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A STUDY OF ACHONDROPLASIA *

INTRODUCING A NEW SYMPTOM — A WEDGE-SHAPED VERTEBRA

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INTRODUCTION

Ita P. appeared in the orthopedic outpatient department of the Children's Hospital for treatment because of a "bunch" on her back. As usual, a roentgen-ray examination was made. The plates showed widely separated vertebral bodies with a peculiar wedge-shaped vertebra at the point of the "bunch." As this did not seem to be due to any of the more common processes, further study was instituted.

Following this, Jansen's "Achondroplasia" was studied, and it was while studying this that the idea suggested itself that the peculiar wedge-shaped vertebra might easily be a result of his "amnio pressure," although he makes no mention of this condition. Furthermore, the significance of the following statement of G. Elliot Smith (of the University of Manchester) became evident. "His (Jansen's) hypothesis cannot fail to serve the even greater purpose of stimulating research, by giving a new point of view, an illuminating suggestion, which is certain to become the nucleus of a whole series of investigations."

The whole work has been done under the helpful supervision of Dr. Robert W. Lovett, who first suggested that the wedge-shaped vertebra be studied further, and who added that Jansen's conclusions might shed some light on the subject. To him is due full credit for stimulating the present inquiries.

The roentgen-ray examinations were made by Miss Dorothy Weil of the roentgen department of the Children's Hospital. Mr. J. V. Footman developed and reduced the plates.

* Because of lack of space, a large number of figures have been omitted. In the original article, there are complete series of photographs of front, side and back views of each of the children with photographs of most of the hands and feet individually. Also there is a roentgenogram of every bone of each child.

For comparison, two complete photographic and roentgenologic series of normal children are shown.

In measuring the cases the method of Dr. Joseph I. Grover of Boston was used.

I take this opportunity to thank the trustees, who through Miss I. C. Smith, superintendent, placed at our disposal the facilities of the Children's Hospital, where all the cases were studied.

REVIEW OF LITERATURE

G. Elliot Smith (1912) has the following to say of dwarfs:

"Nearly fifty centuries ago the most treasured gift the general in command of an Egyptian Expedition brought for his Pharaoh from a foreign country was a dwarf to entertain him and his court by his antics (Schiaparelli: *Una Tomba Egiziana inedita della Via Dinastia*, Rome, 1893), and from that time onward throughout the ages, even until the present day, the quaintness and not overdélicate wit of the dwarf have ever secured him a place in the court of the ruler of Egypt.

"Moreover, the ancient Egyptians selected the dwarf with his misshapen head and limbs as the prototype of Bes, their god of sexual intercourse (Quibell: *Excavations at Saqqara, 1905-1906*, Cairo Museum Reports) and they represent him with genitalia of phenomenal proportions—a fact which assumes special significance in the light of the discussion to be found in this (Jansen, 1912) monograph.

"From this it is evident that the distinctive structural peculiarities and functional proclivities of the dwarf have been realized from the very dawn of history; and no doubt even long before man learned to record his thoughts in written characters he had become familiar with the achondroplastic. But the problem of explaining the genesis and significance of the curious series of physical and mental traits peculiar to the dwarf has always baffled the investigator, even though many of the greatest clinicians, pathologists and embryologists of the last century have attempted to resolve its difficulties.

"The recent appreciation of the marvelous influences exerted in ways so manifold by the internal secretions of a whole series of organs has not unnaturally riveted attention mainly on such factors as the influence of the pituitary body, the thyroid and the sexual organs for an explanation of nanism. But so far the pursuit has been in vain."

Murk Jansen (1912) adds: "From the earliest times recorded in history we meet with scattered instances of dwarfs; thus the ancient Egyptians worshipped the god "Ptah" (Porak et Durante, 1905), who shows (that) stunting of the extremities characteristic of achondroplasia. In the Middle Ages we find achondroplasts at court as 'fools.' The grotesque proportions of these otherwise healthy and ever robust individuals, as well as their liveliness and perhaps a suspicion of impu-

dence, which often characterizes them, may have rendered them particularly fitted for this position.

“In recent times the lot of dwarfs, no longer found in palaces and temples, has been cast amid less exalted surroundings; but, on account of their sense of the burlesque, they afford a lively source of amusement in various places of public entertainment.

Fig. 1.—Emily S. Total length 70.4 cm. This picture shows: (a) the brachycephalic head; (b) the broad face; (c) the flattened and sunken nasal bridge; (d) the cretinistic facies; (e) the rather short neck; (f) the short extremities; (g) the large amount of subcutaneous fat.

“During the last forty years this remarkable form of dwarf growth has so far attracted the attention of scientists as to secure their careful study in tracing its causes. An extensive literature on the subject has arisen, in which the dwarf is described by almost twenty different

names, most of them borrowed from the Greek. From this it is evident that each investigator formed his own idea of its nature, but failed to procure convincing proofs."

Parrot (1878) first used the terms "achondroplasia" in describing the affection which he recognized as an independent form of disease in a number of fetuses. This term was adopted by Porak (1891) and P. Marie (1900) in their papers. Osler (1897) says, "On August 4, 1886, when at Cacouna in the Province of Quebec, I was asked to see two cretins, and found them remarkable rhacitic dwarfs belonging to this type," and "it was some years later that I learned the true nature of the affection, namely, the chondrodystrophia foetalis." Osler also,

Fig. 2.—Emily S. This picture shows the "main en trident" and prominent epiphyses.

with others, for years used the term "fetal rickets." Kaufmann (1892), in the meantime, described the pathologic condition in achondroplasia and adopted the name "chondrodystrophia." "It is," he says, "a disturbance of the endochondral ossification while the ossification on the side of the periosteum is perfectly normal." He distinguished three forms: (1) chondrodystrophia hypoplastica, in which the principle element is a simple cessation in the growth of the cartilage; (2) chondrodystrophia malacica, in which the arrest of the growth is dependent on the softening of the cartilage; (3) chondrodystrophia hyperplastica, in which we are concerned not simply with an arrest of the growth of the cartilage, but with an excessive growth abnormal in its direction (Bullard and George, 1908). Jansen (1912) prefers

the name achondroplasia for he says, "Kaufmann in Germany afterwards adopted the name "chondrodystrophia," thereby indicating that the affection is distinguished less by an absence of the 'cartilage' than by a disturbance of its nutrition. In what follows we shall, however, see that, on the one hand, the trophic disturbance may leave some cartilaginous formations unaffected, while, on the other hand, it may extend even to bones formed in membrane. We shall, therefore, for

Fig. 3.—Emily S. Roentgenogram showing: (a) the brachycephalic head; (b) the small sella turcica; (c) the narrowed nasopharynx.

the present, keep to the name sanctioned by use — achondroplasia, by which we understand an affection characterized by a congenital shortness of the extremities and the base of the skull." Although at present the terms "achondroplasia," "fetal rickets," and "chondrodystrophia" are used interchangeably (Bradford and Lovett, 1915; Whitman, 1917), most writers' descriptions of the disease agree more fully with that of Jansen, and it seems only consistent to use the name he so well vindicates.

Morse (1902) in reviewing the American cases, says, "Very few cases of this condition have been reported in this country and the diagnosis of several of these is open to considerable doubt." For the sake of completeness, I have included his cases in my bibliography, and in addition all other American and foreign cases I could find.

REVIEW OF JANSEN'S "ACHONDROPLASIA"

Jansen (1912) has so skillfully arranged the mass of facts concerning achondroplasia that it seems most profitable to consider our own cases in the light of his work. For that reason, the first main division of his memoir, "The Nature of Achondroplasia," will be reviewed now. The second main division, "The Cause of Achondroplasia," will be reviewed later.

Jansen divided the nature of achondroplasia into two groups of symptoms: (1) Those of dwarf growth, and (2) those which are the result of infolding. "The former," he says, "are quite obvious and lend themselves to the recognition of the achondroplast even at a distance. The latter, on the contrary, are less conspicuous, and have thus, for the greater part, passed unnoticed hitherto. It is these very mechanical malformations, however, which will prove useful in tracing the cause of achondroplasia."

The symptoms of dwarf growth include those involving the extremities, pelvis, vertebral column, thorax and other parts. The extremities are too short, while the trunk is equal in development to that of a normal child of the same age.

He says, "Notice that the shortness of the extremities is not due to any crookedness or bending of the bones, as in rickets or osteomalacia, nor the result of multiple fractures, as in osteogenesis imperfecta; nor is it due to absence of the proximal parts, as in phocomelia or congenital deficiency of the femur, and so forth; nor of the distal parts, as in congenital amputations and in hemimelia. All the bones are present, scarcely or not at all bent; they are simply too short. This shortness affects the proximal more than the distal parts of the extremities, and is called "micromelie rhizomelique," although, as appears in the comparatively broad hand and short fingers, the peripheral parts are not unaffected."

"The "main en trident" is present, the second and fifth metacarpals diverging more than the normal 32 degrees, and usually as much as 40 degrees. The fingers do not group themselves about the middle finger. In addition, the bones of the achondroplastic hand are not only too short, but also too slender, the latter in a less degree than the former. The pelvis lags behind in development, when compared with the other parts of the trunk. The pelvis is small in pro-

Fig. 4.—Emily S. Roentgenogram showing what Jansen says is a tendency of the organs of achondroplasts to be "gaseous."

portion to the size of the body, its cavity is funnel shaped, and the alae ossium ilii are relatively poorly developed.

The vertebral column is often affected. Its length may not be more than one half that of the normal. Occasionally, the size of the vertebral bodies diminishes from neck to sacrum.

The skull, even in the most serious form of achondroplasia known, escapes the dwarf growth. It may be deformed, having a backward basis cranii, more (unossified) cartilage in the petrosal parts of the temporal bones and the basilar, and a short hard palate, but it does not become dwarfed.

The chest is often shortened and consequently is too small for the proper accommodation of the vital organs. The caudal circumference is pressed upward, so that the sternum is directed almost horizontally and its shape comes to resemble a calotte.

The skin is often loose and arranged in oblique and transverse folds reminding one of a pair of knickerbockers.

Achondroplasia occurs in various degrees; in the most serious forms the growth of the oldest parts of the skeleton (the whole of the vertebral column) is defective. They are not viable. Only the slightest forms may survive; in them the trunk reaches the normal length, or very nearly; it is chiefly the extremities — with the pelvis — that are affected.

Henri Dufour (1906) recently described "atypical forms of achondroplasia." These include forms in which the extremities are only very slightly shortened, and forms in which the fourth metacarpal or metatarsal bone is relatively short in otherwise perfectly normal individuals (Chevallier (1910). Jansen would prefer substituting "slightest" for "atypical" and apply it to the former. The latter forms he would group in the manifold forms of kakomelia.

In addition to the characteristic phenomena of growth disturbance in achondroplasia there are often present a group of symptoms connected with sex. A two-year-old girl may have well developed pubic hair. The sexual appetite may be enhanced.

Let us now turn to the symptoms of infolding. These appear to be the direct result of mechanical forces modifying the form of the fetus.

While, as we have seen, except in the more severe forms, the dwarfing process spares the skull, it is the skull that is most affected by the mechanical malformations. The basis cranii is shortened while the breadth of the skull exceeds the normal — brachycephaly (Parhon, Shunda and Zalplachta, 1905). The height of the skull is often increased and the circumference enlarged. Jansen (1912) says that the intellect is often normal and may be above the average; but

Parhon, Shunda and Zalplachta observed that it usually stands in inverse proportion to the circumference. Kaufmann (1892) very clearly pictures the malformation found in the skull. In all of his figures the shortening of the basis cranii and in some of them the premature fusion of its parts, are to be seen. It seems, however, that both he and Virchow overlooked the causes of these conditions. In explaining these facts Jansen (1912) advances the supposition that during its fetal development the achondroplastic skull is submitted to a pressure in front, against the face, and behind, against the occiput. The consequence of this pressure is:

1. That the nasal bone and the squama occipitalis approach each other; that the skull and its base are shortened, thus causing the ossification centers of the basilar bone to come too close together in an early stage.

Fig. 5.—Ita P. Aged $1\frac{1}{2}$ years. Total length 78.3 cm. This picture shows the dorsolumbar kyphos which does not disappear even on lying down.

2. A lessening of the sagittal dimensions of the mouth cavity with a displacement of the hard palate toward the basis cranii (a narrowing of the choanae).

3. Either a kyphosis baseos cranii or a sagittal narrowing of the foramen magnum.

As a result there may be either a depression of the nasal bridge only or a flattening of the nose in toto. The narrowing of the choanae may cause a noisy, snoring respiration and may be mistaken for adenoid vegetations.

With the change in the shape of the skull the brain conforms so that when laid by the side of a normal brain of the same age the characteristic deformity is easily seen.

In addition the sella turcica may be reduced in size even to total obliteration, and, regarding the pituitary body which lies in it, Jansen draws the conclusion from a review of the literature that it is reduced

in size in the serious cases of achondroplasia, and little or not at all in the slightest forms.

Turning now to the spine, we recognize the malformation by which the achondroplast is distinguished from the normal. The three sagittal curvatures which occur in the normal spine of new-born infants are not present. The spine may be curved backward, the normal lumbar

Fig. 6.—Ita P. Roentgenogram showing: (a) the brachycephalic head; (b) the narrowed nasopharynx; (c) the kyphosis basis cranii; (d) the queer angle of the sella turcica; (e) the tendency for the alveoli to project backward.

lordosis being replaced by a dorsolumbar arcuate kyphosis. This is often first noticed in infants because they lie “bent-up” and may persist to adult life where it seems to be a more constant symptom of achondroplasia even than the depression in the nosebridge which is not infrequently missing.

REPORT OF CASES

CASE 1.—Emily S.; Age, $1\frac{1}{2}$ years; Italian parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal diseases. No other deformity in the family.

Patient's History.—Negative. Denies any previous illness.

Present Illness.—Mother brings the child into the hospital because of a "bump on her back." Duration of life. Child recommended to house for study.

Physical Examination.—General; poorly developed but well nourished child.

Head: Brachycephalic, prominent frontal bosses, open anterior fontanel, broad face, flattened and sunken nasal bridge, cretinistic facies.

Neck: Rather short.

Upper Extremities: Very short for length of trunk, epiphyses easily felt.

Chest: Harrison's groove and rosary present, the sternum projects forward at an increased angle, the nipples are noted to be very high.

Abdomen: "Pot-belly," liver and spleen palpable.

Spine: Definite low dorsal rounded kyphos on sitting and lying.

Lower Extremities: Very short for length of trunk, epiphyses are easily felt, legs held in abduction when lying on back, an enormous amount of fat hangs from the legs like pantaloons.

Neuromuscular: Child cannot walk or stand so far as is known, child sits in leaning forward posture usually, supporting the body by the hands resting on the knees.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 2.—Ita P.; $1\frac{1}{2}$ years; Italian parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Four other children living and well. No other deformities in the family.

Patient's History.—Negative. Denies any previous illness. Normal birth history.

Present Illness.—Mother brings the child to the hospital because of a "bunch on its back" present since the age of 2 months. The "bunch" has been growing larger. Child recommended to house for study.

Physical Examination.—General: fairly well developed and nourished baby.

Head: Brachycephalic, marked prominence of the parietal and temporal bosses, broad face suggestive of cretinism, broad nasal bridge, ears project noticeably from the sides of the head.

Neck: Slightly shortened.

Upper Extremities: Short for length of trunk, marked epiphyseal enlargement, enormous amount of fat hanging from arms, fingers seem thickened.

Chest: Marked rosary and moderate Harrison's groove, sternum projects forward at an increased angle, nipple line is very high.

Abdomen: "Pot-belly," liver palpable.

Spine: Marked rounded kyphos in the midlumbar region.

Lower Extremities: Short for length of trunk, abduction limited to 79 degrees, trochanters 2 cm. above Nélaton's line, moderate anterolateral bowing of the femora, slight lateral bowing of the tibiae, large amount of subcutaneous fat.

Neuromuscular: Child cannot walk or stand so far as is known, child leans forward when sitting, usually supporting the body by the hands resting on the knees.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age, although child seems to be both deaf and dumb.

CASE 3.—Frank B.; age, 4½ years; Swedish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Mother had one miscarriage and one still-birth before birth of this child. One other child living and well. No other deformities in the family.

Fig. 7.—Ita P. Roentgenogram showing: (a) the short clubby humerus with evidence of an old fracture; (b) the short ulna and radius with flaring diaphyseal ends; (c) “main en trident”; (d) the short, thin bones of the hand.

Patient's History.—Full term, normal delivery. Weighed 12 pounds at birth. Mother noticed at birth that the bridge of the nose was very much sunken. There was some disproportion of trunk and extremities. Breast fed until 7 months of age and then given modified milk. Did fairly well. Measles at 1 year of age. Frequent colds in the nose and sometimes there was a bloody

discharge. Walked at 12 months of age. Talked late but is very bright for his age. Tonsils and adenoids removed at 3 years of age. Has frequent dislocation of left elbow joint.

Present Illness.—Mother brings child into hospital because of lack of growth, shortness of extremities, and dislocation of left elbow. Duration for life.

Physical Examination.—General: well developed and nourished boy with bright appearance.

Head: Large, prominent bosses, bulging forehead, anterior fontanel just closing, broad sunken nasal bridge, projecting ears.

Neck: Negative.

Upper Extremities: Short for length of trunk, marked epiphyseal enlargement, elbow shows slight limitation of motion, unable to extend forearm fully.

Chest: Negative, except for depression at ensiform and increased forward projection of the sternum.

Abdomen: Distended, otherwise negative.

Spine: Negative.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 4.—Dorothy A.; age, 6½ years; Irish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Two sisters living and well. No other deformity in the family.

Patient's History.—Full term, normal delivery. Birthweight, 8½ pounds. Breast fed for nine months. Measles at 2 years of age.

Present Illness.—Comes to hospital because of knock knees of one year's duration.

Physical Examination.—General: well developed and nourished girl.

Head: Negative.

Neck: Negative.

Upper Extremities: Short for length of trunk, hands are spade-like in shape with a scar where a sixth finger has been removed at the sixth metacarpophalangeal joint of each hand; all finger nails are under developed.

Chest: Negative.

Abdomen: Prominent and very long.

Spine: Six lumbar vertebrae.

Lower Extremities: Short for length of the trunk, double knock knee deformity; on the inner side of each tibia there is a nodule of bony hardness about one inch in diameter projecting from the bone at the upper epiphyseal line, there are six toes on each foot with syndactylism of the second and third.

Neuromuscular: No disturbances.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

CASE 5.—Beatrice R.; age, 9½ years; Irish parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. One brother living and well. Mother had one miscarriage at fourth pregnancy from unknown cause. Two brothers dead of "cholera infantum" and one dead of convulsions at 6 months. No other deformities in the family.

Patient's History.—Full term, instrumental delivery, birth weight 5 pounds. Breast fed for one year. Pneumonia and relapse at 2 years of age. Pertussis

at 3 years of age. Measles and pneumonia at 7 years of age. Chickenpox and bronchitis at 8 years of age. Constipated most of the time.

Present Illness.—Brought to hospital because of knock-knees of three years' duration. Mother says child was queer even at birth.

Physical Examination.—General; well developed and well nourished girl.

Head: fairly large and square; forehead prominent and well marked frontal bosses; poor teeth which are notched; slight prognathia; hoarse voice.

Neck: negative except rather short.

Upper extremities: humeri are short and thick; carrying angle is much exaggerated; hands are short, fat and thick; fingers are short and there is an increase of space between the index and middle fingers of both hands; the finger nails are thick and resemble horn; the left hand shows a linear scar where a sixth finger has been removed.

Chest: flat and narrow, flaring of lower ribs and Harrison's groove, irregular shortened clavicles.

Abdomen: protuberant.

Spine: negative.

Lower extremities: short for length of the trunk; excessive knock-knees; enlarged ends of the diaphyses at the ankles; feet are very short; great toes are normal in length but the four small toes on both sides give the appearance of the bones being too short for the growth of the soft parts; all toe nails show horny overgrowths.

Neuromuscular: on standing, child has marked lordosis, walks with peculiar gait because of knock-knee deformity and flat feet.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Child very intelligent for age.

CASE 6.—Basiliki S.; age, 10 years; Greek parentage.

Family History.—Negative for tuberculosis, rheumatism, joint diseases, central nervous system disturbances and venereal disease. Four other children living and well. No other deformities in the family.

Patient's History.—Full term. Normal delivery. Birth weight, 12 pounds. Breast fed for one year. Has had no illness.

Present Illness.—Mother brings child to hospital because she does not grow large like her other children.

Physical Examination.—General; poorly developed but well nourished girl.

Head: large and square with prominent forehead and bosses; nasal bridge sunken; cretinistic facies.

Neck: rather short.

Upper extremities: very short for length of trunk, marked epiphyseal enlargement.

Chest: moderate rosary and Harrison's groove, nipple line is very high and angle of sternum increased so that sternum projects almost horizontally.

Abdomen: tendency to "pot-belly."

Spine: negative except for lordosis on standing.

Lower extremities: too short for length of trunk; marked epiphyseal enlargement; rather too much subcutaneous fat.

Neuromuscular: negative.

Measurements.—See table.

Laboratory Examination.—Tests for tuberculosis and syphilis were negative.

Mental Examination.—Intelligence normal for age.

TABLE 1.—COMPARING MEASUREMENTS OF ACHONDROPLASTS WITH THE MEASUREMENTS OF NORMAL CHILDREN

	Age, Years	Weight, Lbs.	Circum- ference of Head, Cm.	Circum- ference of Thorax, Cm.	Height, Cm.	Length of Arm, Cm.	Length of Leg, Cm.
Emily S.	1 8/12	25 8/16	45.0	42.5	70.4	24.1	30.0
Normal 1*.....			48.0	48.0		35.0	33.0
Normal 2†.....		25 8/16	46.0	47.7	85.9	32.0	40.5
Ita P.	1 10/12	21 11/16	46.4	45.4	78.3	27.4	34.6
Normal 1.....			46.4	45.4		28.0	36.5
Normal 2.....		27 0/16	48.5	48.6	84.1	29.4	39.8
Frank B.	4 1/12	32 8/16	55.0	51.0	87.0	27.8	36.0
Normal 1.....			49.9	50.9		30.8	41.5
Normal 2.....		36 8/16	50.9	43.9	101.2	33.6	47.2
Dorothy A.	6 1/12	33 1/16	48.8	48.0	90.8	27.2	40.5
Normal 1.....			49.9	50.5		36.0	50.5
Normal 2.....		48 0/16	52.3	56.3	114.3	43.2	60.1
Beatrice R.	9 8/12	67 0/16	51.2	62.1	121.7	43.0	57.0
Normal 1.....			54.0	63.0		46.6	65.0
Normal 2.....		67 0/16	52.0	60.2	134.7	49.5	74.7
Basiliki S.	10	67 0/16	56.2	61.3	107.0	38.8	52.3
Normal 1.....			54.0	63.0		40.0	55.0
Normal 2.....		67 14/16	52.7	62.4	135.7	49.7	74.9

* Normal 1—When compared to children of same weight and height.

† Normal 2—When compared to children of same age.

The foregoing cases illustrate so well the symptoms of dwarf growth and infolding that each will not be taken up in detail here. A complete discussion of the symptoms will be found in connection with the plates at the end of the paper. At this time we wish to mention only a few of the more salient features.

GROUPING OF CASES

1. We seem to have two groups of cases:

- A. That including Dorothy A., Beatrice R. and Basiliki S. shows more the symptoms of dwarf growth, while
- B. That including Emily S. and Ita P. shows the symptoms of infolding.

Frank B. falls between these two groups, having symptoms of each.

2. Emily S. and Ita P. have a feature which seems hitherto undescribed, for we can find no mention of it in the literature.

Each case has an arcuate kyphos with a point of greatest convexity. Emily S. has this in the dorsal region, while in Ita P. it is dorsolumbar.

Roentgen-ray examination of this region shows a wedge-shaped vertebra at the point of greatest convexity.

Since there is no disease of the spine in either of these cases, we have taken the stand that this peculiar vertebra is the result of Jansen's "amnio pressure." The same force which presses on the two ends of the spine producing the kyphos might also very easily, it seems to me, produce this wedge-shaped vertebra.

3. Dorothy A. and Beatrice R. have in addition to the ordinary symptoms of "achondroplasia" certain bony changes which can easily be seen in the roentgenograms. Because of the limitation of time, it

Fig. 8.—Ita P. Roentgenogram showing the wedge shaped vertebra; antero-posterior view.

Fig. 9.—Ita P. Roentgenogram showing lateral view of the wedge shaped vertebra.

has not been possible to work out this added complication, but it seems to me that some of the changes agree very well with those described by Ehrenfried (1915).

PATHOLOGIC CHANGES

Kaufmann (1892) described the pathologic condition in achondroplasia and on it based his three forms: (1) Chondrodystrophia hypoplastica; (2) chondrodystrophia malacica; (3) chondrodystrophia hyperplastica. In the first, he described a simple cessation in the growth of the cartilage; in the second, an arrest of the growth depending on the softening of the cartilage, and in the third, not simply an arrest of the growth of the cartilage, but an excessive growth, abnormal in its direction.

Morse (1902) says: "The most important pathologic process is, in brief, a disturbance of the normal process of ossification of the primary cartilage." He reviews Kaufmann's article and adds "Osteo-

Fig. 10.—Ita P. Roentgenogram showing the poorly developed pelvis.

porosis and osteosclerosis may occur as complications in any case. Fractures may also increase the deformities."

Bullard and George (1908) review the work of Apert (1901) and Durante (1902) and have the following résumé: "Sclerosis of the epiphyseal cartilage while in preparation for multiplication. Lack of serial arrangement of the cartilage cells and deficiency in cartilaginous ossification while processes from the marrow cross the line of ossification. Abundant periosteal ossification produced as well by means of osteoblasts as by direct calcification of the fibrous lamellae, but only eventuating in the formation of a spongy bone with thick resistant lamellae. Sclerosis of the bone marrow."

Jansen (1912) says the ossification of the epiphyses is very much retarded, while the diaphyses, on the contrary, have not only formed

relatively more bone, but the edges of the periosteal bone have grown round the epiphysis in the shape of a funnel. The periosteum often forms a process (Kaufmann) which penetrates between the diaphyses and epiphyses, and Wallaardt Sacré finds the periosteum of long bones showing a more rapid growth at their ends, so that the diaphyses surround the epiphyses very nearly like "cuffs." "All this," he says, "proves that the periosteal bone grows faster than the epiphyseal. The periosteal bone is not completed by the addition of endochondral bone, which the epiphysis normally deposits at the ends of the diaphysis. The epiphysis is at fault, but still the periosteum continues its growth sometimes in the normal direction, forming a funnel around the epiphysis, or sometimes, departing from the right track by separating diaphysis and epiphysis by an abnormal layer of cellular tissue."

"The microscopic picture," Jansen adds, basing his opinion on the work of Kaufmann and Wallaardt Sacré, "of the achondroplastic bones confirms the opinion that in them the specific power of growth is diminished; the chief histologic characteristics of length growth in bone substance is constantly at fault; the columns of cartilage cells are too short, show irregularities in their arrangement and in their direction, or are lacking altogether." He does not pass on any decision as to how normally the cartilage cells are so thoroughly informed both of the direction of muscle action and of gravity, as to arrange their columns so precisely in these directions, but adds: "However that may be, the columns of cartilage cells in achondroplastic bones are situated less precisely in the long axes of the bones than normally. Moreover, they are shorter. Thus, the microscope reveals the picture of a diminution of the growth and the power of growth in achondroplastic bone."

I have not had the opportunity to study achondroplastic bone histologically. The work of others, probably due to lack of material, although describing single stages amply, does not at all exhaust the fields of embryological development of such bone. Such a piece of work would be valuable to consider in view of Jansen's work on the cause of achondroplasia.

THE ROENTGEN-RAY EXAMINATION

Most writers say little of the examination of cases of achondroplasia by the roentgen-ray method. Bullard and George (1908) has described it more fully. They divide the cases into two groups: (1) Those cases which are seen up to puberty without marked deformity; (2) cases with marked deformities of the limbs, or those cases in which there is a secondary joints lesion apparent (Kaufmann, 1892).

Fig. 11.—Ita P. Roentgenogram showing: (a) the short bones of the lower extremities and (b) a definite tendency for the periosteum of the distal end of the femoral diaphyses to form a "cuff" about the epiphyses.

They say, "In the first group of cases the typical roentgen-ray picture of a given bone, the tibia for instance, will show it to be shorter and wider than that of a normal child, having a well developed ossific center for that given age. The shadow produced by the bone generally compares well with that of a normal child. Deformities of the shaft, with the exception of bowing, are rare in this group. The cortex is thicker, particularly in the middle of the shaft, showing considerable deposit of bone and thinning out toward the epiphyses. At the same time, the medulla, though small at the middle of the shaft, is increased in width proportionately with the thinning of the cortex; the bone structure in some cases is practically normal as compared with that of a normal child, but in the majority of cases a coarser and sometimes a more irregular deposit is apparent, particularly in the diaphyses.

"The most characteristic appearance of a long bone under examination in achondroplasia is that near the epiphyseal ends, the diaphyses become cup shaped, producing a T-shaped outline without any disturbance of the epiphyseal line or zone of proliferation, though they may be uneven and take on more or less fantastic shapes as compared with those of a normal individual. They are not, however, as uneven as in the diseases of nutrition, such as rachitis, where there is a definite disturbance of the zone of proliferation, but, as has been stated, the ossific centers have been well formed and the epiphyses are apparently fitted into the cup-like diaphyseal ends. In this first group of cases there is nothing seen in the roentgenograms which could be confused with rachitis.

"The second group of cases which we meet with in a large clinic is characterized by the large rectilinear head, extremities extraordinarily shortened in comparison to the bodies, the upper arms and thighs shortened in comparison to the forearms and legs, but distinguished from group (1) in that the osseous system shows more definite pathological changes such as scoliosis, kyphosis and lordosis of the spine, coxa vara, genu valgum or varum, and ankylosis, partial or complete, of one or more joints, due either to a mechanical inhibition of joint motion or to pathologic changes within the joint.

"In the roentgen-ray examination of these cases, though the underlying appearance of the bone is that of group (1), we have a more definite change of the articular surfaces of the joints, or of the epiphyses in general, to such an extent that one would hardly identify the given joint; there is a great distortion of the bone generally, with a tremendous increase in the size of certain portions, such as the great trochanter of the femur. The joint surfaces are practically absent, with a partial or complete erosion.

“It is to be noted that the epiphyses in this case are all delayed in their development, particularly as these children approach puberty, when there seems to be very little, if any, development of the epiphyses beyond a certain point.”

Fig. 12.—Frank B. Aged 4½ years. Total length 87 cm.

In speaking of the roentgen-ray examination of long bones in which Bullard and George (1908) say the epiphyseal ends of the diaphyses have a “T-shaped” outline, Jansen (1912) refers to this as a “cuff” of periosteal bone and says that the roentgen rays show that the peri-

osteum forms more bone than the epiphysis. Kaufmann (1902) and Jansen (1912) contradict the statement of Bullard and George (1908) that there is not any disturbance of the epiphyseal line or zone of proliferation. They hold with others that there is a growth of fibrous tissue from the periosteum between the epiphysis and diaphysis.

THE CAUSE OF ACHONDROPLASIA

Morse (1902) said, "Little is known as to the cause of this disease." Such a state existed until 1912 when Jansen advanced his hypothesis that the amnion is the cause. His argument is so convincing that I review it here, first giving his summary of the various opinions of other writers on the subject.

He says: "Parrot (1878) who first recognized the affection as a separate entity, and introduced the name achondroplasia, considered it to be the nature of a congenital nutritive disturbance of the cartilage germ cells. Parrot thereby provided us with a circumlocation rather than an explanation of the facts.

"De Buck and Mayet (1900 and 1901) consider this change in cartilage germ cells as a sign of degeneration and consider the achondroplasts as the last member of a pedigree of degenerates." We may plead against this theory that achondroplastic women not frequently bear normal children (Treub, 1904).

Poncet and Leriche and others consider the achondroplasts as a separate race on account of the striking resemblance they show one to another. Against this it has been argued that, on account of the considerable narrowing of the pelvis, natural (Nolen) birth is usually impossible and thus the conditions necessary for the existence of a race as such are not met with. And even those who cling to the idea of a separate race, will feel the need of finding the causes which lead to this change.

"Bohn and Schwob (1868) deem a disturbance or insufficiency of the placenta probable in correlation with the nutritive disturbance." No facts have yet been brought forward in support of this suggestion.

"Klebs (1889) is of the opinion that the umbilical vesicle by an excessive development and a broadening of its stalk is able to compress the limb buds just after their formation, and so to stunt their growth." Even those who firmly believe in the correctness of this hypothesis must seek a further explanation for the changes in the skull.

"V. Franque (1893) and Rindfleisch (1899) have suggested that mechanical pressure of the surrounding tissues on the embryo might be the cause; but the hypothesis has been rejected on account of the symmetry of the dwarf growth in achondroplasia and the strong resemblance of every two cases, both of which characteristics dis-

tinguish it from the asymmetry and diversity shown by deformities known to be the result of external pressure (Sumita).

“Wissermann (Sumita) considers tightness or rather lack of expansion of the skin as a possible cause of the stunting in growth of the

Fig. 13.—Dorothy A. Aged $6\frac{1}{2}$ years. Total length 90.8 cm. This picture shows the short extremities and the extra toes.

bones; but as has rightly been objected, the skin is not lacking in expansion in achondroplasia; on the contrary, its growth is relatively excessive so as even to lie in folds.

"Most of the authors who have written on achondroplasia consider it to be an hereditary infection or intoxication.

"Dor (1893) considers the toxi-infectious agent to affect the cartilage directly: typhoid fever promotes the growth of the skeleton, he argues; whilst on the other hand intestinal infections inhibit its growth. In the latter sense the unknown agent works from an early stage in the development of the skeleton.

"Syphilis and tuberculosis, alcohol and tobacco, the causal agents to which so many ills are attributed, have naturally not escaped being accused, each and all, of being responsible for this affliction; but again, no valid evidence has been brought forward in support of the accusation.

"Cestan (1901) and Reignault speak of intrauterine rickets."—Both in rickets and achondroplasia, indeed, shortening of the extremities occurs. In rickets, however, the disproportion is chiefly due to curvature of the bones; in achondroplasia it depends on their insufficient growth in length. Moreover, an achondroplast is born as such and remains so for life. Rickets, on the contrary, appears after birth and disappears later on in life. To label the two affections with one name would, therefore, create confusion rather than afford a deeper view into the nature of either.

"Porak and Durante (1905) base their opinion on the histological appearance of achondroplastic cartilage. They consider it to be characterized by sclerosis. All substances that exercise a sclerogenetic influence on cartilage may—according to them—be the cause of achondroplasia. New data afterward led them to the conviction that in addition to the theory of hereditary infection or intoxication, which they postulate as a casual agent, certain forms of achondroplasia might be brought about by autointoxication." We doubt whether the insight which the histological aspect of this affection affords, is explicit enough to justify such far reaching conclusions.

"P. Marie expresses himself with more caution: Could there not in this disturbance of development, be something analogous to myxedema; should we not seek the cause of achondroplasia in a deficiency in the function or the development of some gland?

"All glands with internal secretion have indeed been suspected in the attempt to answer this question:

"Leblanc (1902), who found myxedema and achondroplasia combined in a calf, considered the thyroid gland responsible.

"Lugaro also saw the two affections combined in man, and Devay (Parhon, Shunda and Zalplachta, 1905) as well as Collmann, on the contrary, found the thyroid gland enlarged in a case of achondroplasia. In by far the majority of achondroplasts this gland is normally

developed. Identifying the two affections would mean returning to the old standpoint of Virchow who confused achondroplasia and cretinism. Clinicians have since placed the two wide apart. Yet, the relative frequent coincidence of these two affections raises the suggestion that the causes of congenital cretinism and achondroplasia may be related.

"Vargas raises the question, whether the thymus may be the cause; but without procuring any support for this hypothesis.

"Parhon, Shunda and Zalplachta (1905) consider it possible that a hypofunction of the pituitary body, the thyroid gland and the thymus, combined with a hyperfunction of the sexual glands might produce achondroplasia. They strongly emphasize the latter. Before birth this enhanced action of the genital glands might be excited by the ovaries of the mother, and after birth the child's genital glands

Fig. 14.—Dorothy A. This picture shows the extra toes, the second and third being webbed, and the horny irregular toenails.

might begin to exert their influence too early and too powerfully. Especially after the publication of Leriche's (1904) observations, they strongly inclined toward the great influence of the latter, of which Leriche says: 'au rebours du gigantisme avec lequel elle (—la glande interstitielle du testicule et de l'ovaire) est en relation manifeste en certains cas par défaut, la glande testiculaire pourrait peut-être par viciation ou par excès produire un arrêt de croissance.' It is especially the experiments of Leriche's teacher, Poncet, and those of Dor and Maisonave which served as the foundation of his belief. The former, indeed, has ascertained that castration causes excessive growth of the skeleton, while the latter elicited a "sterilization relative" of the diaphyso-epiphyseal cartilage discs and a stunting in the growth of animals in injecting extract of testicle. However, these experiments

have not led to achondroplasia by any means; and it would thus be premature to consider achondroplasia as the effect of an exaggerated secretion of the sexual glands both of the mother (before parturition) and of the child (soon after birth). Moreover, the enlargement of the skeleton by castration is greatly exceeded by gigantism; and the effects of gigantism and castration are not to be identified.

Fig. 15.—Dorothy A. Roentgenograms showing (a) the extra metacarpals and metatarsals, the extra fingers having been removed at operation, the extra toes being present; (b) the character of the metacarpal and metatarsal bones and (c) the epiphyses surrounded by periosteal “cuffs.”

“Ettore Levi (1909), to complete this enumeration of writers, rejects the hypothesis of P. Marie—and in our opinion—he is quite

right in so doing; Levi is ready to admit that gigantism may be caused by a disturbance in the function of a blood gland, and even infantilism, because in these affections all segments of the skeleton are modified. In achondroplasia, however, we cannot see how a blood gland could

Fig. 16.—Beatrice R. Aged $9\frac{1}{2}$ years. Total length 121.7 cm.

be the cause, because the dystrophy is restricted chiefly to the extremities.

“In short, we find that the causes of achondroplasia are still completely enshrouded in obscurity; local nutritive disturbances in the

cartilage, infection—both hereditary and direct—intoxication—both exogenic and endogenic—sclerogenetic influences, race peculiarities, degeneration, defective function of glands, mechanical pressure—form the motley series of possibilities from which science has hitherto been unable to make her choice.

“It will now be our task to find out whether the mechanical malformations, which characterize the achondroplast, and which we have proved to be the results of infolding of the fetus, may put us on the track of the causes of this disproportionate dwarfing of the growing body in achondroplasia.”

Jansen says that the mechanical malformations, characteristic of achondroplasia, could be brought about by three compressing forces which act on the head, the neck and the tail bends of the embryo and, so to speak, roll it up in its long axis. He does not believe that this can be produced by direct pressure from maternal parts, because of the space between the amnion and the fetus. Nor does he believe that pressure on the fetus transmitted by the chorionic liquid could bring about the malformations because this pressure would be the same in all directions and be unable to accentuate the normal bends in the manner found characteristic of achondroplasia.

By exclusion, then, we must find in the amnion the source of the deforming forces. Only two conditions of this need be considered, i. e., hydramnion and smallness of the amnion. That hydramnion does not constantly bring about these malformations may be understood, when we consider (1) that rapid growth or distention of the amnion might soon put an end to the abnormally high pressure, and give the embryo an opportunity of resuming the normal attitude before injury has been inflicted; and (2) that, when the abnormal increase of liquid in the amniotic sac begins (only after the amnion has been lifted from the surface of the embryo) the abnormal axial pressure need not be exercised.

It then remains that, except in rare cases, the deforming forces must be due to the smallness of the amnion. That the amnion is often affected by such a primary disturbance in growth is accepted by such investigators as Dareste (1892), Marchand, Schwalbe, Kocher, von Volkmann and others.

But we have not considered the cause of the dwarf phenomena. If the smallness of the amnion produces the malformations of infolding, can the same cause affect the growth of the deep lying parts? This seems to be the case, and it takes place in the following way. The amnion which folds up the embryo, at the same time impedes the supply of food by producing a closer contact of the cells and a diminution of the nutritive fluids. If it may be accepted that embryos are

rolled up by their amnion, it is also certain that the direct amnion pressure has caused the preponderant axial dwarfing of the pelves and in a lesser degree that of the spine. And that which is true of the direct amnion pressure in one direction, is true of the hydrostatic pressure in all directions; if the axial pressure of the amnion is able to squeeze blood out of the scleroblastematous spine in one direction, then the hydrostatic pressure is able to do the same in all directions. If a direct pressure of the amnion can cause dwarf phenomena in one direction, the indirect hydrostatic pressure can do the same in all directions; in other words, if direct amnion pressure is the cause of the phenomena of infolding in achondroplasia, then indirect or hydrostatic amnion pressure is the cause of the dwarf phenomena.

Fig. 17.—Beatrice R. Roentgenogram showing the misshapen fifth metacarpals where a sixth finger has been removed at operation, and the epiphyses of the phalanges surrounded by the peculiar funnel-shaped "cuff" of periosteal overgrowth.

In view of this we understand that the bones formed in cartilage are most affected because they increase their volume more rapidly than other tissues and because they demand such a large amount of nutrition in their growth. In other words, heightened amnion pressure, through a diminution of blood supply, leads to an "aplasia" of "chondrium," an "achondroplasia." And, the bones formed in membrane (except in the severest forms) pass unmolested because they are not gluttons.

Above all, it becomes clear why the growth disturbance affects the latest formations most, the earliest least, for each younger part of the skeleton forms its cartilage under more unfavorable conditions.

We can now see that the severest forms of achondroplasia must be produced by the smallness of the amnion, while the relatively slight

forms may have been produced by less damaging hydramnion. Further, Jansen (1912) believes that hare lip, micrognathia, apnathy, myxedema, hydrocephalus, gas bubbles in the internal organs, subcutaneous fatty masses and increased sexual function which are often found in the achondroplast, may be considered in relation to this same direct and indirect amnion pressure. His observations on the latter are especially interesting. Summing up his facts, we find in:

castrates:	sexual functions	<→	pituitary	>	growth	>
pregnancy:	sexual functions	<	pituitary	>	growth	>
acromegaly:	pituitary	>	growth	>	→	sexual functions <
gigantism:	pituitary	>	growth	>	→	sexual functions <
achondroplasia:	pituitary	<	(growth <)	→	sexual functions	>

Thus the idea is suggested that the exaggeration of the sexual functions which we observe in achondroplasts may be the consequence of the disturbance in the development of the pituitary body which we found in the severer cases.

THE TIME AT WHICH THE CHANGES OF ACHONDROPLASIA
TAKE PLACE

The question now quite naturally arises as to when this infolding of the embryo takes place. The following things strongly suggest the idea that the embryo, between the third and eighth week of its intra-uterine life, has been, so to speak, bent up, infolded, "coiled up" like an anchor rope:

(1) The degree of retardation of growth of the various parts of the skeleton is determined by the time of their primary formation from the scleroblastema, as can be seen in Table 2.

TABLE 2.—COMPARISON OF DATE OF FORMATION AND RATIO OF ANOMALIES.

A. Date of Formation (Keibel and Mall, 1910)				B. Ratio of Anomalies (Jansen, 1912)		
	Of the sclero-blastema	Of the cartilage	Of the centers of ossification		In smaller dwarf skeletons	In larger dwarf skeletons
Of the cervical vertebrae	3d week	5th week	56th day	Of the breadth of 3d cervical vertebra	$\frac{1}{1.97}$	$\frac{1}{1.31}$
Of the lumbar vertebrae	After the cervical vertebrae	5th week	73d 105th day	Of the breadth of 3d lumbar vertebra	$\frac{1}{3.10}$	$\frac{1}{1.5}$
Of the humerus diaphysis	End of 4th week	5th week	42d day	Of length of humerus diaphysis	$\frac{1}{3.63}$	$\frac{1}{2.5}$
Of the femur diaphysis	Early after humerus 5th week	5th week	42d day	Of length of femur diaphysis	$\frac{1}{3.47}$	$\frac{1}{2.80}$
Of the epiphysis	After diaphysis		10th month or after birth	Of the thickness of cartilage between femur and tibia diaphysis	$\frac{1}{8.33}$	$\frac{1}{3.00}$

Thus we see the formation of the primitive vertebrae starts in the cervical region and proceeds in a caudal direction; and it is only after the sacral vertebrae have been formed that the extremities bud. In these again the epiphyses are the latest formations. And in the same order we see the various parts of the skeleton in achondroplasts affected in a successively increasing measure.

Fig. 18.—Beatrice R. Roentgenogram showing the clubby shape of the femurs; the cortical thickening with resulting decrease in caliber of the medullary canal and the bowing of the femurs, especially the left.

2. It may be remembered that the pituitary body develops between the second and eighth weeks of fetal life and that its larger anterior part is formed by a diverticulum of the roof of the primitive mouth, which pierces the mesodermal covering of the brain vesicle between

Fig. 19.—Beatrice R. Roentgenogram showing: (a) the difference in length of the tibiae. The bowing of the left femur exactly compensates for the increased length of the left tibia for the lower extremities are of the same length; (b) the bulbous ends of the long bones; (c) the small exostoses which are present at the epiphyseal lines; (d) the cortical thickening of the bones and (e) the eccentric medullary canals.

the future presphenoid and postsphenoid, i. e., between the anterior and the middle bone centers of the tribasilar bone. Thus, the fact that the sella turcica may be totally absent, if indicating that the development of the pituitary body has been disturbed may suggest the inference that this disturbance has taken place between the second and eighth weeks of fetal life.

3. In order that the skull shall assume the form often seen in the foregoing discussion the change must have been brought about at a period of fetal life, when the skull was still membranous, either entirely or for the greater part.

4. From Table 2 we see that the scleroblastema formed at the third week begins to change into cartilage about the fifth week, while the formation of bone begins at about the eighth week. The suitable time, then, for the malformations of the spine lies between the third week, when the condensation of the primitive cellular tissue into scleroblastema may be observed, and the eighth week, when the cartilaginous formation begins to harden into bone substance.

5. The form of the normal embryo of 4 weeks is such that (a) pressure on the head curve must needs push the region of the visceral arches and the future face against the organs of the future chest and the chest wall. It is quite intelligible that this is the way in which the region of the future nose has been either partly or wholly flattened and the hard palate displaced in the direction of the base of the skull. Therefore, an accentuation of the normal neck curve subjects the parts of the future face to a compression which fully explains their characteristic malformation in achondroplasia. (b) Similarly, a pressure at the neck curve may have moved forward the parts of the squama occipitalis. It may have narrowed the foramen magnum, when its anterior border, the lower part of the tribasilar bone, was driven against a firm resistance (the hard palate in front), or have displaced it in a forward direction, i. e., kyphotized the base of the skull, when no such bony resistance was met with, the posterior border of the palate being tilted high up. (c) Finally, the forces at the caudal end of the fetus counteracted those acting on the head, and have kyphotized the spine.

6. If we believe the smallness of the amnion to be the cause of the mechanical malformation, the changes must take place between the third and eighth week, for it is during the third week that the amnion obtains the power of folding up the embryo. Up until then the amnion with its mesodermal and ectodermal layers is about as thick as the embryo and hardly inferior to it in firmness. During the sixth week

the amnion probably loses the power of folding up the embryo because the embryo rapidly increases in firmness and by the seventh and eighth week the skeleton finally presents ossification centers.

RESUME

1. The name "achondroplasia" has been chosen for the condition under discussion because the state is an "aplasia" of "chondrium."

2. Achondroplasia is characterized by symptoms of dwarf growth (shortness of extremities, vertebral column and chest and looseness of the skin) and symptoms of infolding (kyphosis baseos cranii, sagittal narrowing of the foramen magnum, depression of the nasal bridge, narrowing of the choanae, reduction in the size of the sella turcica with consequent reduction in the size of the pituitary body, and changes in the spine).

3. The changes of achondroplasia are probably due to the smallness of the amnion, except in rare cases.

4. The changes of achondroplasia are produced between the third and eighth weeks of intra-uterine life.

5. The pathologic changes consist mainly in a retardation of ossification of the epiphysis and the diminished production of endochondral bone, while the periosteum produces a comparatively normal amount of bone.

6. Besides the deformities of the bones, the characteristic roentgenologic appearance of a long bone under examination shows that near the epiphyseal ends the diaphyses become cup-shaped, producing a T-shaped outline without any disturbance of the epiphyseal line or zone of proliferation, though these may be uneven and take on more or less fantastic shapes as compared with those of a normal individual.

7. All the cases presented in this paper bear out all that has been said, and in addition two of them show a new symptom, a wedge-shaped vertebra, which falls in the group of symptoms of infolding, and fortifies the belief that the state of achondroplasia is produced by the smallness of the amnion.

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