralgic pain. The ordinary commercial alkaloid has been used in ointment up to two-per-cent. strength, but that of the pure crystalline alkaloid should be limited to .2 of one per cent. There is great danger of absorption, and it should be applied only to the unbroken skin. Internally, it may be used in pill form or in freshly made solution, in doses of gm. 0.0001 to 0.0003 ($\frac{1}{1\,6\,6\,6}$ to $\frac{1}{5\,0\,0}$ grain), and not more than ten times these amounts per day.

Japaconitine, from Japanese aconite (*A. Japonica* Thunb.), is apparently identical.

Pseudaconitine, from Nepaul or Indian aconite (*A. ferox* Wall.), is equally poisonous. Its properties are under investigation, and it is not unlikely that it may be found worthy of introduction.

H. H. Rusby.

ACORMUS. See *Teratology*.

ACROCHORDON. See *Fibroma of the Skin*.

ACRODYNIA, or Epidemic Erythema.—A somewhat obscure disease, said to bear considerable analogy to pellagra. It was first observed at Paris in 1828, occurring there as an outbreak in one of the infirmaries for old men. The epidemic subsided during the winter months to break out again in the spring, but was considered to have been extinguished during the severe winter of 1829–30. A few cases, however, were noted from time to time during the years 1830 and 1831, since when the affection has not again been observed in Paris. In Mexico, in 1866, during March and April, an epidemic said to be acrodynia broke out among the Mexican and Algerian soldiers at Zitocuaro.

On the Continent it had been observed on a small scale since 1831, chiefly among Belgian and French soldiers and prisoners, the last occasion being in a French regiment stationed at Satory, near Versailles, in 1874. This epidemic was not very clearly demonstrated, however, to have been one of acrodynia, and of late the existence of such a disease has even been questioned. The general symptoms are said to be in some respects similar to those of chronic arsenical poisoning. Commencing with gastro-intestinal irritation, redness of the conjunctiva, œdema of the face or limbs, there are soon added formication, pains in the fingers and toes, a burning sensation, and pricking or shooting pains in the palms and soles, and a feeling of weight in the extremities, especially the lower. Hyperæsthesia of these parts, especially the soles of the feet, and sometimes anæsthesia, are present. Cramps, spasms, and tetanic contractures are almost always constant symptoms. There is no fever, and the disease is rarely fatal, except in the old and feeble or from the diarrhœa which is present in all cases, recovery taking place in a few weeks or months.

The chief cutaneous manifestations of the disease are erythematous and pigmentary.

The erythema makes its appearance early in the course of the disease and may be very general, affecting, however, chiefly the extremities, more particularly the hands and feet, and here especially their palmar and plantar surfaces. It may be preceded or accompanied by the formation, chiefly on the hands and feet, of vesicles or bullæ filled with a clear or at times more or less sanguinolent effusion, and is followed by desquamation or exfoliation of the epidermis, while a dark brown or blackish pigmentation spreads itself over the abdomen, chest, axillæ, and other parts, being more pronounced in the warm region of the body. Alibert, in his description, the only one coming from a dermatologist, says ("Monographie des dermatoses," Paris, 1833, p. 12) that what particularly attracted his attention in most of those afflicted with the disease was this black color which affected the integument, nearly all who presented themselves for treatment having the tint of a chimney sweep.

The pathology of the disease is obscure; there are no special post-mortem changes, but in several cases inflammation of the pia mater and spinal arachnoid was found. Though the disease bears a close resemblance to pellagra, the general and cutaneous symptoms are more varied in acrodynia than in pellagra; and while in the latter the backs of the hands and feet are attacked, it is the palms and soles that are affected in the former. The disease was regarded (Chomel, Récamier, etc.) in Paris as being due to spoiled cereals, but nothing positive on the score has been proven. The most efficient treatment was claimed to consist in counter-irritation of the spine.

Charles Townshend Dade.

ACROMEGALY, or Akromegaly (ἄκρον, extremity; μέγας, great).—(Synonyms: Acromégalie; Akromegalie; acromegalia; pachyacrie; Marie's disease.)

Definition.—Acromegaly is a chronic disease, characterized by an abnormal increase in the size of the extremities of the body, viz., hands, feet, and generally head, due to a hypertrophy of the bones and soft parts of these regions.

History.—The first to recognize this disease as a separate entity was P. Marie, who wrote upon this subject in 1886. This first article of Marie's describes two cases which he had discovered while first assistant to Professor Charcot. He named this disease "Acromégalie" because he found all the extremities of the body enlarged, viz., hands, feet, and cephalic extremity, while von Recklinghausen suggests the name of "Pachyacrie." Since the publication of Marie's first paper, in 1886, a number of cases, reported in literature under various titles, have been discovered, which in all probability were cases of acromegaly.

On the other hand, since 1886, a number of cases have been reported as acromegaly which I do not believe to be cases of that disease. The first cases discovered and reported as acromegaly (in 1885 Wadsworth reported a case as myxœdema which was undoubtedly acromegaly) in America were those of Drs. O'Connor and Adler, both of which were published in 1888.

A complete study of this disease can be made by reference to the New Sydenham Society Reports, London, 1891; to Dr. Joseph Collins' articles in the *Journal of Nervous and Mental Diseases*, December, 1892, and January, 1893; to the alphabetical bibliography in the writer's article in the *Yale Medical Journal*, December, 1897; to Dr. Guy Hinsdale's monograph in *Medicine*, 1898; and to the chronological bibliography of Dr. Harlow Brooks in the *Archives of Neurology and Psycho-Pathology*, vol. i., No. 4, 1898.

Symptomatology.—*General Condition.*—The acromegalic patient comes to the physician complaining of headache, disturbances of vision, severe joint pains, and sometimes ringing in the ears; or the condition is discovered while the patient is under treatment for an entirely different disease. This pain in the head is the most frequent subjective symptom, and is often severe and even terrific. There may be, and frequently are, pains referred to various parts of the body, often to the joints, which are more or less persistent but neuralgic in character. Frequently there is tingling of the hands, feet, or ears, often with numbness of the fingers, but with no great loss of sensibility. There is generally increased and often ravenous appetite, increased thirst, and often dyspepsia and polyuria, and generally constipation. Menstruation is generally absent in the female, and the sexual appetite is generally diminished in the male. The pulse and temperature are almost invariably normal.

Previous History.—In women the cessation of the menstruation is generally the first symptom of the disease. In several cases there has been a history, in the early stages, of profuse and recurring epistaxis.

From the patient or his family proof of the continuous growth of the head, hands, feet, and body can generally be elicited, and commonly an approximate date for the beginning of the disease can be estimated. The weight during this developing period of the disease always increases, and so does the height to a certain extent, at least till the period when kyphosis develops. When this kyphosis is well developed more or less loss of height takes place, even to as much as six inches in Paget's case.

The gradual increase in the size of the hats, shirts, gloves, and shoes worn can always be ascertained, and furnishes positive evidence of growth.

In women the increase in the size of the fingers, as shown by the inability to longer wear the wedding ring, which in many cases has been sawed off, is a positive evidence of growth frequently mentioned in the histories of the cases. In most cases earlier photographs of the patient can be obtained and compared with the present condition.

These signs and facts show a positive and continuous growth, and careful examination of the parts affected shows that this growth is largely of the bones.

Clinical Inspection.—In acromegaly all of the projecting portions of the body are greatly enlarged—hands, feet, chin, lips, nose, tongue, ears, and often the genitalia. Of these parts the bones, cartilages, and soft tissues are all hypertrophied. The face is oval, the cheeks are flattened, the forehead is retreating and low, the nose enlarged and often massive, and exophthalmos may be present. The ears are generally enlarged and the hair of the head is strong and thick.

The intellectual faculties may or may not be impaired, and somnolency is sometimes present. Taste and smell are rarely affected, while hearing is occasionally disturbed and sight is frequently impaired. The voice is loud and deep. The reflexes are generally normal, at least not markedly impaired, and the electrical reactions are normal.

The skin may be dry and harsh and is generally greatly thickened, especially on the affected parts, while the subcutaneous cellular tissue may be either hypertrophied or atrophied. The skin is often yellowish, especially marked on the face, and there is often increased perspiration, either local or general. There is frequently an increased growth of hair, especially on the arms and legs, and molluscous growths often appear on the face, neck, or body.

The superficial veins of the body are often dilated, giving rise to hemorrhoids and varicose veins of the legs.

There may be muscular hypertrophy, local or general, but later there is atrophy of many of the muscles. The heart, lungs, spleen, and liver may be normal, although the heart may be slightly hypertrophied. The kidneys are generally normal, although there is frequently polyuria, and occasionally glycosuria or albuminuria is present.

The cartilages of the nose are enlarged and thickened, as are generally the cartilages of the ears and eyelids. The lower jaw is almost invariably enlarged, and generally to such an extent that prognathism is present. The superior maxillary and malar bones are generally enlarged, elongating the face and giving prominence to the cheek bones. The supra-orbital ridges are generally very prominent, causing the rest of the forehead to apparently retreat, while the skin of the forehead is enormously hypertrophied and thrown into folds and corrugations. The cranial bones, except as to crests and protuberances, are rarely affected.

The bones of the thorax are always enlarged, notably the extremities of the clavicle and the costal cartilages, especially at the junction of the ribs and the sternum, and still more markedly at the xiphoid appendix. The ribs are generally widened, while the scapulæ may or may not be enlarged, and sooner or later the vertebræ and the vertebral cartilages become affected, the latter thickening and ossifying, causing kyphosis and other deformities of the spinal column. On account of this kyphosis and the shortening of the neck the long, projecting chin often almost rests upon the sternum.

The bones of the arm are generally not enlarged except the lower part of the radius and ulna, thus causing an enlarged wrist, while the bones of the hand, the metacarpal bones and phalanges especially, are all widened and thickened.

The soft parts of the hand are especially hypertrophied, giving the large and often enormous acromegalic hand.

The pelvic bones are generally enlarged, this being particularly noticeable at the symphysis pubis and the crests of the ilia. The thigh bones are generally not affected except at the condyles, which are enlarged and, together with the almost constantly enlarged patellæ, produce large knee joints. The tibiæ and fibulæ may or may not be enlarged, though frequently there is some hypertrophy of the extremities of these bones. The ankle joints are generally enlarged, and the feet bones and soft parts are affected similarly to the hands and, like the latter, are enormous.

Critical Examination.—*Head.*—We find the forehead low and retreating, due to the growth forward of the superciliary ridges, which, with the elongation and forward projection of the lower jaw, gives the oval or elliptical face so characteristic of this disease. The hair is thick and strong, and the eyebrows are often heavy. We next notice that the face is entirely too large; that it is out of all proportion to the cranium proper. The skin of the face is thickened and of a yellowish-brown color, most marked on the eyelids, with perhaps here and there a molluscous growth.

The skin of the forehead is often redundant and thrown into many transverse wrinkles and folds. The cheeks are generally flattened, and often appear sunken, largely due to the prominence and projection of the malar bones. The circumferences of the orbits are prominent, and the eyelids are large, due to the thickening and widening of the tarsal cartilages, with more or less hypertrophy of the skin, especially of the lower lid, where it may fall in folds, with occasionally the appearance of œdema. The eyeballs are large and generally more or less prominent, even to the condition of exophthalmos.

The nose, even for the size of the face, is too large, often immense, due to the thickening and enlarging of the nasal cartilages and to the great hypertrophy of the soft parts. It is wide, thick, and may be pugged.

The superior maxillary bones may or may not be enlarged, but are frequently lengthened from above downward; nevertheless they are never enlarged to the same extent as is the lower jaw.

The upper lip is generally thick and projecting, but never attains the size of the lower lip. The lower lip is almost invariably thick, everted, and projecting, and is a characteristic feature.

The enlargement of the lower jaw is one of the landmarks of this disease, although acromegaly can unquestionably occur without the enlargement of this bone. The angle of junction between the rami and the body becomes obtuse, and, while the rami may grow to a considerable extent, the chief growth is in the body. The body of this bone widens and thickens all over, but especially on its alveolar border and at the symphysis, where the mental process becomes very prominent. The rami, however, may be so enlarged and widened as to force outward the lower part of the external ear. The teeth rarely partake of this growth (in the congenital case described by Cènas the teeth were all enlarged); hence the growth of the alveolar process soon tends to separate the teeth from one another by continually increasing intervals, though the teeth may fall out spontaneously. Sooner or later prognathism generally occurs; it is due not only to the growth of the body of the lower jaw, but also to the widening of the angle and the changes in the

glenoid fossa. This prognathism is of all degrees, even to 15 mm.

The external ear is generally increased in size, sometimes even appearing very large. The cartilages and the soft parts both take part in the growth, and the former may become in places as hard as bone, while the external

FIG. 21.—Typical Face in Acromegaly. (Author's first case.)

auditory canal may be lengthened by the growth of its cartilage and the bony canal narrowed by exostoses from its walls.

The bones of the cranium are generally not enlarged, although there have been several exceptions, but the ridges and eminences are often abnormally prominent, especially the occipital protuberance; and in one case there were spiky, osseous protuberances along the sutures of the skull.

The mucous membrane of the nostrils is frequently found hypertrophied. The sense of smell is very rarely affected.

The tongue is broad and thick and frequently double its normal size, almost entirely filling the cavity of the mouth, so that the sides show indentations from the teeth. The upper surface of the tongue is often deeply corrugated and marked by deep lines and fissures, and the papillæ may be prominent and projecting. The speech is rendered thick, heavy, and slow by the massive tongue, which gives the impression of weight and clumsiness, while the prognathism allows the labial and dental sounds to be but poorly articulated. The tongue is generally clean, but may be covered with a grayish-yellow coating.

The soft palate is often thickened, the uvula may be wide and long, even as large as a little finger, and the epiglottis has been found considerably thickened. The larynx is enlarged, either as a whole or in one or more sets of its cartilages. The aryepiglottic ligaments have been found thickened and the vocal cords hypertrophied. These laryngeal enlargements cause the voice to be loud and harsh, while the pitch is much lowered in men and made masculine in women.

The thyroid cartilage is often enlarged, as is also the cricoid cartilage and frequently the hyoid bone. The submaxillary and the lymphatic glands of the neck may be enlarged. The thyroid gland may be normal in size, hypertrophied, cystic, or so atrophied that it cannot be found.

The neck is short and thick, and the head leans forward, which with the cervico-dorsal kyphosis causes the long projecting chin to almost rest on the sternum.

Body.—Sooner or later, but almost invariably if the case is far enough advanced, the irregular growth of bone in the spinal column causes deformities of the spine. This deformity is almost constantly a cervico-dorsal kyphosis, giving a humpback appearance which is very characteristic of this disease. Occasionally scoliosis is also present, and sometimes there is a compensatory lumbar or dorso-lumbar lordosis. The spinous processes of the vertebræ are frequently found abnormally prominent, especially the lower cervical.

The size of the chest is greatly increased, especially at the level of the ensiform cartilage, where it reaches its greatest circumference. Laterally the chest appears flattened, while the antero-posterior diameter is often enormous, due to the forward projection of the lower end of the sternum.

The sternum is generally widened and thickened, with prominent transverse ridges, and there may be triangular-shaped indentations at the sides. There may be a hollowing of the sternum in the region of the manubrium due to an irregular growth of the segments, while the upper end of the sternum may be so thick as to give a dulness on percussion. The xiphoid cartilage is generally hard, wide, and projecting.

The clavicles are most enlarged at the sternal extremities, but the acromial ends are also generally thickened.

The ribs are wide and very oblique, and at their junction with the more or less enlarged and ossified costal

FIG. 22.—Author's Third Case of Acromegaly.

cartilages are generally found bony nodules, not unlike the rachitic rosary, and nodosities may appear on the ribs themselves. The ribs are rendered oblique, and the lower ones are forced outward by the great growth of the costal cartilages. The hardening of the ligaments and cartilages of the chest causes a peculiar stiff and constrained up-and-down or out-and-in motion of the lower part of the thorax during respiration, and the abdominal respiration is increased.

The abdomen is generally flattened and even appears retracted from the forward projection of the sternum and costal cartilages, though rarely it may be large and pendant.

The pelvis is generally enlarged, the ilia are wide apart, the crests broad and prominent, and the pubic bones are especially hypertrophied at the symphysis.

The external genitals may or may not be enlarged. The clitoris may be hypertrophied, and the vagina may be lengthened, but the uterus is generally small and atrophied.

Upper Extremity.—The shoulder joint may be, but rarely is, much enlarged; the elbow joint may be increased in size; the forearm is often enlarged at its lower third, especially just above and at the wrist; the wrist joint is almost always large. The hand, widened, thickened, and often lengthened, is massive and enormous, and appears heavy and cumbersome for the relatively small arm to carry. The ends of the metacarpal bones and phalanges are enlarged, giving prominent joints. The skin of the hand and the subcutaneous tissues are greatly hypertrophied, so that the normal lines of the palm are greatly deepened, even to the appearance of fissures in the flesh. At the upper part of the hand, and over the metacarpal bone of the thumb, and on the ulnar border, the hypertrophy of the soft parts is excessive.

The fingers, by the growth of phalanges and soft parts, become of the same width and thickness at the tips as at the bases, giving the appearance called "sausage-shaped," which is a characteristic feature of this disease.

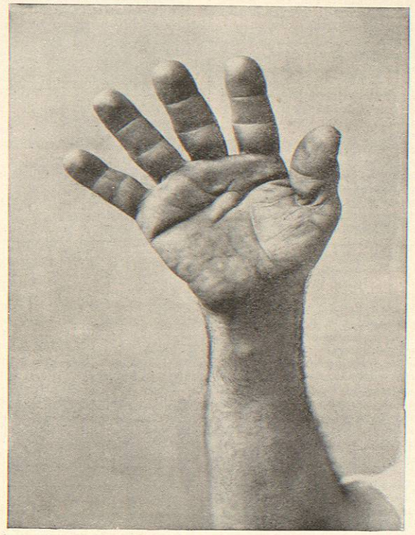

FIG. 23.—Typical Hand in Acromegaly. (Author's case.)

The above-shaped fingers, with the great thickness of the soft parts over the metacarpal bone of the thumb and on the ulnar border of the hand, with the exaggerated palmar lines, and with the abnormal proportion of the hand to the size of the forearm, render the acromegalic hand a landmark not easily forgotten.

The fingers may appear somewhat flattened, and, according to Marie, there is often a swelling at the articulation of the first and second phalanges.

The nails are flattened, short, and sometimes widened, but always appear too small for the enlarged fingers, whose redundant flesh laps over them at the sides. There are strongly marked longitudinal striations, sometimes even with ridges, and there may be transverse striations on the nails. They are often brittle, breaking off or cracking easily, and in Cènas' case the nail of one finger fell off spontaneously and a new one developed.

Lower Extremity.—The thighs are generally not increased in size, although the condyles of the femurs are generally prominent and enlarged, which with the hypertrophy of the patellæ causes a marked enlargement of the knees. The upper ends of the tibiæ and fibulæ may or may not be enlarged, but the lower ends of the leg bones are generally found hypertrophied, causing prominent malleoli and large ankle joints. The tendo Achillis is frequently prominent and hardened, while the foot is described as "massive," "colossal," and "enormous." The bones of the feet are all enlarged, and especially the os calcis, which projects backward, giving a marked prominence to the heel. The foot is thick and broad, with a prominent cushion of thickened skin and subcutaneous tissue on the external border, a characteristic feature of the foot in acromegaly. The toes are all large, but more especially the big toe, which is immense, and crowds the other toes together. The skin of the foot is redundant, hypertrophied, and thickened, especially on the toes, causing them to appear pushed back and turned up, throwing the skin into great folds on the upper surface of the toes. The nails of the toes present appearances similar to those of the fingers.

The projecting os calcis covered with a cushion of hypertrophied skin and fat, the presence of a pad of hypertrophied tissue on the external border of the foot, the immense big toe pushing against the other toes, and the redundant skin, make the acromegalic foot as prominent a landmark as the hand.

Asymmetry.—Acromegaly is primarily a symmetrical disease, one part enlarging correspondingly with its fellow on the other side; but in many cases one side of the body is larger than the other, and the right half of the body is often the larger. In a number of cases data are given showing the growth to have begun in one foot or one hand, or in both feet or both hands, before any other parts of the body were affected.

In fact, the growth probably generally starts in the hands and feet, while later the face and lower jaw are attacked; then, the lower ends of the arm and leg bones; next, the crests, tubercles, ridges, and eminences show growth, and about this time kyphosis develops; while lastly cartilages and tendons all over the body show bone development. Besides the slight asymmetry of the two sides of the body, some atypical cases have occurred in which one or several toes or fingers were found to be larger than their fellows, or one side of the face and head was much larger than the other side.

Muscles.—At first the muscle growth and muscular power are increased, and sometimes the development of the muscles may be very great. Sooner or later, however, the muscles become atrophied in greater or less degree, and the muscular power is greatly diminished, even to the point of compelling the patient to remain in a sitting or reclining posture, or even forcing him to remain in bed. There may be intermittent attacks of great loss

of muscular power, to be followed by periods of improved strength.

The muscles of the arms and legs may become flaccid and shrunken, and some of the kyphosis and scoliosis may be due to muscular debility. Some of the muscles may be atrophied while others are hypertrophied, even to the extent of forming muscle tumors and causing deformity.

Skin.—The subcutaneous fat may be increased or diminished, but later it is generally found diminished, except perhaps on the diseased portions of the body. The skin on the affected parts is hypertrophied, and generally, especially where exposed, is olive brown or yellowish in color. This yellow color is most marked on the face, and here most noticeably on the eyelids. The face may, however, be pale, or the nose may be red, and the skin may be dry and harsh from diminished sebaceous secretion. There is frequently increased perspiration, coming on with slight exercise, or even without exercise, either general or local on the diseased portion of the body, and especially frequent on the legs. This perspiration may have a disagreeable odor. The growth of the hair all over the body is generally increased, especially on the legs, and on the head it is thick, strong, and coarse. There may be pigmentations on the skin, and growths of molluscum fibrosum frequently occur on the face, especially on the eyelids, and on the chest or back, and they are generally pendulous in character. Multiple fibromata of the skin may occur, of the size of a millet-seed, and fatty nodules may be found beneath the skin.

Blood-Vessels.—There are always vasomotor disturbances of the affected portions of the body, as shown by the tingling, flushing, and local sweating. The flushing is often accompanied by a "burning pain." Besides these signs, which denote the dilatation of the small blood-vessels, there is a marked tendency to a dilated and varicose condition of the superficial veins, which is frequently found on the legs. Hemorrhoids are often present, varicocele may be, and profuse epistaxis may occur, while the arteries may show signs of beginning atheroma.

The blood shows no marked or constant changes; the red corpuscles or the hæmoglobin may be decreased.

Internal Organs.—The lungs are normal, although there may be some dyspnœa, especially on exertion; it is due to the impaired respiratory movements of the chest.

The heart sounds are generally normal, but more or less hypertrophy is always present. Late in the disease dilatation occurs with its usual symptoms, dyspnœa, œdema of the lower extremities, palpitation, and perhaps systolic murmurs, and acromegalic cases die most frequently from sudden cardiac failure.

Physical examination does not discover much change in the size of the liver and spleen, though they may be found enlarged.

The kidneys, as interpreted by the examination of the urine, are generally normal, although albuminuria or peptonuria may be present, while polyuria is a frequent symptom. Glycosuria has been so many times present as to suggest some metabolic connection between pituitary disease and the disturbances of the sugar mechanism, and several cases of acromegaly have died of diabetes.

Sight.—The eyes may be normal, but are frequently affected, in all degrees from occasional flashes of light or eye blurs to narrowing of the fields of vision and atrophy of the optic nerves, even to absolute blindness. Exophthalmos is often present, due both to actual enlargement of the eyeballs and to bone growth in the orbital cavities, or perhaps to associated thyroid disease. The pupils are generally normal in size, but may be dilated, and the reaction is generally as usual, though it may be slow to light but normal to accommodation. Nystagmus, both rotary and vertical, has been present, and divergent strabismus has been noted in at least two cases. Narrowing of the visual fields has been found in all degrees, even to bitemporal hemianopsia, and signs of optic neuritis due to pressure may be found even before the vision is much impaired. Optic atrophy, partial or complete, of one or both eyes, is of frequent occurrence. The retinæ may show venous congestion, and the arteries may be small or they may appear pale, or a congestion as of a neuroretinitis may be present.

Hearing.—The hearing is not generally affected, but occasionally there has been decided deafness, and in several cases there has been continuous and unceasing tinnitus aurium, variously described as singing, ringing, rumbling, or swashing sounds. This ringing is often increased on lying down, so that the patient cannot sleep except in the sitting position, and anything that increases the blood pressure even momentarily will increase the tinnitus, and often give it a pulsating character. The drum membrane may be hardened and thickened, and so stiffened as to be immovable.

Smell and Taste.—These are but rarely affected.

Nervous Phenomena.—A most constant symptom is pain in the head, which may be referred to any region, but is generally frontal or vertical, and in one of the writer's cases was located in a small circumscribed spot, tender to pressure, over the region of the anterior fontanelle. This pain may be so mild that it is hardly complained of, or so severe, violent, and excruciating as to almost render the patient insane. The headache is often, like the tinnitus aurium, increased on lying down or by anything that increases the cerebral blood pressure. Pain is often present in the joints, especially the knees, and is often severe in the fingers. Pain is frequently complained of in the chest or abdomen, shooting around the body or confined to one side, or it may be lumbar or sacral. Almost every case of acromegaly has pain, more or less constant and severe, in some part of the body, often without any local cause. Crepitations may be found in some of the joints, which, of course, would account for the pain there, though there is no swelling or any evidence of acute inflammation. Pain sometimes seems to centre at one of the small fibromata which occasionally develop in the skin.

Sometimes a peculiar nervous sensation is complained of, a sensation as of a nervous discharge, or electric shower, starting from the top of the head and passing quickly over the body to the feet. This is sometimes described as giving the sensation of the rolling of shot; hence it has been termed the "shot feel."

There are no marked or constant paræsthesiæ in acromegaly, though slight numbness or prickling of the affected parts is often complained of, most frequently in the fingers. The tactile sense of the fingers may be impaired, so that small objects cannot be readily handled, and sewing, knitting, or even dressing becomes difficult. When this condition is present it may become much improved, though the growth of the body and the advance of the disease may continue; but of course there is always clumsiness in the use of the fingers from the size alone. Sometimes an intermittent vasomotor spasm in the fingers has been noted, causing localized anæmia with severe pain, while formication or hyperæsthesia of the hypertrophied parts may occur. More or less general numbness, anæsthesia, analgesia, or impaired perception of heat or cold, are rare conditions in this disease.

The electrical responses of the muscles and nerves are rarely found abnormal, and the reflexes, both deep and superficial, are generally unimpaired. Occasionally the patellar reflex is diminished, and rarely it is absent on one or both sides.

The mental faculties in the majority of cases are not affected, but the loss of memory, dulness or sluggishness of the mind, apathy or depression have all been recorded. Marie says that there may be a state of great good humor, but, on the contrary, melancholia is more frequent.

There may be great irritability, while there may be delusions, and the patient may be refractory and suspicious; he may develop decided insanity, and may even show suicidal and homicidal tendencies. This condition may be persistent or intermittent, or may last for a short time and not recur.

Another interesting condition which seems quite frequently to occur in acromegaly is a persistent drowsiness even to somnolency. This somnolency may become a profound stupor that lasts for several weeks, does not seem to end in death, and may recur.

Vertigo may occasionally occur and be severe enough to cause the patient to grasp something for support. Attacks of syncope are sometimes a frequent symptom.

Pituitary Enlargement.—I believe that the pituitary gland is enlarged in every case of true acromegaly, but

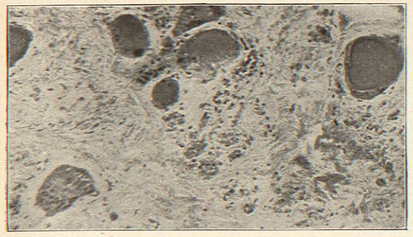

FIG. 24.—Section of Parenchyma of Thyroid Gland. Whole gland weighed 101 gm. (Author's case.)

it may not show evident signs of its growth. A positive sign of the enlargement of this body is the impairment of vision associated with a hypertrophy of the bones.

More than half of all cases of acromegaly show deranged vision or optic signs during some stage of the disease. The physical cause of the ocular disorder is largely the pressure of the growth on the optic chiasma. Where tinnitus aurium is constantly present there is either pressure on the cavernous sinuses by the enlarged pituitary or an actual growth into them of the pituitary tumor. It also seems probable that the conditions showing sudden and serious brain trouble, all of which point to cerebral tumor, are due to the first sharp pressure which the enlarged pituitary body exerts upon the brain, having perhaps suddenly burst from its bony moorings.

That in some cases one eye, in others both, and in still others the ears alone are affected can be explained by the condition of the bony environments of the sella turcica in the individual skull, the enlarging pituitary body tending to escape in the direction of the least resistance. If the middle clinoid processes are small, the pressure will be exerted correspondingly earlier on the optic commissure; or if one of these processes is smaller than the other, the pressure will first be exerted on that side, and but one eye may be affected.

PATHOLOGICAL ANATOMY.—*Pituitary Body.*—In autopsies on cases of acromegaly the pituitary body has been found normal so few times that I question the diagnosis in those cases. I believe that an enlarged or diseased pituitary body is always present in cases of true acromegaly. The enlarged hypophysis may be a normal hypertrophy, an adenoma, a glioma, or a small-celled growth resembling sarcoma, and there may be cystic, colloid, or granular degeneration. Frequently this enlargement or tumor growth has been confined to the anterior lobe of the hypophysis, the prehypophysis.

Thyroid.—The thyroid gland is probably generally abnormal in acromegaly. It may be hypertrophied and give a hypersecretion and all of the symptoms of exophthalmic goitre, or it may be atrophied and cause some myxœdematous symptoms, or, which is probably most frequently the case, the gland is first hypertrophied and then connective-tissue growth displaces the glandular parenchyma, and though the gland is actually enlarged, it is producing a diminished secretion, and a partial myxœdema occurs. This accords with the symptoms of a long-continued acromegalic case, and with the frequent autopsical finding of an enlarged and heavy thyroid gland which, in my case at least, contained a greatly diminished amount of iodine. This gland may also show cystic degeneration. In the writer's case a large supernumerary thyroid gland was found in the upper part of the thoracic cavity, which contained a large amount of iodine.

Thymus.—The thymus gland has not been often mentioned, but several times it has been found enlarged, and in one instance a fatty growth in the region of the thymus has been reported. In these cases instead of thymus glands they may have been supernumerary thyroids. A thymus gland contains no iodine (Mendel).

Another interesting disturbance of the metabolism of the body in this disease is shown by the number of times that sugar has been discovered in the urine.

Brain.—The brain has frequently been found enlarged, but may not be, even in cases which show almost every other organ of the body to be enlarged. This enlargement of the brain seems to be due to a general growth. An increase of the neuroglia cells has been found, but in direct proportion to the general enlargement of the brain substance.

The growth of the pituitary body not only causes enlargement of the sella turcica, but may cause symptoms of pressure with referred pains, paralysis, cerebral irritation, insanity, or even coma. If the bony formation of the sella turcica allows the enlarged pituitary body to press upon the optic commissure, we find pressure atrophy of the optic nerve; or a tumor growing in the sella turcica may press laterally and interfere with the blood flow in the cavernous sinuses, or even in the internal carotids, or may even grow into the walls of the sinuses, causing impaired blood flow in them and a constant tinnitus in the ears.

The pineal gland has been found double its ordinary size, and little tumor growths have been found attached to the base of the brain.

Calcified and even ossified plates have been found in the dura mater, and its attachments to the skull have been found ossified. The arteries at the base of the brain have been found enlarged and thickened, often especially marked in some one artery in the circle of Willis, while another artery or another part of the same artery may be distinctly narrowed. The arteries may become distorted and tortuous, and the posterior cerebral has been found knotted and imperforate. The cranial nerves have been found both normal and enlarged. The nerve changes in the brain and cord, if there are any, are probably sec-

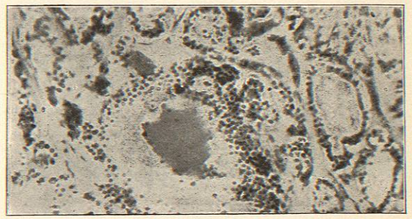

FIG. 25.—Section of Thoracic Thyroid Gland. Whole gland weighed 36.5 gm. and contained a large amount of iodine. (Author's case.)

ondary to the vascular changes. As in this disease we find the blood-vessels almost constantly changed, either narrowed, due to a thickening of the intima, or dilated, due to a thinning of the other coats, we may expect to find all kinds of changes due to a greatly modified blood supply, be it in an organ or in nervous tissue.

Spinal Cord and Nerves.—The medulla and spinal cord are generally normal, but the pia of the cord has been found thickened, and some of the columns of the cord have been found degenerated. Probably, however, as