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TITLE THE PRENATAL DEVELOPMENT OF THE HUMAN FEMUR

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THE PRENATAL DEVELOPMENT OF THE HUMAN FEMUR

by

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of the requirements for the degree of
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Table of Contents

	Page
INTRODUCTION	1
MATERIALS AND METHODS	6
OBSERVATIONS AND DISCUSSION	11
The Dimensions of the Prenatal Femur	11
The Growth Areas of the Prenatal Femur	16
The Process of Femoral Shape Change	29
Gross Development of the Ossified Shaft	48
Environmental Effects upon Femoral Configuration	58
Femoral Torsion and Angular Displacement of the Head	59
Inclination	81
Obliquity	83
Some Proposals for the Solution of the Problem of Environmental Influence in Femoral Development	85
SUMMARY	89
BIBLIOGRAPHY	94

List of Tables

		Page
Tab. 1.	Linear Dimensions of the Prenatal Femur	20-21
2.	Correlation Coefficients and Coefficients of Growth	22
3.	Increments and Percentage Increases in Dimensions between the Smallest and Largest Femurs	23
4.	Relative Changes between Smallest and Largest Femurs	24
5.	Summary Table of Prenatal Torsion	68
6.	Torsion and Angular Displacement of Head	69
7.	Inclination and Obliquity	73
8.	Intersection Point of Load-line with Infracondylar Plane	74

List of Figures

		Page
Fig. 1.	Dimensions of the Femur	10
2.	Dimensions of the Femur	12
3.	Femoral Growth Units and Their Components	15
4.	A representative series of fetal and neonatal femurs at constant total length of shaft	25-26
5.	A representative series of fetal and neonatal femurs at approximately natural size.	27
6.	The regression of log Overall Length of Femur upon log Total Length of Shaft	35
7.	The regression of log Length of Ossified Shaft upon log Total Length of Shaft	36
8.	The regression of log Length of Proximal Cartilage upon log Total Length of Shaft	37
9.	The regression of log Length of Distal Cartilage upon log Total Length of Shaft	38
10.	The regression of log Bicondylar Width upon log Total Length of Shaft	39
11.	The regression of log Anterior-posterior Diameter of Condyles upon log Total Length of Shaft	40
12.	The regression of log Head-trochanter Width upon log Total Length of Shaft	41
13.	The regression of log Diameter of Head upon log Total Length of Shaft	42
14.	The regression of log Diameter of Chondro-osseous Junction upon log Total Length of Shaft	43
15.	The regression of log Minimum Diameter of Shaft upon log Total Length of Shaft	44
16.	The regression of log Minimum Anterior-posterior Diameter of Shaft upon log Total Length of Shaft	45

List of Figures (cont.)

Page

Fig. 17. The developmental shape changes in the proximal and distal ends of the ossified shaft 46

18. The regression of log Torsion upon log Total Length of Shaft 66

19. The regression of log Torsion upon log Total Length of Shaft (Altmann and de Cuveland data) 67

20. The regression of log Angular Displacement of Head upon log Total Length of Shaft 70

21. The regression of log Inclination upon log Total Length of Shaft 71

22. The regression of log Obliquity upon log Total Length of Shaft 72

INTRODUCTION

It is a surprising fact that despite the large volume of literature dealing with skeletongenesis, the manner of growth of prenatal human long bones has never been subjected to comprehensive investigation. Only in the very early stages of development, up to the beginning of ossification, can it be said that the topic has been well explored. Beyond that developmental level, only certain characteristics (e.g., torsion) have been studied intensively.

In the early phases of an investigation of femoral torsion and its possible relation to congenital dislocation of the hip, the lack of information on the prenatal development of the femur was critical enough to warrant beginning the study by an investigation of the growth of the femur itself. It was felt that unless the trend of development of the bone as a whole was known, any investigation of a single facet of its organization would have only limited utility. In this study the developing femur has been investigated quantitatively and qualitatively. Growth and groth rates along several dimensions have been determined and expressed graphically. An attempt has been made to relate the observed growth to certain basic processes already described in the literature.

The most comprehensive study of the prenatal human femur so far available is the work of Pitzen ('23). He reported upon the general proportions of the femur at different levels of fetal development and compared these to those of the child, adolescent and adult. It is to be regretted that indices rather than actual measurements were used throughout his paper and that no consideration was given to rates of growth. Other works of lesser developmental range and more specific interest will be referred to and discussed

in the text where most pertinent.

The series presented in this paper deals with the macroscopic development of the femur from approximately the ninth fetal week to shortly after term. The major contribution to our knowledge of the morphogenesis of the femur during its earlier developmental phase is the classic work of Bardeen and Lewis ('01) and Bardeen ('05) who traced the femur through the first two months with the aid of sectioned material and reconstructions. Braus ('04) dealt with the early development of the vertebrate femur including that of man. Friedländer ('01) and Altmann ('24), interested chiefly in the question of femoral torsion and congenital dislocation of the hip, utilized reconstructions to show shape changes and angles. The works of Murray and Huxley ('25), Murray (26, '28, '36), Murray and Shelby ('30), Fell ('28), and Fell and Robison ('29), have pointed to critical factors in the determination of femoral configuration and growth in the primordial period. Although concerned with the humerus rather than the femur, Streeter ('49) has illustrated the general progress of long bones in this period of development. Utilizing the fundamental works of the above mentioned investigators, supplemented by a study of serial sections available in the University of Michigan embryology collection, the pertinent steps in the early development of the femur may be briefly summarized.

The posterior limb bud appears in the fourth week as an extension of the bodywall composed of ectoderm overlying a homogeneous core of dense, rapidly proliferating mesenchyme. During the fifth week regional differences in density arise, due to local differences in rate of proliferation

(Streeter, '49). In an 11.5 mm embryo (late sixth week) an area of markedly greater density exists along the central axis, blending without sharp demarcation into the otherwise homogeneous mesenchymal mass. This axial condensation, as pointed out by Bardeen ('05), represents the common anlage of the femur and the acetabular region of the pelvis. Bardeen reconstructed the femoral anlage of this age with the use of admittedly arbitrary lines of demarcation. It appears as a paddle-shaped mass of mesenchyme constituting the distal end and the shaft of the future femur. In frontal view it is about half as wide as it is long.

The culturing of cells from chick limb buds of the homogeneous mesenchyme period has demonstrated (Fell, '28) the early determination of the femoral anlage. Cultures of central and peripheral mesenchymal cells show sharp differences in capacity; those from the center eventually differentiate and produce cartilage, those from the peripheral areas do not. Thus, the differentiation of the femoral anlage is not due to the induction of the centrally located cells toward that end but rather is an inherent capacity of the cells that assume the central position and there proliferate.

The mesenchymal anlage enlarges by proliferation until at about 16 mm C-R (6th week) the central region of the shaft has entered the so-called precartilage phase. By this is commonly understood, along with the loss of the processes characteristic of mesenchymal cells, an increase in cytoplasm and the beginning production of intercellular matrix. In the rest of the shaft the changes presaging chondrification are only slightly indicated while the proximal and distal enlargements are still mesenchymal.

Young cartilage has developed in the middle of the femoral shaft by the end of the seventh week (18 mm C-R). Progressively less mature cartilage is seen toward either end, and the head-trochanter and condylar enlargements are barely entering the precartilage phase. As chondrification progresses into the proximal and distal enlargements the center of the shaft matures. Before either end has attained the degree of development seen at the end of the seventh week, the cartilage cells of the shaft have begun to enlarge and show vacoulization (20 mm, 8th week).

The drawings of the reconstructions made by Friedländer ('01), Bardeen ('05) and Altmann ('24) indicate that the femur, which is short and wide in the mesenchymal stage, elongates rapidly with its progressive chondrification. Particularly in Bardeen's reconstructions, the femur at 20 mm C-R is considerably longer in relation to bicondylar width than at 14 mm C-R. This observation taken in conjunction with the findings of Streeter ('49) concerning the sequence of maturation of cartilage in expanding areas along the length of the femur indicates that the cartilaginous femur, at the time ossification begins, is growing in length faster than in breadth.

Of critical importance to an understanding of long bone growth is the relative autonomy of skeletal development. Murray and Huxley ('25), Murray ('26), Fell and Robison ('29), Murray and Shelby ('30) and Murray ('36) describe femurs or portions of femurs of the chick grown in chorioallantoic grafts. These specimens exhibit essentially normal proportions and features. The major deviations from normal configuration are those induced by the pressures and tensions of the host area and are manifested mainly as bending of the shaft and the formation of bony buttresses to

counter the abnormal forces. Condyles, head and processes appear about as one would expect in the naturally growing bone. Although a quantitative study of these femurs was not made, it is nevertheless apparent that the early development of femoral configuration is inherent and, in basic aspects, independent of the modeling influences of the developing muscles and of adjacent skeletal units.

MATERIALS AND METHODS

The femurs used in this study were taken from a series of 53 human fetuses and children available in the Embryology Collection and from the morgue of the Department of Anatomy of the University of Michigan. The crown-rump (C-R) lengths ranged from 37 to 500 mm and the spine lengths (A-R) from 26 to 410 mm. The minimum and maximum ages estimated from these measurements were ninth week to term and one infant three weeks postnatal. The age-size data of Mall ('18) and Streeter ('21), as modified and used in the Michigan Department of Anatomy, (Patten, '46) were used in these estimations.

The femurs were carefully removed from left or right sides, with no selection being made as to side. The superfluous tissue was dissected off as completely as possible, but the periosteum was left intact. The femurs were then stained with Alizarin Red S in KOH in order to demonstrate the extent of their ossification with the greatest possible sharpness. Finally the specimens were cleared in glycerin. In general the process follows that utilized by Noback and Noback ('44) with variations in the strength of KOH depending on the size of the specimens. Measurements taken before and after processing indicated that distortion of cartilage or bone was insignificant. All but two of the fetuses of 150 mm or greater C-R length were morgue specimens preserved by freezing rather than by chemical means. Almost all of the remaining fetuses were taken from a group classified as unsuitable for standard histological sections due to their poor condition upon arrival in the Department. These had been preserved for varying lengths of time in formalin. As a result, it was impossible to account for shrinkage or swelling of the tissues of the femur

prior to its removal from the thigh. This should not, however, be considered a critical factor for, as has been pointed out by Krahl and Mueller ('47), no significant shrinkage or swelling of either cartilage or bone should be encountered during or following formalin fixation.

In order to be able to measure the smallest femur with essentially the same degree of accuracy as the largest, and to prevent distortion or damage of the more delicate specimens, I devised a procedure by which all measurements were taken from line drawings of constant magnification. The first step was the taking of a photograph of the frontal aspect of the femur under a vertical camera. On the line drawing made from a projection of this negative a series of 11 points were placed, one at the center and five on either side of center, along the middle half of the shaft. Through these points a line was drawn extending the length of the femur outline. This arbitrary, but constant, longitudinal axis served as a line of orientation for the various measurements taken on the frontal drawing, and as a means of positioning the femur for further photographs of the medial, superior, and inferior aspects.

Because of the difficulty in handling the smaller femurs, photographs of the medial, superior, and inferior aspects were made with the aid of a mirror-apparatus. The femur was so placed on a glass slide of appropriate length that the previously determined longitudinal axis could be visualized as being directly above an orientation line scribed on the glass. This could be done with great accuracy under a dissecting microscope and checked with measurements on the frontal drawing. Next the glass with the femur was fixed on a platform in front of the right angle mirror. Then by rotating the platform and focusing on the reflected image, it was possible to

take photographs parallel with (medial aspect) or at right angles to (superior or inferior aspects) the original longitudinal axis.

All the line drawings were made to an approximately constant enlargement of 22 cm for the overall length of the femur. This size was chosen because, without being too large, it approaches that of the femur of a three year old child and permits accuracy comparable to that attained in postnatal studies. Measurements were taken with a millimeter rule (one half millimeter scale), dividers and protractor to the nearest half millimeter or degree. In converting the linear measurements taken from the line drawings, the figure was divided by the times magnification, (that value depending on the original size of the specimen) and expressed in millimeters and tenths of millimeters. Repeated measurements of a sample series of drawings indicated that accuracy was within a tenth of a millimeter.

The various dimensions of the femurs in the series have been plotted on a log-log scale after the technique first used by Huxley ('24, '32) and further developed by Huxley and Teisser ('36). This technique has recently been discussed by Kesling who has suggested simplifications in its use ('51). Although there are other ramifications to the method, the particular interest to this study is the use of the tangent of the angle made by the log-log with the horizontal. In this fashion, Huxley derived what he termed the coefficient of growth or k. Thus, if the two dimensions plotted against one another have identical growth rates, the angle is 45 degrees and the tangent of k is equal to 1.00. If either dimension has a greater rate of growth than the other, the k varies more or less than 1.00. As pointed out by Huxley, a very small difference in

k can have a very large terminal result.

The use of log-log graphic expression of long bone growth is not new. Hesdorffer and Scammon ('28) tested the value of this method in long bone studies with an investigation into the growth in length of the prenatal human tibia. A similar study was made by Robb and Clarke, ('34) using dried diaphyses. Aries ('41) has published a rather complete analysis of femur growth in the rat, utilizing both log-log and arithmetic graphic presentations.

In my series, the log-log regression line was traced through computed mean points for five units of the series. The angle was then determined with a vernier protractor, as suggested by Kesling ('51). Repeated tracings of the line and measurements of the angle, in addition to a computation check on some lines, showed that the accuracy attained by this manual method was consonant with the overall accuracy of the investigation. Variation in the various dimensions was determined by the simple computation of correlation coefficient with total length of shaft. It is obvious that one cannot judge the variation in the log-log graphs visually for variation about the line appears less for points of high angle, more for those of low angle.

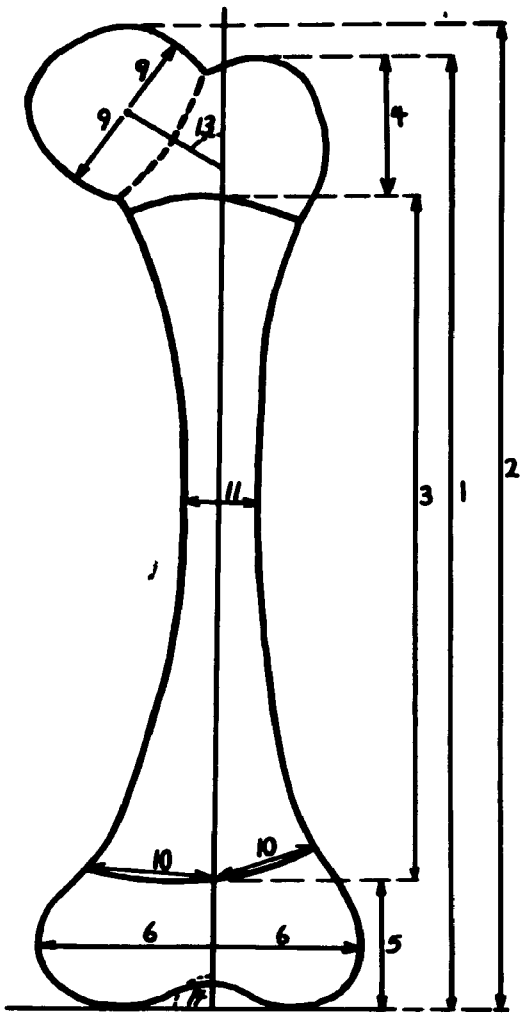


Fig. 1. Dimensions of the Femur
1. Total Length of Shaft
2. Overall Length of Femur
3. Length of Ossified Shaft
4. Length of Proximal Cartilage
5. Length of Distal Cartilage
6. Bicondylar Width
9. Diameter of the Head
10. Diameter of Chondro-osseous Junction
11. Minimum Diameter of Shaft
13. Inclination
14. Obliquity

OBSERVATIONS AND DISCUSSION

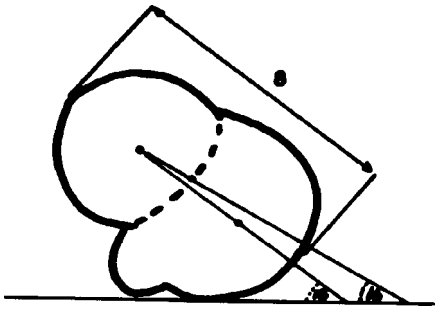
1 - The Dimensions of the Prenatal Femur

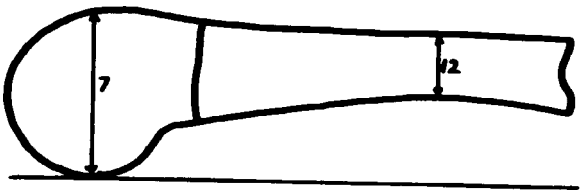
Each dimension used in an investigation of this type should fulfill two requirements. First, it should represent, in its changes, a part or all of the growth of one, or in special summation cases more than one, of the various regions of the femur throughout the period covered by the study. Second, the dimension should be such that the technique utilized in its determination is as equally applicable to the oldest as it is to the youngest specimen in the series being studied. In view of this, the dimensions measured in the present series have been kept to a minimum. From the following definitions of dimensions, it will be seen that some are adaptations of the standard osteometric techniques used previously (e.g., Martin, '28, Hrdlicka, '20, Ingalls, '24), while others were devised to fulfill the exigencies of this particular study and its developmental problems. The various dimensions used in this study are listed and defined below and indicated in figs. 1 and 2. Figure numbers in parentheses are those of appropriate graphs.

(1) Total Length of Shaft, distance from infracondylar plane to highest point of greater trochanter, measured on the determined longitudinal axis of the femur.

(2) Overall Length of the Femur, (fig. 6) distance from infracondylar plane to highest point on femoral head, measured on a line perpendicular to the infracondylar plane. The value of this dimension is affected by torsion, by inclination, and by obliquity of the shaft.

(3) Length of Ossified Shaft, (fig. 7) distance from highest to lowest point on ossified shaft, measured along the determined longitudinal axis.





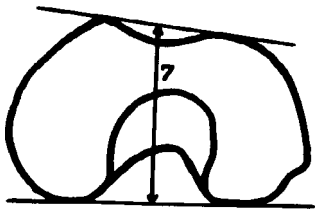


Fig. 2. Dimensions of the Femur
7. Anterior-posterior Diameter of Condyles
8. Head-trochanteric Width
12. Anterior-posterior Diameter of Shaft
15. Torsion
16. Angular Displacement of Head

of the femur. (fig. 7)

(4) Length of the Proximal Cartilage, (fig. 8) distance from proximal chondro-osseous junction to highest point on greater trochanter, measured along the determined longitudinal axis of the femur.

(5) Length of the Distal Cartilage, (fig. 9) distance from distal chondro-osseous junction to infracondylar plane, measured along the determined longitudinal axis of the femur.

(6) Bicondylar Width, (fig. 10) distance across condyles, measured at greatest width perpendicular to the determined longitudinal axis.

(7) Anterior-posterior Diameter of Condyles, (fig. 11) the distance retrocondylar plane to a point midway between anterior-most surfaces of the two condyles.

(8) Head-trochanter Width, (fig. 12) greatest distance across head and greater trochanter, measured on the line drawing of the superior view. Measured in this manner the dimension is affected only by the inclination of the head and neck, not by torsion; measured on the frontal drawing, it would be affected by both.

(9) Diameter of the Head, (fig. 13) an average of two measurements of greatest head diameter, one perpendicular to the line established for inclination, and one perpendicular to the line for torsion.

(10) Diameter of the Chondro-osseous Junction, (fig. 14) in the younger specimens in which the ends of the ossified shaft are fairly straight, this dimension is measurable as the distance across the junction of cartilage and bone. In the older specimens the junction is curved or angulated and the measurement is taken from each side to the intersection of the junction with the determined longitudinal axis of the femur. In

these older specimens only the distal chondro-osseous junction can be accurately measured, the proximal dimension being distorted by the degree of torsion present.

(11) Minimum Diameter of the Shaft, (fig. 15) diameter of ossified part of shaft at narrowest point, medial to lateral.

(12) Minimum Anterior-Posterior Diameter of the Shaft, (fig. 16) diameter of ossified part of shaft at narrowest point, anterior to posterior.

(13) Inclination of the Head and Neck, (fig. 21) angle with the determined longitudinal axis of femur made by a line drawn to it from determined center of head and passing through a point midway across the junction of head with neck. Although it would be more desirable to carry this line through center points in the neck, the extreme shortness of that region and the fact that torsion in many older specimens causes it to appear nonexistent make such a procedure impractical. As determined thus, inclination is affected by the degree of torsion.

(14) Obliquity of the Shaft, (fig. 22) laterally opening angle made by infra-condylar plane with the determined longitudinal axis of the femur.

(15) Torsion, (fig. 18) angle with the retrofemoral plane made by a line extending from the determined center of head through to a point in center of greater trochanter. The retrofemoral plane, that plane on which the femur rests on condyles and trochanter, is here assumed to be identical with a frontal plane through the femur.

(16) Angular Displacement of the Head, (fig. 20) angle made with the retrofemoral plane by a line extending from the determined center of the head through the middle of the head-neck junction.

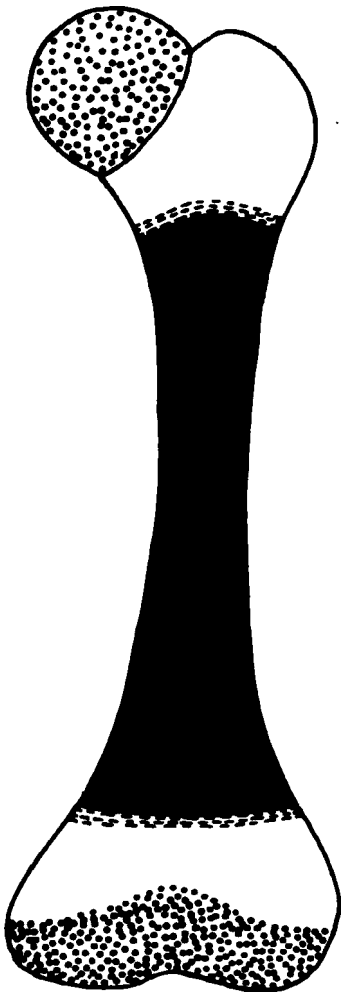


Fig. 3. Femoral Growth Units and their Components
Black area, ossified shaft; above, the proximal cartilage, below, the distal. Components are: intracapsular (stippled), extracapsular (white), and juxtaosseous (lined) cartilage.

2 - The Growth Areas of the Prenatal Femur

In order to analyze the growth of the long bone it is necessary to relate the progressive morphological changes, as much as possible, to the basic features of its histogenesis. One must visualize the configuration of specific regions in terms of the behavior of their constituent tissues during the developmental period. The growth of the whole bone is, then, the resultant of these several growth processes. This approach has been used in reference to the postnatal development of the femur and of long bones in general, but as yet has not been extended to their prenatal development.

In the prenatal period it is possible to visualize essentially the same processes as in the postnatal. In short, the generally accepted concepts of appositional and interstitial growth in cartilage, of appositional growth alone in bone, of row formation and associated phenomena in cartilage adjacent to advancing ossification, and of resorption, all hold true for the prenatal period. The differences between the pre- and postnatal periods are, as will be discussed at length in a later section, mainly differences in the relative proportions and spatial relations of the active tissues to one another.

Throughout the age range covered in this study the femur may be regarded as consisting of three growing units: the proximal cartilage, the ossified shaft, and the distal cartilage. It is in terms of the developmental behavior of the tissues of these three units that all the growth in the prenatal period must be interpreted. It should be pointed out that the terms diaphysis, metaphysis, and epiphysis, used in standard textbooks and references (e.g., Maximow and Bloom, '48, Ham, '50, Weinmann and Sicher, '47),

are of little value in the designation of prenatal growth areas. The areas to which they are applied in postnatal long bones are, at different periods of prenatal development, made up of tissues with differing modes of growth, or even of entirely different tissue types, as in the case of the advance of ossification from the diaphysis into the metaphysis. The rather non-specific terms proximal and distal cartilages and ossified shaft would seem more appropriate than the terms proximal and distal extremities and diaphysis used by Lacroix in his recent monograph ('49), particularly because the use of diaphysis without epiphysis is somewhat incongruous. If one accepts this simple major division then both the proximal and distal cartilages may be divided, on the basis of certain anatomical and growth characteristics, into three components: intracapsular, extracapsular, and juxtaosseous.

The Intracapsular Component. (fig.3, stippled areas) The femoral head and those portions of the neck and condyles lying within their respective joint cavities but not covered by capsular reflections may be grouped together under the designation of intracapsular cartilage. From the time the joint cavities open these areas are without a perichondrium. With the absence of the perichondrium which is primarily responsible for the appositional growth of cartilage, increase in mass of this component must be accomplished by interstitial growth or by proliferation from the connective tissues at the margins. The time at which the two articular cavities open has recently been carefully re-studied. That of the hip was observed to be open in specimens of 30 mm C-R length (Gardner and Gray, '50), and that for the knee somewhat later, in 33 to 37 mm C-R length specimens (Gray and Gardner, '50).

Despite the fact that the process of cartilage replacement and the attendant phenomena have been so well explored, the question of interstitial and appositional growth of cartilage and their inter-relation has hardly been examined. Harris and Russell ('33) studied the proliferating cartilages of human fetal long bones and mapped mitotic figures. Their illustrations show that interstitial growth, as indicated by the distribution of these figures, is nearly absent in the central region of the cartilages, but is progressively more evident as the peripheral areas are approached. The other possible source of increment to the intracapsular cartilage, namely proliferation from the connective tissue at the articular margin, has been cited by Weinmann and Sicher ('47), but it would seem that this is a relatively more important source in postnatal life when only the thin articular cartilage remains.

The Extracapsular Component. (fig. 3, white areas) The designation extracapsular component covers the remainder of the cartilages except for a narrow zone immediately adjacent to the ends of the ossified shaft. The presence of a perichondrium makes possible appositional as well as interstitial growth.

The Juxtaosseous Component. (fig. 3, lined area) The cartilage immediately adjacent to the ends of the ossified shaft may be regarded as the precursor of part of the well defined epiphyseal plate of the postnatal period. Except in microscopic sections, it cannot be distinguished from the extracapsular cartilage. The juxtaosseous cartilage is that in which the cells are arranged in rows parallel to the long axis of the femur, where the cellular hypertrophy and final degeneration occur, and where the intercellular matrix is seen to be calcified.

This area has been the subject of intensive investigation on the part of Ham ('32), Dodds ('32), McLean and Bloom ('40), Bloom and Bloom, ('40) and Lacroix ('49). For the present paper, two characteristics of this component are of vital importance: the orientation of the cell rows or columns and their replacement by bone, and the fact that the intercellular matrix undergoes calcification. This is a zone of lost potential, as far as interstitial growth is concerned; the proliferation of cells is accompanied by a reduction rather than an increase in the amount of matrix. As a result, although the tissue organization is modified, there is no growth. In addition, the rigidity of the calcified matrix, which extends at least three or four rows in front of the advancing chondro-osseous junction (Dodds and Cameron '34), precludes even the possibility of diameter increase by cellular hypertrophy. Finally there is the possibility of a retardation in appositional growth from the periosteum in this zone of transition from perichondrium to periosteum.

The Ossified Shaft. (fig. 3, black area) As in the postnatal femur, the ossified shaft increases in external diameter by apposition, in internal diameter by resorption (Payton, '32, Brash, '34, and Aries, '41). The ultimate determiner of its configuration is the cartilage which at either end forms an area of preparation for osseous replacement. Although the osseous tissue is not identical in organization pre- and postnatally, no essential differences in the overall growth process have been demonstrated (Lacroix, '49).

In order to emphasize the specific changes in the growth units of the prenatal femur over the extent of time covered in this study, it is

Table 1

Linear Dimensions of the Prenatal Femur

Crown-Rump Length	Total Length of Shaft	Overall Length of Shaft (Fig. 6)	Length of Ossified Shaft (Fig. 7)	Length of Proximal Cartilage (Fig. 8)	Length of Distal Cartilage (Fig. 9)	Head-trochanter Width (Fig. 12)	Biocondylar Width (Fig. 10)	A-p Diameter of Condyles (Fig. 11)	Diameter of Head (Fig. 13)	Minimum Diameter of Shaft (Fig. 15)	A-p Diameter of Shaft (Fig. 16)	Diameter of Chondro-osseous Junction (Fig. 14)
31.0	8.4	10.0	6.5	.95	.95	2.1	2.2	1.3	1.1	.65	.65	1.4
32.0	9.2	9.8	3.6	2.8	2.8	2.0	2.2	1.4	1.3	.52	.64	.96
45.0	11.5	11.1	1.1	5.1	5.3	2.8	3.1	1.8	1.1	.85	.68	.12
51.0	11.9	12.0	4.9	3.4	3.6	3.3	3.2	2.6	1.9	.98	.94	1.4
45.0	12.2	12.5	5.0	3.7	3.5	3.1	2.8	1.8	1.7	.71	.89	1.3
50.0	13.0	13.3	5.7	3.9	3.4	3.8	3.6	2.1	2.1	1.1	1.0	1.8
55.0	13.2	13.3	7.6	2.7	2.9	3.6	3.7	3.4	2.1	.74	1.0	2.2
63.0	14.4	15.7	5.4	3.3	5.7	4.3	4.3	2.9	2.3	1.4	1.3	1.6
50.0	14.9	14.4	7.8	3.0	3.0	3.1	3.2	2.3	1.8	.74	.89	2.1
57.0	15.1	15.7	7.8	3.4	3.9	3.6	3.9	2.8	2.1	1.2	.97	2.1
70.0	15.5	15.9	7.9	3.8	3.8	3.7	3.5	2.4	2.2	.93	1.1	2.0
62.0	16.6	17.0	8.9	3.6	4.1	3.6	3.6	2.6	2.1	.79	.94	1.9
75.0	18.3	19.1	10.0	4.6	3.7	4.1	4.1	3.3	2.5	1.1	1.5	2.4
81.0	19.7	20.4	11.3	4.2	4.2	4.7	4.4	2.9	2.7	1.5	1.7	3.0
62.0	20.4	21.0	11.4	4.7	4.3	4.7	4.9	3.3	2.6	1.5	1.4	2.8
75.0	23.9	21.5	11.7	6.3	5.9	5.1	5.0	4.0	3.0	1.6	1.7	2.8
78.0	25.0	25.5	16.2	4.6	4.2	6.0	5.5	3.8	3.1	1.8	2.0	3.8
90.0	25.0	26.0	10.5	7.3	7.3	6.4	6.1	4.3	3.5	1.7	2.0	3.0
85.0	26.5	27.5	16.6	3.1	6.8	5.6	5.9	3.9	3.2	1.7	2.1	3.7
94.0	30.1	31.1	19.3	5.4	5.4	7.6	7.2	5.5	4.1	2.1	2.4	5.1
96.0	31.3	32.2	20.4	4.3	6.6	7.9	7.6	6.2	4.1	2.1	2.7	5.0

98.0	31.8	32.6	23.0	4.5	4.3	7.3	7.8	5.2	4.3	2.5	2.9	5.9
108.0	37.8	38.9	26.6	6.0	5.2	9.3	9.8	6.4	5.0	2.3	3.1	7.6
101.0	39.1	40.0	27.9	6.4	4.8	9.6	10.5	6.9	5.6	2.6	3.1	8.2
134.0	43.9	44.7	30.1	6.9	6.8	11.5	11.9	8.6	6.1	3.0	3.6	8.1
119.0	44.3	44.3	29.6	7.5	7.2	10.3	19.1	8.2	5.9	2.9	4.0	8.2
111.0	44.8	45.0	29.8	7.7	7.5	9.0	12.1	7.5	6.2	3.1	1.9	8.2
155.0	45.3	46.2	30.4	7.7	7.2	11.7	11.4	7.9	6.3	3.2	3.3	7.2
153.0	47.2	49.1	39.0	3.0	5.2	12.1	13.5	8.7	7.2	3.5	3.9	12.1
163.0	49.6	50.6	35.4	7.4	6.8	14.4	15.2	9.4	7.2	3.7	4.4	12.0
150.0	51.5	52.2	38.1	8.0	5.4	13.8	14.4	9.7	7.3	3.6	4.7	12.2
165.0	54.4	55.9	39.4	8.4	6.6	13.7	14.7	9.4	7.5	4.0	5.0	12.0
183.0	57.7	59.1	48.2	4.7	4.8	15.9	17.0	10.2	8.6	3.8	4.9	12.6
190.0	63.3	64.0	49.0	6.9	7.4	14.0	18.7	12.7	9.9	5.7	5.5	16.1
175.0	65.9	70.2	53.0	7.6	5.3	22.3	20.5	13.4	10.3	5.0	5.3	16.7
210.0	68.5	71.0	51.3	7.4	9.8	21.7	22.1	13.8	11.3	4.9	4.9	17.4
220.0	72.9	73.6	53.5	8.0	10.4	22.6	22.4	15.9	11.5	5.5	6.7	18.4
220.0	74.4	74.5	53.6	10.0	10.8	21.2	25.5	15.1	12.0	5.2	6.6	15.9
250.0	76.2	78.1	56.6	9.6	10.0	20.0	23.6	14.8	12.3	5.5	5.6	18.6
230.0	77.1	79.5	58.9	7.5	10.7	23.5	24.0	15.3	12.8	5.8	6.2	17.1
260.0	77.2	78.7	57.6	9.2	9.4	23.0	22.9	15.0	12.0	5.3	5.8	16.8
270.0	78.1	82.0	58.1	5.2	14.8	22.3	25.1	16.6	14.3	6.2	5.8	18.9
280.0	80.0	81.0	61.2	8.0	10.3	26.6	26.5	15.2	17.3	6.0	6.1	20.5
280.0	81.8	83.3	59.1	10.2	12.5	25.4	27.2	18.4	15.2	6.6	6.4	20.8
288.0	84.6	87.8	61.7	7.1	15.8	24.6	25.5	16.1	14.1	5.7	5.6	21.2
270.0	88.7	91.8	58.5	6.1	9.0	23.8	26.0	17.7	14.7	6.5	6.5	18.0
300.0	91.5	94.4	73.6	7.7	10.2	24.6	27.2	17.2	13.4	7.4	7.5	24.9
300.0	96.7	99.1	75.7	10.0	10.8	31.7	31.0	21.2	16.4	8.1	8.3	25.7
310.0	99.5	101.7	76.7	9.7	13.1	25.4	27.1	18.7	15.2	6.7	5.9	21.4
300.0	100.9	105.2	82.1	7.1	11.7	26.0	31.0	20.3	16.0	7.1	7.1	25.0
330.0	102.9	104.9	84.3	9.3	9.3	30.4	29.4	21.1	15.0	6.4	8.4	25.6
513.0	105.3	109.0	89.9	7.1	8.3	28.6	31.7	20.1	17.1	9.0	9.8	31.7
485.0	110.6	113.6	94.0	6.8	9.8	30.9	35.0	20.7	16.1	9.5	9.8	30.4



Table 2

Correlation Coefficients and Coefficients of Growth

Dimension	r	k
Overall Length of Femur	.99	.97
Length of Ossified Shaft	.99	1.28
Length of Proximal Cartilage	.77	.51
Length of Distal Cartilage	.84	.62
Bicondylar Width	.99	1.15
Anterior-posterior Diameter of Condyles	.99	1.09
Head-trochanter Width	.98	1.11
Diameter of Head	.98	1.15
Diameter of Chondro-osseous Junction	.99	1.38
Minimum Diameter of Shaft	.98	1.03
Anterior-posterior Diameter of Shaft	.99	1.04
Inclination	.17	.03
Obliquity	.51	-1.00
Torsion	.74	.18
Angular Displacement of Head	.64	.11

Table 3

Increments and Percentage Increases in Dimensions between Smallest and Largest Femurs

Femur as a whole	Increment	% Increase
Total Length of Shaft	99.2 mm	1230 %
Overall Length of Femur	101.4	1120
Bicondylar Width	31.1	1511
Head-trochanter Width	27.6	1410
Head-Diameter	15.4	1380
Minimum Diameter of Shaft	8.6	1580
A-p Diameter of Shaft	8.7	1450
A-p Diameter of Condyles	19.0	1460
Proximal Cartilage		
Length of Proximal Cartilage	5.0	360
Head-trochanter Width	27.6	1410
Head Diameter	15.4	1380
Distal Cartilage		
Length of Distal Cartilage	7.2	480
Bicondylar Width	31.1	1511
A-p Diameter of Condyles	19.0	1460
Diameter of Chondro-osseous Junction	29.9	2590
Ossified Shaft		
Length of Ossified Shaft	87.0	1840
Minimum Diameter of Shaft	8.6	1580
A-p Diameter of Shaft	8.7	1450
Diameter of Chondro-osseous Junction	29.9	2590

Table 4

Relative Changes Between Smallest And Largest Femurs

Relative to Total Length of Shaft	Smallest	Largest	Change
Bicondylar Width	.25	.31	.06
Head-trochanter Width	.24	.27	.03
A-p Diameter of Condyles	.16	.19	.03
Minimum Diameter of Shaft	.07	.08	.01
A-p Diameter of Shaft	.07	.09	.02
Diameter of Chondro-osseous Junction	.13	.29	.16
Length of Ossified Shaft	.52	.85	.33
Length of Proximal Cartilage	.22	.06	.16
Length of Distal Cartilage	.22	.08	.14
Relative to Length of Ossified Shaft			
Diameter of Chondro-osseous Junction	.24	.34	.10
Minimum Diameter of Shaft	.12	.10	.02
A-p Diameter of Shaft	.12	.10	.02
Relative to Bicondylar Width			
Length of Distal Cartilage	1.00	.28	.72
A-p Diameter of Condyles	.64	.61	.03
Relative to Head-trochanter Width			
Length of Proximal Cartilage	.90	.23	.67
Diameter of Head	.55	.57	.02

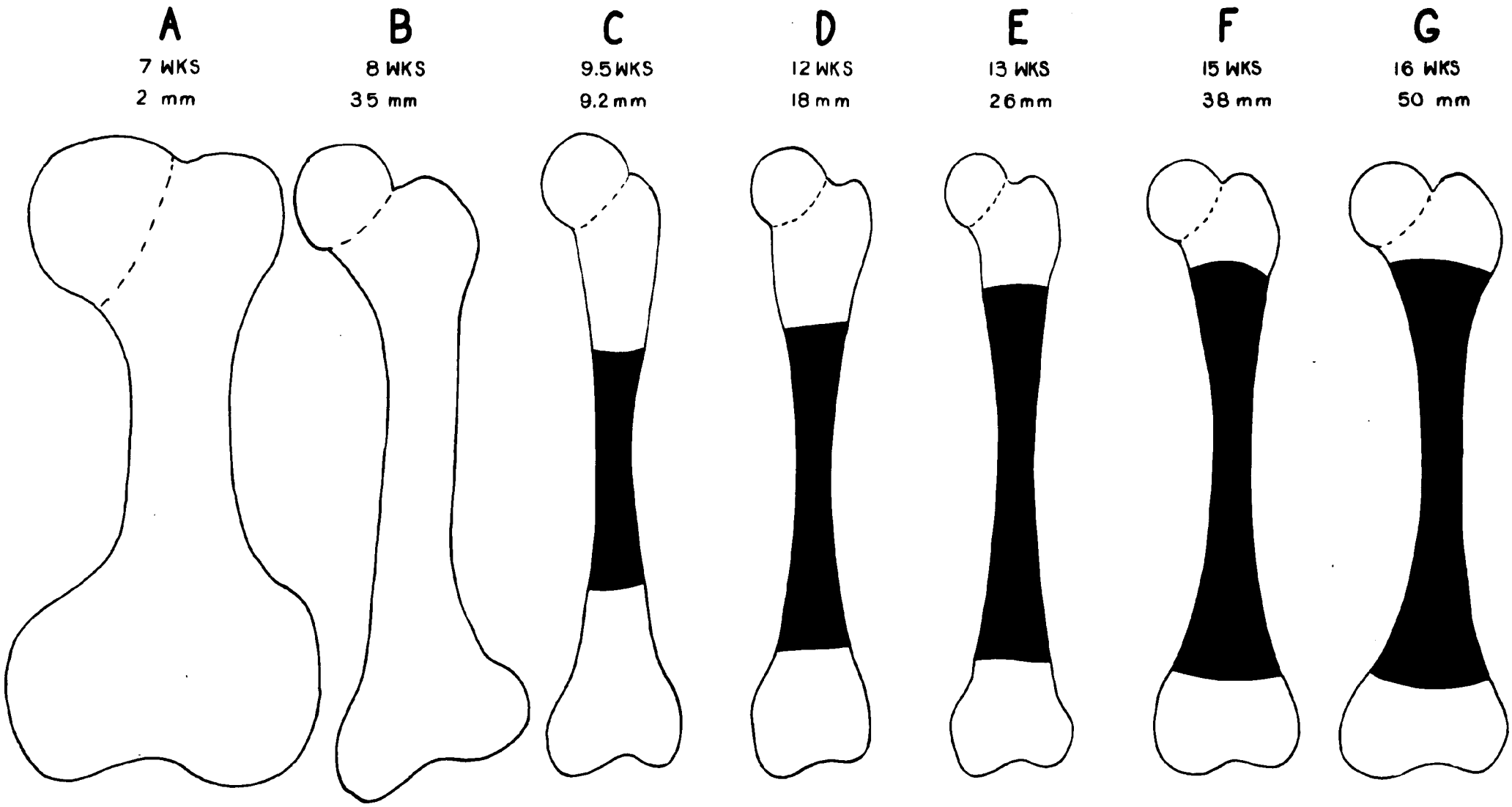


Fig. 4. (See caption on facing page.).

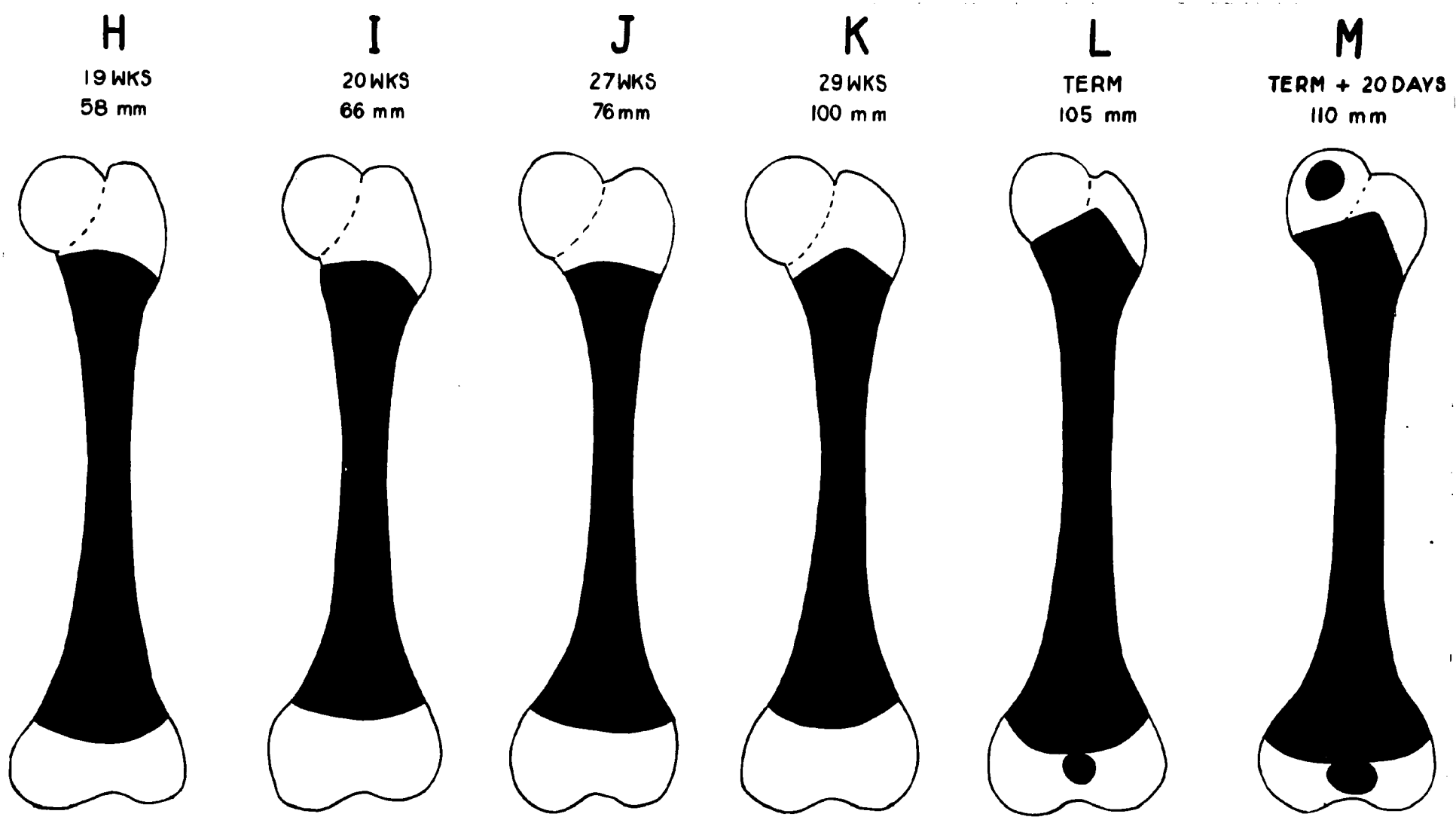


Fig. 4. A representative series of fetal and neonatal femurs at constant total length of shaft.

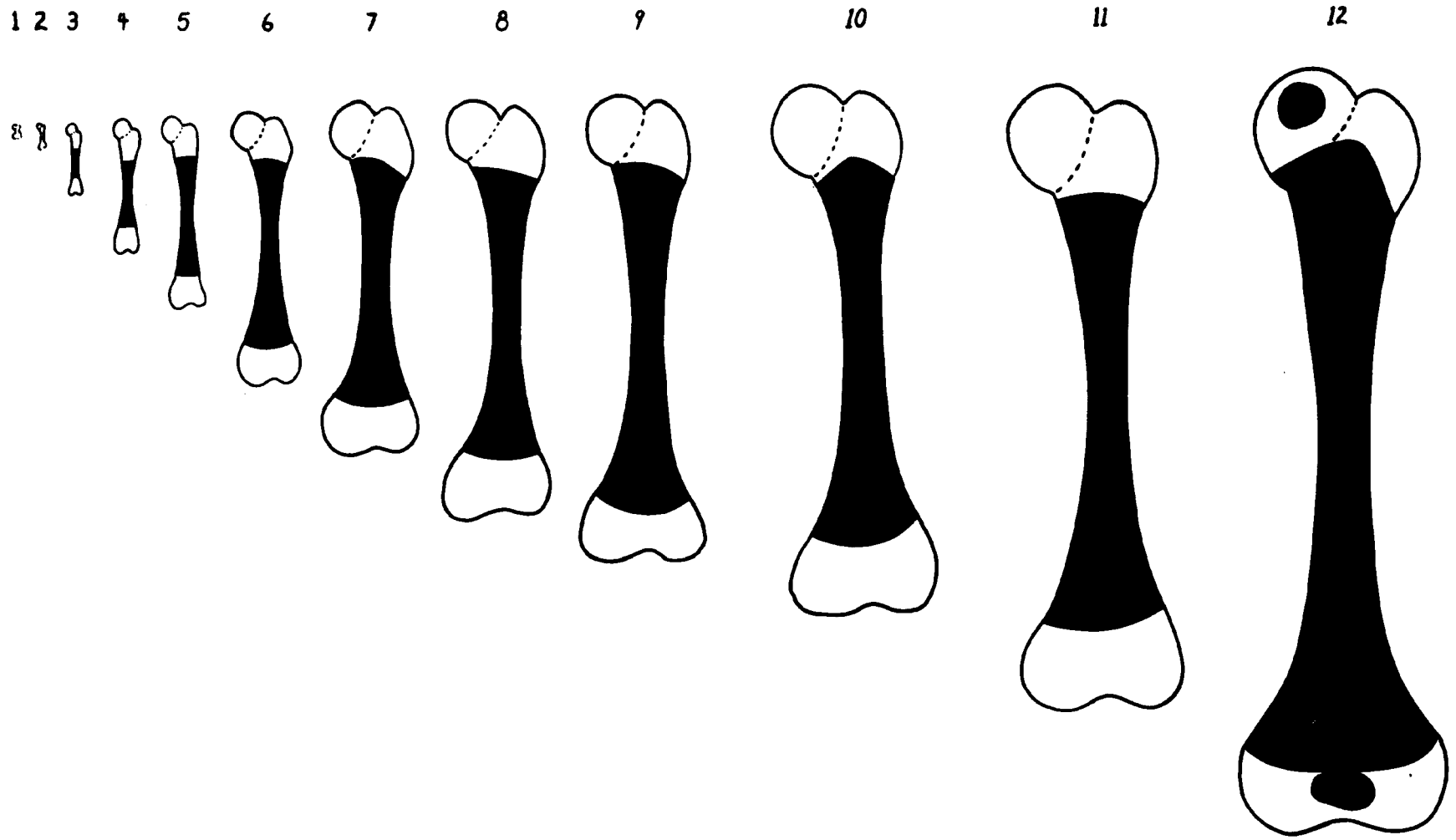


Fig. 5. A representative series of fetal and neonatal femurs, approximately natural size. The first two specimens are modified from Altmann; lengths are 2 mm and 3.5 mm . Lengths of the rest of the series are (3), 9.8, (4), 15.7, (5), 25.0, (6), 37.8, (7), 44.8, (8), 54.4, (9), 57.7, (10), 68.5, (11), 80.0, and (12), 110.6 mm .

desirable to compare the femurs of the smallest and of the largest fetuses in the series. The essentially linear progression in the growth of most of the dimensions, as well as the generally rather small variations about the trend, makes possible such an approach. The individual variability is, however, such that the least value for a femoral dimension does not always occur in the smallest fetus, nor does the greatest value invariably appear in the largest fetus. In view of this fact, averages of the femoral dimensions of the two smallest fetuses are compared with those of the two largest. This comparison, represented by indices, index change, increments and percentage increases, is presented in tables 3 and 4. In general, the tabular data are self-explanatory and may be presented at this point without comment. Certain features are, however, of sufficient importance in the immediately following discussion to warrant comment.

In both cartilages the most striking changes are in length. The percentage increases are the smallest for any femoral dimension. The decreases in length relative to total length of shaft are great; the decreases relative to cartilage breadth are greater than any others in the femur. These changes are obviously due to osseous replacement of cartilage.

In breadth of cartilages the percentage increases are notably high, the greater increase being in the distal cartilage. Relative to total length of shaft the changes are not as great as one might expect from examination of the drawings (fig. 4). They are, however, greater than any other positive changes except for the ossified shaft. It is noteworthy that the proportional change within the distal cartilage is such

that the condylar mass in the larger femurs is wider relative to its anteroposterior diameter than it is in the smaller femurs. This was also observed by Ingalls ('27).

The length of ossified shaft increases greatly and in proportion to the relative decrease in length of cartilage; the percentage increase is second only to that for the diameter of the chondro-osseous junction. Relative to total length of shaft, the ossified shaft length undergoes a change greater than that of any other dimension. The minimum diameter of the shaft is so very small initially that the increase occurring is reflected in a very high percentage figure. Relative to total length of shaft the increase is slight, and in ratio to length of ossified shaft there is a small decrease in the dimension. The anteroposterior diameter of the shaft shows a similar progression.

3 - The Process of Femoral Shape Change

The total configuration of the femur is at any time in its development the manifestation of the total previous interaction of the growth rates of the several tissue regions. Because of its greater bilateral symmetry and lesser complexity of configuration, the distal half of the femur, rather than the proximal, is the preferred area in which to investigate this interaction and attempt to explain its role in femoral morphogenesis.

Although one of the most striking features of femoral development, the increase in length of the ossified portion of the shaft cannot of itself be regarded as contributing to increase in the total length of the femur. This has been demonstrated no where as clearly as in the

recent work of Paff and Eksterowicz ('50) who have found that ossification in long bones cultured in vitro can be retarded or stopped completely by alizarin. In such specimens (metatarsals) it was found that there was no retardation or cessation of growth in overall length. In the proven absence of interstitial growth in bone, it is obvious that increase in length of the ossified shaft is nothing other than a replacement of cartilage by bone at a rate considerably in excess of that of increase in total length of the shaft. This is demonstrated in this series by the coefficient of growth (k) of the ossified shaft in length, 1.28.

The distal cartilage increases in length by interstitial growth and to an unknown, but probably lesser, degree by the differentiation of cartilage from the fiberous connective tissue bordering the articular surfaces. Breadth (bicondylar width) increases by both appositional and interstitial modes of growth. As we have seen, breadth increases much more rapidly than cartilage length. The differences in the growth rates of cartilage along these two dimensions is clearly shown in a comparison of growth coefficients: breadth 1.15, length .62. In view of the fact that at the time ossification begins the cartilaginous femur, as was pointed out earlier, is increasing in length faster than in breadth, it must be assumed that this relative decrease in distal cartilage length can be due only to the process of relatively more rapid replacement of cartilage by bone at the chondro-osseous junction.

The juxtaosseous cartilage constitutes an area where growth potential, in terms of elongation of the shaft or diameter increase, has been lost, except perhaps for some appositional growth. This cartilage may be regarded as essentially a narrow zone of lost growth potential moving pro-

gressively along the length of the femur away from the middle region of the shaft. The movement is propagated by the continuous replacement of cartilage by bone on one side, and the concomitant addition of cartilage from the extracapsular component on the other side.

Ahead of the encroachment of the juxtaosseous zone and the accompanying osseous replacement, the extracapsular cartilage continues to increase in diameter, and, of course, in length, as the level occupied by the juxtaosseous zone, for all practical purposes, ceases to do so. Consequently the juxtaosseous cartilage, while probably not increasing to any great extent by its own growth, nevertheless comes to occupy a progressively greater diameter of the femur. This integrated process is responsible for the major proportional change in the prenatal femur. The rapidly growing cartilage, after alteration and loss of growth potential, is replaced by bone. This replacement occurs relatively and absolutely faster than the longitudinal growth of the distal cartilage, but not sufficiently fast to prevent considerable expansion of the cartilage transversely prior to replacement. Thus the predominant growth direction at the end of the femur is transverse, and the ossified shaft, at either end, assume/ the ever larger diameter of the cartilage it is replacing. At the minimum diameter of the shaft, which we may consider to represent the original diameter of cartilaginous shaft increased by the deposition of bone, apposition occurs with a coefficient of 1.03. The growth rate of the chondro-osseous junction, on the other hand, may be represented by a coefficient of 1.38, the highest for any femoral dimension. Related to this is the value for bicondylar width, 1.15, the highest for cartilage.

Although the ratio of bicondylar width to total length of shaft does undergo an appreciable and important change during development, this change is not extreme. Moreover, there is hardly a change in the ratio of minimum diameter of the shaft to shaft length. It becomes obvious from this that the major morphological alteration in the femur is a loss of gracility and an ever-increasing flare of the shaft away from its center, (fig. 4). As Pitzen termed it ('23), the index of massiveness rises with development. The determining mechanism at the basis of this is the process of ossification which, although without effect in length increase, is so related to cartilage growth as to result in a femoral configuration change.

It appears that such changes in the direction and rate of growth occur near birth as to allow one to speak of prenatal and postnatal growth patterns in the human femur. Such is indicated in the relationship of the widening chondro-osseous junction to bicondylar width as well as by the position of that junction relative to the distal end of the femur and to the distal center of ossification when that center appears about the time of birth.

As a result of the rapid rate of elongation of the ossified shaft, its distal end is, by the time of birth, at approximately the same level as the greatest width of the distal cartilage (figs. 4 and 5). When the distal center of ossification appears it is only a very short distance in front of the advancing shaft ossification; an average of only 5 mm in the two oldest fetuses in the series. If the growth processes characteristic of the fetal period were to continue, the small extent of cartilage remaining between the growing bony elements would quickly be replac-

ed and there would be an "epiphyseal closure" only a short time after birth. Were such to occur, there would be essentially the same condition at birth as exists in the adult, rather than the stabilized condition of the immature postnatal skeleton in which each unit of cartilage replaced by bone is compensated for by cartilage proliferation, the growing area remaining approximately the same thickness.

Comparison of some of the major proportions of a postnatal femur of 250 mm total shaft length (recorded age about 4 years) with those of the term femur and one constructed from prenatal growth trends projected to 4 years is pertinent at this time.

	Term Shaft	Projected Shaft	Actual Shaft
Minimum Diameter of Shaft	.06	.09	.05
Bicondylar Width	.31	.39	.22
Length of Ossified Shaft	.85	1.31	.90
Diameter of Chondro-osseous Junction	.29	.50	.28
Length of Distal Cartilage	.08	Obliterated	.10
Minimum A-P Diameter of Shaft . . .	.09	.12	.06
Minimum A-P Diameter of Condyles. .	.19	.22	.13

(In the above, length of epiphysis is substituted for the length of distal cartilage in the postnatal actual).

It is at once apparent that such a projection as is given on middle column above is in many ways invalid. For example, the length of the ossified shaft cannot exceed the total length of the shaft, nor can the diameter of the chondro-osseous junction exceed bicondylar width, except in so far as it curves and presents a line greater in width than the distal end of the femur. For the most part, however, such projection represents the dimensions the femur would attain were it to grow unchecked along the lines followed in the prenatal period. It is obvious that this does not occur. Comparison of the three series of dimensions shows that

the predominant direction of growth in the postnatal period is longitudinal, and that all the transverse dimensions are less relative to total length of shaft than they were during the prenatal period.

No attempt can be made here to point to the exact time at which the shift in growth direction occurs; the scarcity of postnatal material at the time this study was made precluded the collection of anything but scattered data on that period. It is, however, my conviction that the conditions contributing to the shift come into being in the immediate circumnatal period as the end product of the prenatal growth processes. In the absence of more complete data and especially experimental evidence, no more specific suggestion would be justified. It is sufficient here to indicate how the inter-relation of the growing units in a specific fetal long bone may logically effect such an alteration in its growth pattern.

By the time the femur at term has reached an approximate total length of shaft of 110 mm the diameter of the chondro-osseous junction has nearly come to equal the greatest diameter of the distal cartilage. In this circumstance there is the certain indication of the approaching termination of the previous relationship of juxtaosseous to extracapsular cartilage in which the zone of growth potential loss moved into the mass of rapidly growing cartilage. In addition, the advance of ossification has reached, in its proximity to the newly formed distal center of ossification, practically its definitive level relative to the end of the femur. Finally the existence of the rapidly growing distal center of ossification within the cartilage may be taken as an indication of the deviation of the activity of that mass toward the preparation of the

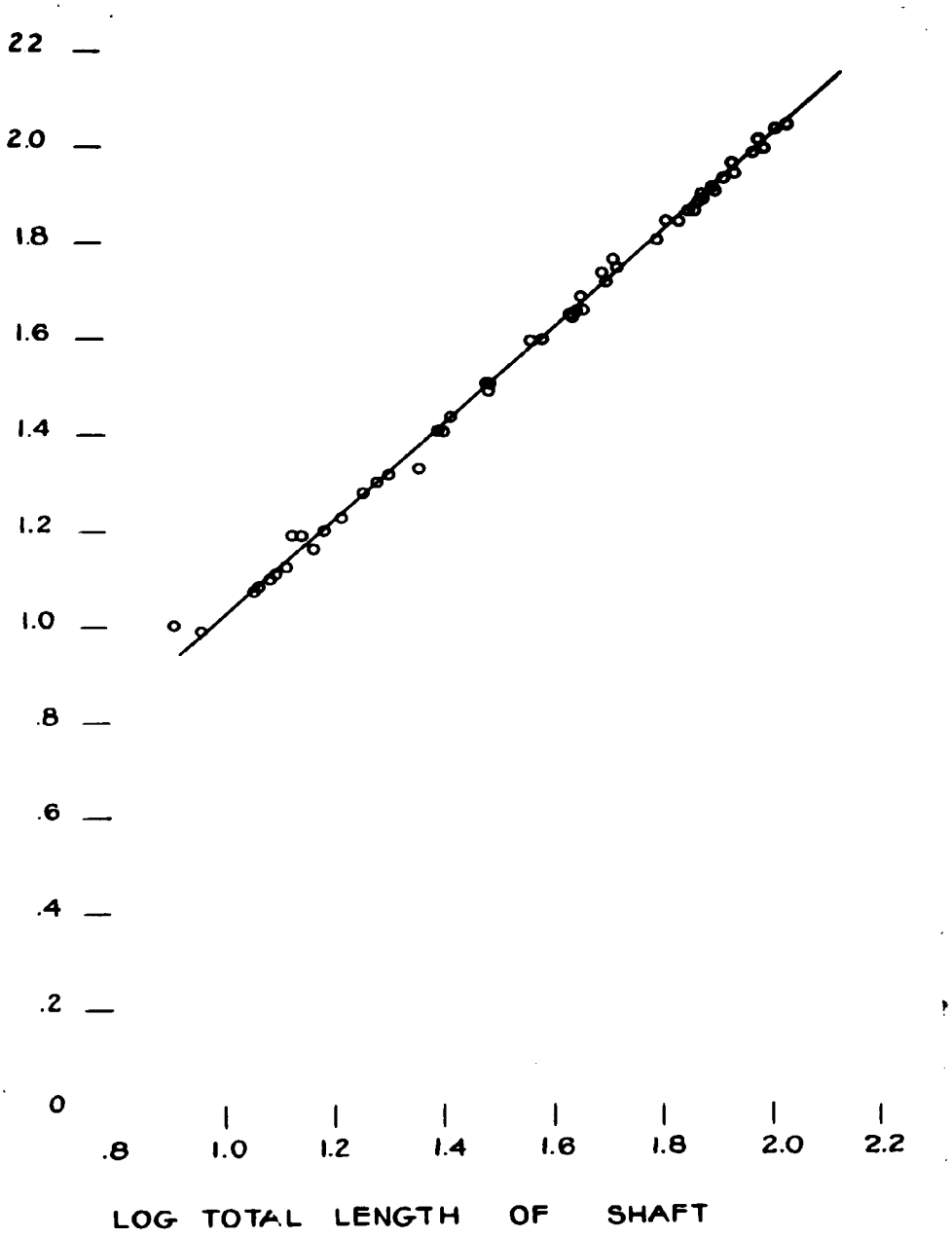


Fig. 6. The regression of log Overall Length of Femur upon log Total Length of Shaft.

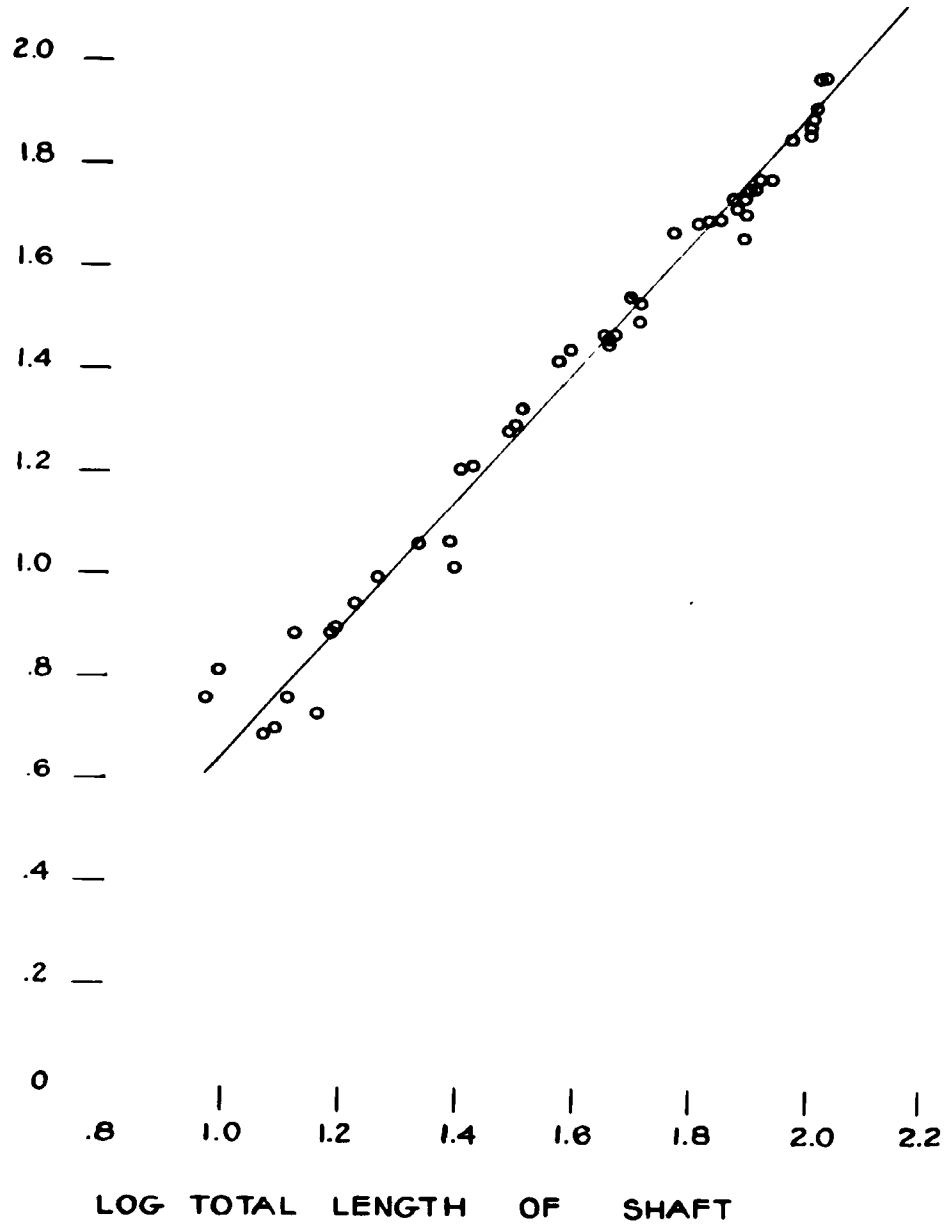


Fig. 7. The regression of log Length of Ossified Shaft upon log Total Length of Shaft.

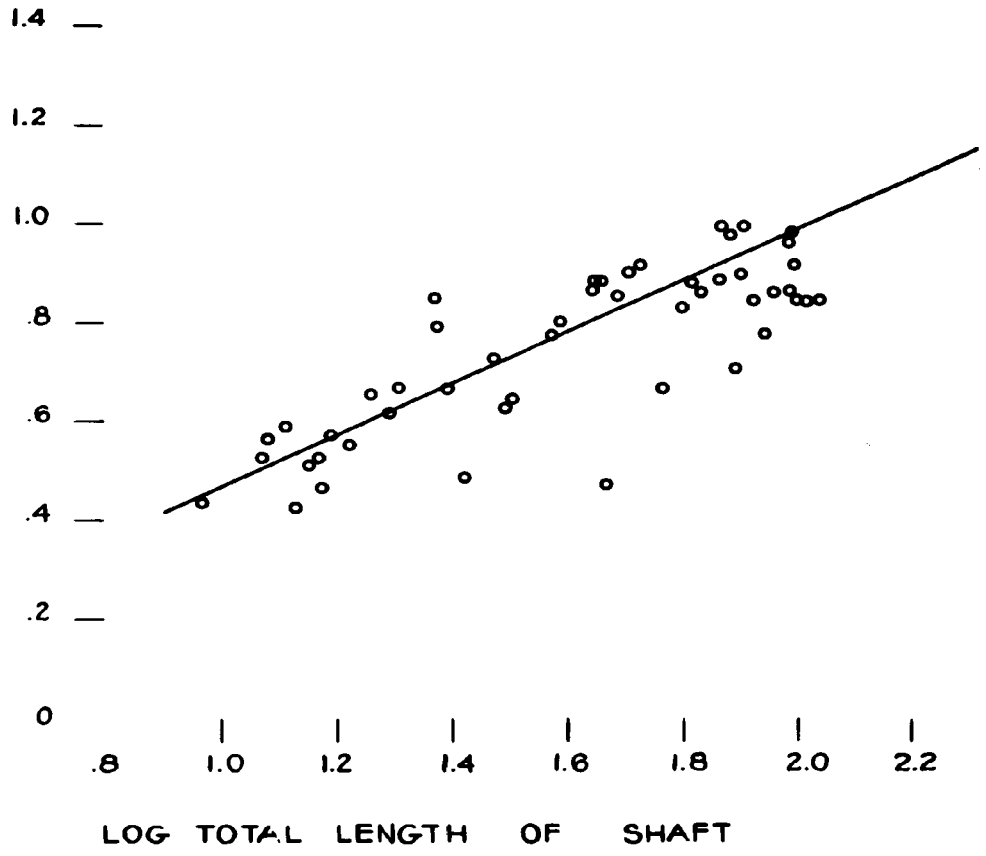


Fig. 8. The regression of log Length of Proximal Cartilage upon log Total Length of Shaft.

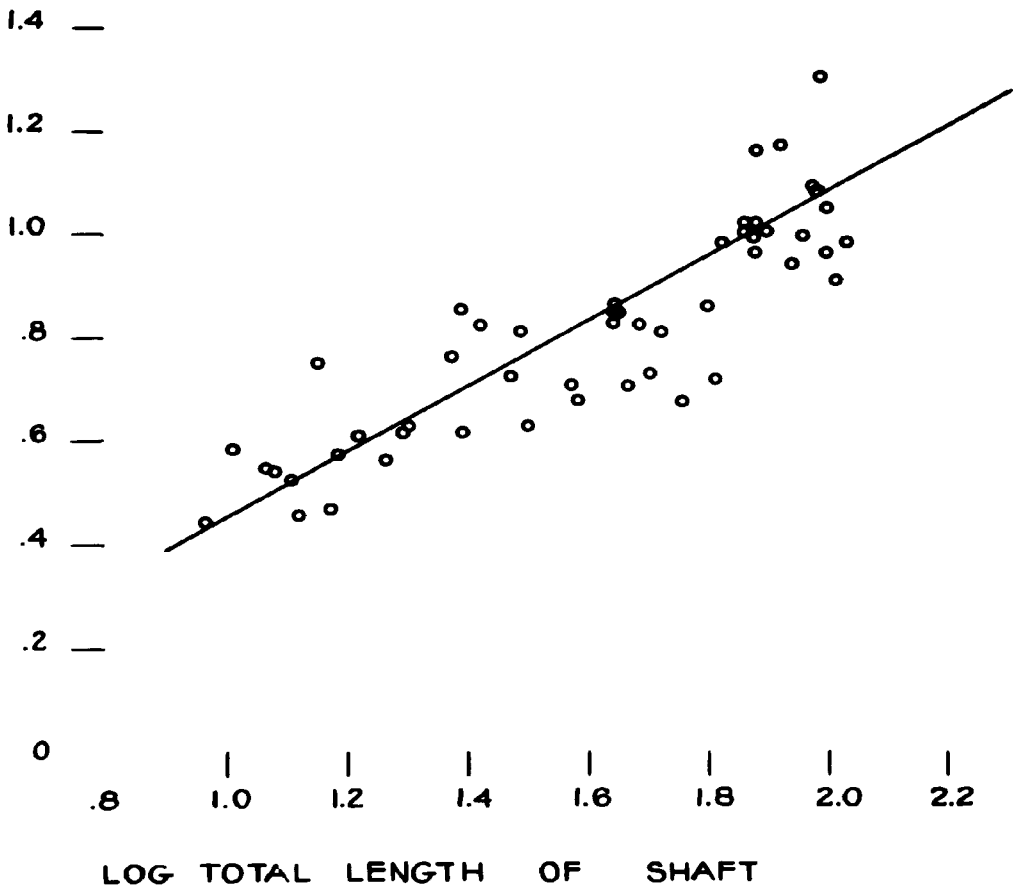


Fig. 9. The regression of log Length of Distal Cartilage upon log Total Length of Shaft.

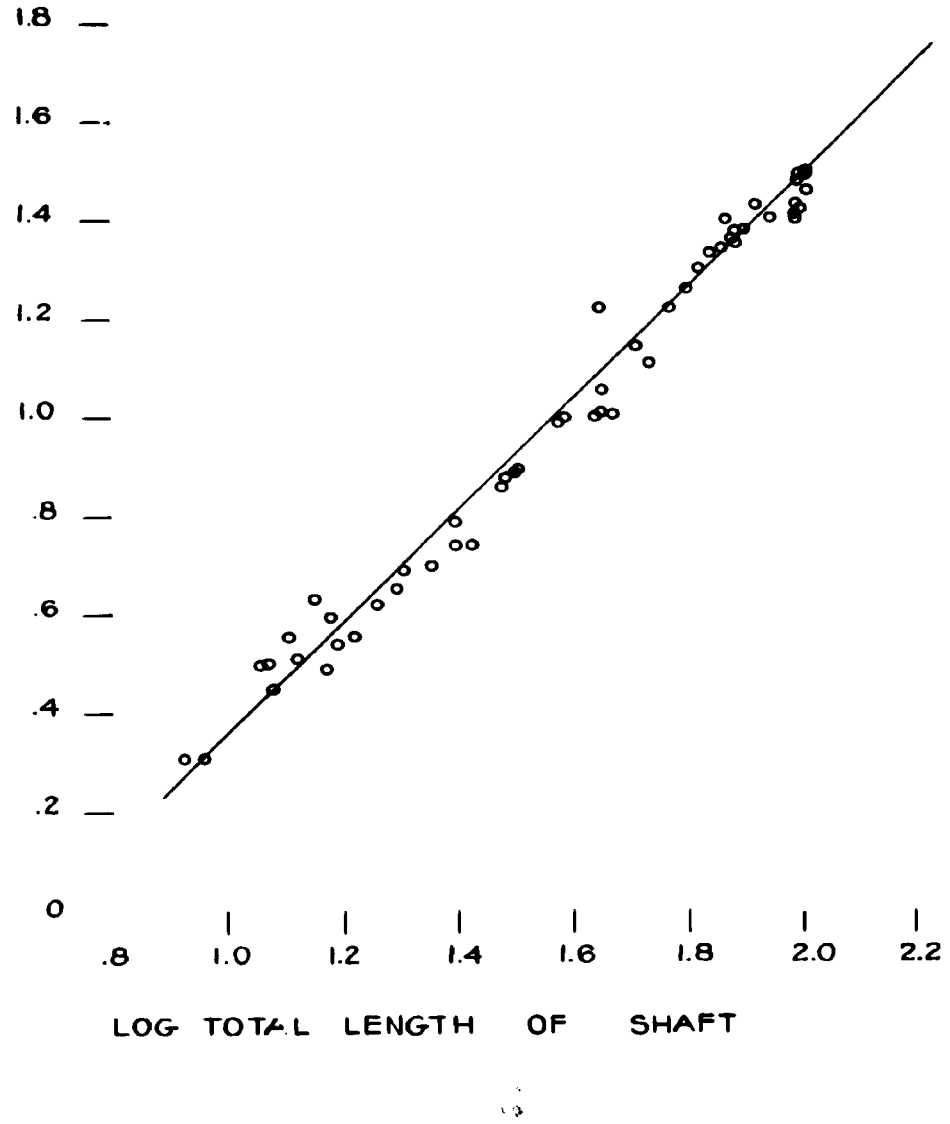


Fig. 10. The regression of log Bicondylar Width upon log Total Length of Shaft.

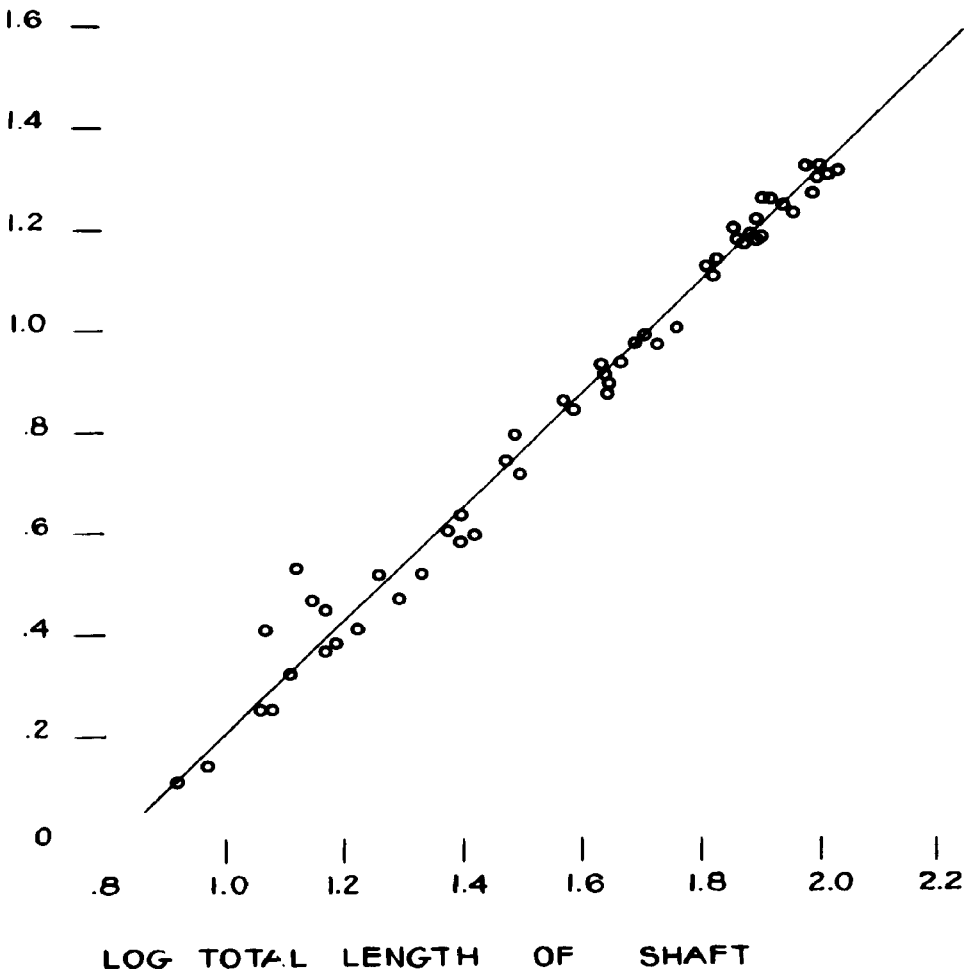


Fig. 11. The regression of log Anterior-posterior Diameter of Condyles upon log Total Length of Shaft.

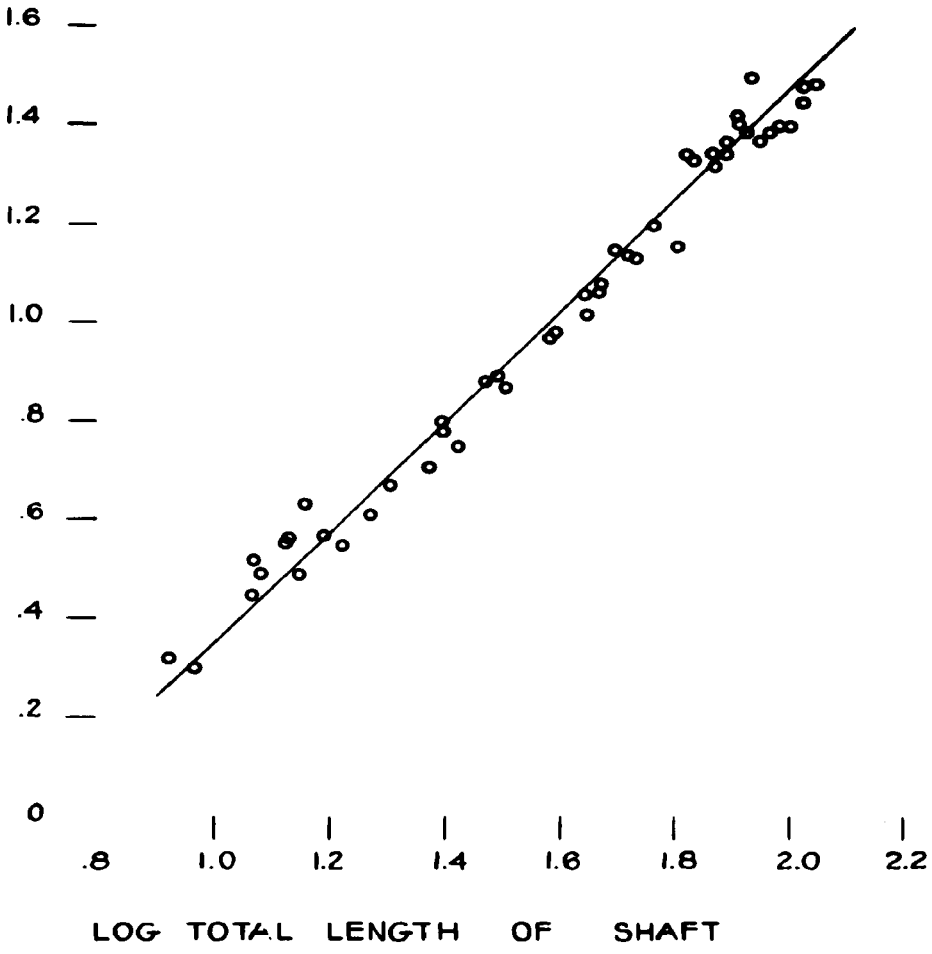


Fig. 12. The regression of log Head-trochanter Width upon log Total Length of Shaft.

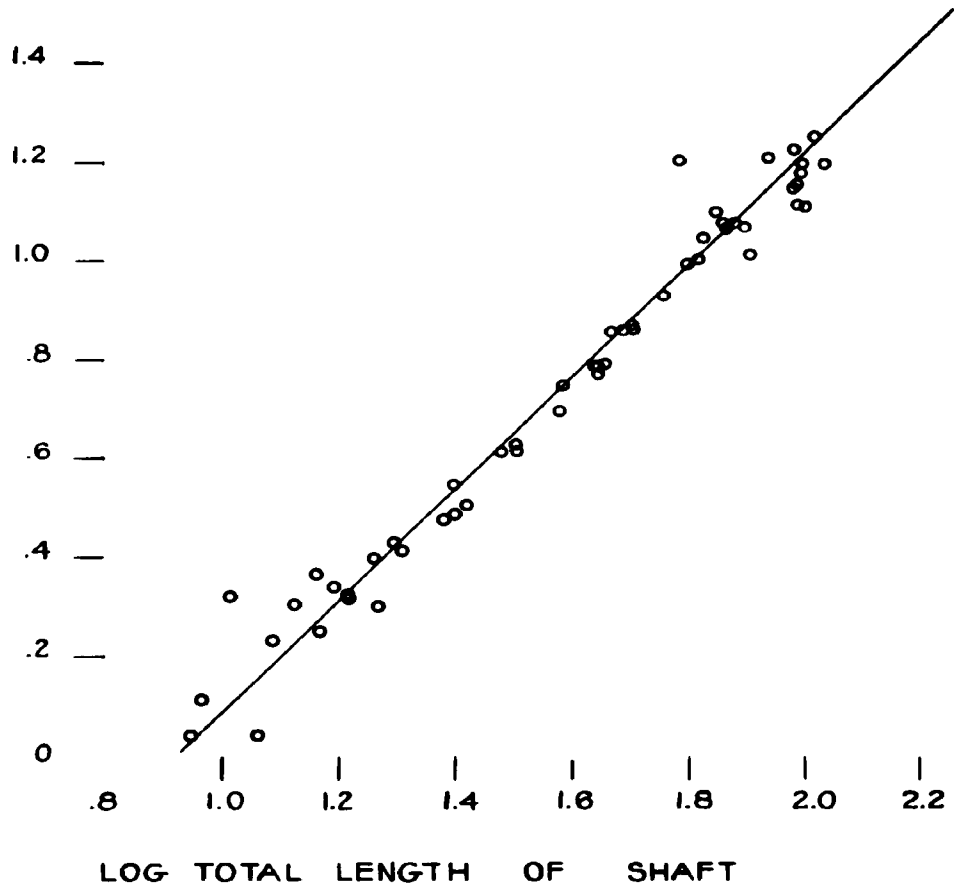


Fig. 13. The regression of log Diameter of Head upon log Total Length of Shaft.

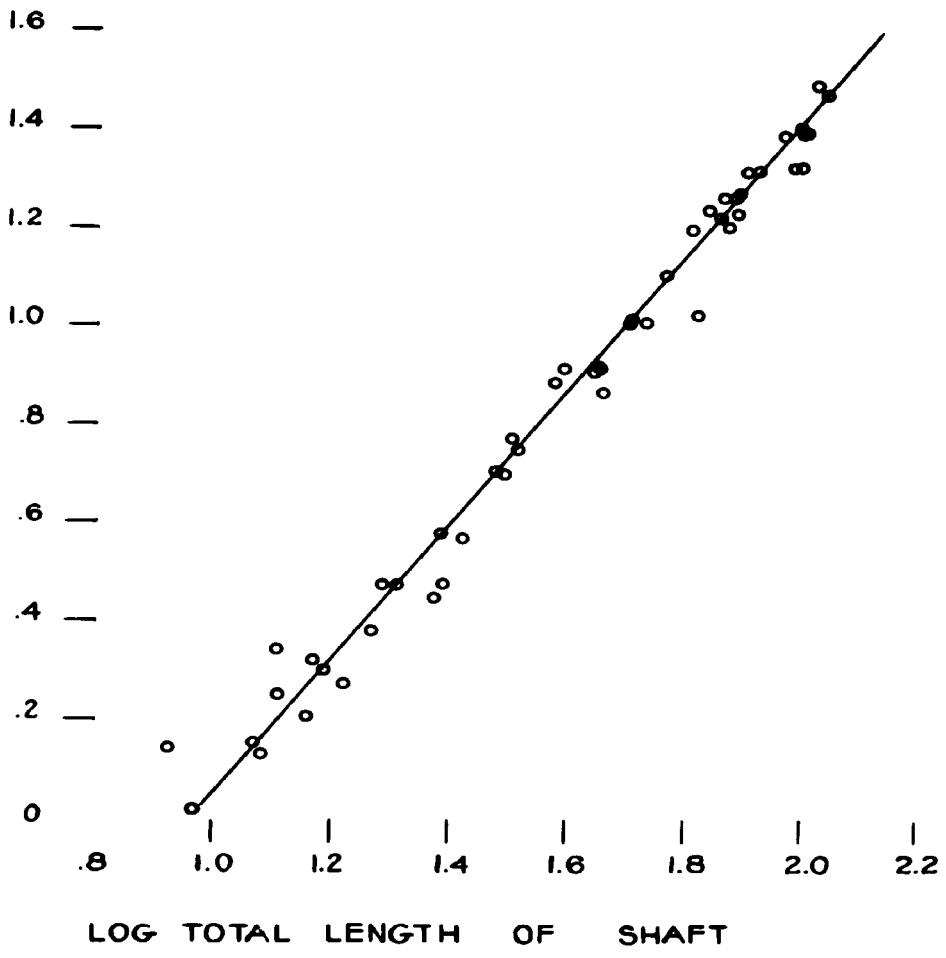


Fig. 14. The regression of log Diameter of Chondro-osseous Junction upon log Total Length of Shaft.

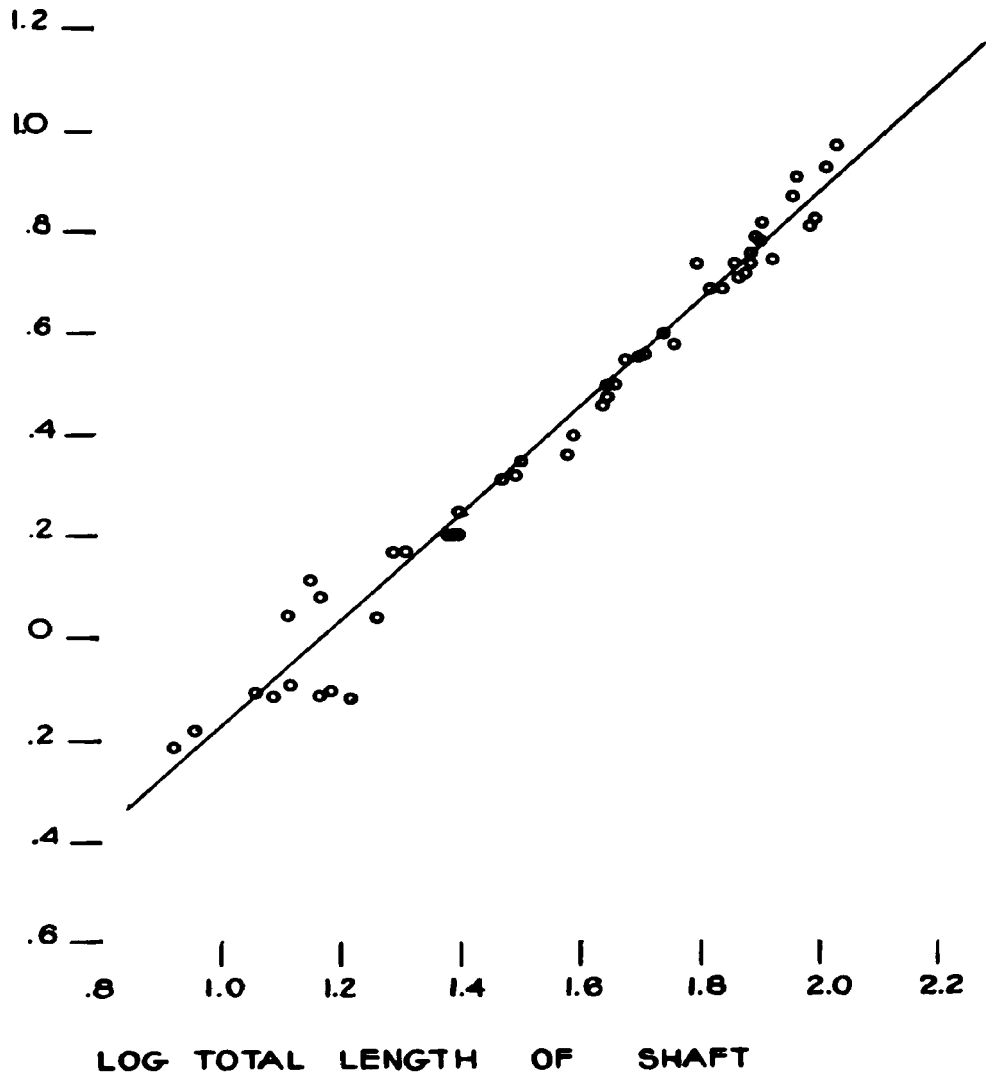


Fig. 15. The regression of log Minimum Diameter of Shaft upon log Total Length of Shaft.

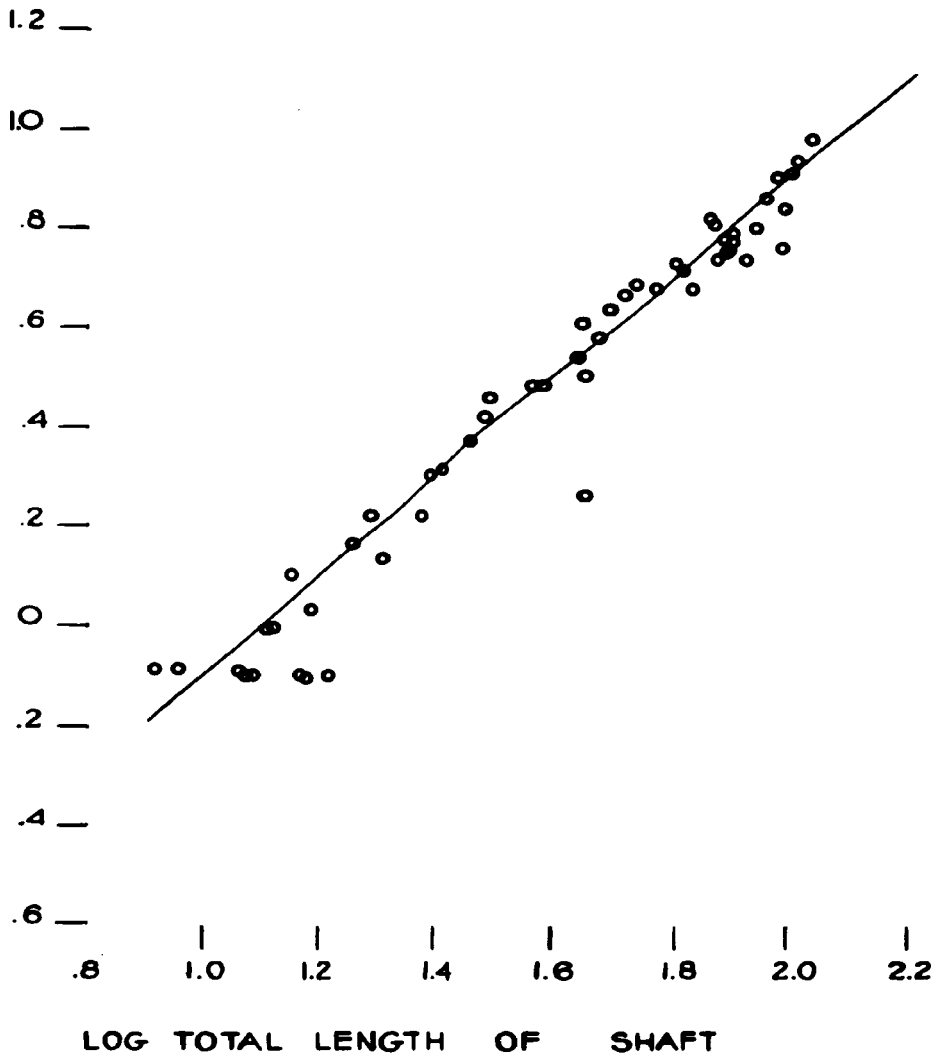


Fig. 16. The regression of log Minimum Anterior-posterior Diameter of Shaft upon log Total Length of Shaft.

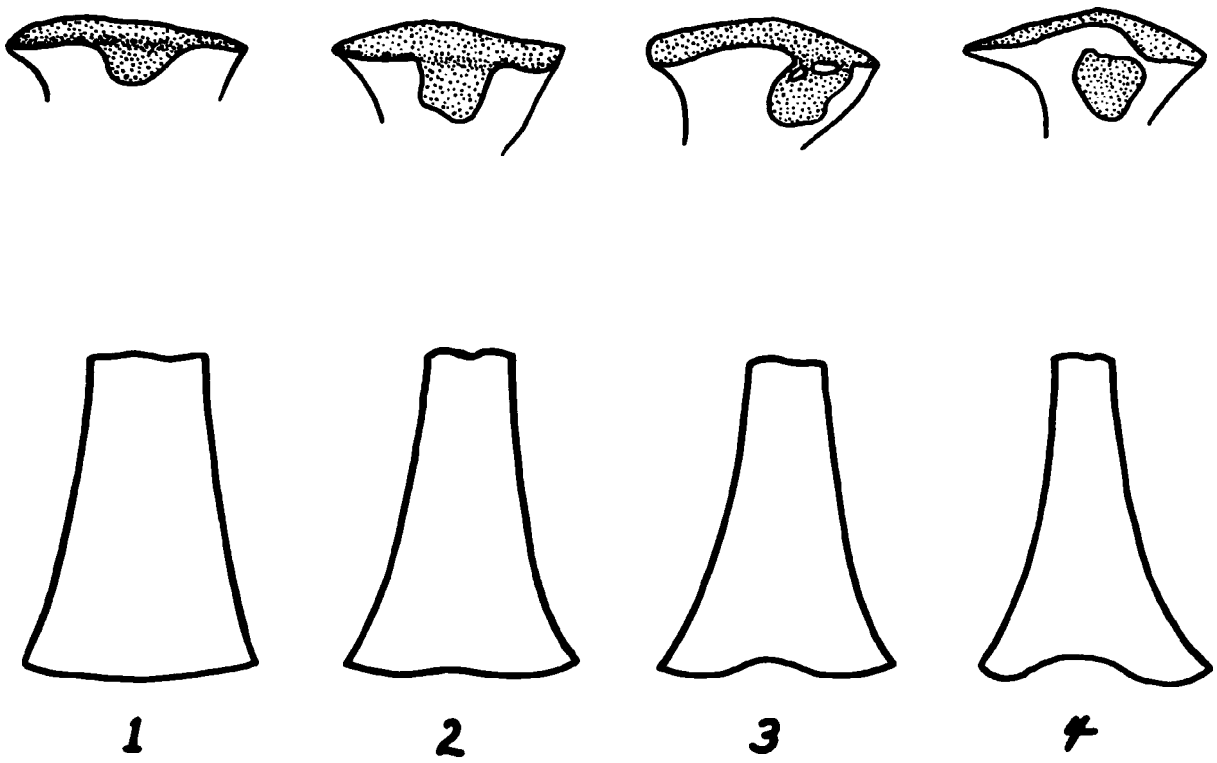


Fig. 17. The developmental shape changes in the proximal (above) and distal (below) ends of the ossified shaft. Note the progressive separation of the plane of the lesser trochanter from the main proximal plane and the increasing angulation of the latter. The frontal sections of the distal end illustrate the change from convex to concave. Total Length of Shaft: (1), 25.0, (2), 54.4, (3), 105.3, and (4), 160 mm . Secondary center of ossification present in last two.

scaffold-work for osseous invasion. (For further discussion of this last point, the reader is referred to page 51).

In short, it appears that the juxtaosseous zone ceases to move along the femur and that, backed up by the remaining extracapsular cartilage and the growing center of ossification, it becomes a major part of the definitive epiphyseal disc (a better term is "cartilage of conjugation" used in Lacroix's recent work). In this situation it proliferates in its basal portions as fast as it contributes to the scaffold for osseous invasion at the chondro-osseous junction. It should be noted that the bicondylar width, whose increase is the indication used here of transverse cartilage growth, is never transgressed by the distal chondro-osseous junction. Rather, once the junction is stabilized relative to the end of the femur, increase in bicondylar width is dependent upon the transverse growth of the cartilage just behind the junction - cartilage largely related to proliferation of the epiphyseal disc area. This may well account for the lower growth rate along the bicondylar dimension in the postnatal period.

It would be unfortunate were the impression created that the process just considered was regarded as the only one in operation in the prenatal femur. Several secondary processes are clearly going on concurrently although they cannot be so readily understood. The fact that certain areas without a perichondrium grow as rapidly or more rapidly than those with that formative layer (e. g., the femoral head and the head-trochanter width) is extremely interesting. This raises a question as to the relative importance in cartilage growth of the interstitial and appositional modes. Again, the possibility of discrete but as yet undetected differ-

ences in growth rates between very localized areas must be recognized. That such an inherent difference in growth rates can exist in a single tissue mass is evidenced by the more rapid growth of the distal cartilage in the transverse than in the sagittal axis and the greater growth in the lateral than in the medial condyle. On the other hand, although there is considerable difficulty in demonstrating the fact, it would seem that relative decrease in length of the femoral neck with development is more likely due to the proportional changes concomitant with cartilage growth in all directions than to an actual difference in growth rates of adjacent areas.

The more rapid longitudinal cartilage growth evidenced in the distal cartilage agrees with the generally accepted statement that growth occurs more rapidly and persists longer at that end of the long bone in which the secondary center of ossification first appears (Payton, '32, Brash, '34, Weinmann and Sicher, '47). This agrees too with the present findings concerning the proportionality of osseous growth occurring at either end of the shaft. It is not without interest that the greater proportion of osseous growth occurs at the same end of the shaft as the greater proportion of cartilage growth.

4 - Gross Development of the Ossified Shaft

Thus far considered as a unit within the developing femur, the ossified shaft is of sufficient importance to warrant a separate discussion. It will be shown that the characteristics of this osseous unit are largely dependent upon the cartilage it replaces and the manner in which this replacement takes place.

Examination of sectioned embryos of ages less than that of the youngest specimen in the present series shows that the ossified shaft originates early in the eighth week as a thin "periosteal collar" surrounding and extending for some distance on either side of the area where hypertrophy of the cartilage cells has commenced. With the intrusion of osteogenetic tissue into the degenerate cartilage, there quickly develop irregular spicules of bone inside the middle portion of the periosteal collar. As a small central medullary cavity forms, the spicules become more regular in form and parallel in orientation. At the same time, the chondro-osseous junction from which the spicules arise moves rapidly toward the ends of the sub-periosteal collar, which by this time has thickened into a more substantial cortex. In the tenth week, at which time the ossified shaft has attained a length of about 9 mm, the chondro-osseous junction is within approximately a quarter of a millimeter of the ends of the periosteal collar and thereafter the projection is so slight as to be generally indistinguishable and is lost in the removal of the cartilages from the shaft.

The ends of the ossified shaft (i. e., chondro-osseous junction) are, in the younger stages of development, neither convex nor concave (fig. 4, C., D.). However, as ossification progresses both ends, especially the proximal, become more convex (fig. 4, F., G.). The convexity is always and progressively greater in the medial-lateral axis than in the anterior-posterior.

In further development the proximal end of the shaft goes out of round and attains, by cartilage replacement, a diameter progressively greater in the medial-lateral axis than in the anteroposterior. Con-

comitantly, convexity in the mediolateral axis increases rapidly, while that in the anterior-posterior has almost no increase. By the time the end of the shaft has progressed to a level superior to the site of the lesser trochanter, this convexity has altered to a rather distinct angulation (fig. 4, K-L). In this manner the proximal end of the shaft, in terms of growth, the chondro-osseous junction, becomes divided into two major planes, neither of which is anywhere near perpendicular to the long axis of the femur. The medial plane underlies the cartilage of the neck, the lateral, that of the greater trochanter (fig. 4, M). It is not until the first months of postnatal life, however, that the angulation becomes great enough, and the neck segment advances into the cartilage far enough that the two planes become discrete. Although it is difficult to determine exactly, it appears that bone from the shaft never grows quite a third of the way toward the apex of the greater trochanter; replacement by bone from the shaft, on the other hand, does occur throughout the neck and the basal half (or a little less) of the head. The proximal centers of ossification are not prenatal in origin. That of the head appears in an early postnatal specimen in the present series, that of the trochanter does not appear until well beyond the age range of this study.

Except in its basal portion the lesser trochanter, like the greater, remains cartilaginous throughout the fetal period. The small chondro-osseous junction at the base of the lesser trochanter does not, however, arise by the angulation of a portion of the proximal end of the ossified shaft away from the major plane, as described for the greater trochanter. Rather, it appears that as ossification of the proximal end of the shaft progresses past the base of the cartilaginous lesser trochanter a carti-

laginous preparation area for osseous replacement comes into existence in the basal part, and a small chondro-osseous junction is formed perpendicular to the main proximal one. The first manifestation of this can be observed on the bare ossified shaft in a small, low triangle the base and surface of which are continuous with, and at right angles to, the edge of the proximal end of the shaft (fig. 17, 1-2). As the shaft elongates this roughly triangular platform becomes detached from the end of the shaft; it is entirely detached by the time the proximal end of the shaft first evidences a definite angulation into trochanteric and neck planes.

While the proximal end of the ossified shaft has thus advanced into the complex region of the neck and trochanters and has undergone the alterations in configuration just discussed, the distal end has changed in an interesting, if less radical, manner. In the process of replacing the cartilage of the lower shaft, the distal end of the ossified shaft widens greatly on its mediolateral axis and much less so on the anteroposterior. The distal end plane, like the proximal, is at first flat, but becomes progressively more convex (fig. 17, 1-4). Convexity increases as the shaft elongates until the end has attained a level nearly at the site of the future distal center of ossification. In ossified shafts of greater than approximately 75 mm length (overall length of femur, about 92 mm) it can be observed that the mediolateral convexity has been lost and instead there is a depression in the middle of the end plane (fig. 17, 2-4). It appears from this that there is a falling off of the rate of elongation of the ossified shaft, i. e., a reduction in the rate of cartilage replacement in the area immediately adjacent to the

site of the distal ossification about a month before the actual distal center of ossification appears. The replacement of cartilage by bone progresses at a high rate around this area, particularly medially and laterally, and the convexity is replaced by an irregular concavity (fig. 17). (See foregoing comment upon the effects of the occurrence of the distal center of ossification upon the advance of the ossified shaft, pages 34 and 47.)

Comparison of the ossified shaft of the prenatal with the postnatal femur makes clear the fact that there must be a striking difference between the two in the proportion of growth in length which can and does occur from either end. Throughout more than half of the fetal period the chondro-osseous junctions, although they undergo changes in curvature, are approximately perpendicular to the longitudinal axis of the shaft. Assuming for the moment that cartilage is replaced by bone at the same rate, on the average, at both ends of the shaft, the two ends would contribute equally to elongation. It has been pointed out by other authors (Keith, '19, Weinmann and Sicher, '47) that growth of the postnatal femur in length occurs mainly from the distal epiphyseal cartilage disc because only that, of the four discs of the femur, lies perpendicular to the shaft's axis. In this position, all of its contribution to length is effective. The remaining growth discs contribute only to the elongation and enlargement of their respective processes, except that some addition to length can be gained with the incorporation of the basal areas of the angulated neck and greater trochanter. In the early and progressive deviation of the proximal chondro-osseous junction into neck and trochanteric planes there can be seen the origin of the inequality of contribution to

the length of the femur. The process of deviation is, as we have seen, a gradual one and the results are probably not critical until some time after birth when deviation is more or less complete and the proximal chondro-osseous plane has become separated into two distinct entities.

In the discussion immediately above, the assumption was made that the rate of cartilage replacement was the same at both ends of the femur, but the effectiveness of the contribution from the two ends was different. Another possibility exists, namely that the rate at one end, as a regular developmental characteristic, exceeds that at the other. Hales, as long ago as 1727, observed that growth in the tibia of the growing postnatal chicken, as measured from awl holes previously placed in the shaft, occurred more rapidly from the proximal end. This technique was elaborated upon only slightly by a series of later investigators who placed in awl or drill holes in bone shafts various particles of silver, lead, or steel: Duhamel (1743), Hunter (1837), Flourens (1861), Gatewood and Mullen, ('27), and Bisgard and Bisgard ('35). All of the experiments utilizing this technique were carried out on postnatal animals and on several different long bones with results which have become standard reference book information (Weinmann and Sicher, '47). The feeding of madder for staining growing long bones, the production of reaction lines or areas by the feeding or injection of chemicals, and the radiographic observation of lines of arrested growth occurring in the bones of children who have suffered prolonged or severe illness have all contributed to knowledge on this point. Humphry (1861) was the first to record the observation that in madder stained bones of the pig, more growth occurred at one end than at the other. Although

the same technique had been used previous to Humphry's time, by Belchier (1736), Duhamel (1743) and Hunter (1837), differences in growth rate at the two ends were not reported. The major contribution of these workers was the basic observation that growth occurred at the ends of long bone shafts.

The most thorough utilization of the madder technique is found in the work of Payton ('32) who investigated the growth of all the major long bones in the young postnatal pig. He showed that the general pattern of long bone growth in the pig is that the adjacent ends of the tibia and femur and the opposite ends of the humerus and radius grow more rapidly. A more intensive investigation of single long bone, the femur, has been done by Aries on the alizarin injected rat ('41) in which it was found that the greater amount of growth takes place at the distal end.

Harris ('26, '31), utilizing as landmarks the lines of arrested growth visible in roentgenograms of the long bones of children who had suffered severe illnesses, demonstrated that the tibia grows faster at the distal end than at the proximal and that growth at the knee is a little more rapid than at the hip. Bisgard and Bisgard ('35), while supporting in their results from the postnatal period the findings of Payton, observed that in the prenatal period, as indicated by measurements from phosphorous reaction lines, there is a more nearly equal contribution of growth from each end of the femur. It is significant that this was found to be particularly true of the early prenatal period.

It was first suggested by Berard (1835) that the canal of the nutrient artery of long bones was inclined toward that end of the bone at

which epiphyseal closure first occurred. Humphry (1861) stated that the inclination of the canal was the result of the unequal growth from the ends of the shaft and that the periosteum was dragged, as it were, toward the end with the greater rate of growth. This would cause the newer additions to the canal to be displaced toward that end. Schwalbe (1876) developed Humphry's concept. Langer, in the same year, showed general agreement. Piollet ('05) held that the canals were directed at first perpendicular to the longitudinal axis of the shaft and that as growth progressed they were inclined away (medially) from the end with the greater growth rate. Digby ('16), who examined the adult human long bones in admittedly small numbers, concluded that the nutrient artery represented the vascular portion of the original periosteal bud and that the site of the original ossification (endochondral) from which growth progresses in either direction could be located at the intersection of the axes of the canal and the shaft. He presented data to show the percentage of the shaft lying on either side of this central point.

Although there has been general agreement that the nutrient artery and its canal are related to the initial ossification, more recent investigators have contested the conclusions and even the observations referred to above. Bisgard and Bisgard ('35) supported Digby's conclusions. Payton ('34) took strong issue with the concept of the fixed central point after finding that in his series of madder-stained pig bones the nutrient foramen appeared to have a variability of position independent of shaft growth. He came to the additional conclusion that the canal was dependent in direction and angle upon its proximity to areas

where new additions of lamellar bone were being laid down. Although offering no substitute explanation, Hendryson ('45) questioned the validity of Digby's conclusion and reported that in his own series of human bones the variation about the mean position for the central point was so great as to cast doubt upon its utility as a landmark from which to measure. More recently ('50), Lütken published essentially the same observations as Hendryson.

In an investigation such as the present one, restricted as it is to gross morphology and unsupported by experimental procedures, only slight additions can be made to our knowledge of the questions just discussed. Nevertheless, some of the facts to be presented may be of value because they are concerned with the prenatal period of human skeletal development which has been much less intensively studied. Of the previous investigators, only the Bisgards treated of the prenatal period and that in the goat.

Roentgenographs were made of the lateral projections of a series of ten carefully selected femurs. Upon enlarged tracings of these pictures the central point was determined in the manner used by Digby and Payton. It was observed that the point of intersection of the axis of the nutrient canal with that of the medullary cavity was in all cases almost exactly at the narrowest diameter of the medullary cavity. In two cases there were double nutrient canals, one pointing inward and distad and the other inward and proximad. In these cases the central point was considered to be midway between the two points of intersection.

In the ten femurs thus examined the position of the point of intersection was an average of 48.6% of the total length distad of the proxi-

mal end of the ossified shaft. The standard deviation for this value is 2.21 (4% of the mean). The maximum was 52%, the minimum 44%. The youngest (smallest) specimen had a value of 50%, the oldest, 47%. A general expression of the slight change in the position of the point of intersection from the youngest to the oldest specimens was obtained by the algebraic addition of the increase or decrease in the percentage between successive specimens in the series, i. e., the sum of increases subtracted from the sum of the decreases. The change thus determined amounted to 2%.

These findings, although from a relatively small series of femurs, lead one to believe that, at least in the fetal period, the point of intersection may well be a central point on either side of which the ossified shaft elongates. The fact that the point nearly coincides with the narrowest diameter of the medullary cavity is of importance because that diameter, in the sharply constricted cavity of fetal long bones may in itself be considered a "central point" for the narrowest internal diameter of the growing femur must coincide with the original central portion of the early periosteal collar.

The decrease in the percentage of the ossified shaft proximal to the central point, however small, is of interest. In the smallest femur in the series (18.3 mm total length of shaft) the 10 mm ossified shaft is divided 5 mm either side of the point. In the largest specimen (109 mm) the 84.3 mm ossified shaft is divided into 40.0 mm proximal and 44.3 mm distal. This is an actual increase of 3%. The increase may be due to either one or both of two factors: the beginning deviation of the proximal chondro-osseous junction or an actual difference

in the rate of cartilage replacement at the distal and proximal chondro-osseous junctions, the distal predominating. On the basis of the material used in this study and the data gathered from it, no distinction or conclusion can be drawn.

5 - Environmental Effects Upon Femoral Configuration

In the earlier sections of this paper the emphasis has been on the developmental characteristics of the femur that could be attributed directly to growth per se, that is to say, things that were manifestations of cellular activity and tissue increase along certain genetically determined lines. As has been shown by experiments in which long bones were cultivated in vitro, this inherent pattern is rather rigid. Yet the femur or any other long bone is acted upon, in its normal environment, by the circumjacent connective tissues and muscles, the presence of which sets up pressures and tensions. It is affected, also, by the postural habits of the organism, and, quite likely, in the fetal period, by the confining action of the uterine wall within which the organism exists. Within certain poorly defined limits the affector forces can be effectively countered by the inherent configuration and substance of the femur; beyond these limits there is an adaptation of the inherent configuration to meet the individual situation.

Precisely how much adaptation to the environment is hidden in what one usually terms the inherent developmental pattern is a question. There has never been a quantitative study of the exact differences existing between a series of long bones grown normally and one grown in vitro. There are, however, several femoral characteristics which because of their high

degree of invididual variation, can be readily classified as functional adaptations as such or in some cases as inherent features with a superimposed variation in the individual adaptation. These characteristics are all such as can be expressed in degrees of angles and are, in the order in which they will be discussed, torsion, angular displacement of the head, inclination, and obliquity. Examination of table 2 shows these four dimensions, although differing greatly among themselves in variability, are as a group rather distinct from the rest of the femoral dimensions. Inclination, for reasons which will be explained in turn, is an unreliable dimension, the much lower correlation coefficient of which should not prejudice opinions concerning the other angular dimensions. Although it might at first be considered that the angular dimensions cannot be measured as accurately as, for example, bicondylar width, it should be noted that obliquity (correlation coefficient, .51) in particular, is determined from landmarks as easily and as reliably located as those for the bicondylar dimension. Torsion and angular displacement of the head (r values, .74 and .64), although determined from artificial points, can hardly be considered as any more than slightly influenced by artifacts of point location. Finally, and most critically, the high individual variation of the angular dimensions is apparent on the actual specimens and is not dependent upon measurement for elucidation.

a. Femoral Torsion and Angular Displacement of The Head.

Torsion of the femur, that is to say the angular displacement of the head and neck anterior or posterior to the frontal plane, has been the sub-

ject of considerable interest and investigation. Before presenting the findings concerning the development of torsion, a brief review of the adult condition is necessary. Adult torsion values have been reported since before the beginning of this century. Although there have been a large number of papers in the clinical literature, only those based on wholly adult series will be noted here. This stipulation rules out the majority of these reports.

Mikulicz (1878) presented a series for which Elftmann ('45) computed a mean of 11.67 degrees. Le Damany ('03 a, b) showed a variation between left and right femurs with an average of 11.33 degrees on the right and 14.07 on the left. Pearson and Bell ('19) found roughly the same condition: 11.63° for the right and 14.71° for the left. However, the opposite variation was observed by Ingalls ('24) whose series had an average of 11.76° on the right and 9.73° on the left. Elftmann ('45) gave a bilateral average of 11.23°. In a recent investigation, Kingsley and Olmstead ('48) found values of 7.47° for the left and 8.54° for the right, the average being 8.02°. As illuminating as the means are the variations expressed in the standard deviations computed by several of the authors: Pearson and Bell, 8.80, Ingalls, 7.87, Elftmann, 6.21, and Mikulicz (computed by Elftmann) 9.61. Ingalls, commenting on the femur as a whole, stated that the differences between the left and right are very small and that, of the two, the right seems to be slightly more constant.

There are, naturally, differences in the techniques of measuring torsion employed by the various investigators, but these differences do not appear significant. Certainly there is not enough difference in

method to account for the range within and between the reported series of measurements.

Doubtlessly the most significant feature of human femoral torsion is the manner in which it progresses through ontogeny. Altmann ('24), in a phylogenetic study of hip joint and femur development from the salamander to man, showed that the lower animals, although possessing torsion to an extent varying with the taxonomic group, do not undergo a reduction of torsion after birth. Le Damany ('04 a) presented torsion values for several animal groups but, in the absence of early embryonic material, did not make this critical observation.

Although the degree of torsion present in the femur of the infant, child and adolescent has been investigated well enough to permit generalizations to be made, information concerning this period as a whole is still far from complete. Mikulicz (1878) presented the following values for 38 specimens: 0-2 years (14 specimens), -19 to 39; 2-5 years (13), -8 to 22; 5-18 years (11), 4 to 28. Le Damany ('04 a) gave data on the left and right femurs of eight term fetuses. Computations from his data yield an overall mean of 35 degrees, with a range of from 21 to 50. A fairly well distributed series was presented by Rogers ('31, '34) from whom the following table of means and ranges was adapted:

Number	Age Range	Torsion	Torsion Range
9	6 mo to 2 yrs	44 degrees	15 to 57 degrees
9	2 yrs " 4 "	33 "	15 to 57 "
11	4 " " 6 "	27.5"	17 to 35 "
15	6 " " 8 "	19.5"	8 to 28 "
25	8 " " 10 "	19 "	8 to 33 "
29	10 " " 12 "	20.5"	8 to 38 "
2	12 " " 14 "	16 "	None

Kingsley and Olmsted ('48) have published findings on torsion in 32 infants and children, two to 15 years of age. Their average for the left femur was 16.4 degrees (range: -4.5 to 38) and for the right, 17.9 degrees (range: .5 to 33). The bilateral average was 17.2 degrees.

From the data just reviewed it is apparent that femoral torsion is slightly more variable in the early postnatal developmental period than in the adult. The generalization may be made that from a circumnatal value of between 30 to 40 degrees there is a reduction in torsion toward the average adult value of approximately 12 degrees. Apparently this reduction occurs most rapidly in the immediate postnatal period.

During the prenatal period quite the opposite trend is seen. Several authors have given values for torsion in the developmental period prior to the level at which this series begins (less than 30 mm C-R length). As is shown on table 5, Altmann's reconstructed femurs of less than 5 mm overall length had a torsion range of from -10 to -4 degrees. The actual figures were: 2 mm femur, -10 degrees; 2 mm femur, -9 degrees right, -6 left; 3.5 mm femur, -4 degrees right, -9 left. The lengths of the embryos were: 17, 19.7, and 28.5 mm (apparently C-R). Friedlander ('01) gave a beginning value for torsion of -10 degrees. Pitzen ('23), in three fetuses under 29 mm length, found torsion of -4, -15, and -22 degrees. From these data it appears quite certain that the initial torsion of the femur is negative and that the anlage of the femur is differentiated with that orientation.

Table 5 lists the torsion values for the femurs of this series and for those of Altmann ('24), Brandt ('28) and de Cuveland ('50). Only these three series have presented the femur lengths corresponding to the

torsion values. Because there appeared to be no significant difference in the techniques used in collecting the four sets of data, the four columns are considered to be representative of the range of torsion possible over the femur length range covered. From these data it is obvious that torsion, at any given fetal level, shows a high degree of individual variation and that its increase in the prenatal period is even greater than its postnatal decrease.

An interesting characteristic of the logrithmic graphs of both the present torsion series (fig. 18) and of the previous series combined (fig. 19) is the indication of a higher rate of increase in the second than in the first half of the fetal period. This is more obvious in the first graph. Although the relatively small number of specimens involved precludes the drawing of two lines on the graph, there seems to be little doubt that such a break actually occurs.

Gruenwald ('19), in a study of the torsion of the adult femur, came to the conclusion that the neck and head are somewhat independent in the degree of torsion each may attain. Because of the extreme shortness of the neck in the fetal femur it was not possible to utilize the procedure he used with adult bones (involving the drawing of separate axes for the head and neck). It has been possible, however, to determine the angle of the head to the frontal plane, and the angle of torsion as separate features. These two series of angles are shown in table 6. The angular displacement of the head has a somewhat lower correlation coefficient with total length of shaft than does torsion (.64 for angular displacement, .74 for torsion), but both are in the same general class of correlation as compared with other non-angular

dimensions. In only two cases was the angle of the head the same as that of torsion (12 mm femur, 30°, and 49.6 mm femur, 6°). In one case both were negative angles (14.4 mm femur, -32 and -26 degrees), while in four cases the head angle was negative and the torsion angle positive (13 mm, 18.3 mm, 25 mm, and 30.1 mm femurs). In the first ten specimens the ratio of head angle to torsion was .63 with a standard deviation of 1.27. Although lower, .62, in the second ten specimens, the ratio thereafter increased: .66, .77, .82. At the same time the S.D. decreased: 1.03, .28, .19, .11. In general then, the angular displacement of the head and torsion both increase, with considerable general variation between individuals, throughout the series, the first doing so at a greater rate than the second. As the two angles attain a closer correspondence to one another (about a 20 degree change in proximity over the series), the variation in the relationship also decreases (the S.D. Lessens 1.2 over the series). It should be noted, too, that the graph of angular displacement of the head shows the same indication of a bipartate progression as does torsion. However, it would seem that this difference in the rate of increase in later angular displacement of the head exceeds that in the case of torsion. This is most likely the cause of the seeming contradiction between the lower $\underline{k}$ of angular displacement in general (.11 as compared with .18 for torsion) and the fact that its ratio to torsion increases with fetal development.

Pitzen ('23) found that torsion was not restricted to the proximal region of the fetal femur but was present throughout its length. In order to determine this in the present series, four femurs of distinctly varying degrees of torsion were sectioned and, as well as possible, the torsion

of each section determined. Femurs A to D, listed below, represent low, moderate, moderately high values of positive torsion, and high negative torsion, respectively. The technique for handling these selected specimens was more elaborate than that described for the series as a whole. They were decalcified in 1% HCl, washed, and infiltrated with a 10% gelatin solution, then embedded in 25% gelatin. Care was taken to have the condyles and trochanter on a level with the bottom of the block, that is, the femur was orientated relative to the base of the block in the same manner as it was to the turntable on which previous photographs were taken. The gelatin was allowed to set in cold air, and was further hardened overnight in a 10% solution of formalin. Sectioning was done with a razor at five stations along the length of the femur: through the head and neck, through the lesser trochanter, at midlength, through the condyles and at a point between the last two.

A protractor was so arranged that its center coincided with that of a cross-line on a counting ocular for a compound microscope. The cross-line was adjusted, by rotation of the ocular and manipulation of the mechanical stage, so that it was parallel with the base of the gelatin section on a slide. A zero reading was taken on the protractor. The section was then moved on the stage until the cross-line, by further adjustment, appeared to pass through the major longitudinal and transverse axes of the section of cartilage or bone. The torsion at the station was read as the difference between the first and a final reading of the position of a fixed needle on the protractor. It must be admitted that, by this technique, one is not measuring equivalent things at each level of a femur. The torsion thus determined is based upon the shape of the external out-

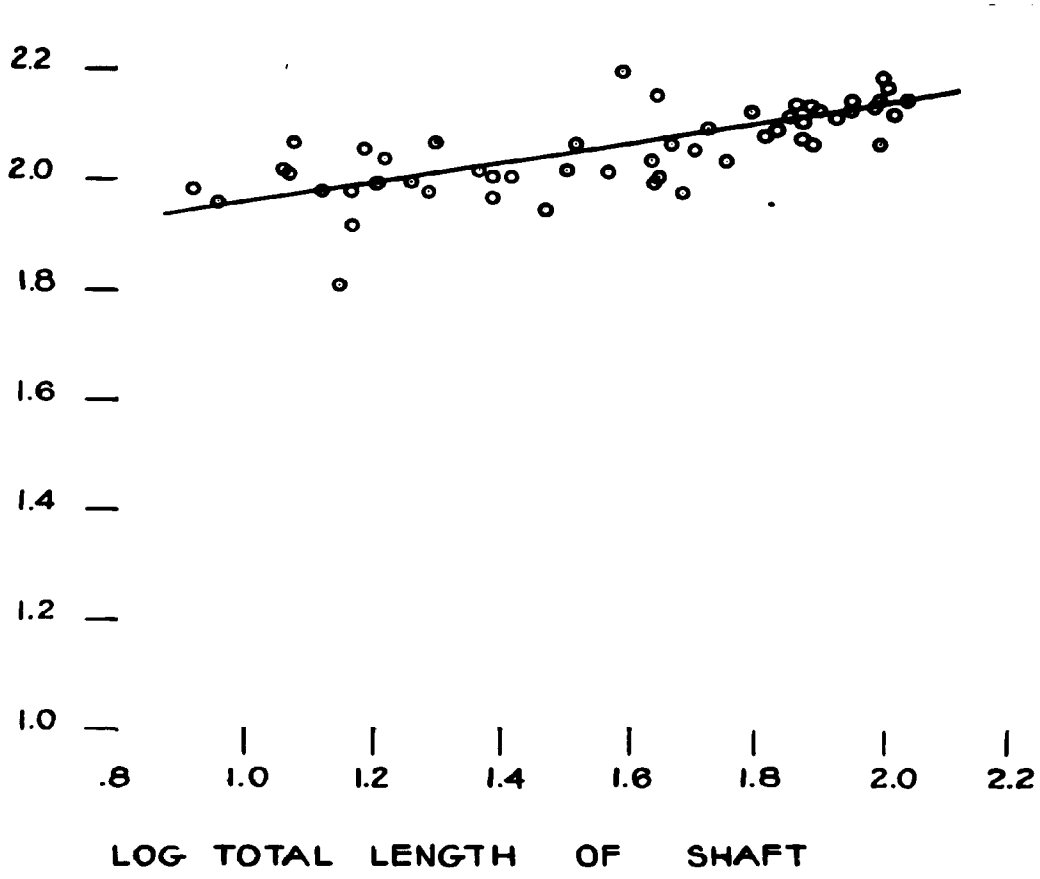


Fig. 18. The regression of log Torsion upon log Total Length of Shaft.

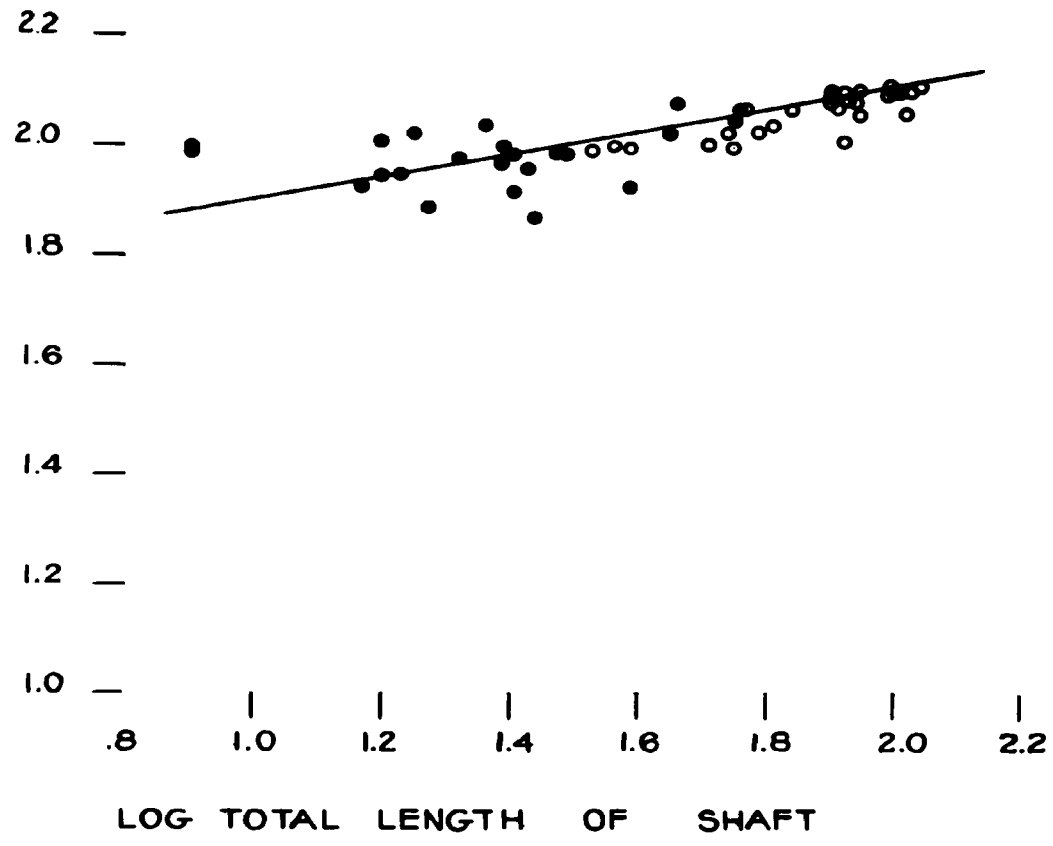


Fig. 19. The regression of log Torsion upon log Total Length of Shaft. Black dots are Altmann's values, the circles those of de Cuveland.

Table 5

Summary Table of Prenatal Torsion

Shaft	Felts	Altmann	Brandt	de Cuveland
0-5 mm		(6)-10.0/-4.0		
6-10	(2) 2.0/7.5	(2) 9.5/10.0		
11-15	(7)-26.0/30.0	(1) -4.0		
16-20	(3) 6.0/20.0	(5) 0.0/16.0		
21-25	(3) 11.5/15.0	(2) 4.0/19.0	(1) -8.0	
26-30	(2) 4.0/12.0	(5)-15.0/11.0	(3)-12.0/0.0	
31-35	(3) 1.0/28.0	(1) 1.0	(5) -5.0/16.0	(1) 6.0
36-40	(2) 15.0/16.0	(2) -5.0/12.0	(3) 20.0/26.0	(2) 10.0/11.5
41-45	(2) 12.0/20.0	(1) 16.0		
46-50	(3) 6.0/56.0	(1) 31.0	(1) 32.0	
51-55	(2) 25.0/38.0		(3) 20.0/38.0	(2) 14.3/17.1
56-60	(1) 18.5	(2) 22.0/27.0		(2) 9.2/26.3
61-65	(1) 47.0			(2) 18.1/22.0
66-70	(1) 34.0			(1) 28.2
71-75	(3) 36.0/49.0		(1) 26.0	
76-80	(2) 28.0/31.0			(3) 29.7/37.0
81-85	(3) 45.0/49.0			(5) 14.0/34.5
86-90	(1) 37.0		(2) 24.0/32.0	(2) 29.3/35.1
91-95	(2) 30.0/50.0		(2) 27.0/36.0	(1) 6.0
96-100	(1) 50.0		(6) 18.0/40.0	(5) 31.7/39.2
101-105	(3) 52.0/64.0		(2) 30.0/32.0	(1) 53.0
106-110	(1) 43.0			(3) 24.5/38.0

From left to right in each column: number of specimens, maximum negative value or minimum positive, then maximum value for torsion.

Table 6

Torsion and the Angular Displacement of the Head

Shaft	Torsion	A.D. of Head	Shaft	Torsion	A.D. of Head
8.4 mm	7.5°	11.5°	45.3	56.0	45.0
9.2	2.0	10.0	47.2	28.0	5.0
11.5	16.0	8.0	49.6	6.0	6.0
11.9	13.0	3.0	51.5	25.0	12.0
12.2	30.0	30.0	54.4	38.0	39.0
13.0	9.0	-5.0	57.7	18.5	6.5
13.2	8.0	12.0	63.3	47.0	24.0
14.4	-26.0	-32.0	65.9	34.0	29.0
14.9	6.0	4.0	68.5	36.0	33.0
15.5	27.0	17.0	72.9	44.0	36.0
16.6	20.0	8.0	74.4	49.0	38.0
18.3	10.0	-14.0	76.2	31.0	23.0
19.7	6.0	7.0	77.1	28.0	21.0
20.5	12.0	5.5	78.1	49.0	39.0
23.9	15.0	9.0	80.0	45.0	48.0
25.0	11.5	-2.0	81.8	45.0	39.0
25.0	4.0	5.0	84.6	37.0	30.0
26.5	12.0	0.0	88.7	50.0	38.0
30.1	1.0	-7.0	91.5	30.0	25.0
31.3	28.0	16.0	96.7	50.0	37.5
31.8	15.0	1.5	99.5	64.0	61.0
37.8	15.0	11.0	100.9	58.0	34.0
39.1	16.0	11.0	102.9	52.0	43.0
43.9	20.0	15.0	105.3	43.0	44.0
44.3	12.0	9.0	110.6	52.0	44.0

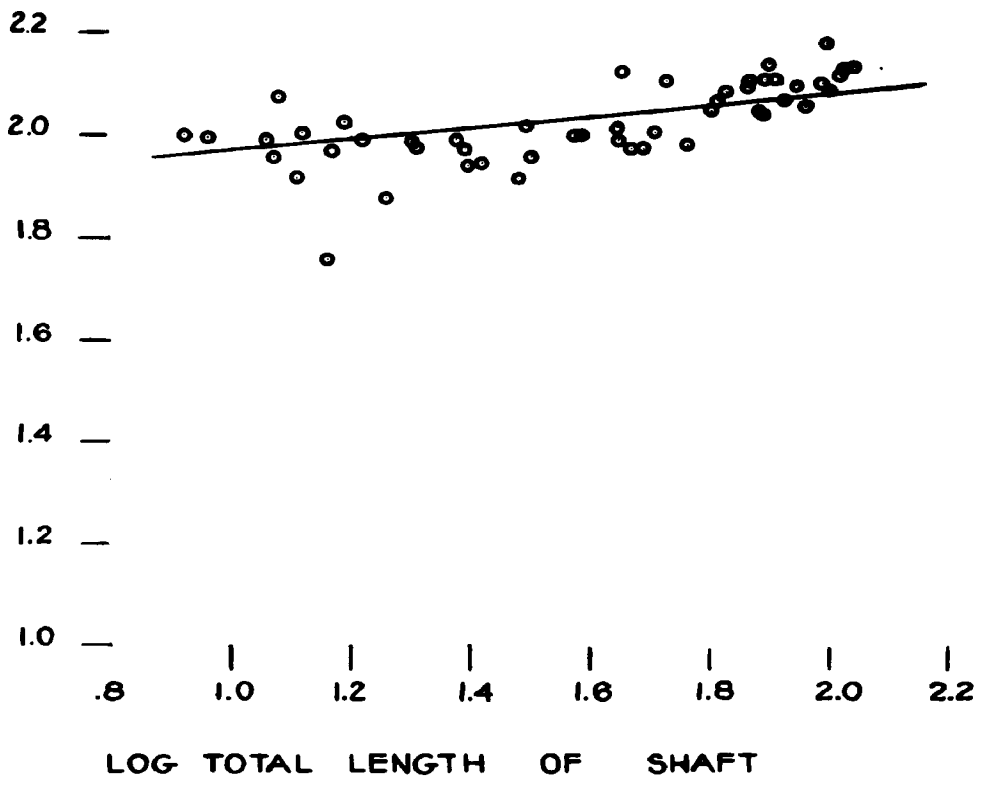


Fig. 20. The regression of log Angular Displacement of Head upon log Total Length of Shaft.

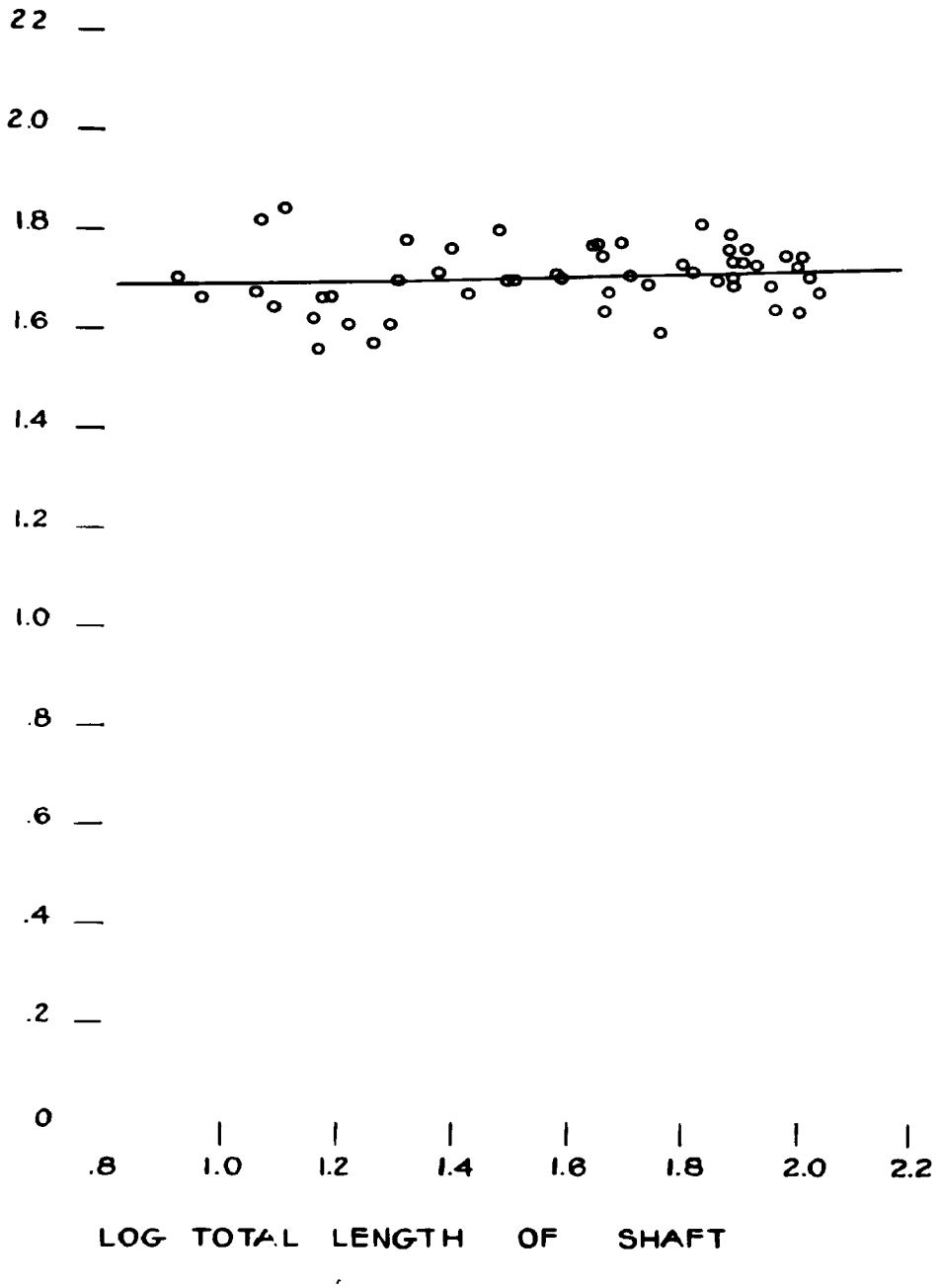


Fig. 21. The regression of log Inclination upon log Total Length of Shaft.

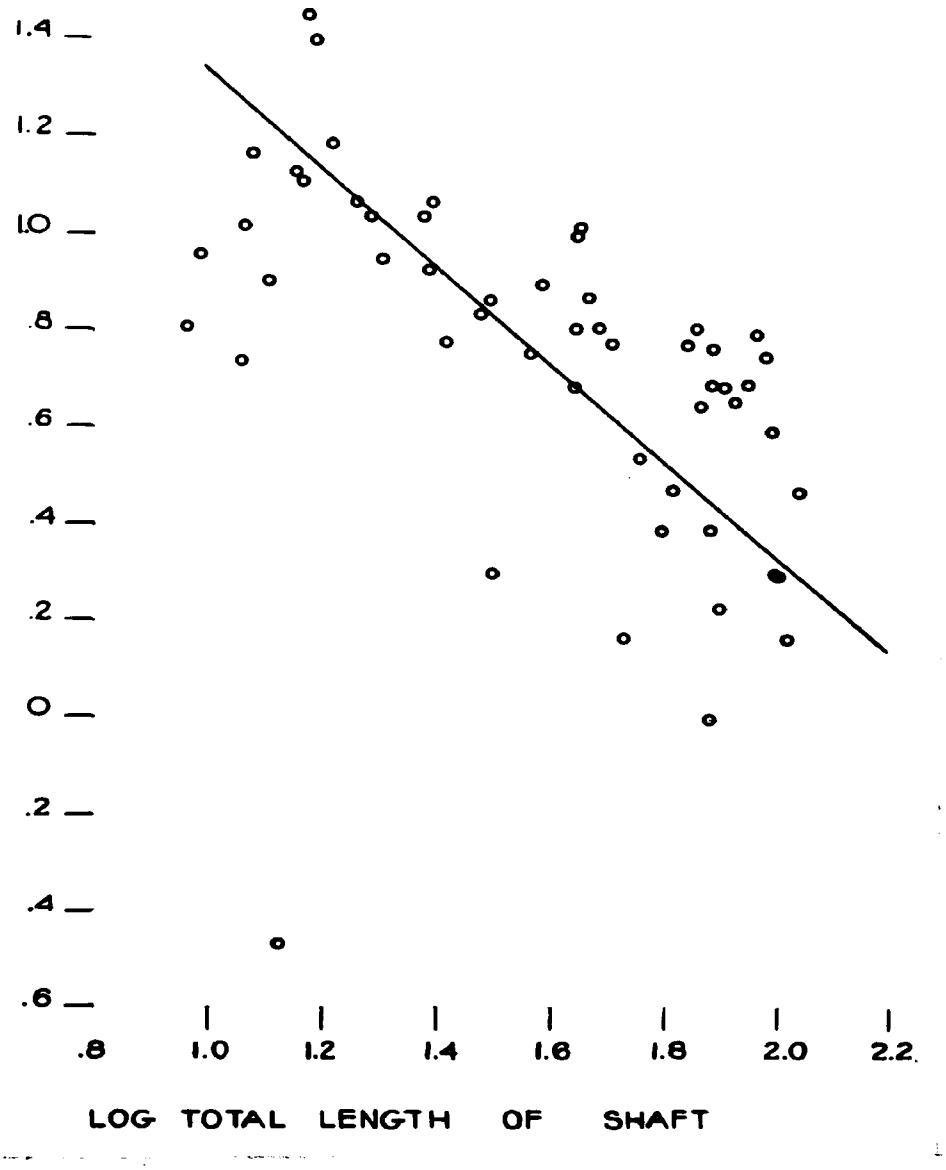


Fig. 22. The regression of log Obliquity upon log Total Length of Shaft.

Table 7

Inclination and Obliquity

Shaft	Inc.	Obl.	Shaft	Inc.	Obl.
8.4 mm	51.0°	9.0°	45.3	49.0	10.5
9.2	46.5	6.5	47.2	48.5	7.5
11.5	48.0	5.5	49.6	61.0	6.5
11.9	67.0	10.5	51.5	53.0	6.0
12.2	45.0	15.0	54.4	50.5	1.5
13.0	71.5	8.0	57.7	40.0	3.5
13.2	62.0	-3.0	63.3	55.0	2.5
14.4	43.0	13.5	65.9	54.5	3.0
14.9	36.5	28.0	68.5	67.0	6.0
15.1	47.0	13.0	72.9	51.0	6.5
15.5	47.0	14.0	74.4	65.0	4.5
16.6	41.0	15.5	76.2	59.5	1.0
18.3	38.0	12.0	77.1	52.0	5.0
19.7	42.0	11.0	77.2	56.5	2.5
20.4	51.5	9.0	78.1	50.5	5.5
23.9	52.0	11.0	80.0	56.0	17.0
25.0	58.5	12.0	81.8	59.0	5.0
25.0	53.0	8.5	84.6	55.0	4.5
26.5	48.0	6.0	88.7	50.5	5.0
30.1	65.0	7.0	91.5	45.5	6.5
31.3	51.0	7.5	96.7	58.0	6.0
31.8	51.5	2.0	99.5	55.0	4.0
37.8	53.0	6.0	100.9	45.0	2.0
39.1	51.5	8.0	102.9	57.0	2.0
43.9	61.0	5.0	105.3	53.0	1.5
44.3	60.0	6.5	110.6	48.5	3.0
44.8	58.0	10.0			

Table 8

Intersection Point of Load Line with Infracondylar Plane

Shaft	1	2	3	4	5	6	7
8.4 mm		x					
9.2			x				
11.5	x						
11.9			x				
12.2	x						
13.0				x			
13.2			x				
14.4				x			
14.9	x						
15.1	x						
15.5	x						
16.6	x						
18.3	x						
19.7	x						
20.4	x						
23.9			x				
25.0	x						
25.0			x				
26.5		x					
30.1	x						
31.3			x				
31.8							x
37.8				x			
39.1			x				
43.9					x		
44.3			x				
44.8			x				

1, lateral to lateral condyle
2, at point of contract of the lateral condyle
3, lateral to midway between points of contact of condyles
4, at point midway between points of contact of condyles
5, medial to midway between points of contact of condyles
6, at point of contact of medial condyle
7, medial to medial condyle

Shaft	1	2	3	4	5	6	7
45.3	x						
47.2			x				
49.6			x				
51.5				x			
54.4					x		
57.7					x		
63.3						x	
65.9					x		
68.5				x			
72.9			x				
74.4				x			
76.2						x	
77.1			x				
77.2			x				
78.1			x				
80.0			x				
81.8				x			
84.6					x		
88.7			x				
91.5			x				
96.7				x			
99.5			x				
100.9					x		
102.9					x		
105.3					x		
110.6					x		

line of the section and not upon a true mechanical axis common to all sections of the specific femur. Nevertheless, approximately the same thing is being measured at any one level in all four femurs and the torsion in a given section is higher or lower depending upon whether or not the femur in question has a greater or lesser degree of torsion at the proximal end.

The values for torsion along the length of the examined specimens were:

Femurs	A	B	C	D
Standard Torsion Value	1.0	8.0	30.0	-26.0
Station 1 torsion	0.0	7.0	28.5	-19.0
Station 2 torsion	0.0	5.5	22.0	-11.0
Station 3 torsion	0.0	0.0	14.0	- 6.0
Station 4 torsion	0.0	0.0	6.0	- 0.5
Station 5 torsion	0.0	0.0	0.0	0.0

The values just given make it evident that the torsion of the femur is not a phenomenum restricted to the one end in a very localized area as is the case in the humerus. As was pointed out by Krahl ('47, '48), torsion in the humerus occurs at the junction of the diaphysis and the proximal epiphysis. In the femur, on the basis of the work of Pitzen and above values, torsion is a total femoral characteristic, present throughout the shaft. In the final analysis, of course, the end of the femur with the greatest torsion is the opposite one from that which the investigator places at a zero level in taking the measurement. In other words, if the head and trochanter were placed parallel to the orientation surface at the time of measurement, the condylar plane, rather than the head-trochanter, would have torsion values of approximately 1.0, 8.0, 30.0, and 26.0. This important fact should be kept in mind in any discus-

sion of the extent of torsion and the forces causing it.

The causal factors in the phenomenum of femoral torsion and in the uniqueness of its progression in ontogeny have been the subject of considerable examination and discussion. That the problem is not a simple one is attested to by the fact the over the course of approximately half a century a series of theories have been offered several of which are mutually contradictory. In general these theories fall into three categories: those which are in opposition to the stand already taken in this paper, i. e., theories that credit only a mechanism inherent in the femur as causing torsion; theories that look to a functional relationship of the femur to another portion of the body or to an extra-fetal mechanism, and lastly, those theories pointing to muscular function as the cause of torsion. These categories, it must be admitted, are poorly defined as the result of certain combinations of theories.

Gruenwald ('19) contended that femoral torsion is the result of an inherent tendency of the femur to grow into a state of torque. In other words, this would be a process similar to that in which some plants grow in a spiral (Martins, 1857, Thompson, '42). Although Altmann ('24) stated that the reduction of the high torsion of the newborn to that of the adult is probably due to mechanical factors related to erect posture, he expressed the view that the increase in torsion in the fetal period is a process inherent to the femur. As proof of this he cited two cases of spina bifida (one sacral, the other lumbar) in which the torsion present was similar to that in normal specimens of like age. In his recent work on torsion in whole lower extremity,

Elftman ('45) expressed a more moderate view. He found that torsion of the tibia and of the femur both show a progressive increase with fetal age, the femur attaining higher values than the tibia (essentially the same results as Mikulicz, 1878). While taking cognizance of the theories concerning environmental factors and noting the possibility of such conditions, Elftman pointed out that such investigations as those of Fell ('28), Murray and Huxley ('25) and Murray ('26) have too well demonstrated the autonomy of long bone primary development to permit one to discount an inherent tendency toward torsion.

Although a proponent of the effects of extrinsic forces, Murray has been willing to concede the possibility of an inherent femoral tendency toward torsion. Thus, after citing the work of Appleton ('22 a, '25 b) and Wermal ('35) in which it was found that torsion could be produced by forcing the limbs into a state of torque, Murray stated that "Facts such as these can leave only a small doubt that normal torsions must be the result of muscular tractions and similar forces, but perhaps some possibility may remain of the existence of an undiscovered intrinsic tendency of the bones to grow with a torsion". ('36, p. 78).

Friedlander, who was apparently the first ('01) to investigate the causation of fetal torsion, seems to have regarded the rotation of the limb bud, and later the early limb, into the definite position as an intrinsic growth process of the limb <u>in toto</u>. He stated that the early course of torsion (apparently the reduction of negative torsion) is the consequence of the change in the orientation of femur and limb prior to the formation of a flexible connection between femur and pelvis, i. e., before the hip joint cavity opens. However, he attributed positive tor-

sion to the function of the adductors as medial rotators and gluteals as lateral rotators, each opposed to the other in a mechanical couple. He introduced an additional factor in torsion development by citing cases in which there was found to be a correlation between the presence of ectopic or overly large viscera and the retention of low torsion. From this he concluded that the visceral mass prevented the completion of limb rotation and flexion of the thigh into the normal fetal position, and, consequently, that torsion is a corollary of the attainment of this normal position.

Le Damany has probably had more influence than any other investigator upon thought concerning torsion and its causation. In the first of a series of publications on this topic ('04 a) he made observations upon torsion in the various lower forms and in man. In this he noted that in the lower animals the degree of torsion was matched by the angular orientation of the acetabular margin, but in man torsion progresses more rapidly than does the change in acetabular orientation. This results in a poor reciprocal relationship between the two articular surfaces and, when torsion is great, a dangerous one in terms of hip joint dislocation. In regard to the changes within the pelvis, Le Damany's observations agree with those of Thomson (1899). According to them, the pelvis as a whole develops in such a fashion that the acetabulum is directed at first almost perpendicular to the transverse and sagittal body planes; in the definitive form it is directed forward and down.

In the same year ('04 b) LeDamany published what is probably his most significant work. He found that in the lower animals (sheep, goats, dogs) the ratio of acetabular depth to width remained about the same

throughout the fetal and postnatal periods. In man, on the other hand, the ratio decreased from midterm to about the middle of the first postnatal year and increased thereafter. In the adult it exceeded that of the greatest fetal value. Representative ratios are: fourth and sixth prenatal months, .56 and .46; newborn, .41; four months and seven months, .39 and .50; one year and two years, .47 and .53. The adult series had an average index of .65. Le Damany presented a parallel table of acetabular indices and torsion values which shows the close correspondence between the two features, the relationship being, of course, inverse. He concluded that in the human fetus torsion is produced as a result of uterine pressure upon the knee which forces the thigh into extreme flexion. He believed that in this position the anterior superior spine of the ilium acts as a fulcrum, the force being at the knee and the resistance being offered by the hip joint. In this situation torsion would be produced and the articular surfaces separated. The acetabular depth would lessen in the absence of articular pressure.

Le Demany was able to demonstrate by experimentation that shallowing of the acetabulum and torsion can be produced in dogs and rabbits by the creating of an artificial fulcrum in their narrow pelves. It is interesting to speculate, however, as to the mechanism this author would have visualized to explain the total course of fetal torsion had he been aware of the fact that torsion exists prior to the fourth fetal month. That he was actually unaware of this is shown by his statements that the conditions producing torsion come into being at about the fourth fetal month and that prior to that torsion is zero.

Le Damany's explanations of the reduction of torsion due to the attainment of erect posture and a shift in body weight were published in 1905 and a summarizing paper followed in 1908. Similar studies of changes in acetabular proportions and orientation have been made by Dega ('33) and Kleinberg and Lieberman ('35).

The investigations of Friedlander and Le Damany have led to what might be termed two loosely defined schools of thought concerning the cause of torsion. Gruenwald ('12) attributed the progress of torsion to the opposed actions of the medial and lateral rotators of the thigh in a situation of extreme flexion. Pitzen and Lange ('21) and Pitzen ('23) followed almost word for word the concepts of Friedlander. Brandt, ('27) did much the same. Bleischmidt ('43), although explaining the cause of positive torsion in a similar manner, set forth an interesting possibility concerning the action of muscles in the pre-functional period. He suggested that the expansion of proliferating myogenic masses along the course of future functional muscles might have the effect of causing torsion. This force, if real, would be instrumental in reducing negative torsion and affecting limb rotation in the very early period. Badgley ('43) has presented a theoretical discussion of the role of the thigh muscles in femoral torsion and the relationship of early or congenital muscular paralysis to the congenital dislocation of the hip. De Cuveland ('50) has been the most recent advocate of muscular forces in torsion causation.

Nauck ('34) suggested forces similar to those postulated by Le Damany: the recurring action of the uterine wall upon the fetus and, in this respect more definitely than Le Damany, the migration of the acetabu-

lum as an altering force upon the femoral head in the production of torsion. In the same year, Böhm suggested acetabular migration as the major cause of torsion.

b - Inclination

Almost nothing concerning the prenatal state of this dimension was found in the literature. Friedlander ('01) noted that the angle of the head and neck to the femoral shaft is generally highest in the very early fetuses (i. e., the neck is more nearly in line with the shaft). Pitzen ('23) commented that in the 11 mm human femur inclination amounts to 130° and that there is apparently little change in this angle during the fetal period. It has been indicated by Strayer ('43) as well that the head and neck deviate from the shaft very early in development. It is indeed surprising that the angle of inclination has been ignored in almost all the studies of early torsion development, especially considering the fact that both angles are, superficially at least, measurements of the same anatomical complex in different planes. Compared with torsion, inclination in the adult femur again has been less well examined. Humphry (1889) stated an adult value of 124°, Pearson and Bell ('19), 126°, Ingalls ('24), 129.6°, and Pick et al. ('44), 126.40°. These figures clearly indicate a very slight increase in the angle through ontogeny. The cause of the increase in inclination is generally stated to be the traction of the developing and functioning muscles of the thigh as well as an inherent femoral factor.

Perhaps the major reason for the general lack of data on fetal inclination lies in the difficulties related to its accurate determination,

particularly in the smaller fetuses. In the present study, no procedure could be devised that would allow the femurs to be so manipulated as to permit photographing the head-neck region perpendicular to the plane of inclination without jeopardizing the practicability of the overall technique. As a result, the degree of torsion present in a given specimen will affect the amount of inclination seen in a frontal photograph. What is presented here, then, is apparent inclination and, other factors being equal, the head-neck axis will appear more in line with the shaft in a specimen with high torsion. The present inclination values can be considered, therefore, as subject to two variables: the probable high individual variation in actual inclination and the artifact introduced by equal or greater variation in torsion. This more likely accounts for the extremely low correlation coefficient of inclination with total length of shaft (.17).

Although presented with definite reservations, the inclination values in this series are not without some value (table 8). As indicated by the coefficient of growth (.03), inclination exhibits only a slight increase during the period covered by the range of this series. In spite of the great scatter in angle values, group averages show a striking constancy. Below are presented means and standard deviations of five consecutive groups of femurs:

1.	10	femurs	Mean:	51.7	S. D.:	10.9
2.	10	"	" :	49.6	" :	7.9
3.	10	"	" :	54.5	" :	4.7
4.	10	"	" :	54.7	" :	7.2
5.	13	"	" :	53.0	" :	14.1

In this study, inclination has been measured as an angle opening superior to the head-neck axis rather than inferomedially as is traditional in

osteometric technique (Martin, '28, for example). This was done simply because it takes cognizance of the direction of the change and because it demonstrates the alteration from the primordial condition in which the head-neck and shaft axes are most nearly a single line (blastemal stage). If the above figures are subtracted from 180°, they become: 128.3, 130.4, 125.5, 125.3, and 127.0. These are in keeping with the observations of Friedlander and Pitzen, and elucidate the fact that inclination attains a mean value near that of the adult early in the fetal period, and that there is high individual variation about the mean. Taking into account the effect of increasing torsion, it appears that the actual inclination probably is still nearer to the adult state.

c - Obliquity

Nothing was found in the literature concerning the measurement of this dimension or the specific changes in the angle during the period of fetal development. Pitzen ('23) observed that the angle of the infracondylar plane to the axis of the femur is greater throughout most of the prenatal period than it is in the postnatal. The figures of the reconstructions of Bardeen ('05) and Altmann ('24) also indicate this. Neither of these authors discuss the point. Ingalls ('27) stated that at term obliquity is less than in the adult femur. For the adult, Pearson and Bell ('19) gave figures of, for right, 8.69°, for left, 11.59°. Grossberg ('24) had higher values for right (10.32°), but lower for left (8.56°), while Ingalls gave right and left figures of 8.63°and 8.70°.

decrease (k value, 1.00). The maximum was 28.0° (at 14.9 mm shaft), the minimum, 1.0 (at 76.2 mm). One specimen had a negative angle (3.0°). The smallest specimen had an angle of 9.0°, and the largest, 3.0°. The correlation coefficient of .51 indicates very high individual variation about the trend. It appears that the lateral condyle increases in mass more rapidly than the medial (Ingalls, '27). If that is the case, such a differential process could lower the infracondylar plane on the lateral side and so decrease the angle. For that reason I did not at first consider that obliquity belonged in the category of the environmentally influenced characteristics. It was the fact that the correlation coefficient of this dimension with total length of shaft is less than those of torsion and angular displacement of the head that finally lead to the present classification of obliquity. If an inherently greater rate of growth of the cartilage of the condyle is responsible for the decrease in the angle, then this factor must be modified by others of approximately the same range of magnitude as those operating in the case of torsion, etc.

Obliquity is considered (e. g., Martin, '28) as the expression of the angular relationship between the shafts of the femur and tibia in erect posture. It is immediately obvious that in fetal position the infracondylar plane represents neither a typical nor an average relationship of these two bones. Our interest here then is in the development of what is essentially an adult characteristic. As such, obliquity must be dealt with in relation to the load or weight line, that is a line from the center of the head to the infracondylar plane, perpendicular to that plane, and representing the vector of the force transmitted

from pelvis to tibia. The point of intersection of this line with the infracondylar plane has been generally described, by Fick ('04), Pearson and Bell ('19), Ingalls ('27), Martin ('28) and Walmsley ('33), as being at or just medial to the point of contact of the lateral condyle with the tibia. The location of this point can be considered as dependent upon three factors: the degree of obliquity, of inclination, and of torsion. For any angle of obliquity, the point of intersection will be more lateral with high torsion and low (present method) inclination. In addition, with the same degree of obliquity, the point will be more lateral in a short than in a long femur (Walmsley, '33). The manner in which these factors combine is shown on table 8. The general trend, with marked individual variation, is from a position lateral to the lateral condyle to one about at the contact point of the medial condyle. As in obliquity, the late fetal and term value of which is less than the adult, there must be a postnatal reversal in the direction of migration of the load-line; The point of intersection must move in the opposite direction before the definite state is attained.

d - Some Proposals for the Solution of the Problem of Environmental Influence in Femoral Development.

As has been shown, there is in the literature a very considerable amount of speculation about, and partial explanation of, the possible roles of certain intrinsic and extrinsic factors in the causation of torsion, inclination and obliquity. In general, such treatment as has been given the problem has been restricted to one developing characteristic (e. g., torsion) and a single causal factor (e. g., function of medial and lateral rotators). Thus far there has been little regard given to

the development of a well documented concept of the total field of either intrinsic or extrinsic forces, or both, which may be operable upon a growing long bone. As an illustration of this point, a current theory of torsion causation may well be inadequate in explaining the developmental course of obliquity. Indeed, little is known concerning what, specifically, the intrinsic and extrinsic factors may be. What is needed is an understanding of what factor or group of factors may be responsible for the simultaneous causation of all the angular changes. It is not the present purpose to describe the total force field in which the femur develops; tempting though the undertaking may be, the limitations of this study are such as to preclude the possibility. Rather, it is my purpose now to set forth a general, but by no means definitive, program for such research as might clarify the situation.

1. It is suggested that a comprehensive study be made of the specific differences between long bones grown in vitro and those grown in the normal limb. Our knowledge on this point, in spite of the work of Fell, Murray and others, is quite fragmentary, being based upon a few specimens and not expressable quantitatively. This study could be carried out on a parallel series for as long a period as the culturing of individual long bones could be maintained (hardly beyond the periosteal collar stage). Measurements could be taken that would demonstrate the growth of the various dimensions. Significant difference tests could then be made to determine which dimensions are affected by the differences in the environment and to ascertain the degree of response in each case. This would be in addition to the application of the usual techniques for demonstrating growth rates and proportion changes.

2. As a reasonable sequence to the approach outlined above a quantitative study could be made of the total fetal development of the femur in a denervated limb. This could be accomplished by the removal of the posterior spinal cord in chick embryos or in mammals in utero. This procedure could be employed in two ways:

a. The operation could be performed at a constant minimal age and the specimens sacrificed at various ages up to term.

b. The operation could be performed at different age levels and the specimens be either allowed to complete development or sacrificed at a constant postoperative date.

These two series would allow one to determine the effects on femoral configuration of, in the one case, a total history of non-function of musculature up to each of several age levels, and in the other case, the effects of non-function of musculature instigated at different age levels and prolonged for a constant or variable period. The data accumulated in this study could be treated in the manner proposed in 1., above.

3. In the human embryo and fetus, rather than in the experimental animal, two lines of investigation seem profitable. That these are closely related is obvious; they could, however, be carried out as separate problems.

a. An investigation of the possibility of developmental changes in the direction of traction and the effectiveness of the various pelvic and thigh muscles and muscle groups in acting upon the femur and altering its configuration would certainly be profitable. The present explanations of torsion, for example, depend largely upon the work of Fick ('04) whose material was adult and whose conclusions as to the mechanics of the pelvis

and thigh are not necessarily applicable to the same areas in the fetus. In view of the general differences between the adult and fetus in pelvic and thigh proportions, such a transposition of data from one age group to another may well be invalid. The investigation in the prenatal could begin with an adaptation of Fick's techniques to the fetal material.

b. To ascertain whether or not different muscles may not be dominant over others in functional level at different fetal stages, it might be worthwhile to investigate the development of the physiologic cross-section of the various muscles attaching to the femur. This approach might be most profitably correlated with a quantitative study of the apparent functional ability of the fetus as shown in such motion pictures as those of Hooker ('50).

In summary, it may be said that the techniques which have been applied to the problem thus far are essentially adequate to derive the correct solution. What is needed is enough data covering the whole of the developmental period in question to allow quantitative expression of the manner in which the total force field acts to effect simultaneously an alteration in several dimensions.

SUMMARY

1. This study was instigated by the general lack of information of a quantitative type concerning the development of the human long bones in the fetal period. The femur has been the subject of the investigation because of its traditional place in anthropologic and orthopedic works. The intention has been to present a quantitative and qualitative picture of the growth of the femur and to relate certain growth processes, as are demonstrated by changes in dimensions and proportions, to those underlying histogenetic processes already in the literature.

2. The material upon which this study is based is 53 femurs, mixed left and right sides, 8.4 to 110.6 mm in total shaft length, from fetuses and neonatals 37 to 500 mm in crown-rump length (ninth fetal week to third postnatal). Specimens were stripped to the periosteum and cartilage, alizarin stained in KOH and cleared in glycerin. Major dimensions were measured from projected line drawings taken from photographs (four views) of these specimens. In addition to linear dimensions, the angles of torsion, displacement of the head, inclination, and obliquity were determined.

3. Data are presented in tabular form, and growth rates are expressed by Huxley's coefficient of growth as determined from log-log graphs. The indication of variation about the relative growth trend is shown by the correlation coefficient of each dimension with total length of shaft. In addition, line drawings of a graded series of femurs are given, to scale, and to constant length.

4. The femur is described as consisting of three growing units:

the proximal and distal cartilages and the ossified shaft. Each cartilage is further divided, on the basis of its growth processes, into intracapsular (bare), extracapsular (perichondrium covered) and juxtaosseous (adjacent to the advancing ossification and concerned with the process of osseous replacement). The first is considered as growing by interstition, the second by interstition and apposition, the third by apposition alone.

5. The absolute increments and percentage increases along the various dimensions and the proportional changes between the smallest and largest specimens are represented in tabular form. Relative to total length of shaft, transverse dimensions increase by from .01 (minimum diameter of shaft) to .33 (length of ossified shaft). Relative to length of ossified shaft, the width of the end of that shaft increases .10. In short, the femur becomes more robust, mainly as a result of an increasing flare of the shaft away from the middle region and the rapid growth of the cartilages. The same picture is given by the listed coefficients of growth for the total series.

6. It is shown, by relating these changes to known histologic processes, that the increasing flare of the femur is due to the relationship of the growth processes of the extracapsular and juxtaosseous cartilage to one another and to the ossifying shaft. As ossification progresses along the shaft, replacing cartilage but not increasing the overall length of the femur, the cartilage just in advance of it (juxtaosseous) ceases to grow and prepares the way for ossification. The rest of the cartilage (extra- and intracapsular) continues to increase in width rapidly. As a result, the end of the ossified shaft acquires an ever-

larger diameter away from its mid-point. The rapidity of transverse cartilage growth relative to the rate of shaft ossification determines the extent of the flaring.

7. It is pointed out that there are indications of a shift in the direction of the major femoral growth in the circumnatal perior or shortly after, and that the general trend in the postnatal period is for longitudinal growth to exceed transverse. Comparison of the dimensions of a femur of term and of four years of age, relative to total length of shaft, shows that only the longitudinal dimensions are greater in the four year old than at term; all the transverse dimensions are less. This alteration is thought to be due to the fact that the cartilages become reduced to epiphyseal discs between the ossified shaft and the secondary ossification of the epiphysis. The cartilages are thereafter related almost entirely to longitudinal growth (preparation for ossification) and increase in diameter only by apposition. It is suggested that even apposition may be lessened.

8. Features of the development of the ossified shaft are discussed under a separate heading. It is shown that the angular deviation of the proximal end of the shaft into trochanteric and neck planes begins in the latter third of the fetal period and progresses rapidly. The distal end of the shaft is shown to become concave a considerable period before the onset of ossification of the secondary center. These changes are discussed in relation to their possible effects upon shaft elongation.

9. Some consideration is given to the literature dealing with inequalities in the amount of growth occurring at either end of the ossified shaft. On the basis of a small series of femurs for which roent-

genographs were available, it is concluded that there is a very slightly greater contribution from the distal than the proximal end of the shaft, more in the late fetal period than earlier.

10. The angular dimensions, torsion, angular displacement of the head, inclination and obliquity are discussed under the classification of "environmentally influenced" characteristics. This classification is based upon the marked difference between the correlation coefficients (with total length of shaft) of these as a group, and most of the other dimensions.

11. The major literature concerned with fetal and adult torsion is discussed and summarized. The present findings are that torsion increases in the fetal period with considerable individual variation about the trend and that there is some indication of a greater rate of increase in the second than in the first half of the period. The lowest value in this series is -26.0° (in a 14.4 mm femur), the highest, 64.0° (in a 94.0 mm femur); in the smallest femur, 7.5° and in the largest, 52.0°. A study of sections of the femur indicates that torsion is distributed along the length of the femur and is not restricted to the head-neck region.

12. The angular displacement of the head is then treated as distinct from torsion. It is seen that this angle increases in the same sense as torsion, that the two angles are nearer to the same degree in the late fetal period, and that there is often marked individual variation in the relationship of the two.

13. Inclination is not an isolated dimension as measured in frontal line drawings, but is increased (apparent inclination) by high torsion.

On the basis of direction of development, inclination is measured as an increasing angle from the vertical, rather than as is traditionally done. In this series, inclination is almost at the adult level throughout, particularly in the larger specimens.

14. Obliquity, the angle of the infracondylar plane, decreases throughout this series and falls below the adult degree in the largest specimens. The load-line of the femur is described as also migrating across the infracondylar plane and lying more medial in the late fetus than it does in the adult.

15. The author does not attempt to present, on the basis of the available data, an explanation of the causation of any of the angular dimensions. Instead, there is suggested a tentative program of attack upon the problem of discovering and expressing the nature of the overall long bone-environment relationship as a substitute to the presentation of theories which attempt to explain only one functional relationship and one characteristic change.

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