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Bony Gauges of Growth, Age and Disease*

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INTRODUCTION

THE recognition of the fact recently reported by Ariev[1] that every bone has its own distinct sound when tapped, is not new. According to Welsh tradition, it was an ancient custom for the soothsayer to detect a murderer by spelling out his name from the sound of the victim's bones when dropped, one by one, into an empty caldron. Yet Ariev's use of this knowledge, through oscillograms or kymographic records of the sound waves set up when bone in the living subject is tapped, is new and valuable. Oscillograms may be a new instrument of diagnosis for fracture, inflammatory conditions and the soundness as well as the age of bone in general.

Similarly general cognizance of the phenomena to be discussed this evening is not new, but new knowledge has greatly increased their importance in relation to medical problems of growth and development; endocrine disorder, and senile decline.

SKELETAL CHANGES

The hard and durable character of the skeleton and the circumstances under which it is usually observed have too frequently caused the skeleton to be regarded as a permanent and unchanging bodily structure, once it has been formed. This concept, however, has lately been greatly modified by evidence that the skeleton is a great storehouse of calcium which is constantly drawn upon according to physiological needs. Thus the mineral content and often the roentgenographic appearance of the bones are correspondingly altered. The skeleton also undergoes a continuous phyletic pattern of differentiation from fetal life to old age, no two stages of which are the same. In addition, the bony framework exhibits many forms of secondary modifications developed in response to environmental conditions.

BONY GAUGES OF GROWTH

The outstanding features of growth in the long bones are well known. Growth refers to increase in dimensions as contrasted with development, which connotes increase in complexity of structure. Bones grow in both diameter and length. Growth in circumference is effected mainly by subperiosteal osseous deposit. This process usually results in compact bone, the organization and distribution of which are largely controlled by mechanical factors. Growth in circumference is effected mainly by subperiosteal osseous deposit. This process usually results in compact bone, the organization and distribution of which are largely controlled by mechanical factors. Growth in length is produced chiefly by the extension of endochondral ossification into growing diaphyso-epiphyseal cartilage. In general, the increment of growth in length diminishes with age as adult size is approached. The rate of increase diminishes more rapidly at the end with the lesser increment, that is at the end with the first epiphysis to unite.[2] The individual bones, however, do not grow at the same rate relative to each other. The maximum rates of increase of the bones of the arm and forearm and of the thigh and leg are each at different periods as we shall shortly see in the case of the crural index.

In the fetal period, growth in all dimensions of the body, which are basically skeletal dimensions, is directly proportional to the body length. This proportion may be expressed by a mathematical formula, employing constants which indicate the changes in relative size which the several dimensions undergo. The length of the

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leg increases more relative to body length than the length of the thigh and the forearms more than the arm in fetal period. The growth curves of the bodily dimensions and of the organs during the fetal period, assume the form of a parabola, that is to say, the dimensions and organs show a rapid increase in the beginning of the fetal period and a steady decline thereafter. [3]

In post-natal life the growth rates of the various regions and organs do not bear such a uniform relation to each other and must be considered separately. The changes in the crural index are of particular interest.[4] The crural index is the length of the tibia expressed as a percentage of the length of the femur. The crural index tends to increase from about 83 at six years to about 93.5 at eleven or twelve years and then to diminish to the adult average of 85. This means that between six and twelve years the leg is growing faster than the thigh, whereas during adolescene tibial growth is damped and gives way to relatively faster increases in femoral length.

Since leaping animals have the longest tibiae in relation to femoral length, Davenport has gone so far as to suggest a relationship between the child's fondness for leaping games in the period when the crural index is highest and the fact that he is mechanically best adapted for leaping and jumping at that time.

Technical considerations and the error of measurement[5] render bodily (skeletal) dimensions and proportions of limited value when applied to individual cases presenting problems of growth. Detailed figures for dimensional increase or growth, with analyses and correlations may be obtained in specialized studies such as that of Wallis.[6] With the observation that, unlike prenatal growth, growth after birth does not progress at a definite rate but occurs in spurts which take place in childhood and in adolescence with wide individual variability as to time of occurrence, we may turn from the subject of growth to that of development.

GAUGES OF AGE AND DEVELOPMENT

In daily life we frequently make estimates of the maturity of individuals, comparisons of physiological age with chronological age. We say that one fellow is 'old for his years' while another has 'never grown up.' If one desires to render an estimate of maturity more accurate by the use of scientific criteria, he finds that several such criteria are available, but that most have decided limitations in scope.

The most commonly used standard is the height-weight ratio. This is very useful as an index of nutrition, but in the absence of definite pathology physicians are rightly very cautious in ascribing specific developmental significance to a child's deviations from the average in weight or height. The normal limits of these dimensions are too ill-defined. The fluctuation in height-weight relationship is such that this index cannot be separately employed as a measure of health and maturity without adequate clinical history. The Baldwin-Wood tables for example,[7] a national height-weight standard, classify all individuals in each age group except the highest and lowest 12.5 per cent as medium. The remainder are designated tall and short respectively, but this arrangement obviously gives a very wide range to the medium group.

The dentition has been studied as a measure of development by Bean,[8] Matiegka,[9] Hellman[10] and others.[11] Though sex and racial differences have been determined on the basis of the eruption of teeth, the standard deviation or average variability of the time of eruption of each permanent tooth is more than a year, so that the dentition is not more accurate than the height-weight ratio as an index of development in individual cases, because a range of three years is too wide to be of practical value. (A deviation to be in itself significant must be at least three times the standard deviation. The latter is more than one year for the eruption of individual teeth.)

Similarly pubertal changes and mental age as determined by combined intelligence tests, show too great a variability to be used alone as measures of development or maturity in individual instances. A much closer gauge of development is the state of differentiation of the skeleton. The standard deviation for the skeletal age of growing individuals is three months.[12] Therefore, a child whose skeletal record differs from the modal value by more than nine months may be classified as accelerated or retarded in development irrespective of what his stature, weight or dentition may be.

Progress in sub-adult skeletal differentiation is registered by three kinds of phenomena. Between birth and five years the appearance of centers of ossification is the indicator, but this is one of several measures of mineralization and not an index of developmental maturation. Between five and fourteen years the penetration of cartilaginous areas by bone is the gauge. From fourteen to twenty-three years, skeletal age is registered by epiphysial union. A series of roentgenograms of the hand and wrist, elbow, shoulder, hip, knee, and foot and ankle readily disclose the stage of bony development.

Ossification is well established in the shafts of the long bones in fetal life. At birth, however, there are only six centers of ossification present in the epiphyses and carpus and tarsus. These are for the calcaneous, talus, distal femur, proximal, tibia, humeral head and cuboid. Before the third birthday in girls and the fourth birthday in boys sixty-four ossific centers have appeared. In the interval ossification centers have appeared for the carpus and tarsus, the metacarpus and metatarsus, the phalanges, the epiphyses of the radius, ulna and fibula and the remaining epiphyses of the humerus, tibia and femur.

The order of appearance of these centers is very erratic, and the period of early childhood is one so susceptible to environmental influences that the average date of appearance of a center is too crude a measure to be used as a standard. The earliest date at which a center has been found is the best standard available at present.[12]

Between five and fourteen years the penetration of cartilage by the ossific centers of both epiphyses and diaphyses is used as the criterion of development. It will be borne in mind that the complete form of bone is already well modelled in cartilage. What we watch in this period is the replacement of the cartilage by osseous tissue. So definitely patterned is the manner in which this bony penetration occurs that the maturation changes recognizable on the roentgenogram at the diaphyso-epiphysial junction may be divided into nine stages.[13] Interpretation of the skeleton at this stage is more difficult than in the periods of appearance of ossification centers or epiphyseal union, and requires considerable experience for satisfactory results.

Between fourteen and twenty-two years the epiphyses are joined to the shafts and growth, but not development, perforce ceases. Subcutaneous and visceral fatty accumulations may thereafter alter the bodily form but cannot change the limits of size determined by the adult skeleton. The epiphyses unite in a very definite order and extensive investigations by Todd have demonstrated "the essential unity in order and relationship of epiphysial union throughout the mammalia."[14]

In man the epiphyses of the humerus both open and close this period of development. The first epiphysis to unite is the distal extremity of the humerus, followed in order by the proximal ulna, medial epicondyle of humerus, lesser trochanter, femoral head, greater trochanter, distal tibia, distal fibula, radial head, proximal tibia, distal femur, proximal fibula, distal radius and distal ulna. The last epiphysis to unite is the proximal end of the humerus.

If, as Alexis Carrel has done,[15] we compare physiological time and chronological time to two trains running on parallel tracks extending between birth and old age, we should note that the chronological train runs at a constant and unvarying speed for the entire life span, but the train representing physiological time runs very swiftly far ahead of its companion during the years preceding adult life, then slows down is passed by chronological time and runs on a very irregular schedule until old age is reached when it rapidly accelerates and catches up with chronological time at death.

So in the skeleton the stamp of the periods of youth and age is definite, but the appearance of the bony framework during early and middle adult life is so variable that no single criterion of age can be used alone, and in occasional instances several criteria used together will not prove satisfactory. However, a skilled observer can determine the age of an adult skeleton to within about six years.[16]

The features which furnish the basis for estimate during this time are: the condition of the sutures, the differentiation of the pubic symphysis, the lipping of long bones, changes in the bony texture and the wear of the teeth.

To be mentioned also because they are of value in the third decade are the stragglers among the epiphyses, those of the bodies, spines and transverse processes of the vertebrae and the heads of the ribs, which fuse before twenty-five.

The bones of the cranium have been in a latent state for many years before suture closure commences and most of their capacity for growth has been utilized before adult life is reached. This fact is related to the very precocious development of the human brain case. At two years the cranium is half its adult size and at six years has attained seven-eighths of its full growth. Increase thereafter is very slow and amounts to about ten to thirty cubic centimeters in cranial capacity per year.[17]

A ready illustration of the fact that the cranial bones have used most of their growth and regenerative capacity early in life, is that a trephined opening does not close in healing. In a sense therefore the parietal of a man of twenty-one is physiologically as old as the femur of a man of sixty-five.

After their long dormant period the cranial bones manifest a period of renewed activity in the form of suture closure.[18] This activity reaches its height between twenty-six and twenty-nine years. Suture closure is essentially the same from both endocranial and ectocranial surfaces but is slightly more uniform endocranially. The first suture to close is the sagittal which begins to unite at 22 and is practically closed at 31. Next is the coronal which begins fusion at 24 and has almost completed it at 38. The lambdoid begins union at 26 and has practically completed it at 47. The parieto-temporal exhibits slight union at 37 but remains inactive until 62. Then it has a burst of progress in closure until 81 when it is about three-fourths closed. Cranial suture closure constitutes a useful though not very reliable indicator of age over a long period of adult life.

Equally valuable for this purpose is the differentiation which occurs at the pubic symphysis.[19] This maturation process begins shortly before nineteen years and is complete at about forty-five. It may be divided into ten stages which cover the transformation of the pubic symphysial surface from an irregularly outlined area marked by transverse ridges and furrows into a distinctly demarcated oval articular surface surrounded by rim. After forty-five, secondary erosions begin to destroy the ventral rim of the completed symphysial surface so that even later the area has some value as an age indicator.

Another phenomenon which begins to appear at about thirty-five years and is therefore suggestive of age is the formation of a rim around the articular margins of the long bones, principally at the elbow, wrist, shoulder, hip, knee and ankle. This rim is, in time, transformed into a lipping which may progress until it is very marked. It is essentially an age change not to be confused with hypertrophic arthritic changes which sometimes resemble it but have a totally different (earlier) age incidence.[20]

Beginning at about fifty years the texture of the skeleton begins to undergo a change. The surface of the bones loses its smooth waxy character and acquires a granular feel. This change is best marked on the vertebral bodies where the texture may be called cinder-like. In addition there is usually noticeable in old bones a decided lightness of weight indicating loss of calcium.

DIFFERENCES RELATED TO SEX AND RACE

To a satisfactory extent differences in skeletal maturation due to sex and race have been investigated. In the appearance of centers of ossification, girls at two years begin to show an acceleration of development over boys, of about six months. At three years this lead over boys has increased to a year and a half. In bony penetration there is a female acceleration of six months at five and a half years. This has been increased to two years at ten and a half years. During the period of epiphysial union the female acceleration gradually diminishes until at fifteen years the female lead is again six months and from sixteen years on there is no difference between the sexes.[21]

Comparisons between White and Negro children show no significant differences in skeletal development. Both groups follow the human pattern. This statement applies also to suture closure and differentiation at the pubic symphysis, although in the Negro the lambdoid suture exhibits somewhat greater variability in time of closure than in the White and there is more adequate ossification of the epiphyses at the pubic symphysis than in the white[18, 19].

SKELETAL EVIDENCE OF DISEASE

The skeleton is very sensitive to metabolic derangements. Disturbances of health in children such as bronchitis, pneumonia, otitis media, bloody stools, secondary anemia or continued fever may be recorded in the roentgenogram by a delay in the appearance of centers of ossification which should appear at the time of illness. The degree of interruption of the sequence of ossification depends upon the severity of the disease. Once health is restored, the appearance of scheduled ossification centers takes place as though no disease had intervened, but the centers inhibited during the illness appear out of order and their progress is greatly retarded. Such is the basis of irregularities in the age order of appearance of centers of ossification.[12]

Similar in origin to irregularities in the appearance of ossific centers are the rings or transverse lines which appear in all long bones near their diaphysial extremities after the exanthemata. A mass of these rings at the lower end of the tibia and less frequently at the lower end of the radius indicates a dietetic problem or a long continued low or intermittent fever. The lines mark pauses in bony growth, and may remain indefinitely as records of disease at the time at which they were laid down. This phenomenon has been studied by Harris[22] and others.

Glandular dyscrasias may upset the orderly maturation of the skeleton. In hypothyroidism the epiphyses may remain ununited after thirty, whereas in achondroplasia union may occur too early as the bones mature before they have attained full growth. Recently T. T. Zuck has obtained promising results with achondroplasts by stimulating their growth with thyroid extract and guardedly promoting differentiation with anterior pituitary extract. The administration of too much pituitary substance will cause the epiphyses to unite before growth has been completed. Thus it would appear that the two phenomena of growth and development are under separate endocrine regulation. The parathyroids also have a very vital influence upon the skeleton. The recent work of J. L. Johnson[23] in experimentally producing osteitis fibrosa, or von Recklinghausen's disease, in animals by injections of parathyroid hormone has been of distinct importance in claryifying the role of the parathyroids in the metabolism of bone.

In adult life as well, disease and defect exert an influence upon skeletal features although physical maturation has no necessary relationship to certain diseases and defects. Microcephaly, various forms of insanity, syphilis and to a less extent tuberculosis may increase the apparent age of the skeleton. Rickets retards the skeletal age. Affections of the pituitary gland have a real effect which is being vigorously investigated in many centers.

There are many other secondary modifications of bone which it will not be possible for us to enter upon tonight, but we have brought for your inspection a few specimens which illustrate certain additional types of bony modification. Of especial interest are the various kinds of hypertrophic bone changes which represent the reaction of bone and joint to the wear and tear of life. These bone changes are permanent and may or may not produce symptoms. When symptoms are produced treatment must be directed toward the removal of all possible sources of continued irritation.[24]

We are very grateful for your indulgence during these warm moments this evening and hope that in some measure at least you have sensed the biological drama which is inherent in the life history of the skeleton.

SUMMARY

1. The skeleton undergoes constant change manifested by (a) alterations in the mineral content of the bones in accordance with physiological requirements; (b) a continuous phyletic pattern of differentiation from fetal life to old age; (c) secondary modifications developed in response to environmental conditions.

2. The following features are convenient gauges of skeletal age: between birth and five years—the appearance of centers of ossification; between five and fourteen years—the penetration of diaphyso-epiphyseal cartilage by bone; between fourteen and twenty-three years—the progress of epiphyseal union; between twenty-three and about fifty years—the condition of the sutures, pubic symphysis and articular margins of the long bones; from about fifty years to old age—atrophic changes such as the assumption of a granular cinder-like texture by the bony surfaces, especially those of the vertebral bodies, loss of weight by the bones due to decreased mineral content and erosion of surfaces in the symphysial area.

3. Disturbances of health or endocrine imbalance may produce interruptions of growth and development evidenced by (a) delay in appearance of ossific centers; (b) retardation of bony penetration and epiphyseal union; (c) transverse lines on long bones and osteoporosis visible radiographically.

4. Roentgenographic examination of selected sites in the living discloses the stage of developmental maturation attained and indications of past health history.

5. Bony changes of adult life, varied and common but difficult of classification (arthritides, excrescences, exostoses, spondylitis) have been illustrated by specimens available at the Laboratory for further examination by physicians at any time.

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