

Morphometric Study of the Fetal Development of the Human Hip Joint: Significance for Congenital Hip Disease

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Hip joints (280) from 140 human fetuses, obtained from abortions and deaths in the perinatal period, were studied. The fetuses ranged from 8.7 to 40 cm in crown-rump length and are believed to be between 12 and 42 weeks in age. The joints were dissected, morphology inspected, and measurements taken of the depth and diameter of the acetabulum, the diameter of the femoral head, length and width of the ligament of the head, the neck-shaft, and torsion angles of the proximal femur. Regression models were fitted to determine which would best predict the growth pattern.

Multivariate analysis of variance showed no significant differences between males and females or between the right and left sides. Acetabular depth was shown to be the slowest-growing hip variable, increasing less than fourfold in the period studied. Acetabular indices less than 50 percent indicate a shallow socket at term. Femoral head and acetabular diameter demonstrated a strong relationship ($r = 0.860$) and in many joints the femoral head diameter exceeded that of the acetabulum. Considerable variability was demonstrated in both femoral angles. The femoral angles showed only low correlation with the other hip variables.

These observations indicate that soft tissue structures about the joint must play an important role in neonatal joint stability. The explanation of greater female and left side involvement in congenital hip disease must lie in factors other than growth changes of hip dimensions. Neither angle appears to be a useful indicator of normal joint development.

Although the hip joint is one of the most intensively studied joints in man, most of the work on its development describes isolated characteristics for small sample sizes [1-13]. Definition of abnormal development, as seen in congenital hip disease (CHD), is dependent on a knowledge of the limits of normal growth and development of the hip joint. Frequently observed characteristics of CHD are abnormal femoral angles, nonspherical head of femur and socket, a shallow socket and a lengthened ligament of the head of the femur. Le Damany [14], Felts [6], Stanisavljevic [15], Ralis and McKibbin [11], Watanabe [16], and Skirving and Scadden [17] reported measurements of dimensions of the hip joint, but none provided quantitative data for all of the hip dimensions, nor did they use adequate samples at regular intervals of age throughout the fetal period.

Le Damany [14] and Ralis and McKibbin [11] showed that acetabular indices decrease toward term but it is still not clearly established whether depth of the acetabulum maintains a constant growth rate or whether, in relation to socket diameter, depth progressively decreases so that the socket is shallower at birth. There are no reports on the variability of depth values at different ages. Individual case values [14] or mean values [16] may be misleading.

Sex differences in the morphology of the postnatal acetabulum have been published [18-24]. No study on hip dimensions of human fetuses has separated data by sex and/or side. However, females and the left side are more frequently involved in reported cases of CHD [25].

This paper reports a study of the growth of the human hip joint in fetuses believed to be between 12 and 42 gestational weeks. Measurements are reported for acetabular depth, acetabular diameter, femoral head diameter, width and length of the ligament of the head of the femur (LHF), the neck-shaft, and torsion angles of the proximal femur. The aims of the study were to determine if a significant difference existed in the growth of hip joint dimensions between males and females, between the right and left sides, if leg crossing of the fetuses was correlated with any of the hip dimensions, to determine the strength of association between hip dimensions both within-side and between-sides, and lastly to determine the model that would best predict the growth of fetal hip joint dimensions.

MATERIALS

Sample

One hundred and forty fetuses, of which 66 were male and 74 were female, were obtained from Pathology and Anatomy Departments in Canada and the United States (Table 1). Specimens were obtained after elective abortion (62.2 percent), stillbirth (23.7 percent), and death during the perinatal period (14.1 percent). Criteria for inclusion in the study of normal development were: absence of malformations, minimal maceration [26], duration of postnatal viability not greater than 24 hours, normal hip joint morphology as determined by gross examination and a magnification of ten, and an estimated gestational age between 12 and 42 weeks. Because the embryonic development has been well described and cavitation is reported present in the early fetal period [27], a minimum crown-rump length (CRL) of 8.7 cm was arbitrarily selected. Several investigators cite CRL values of about 8 cm for an estimated fertilization age of 12 weeks [26,28-30]. The sample was grouped for analysis into two-week age intervals, from 12 to 42 weeks (Table 1) to accommodate eight fetuses, in the difficult-to-obtain third trimester period, that had only an estimated gestational age reported.

Because 90 percent of fetuses were received prefixed in neutral 10 percent formalin, mobility of the hip was not used as a criterion for normality of the joint, although the range of motion was assessed before and after cutting the joint capsule. A hip joint was classified as normal if the morphology conformed to the descriptions given in standard anatomical texts of a joint with a spherical femoral head and socket, a labrum of even thickness with the free margin appearing as a sharp edge, absence of the tissue interposed between the femoral head and the acetabular socket, and no displacement of the femoral head within the socket as determined by dissection and inspection [31,32].

Prior to any statistical analysis, fetuses were initially separated into two groups according to their hip morphology. Ninety-four fetuses presented the expected mor-

TABLE 1*
Gender of Fetuses and Crown-Rump Length (CRL) Summary Statistics in Two-Week Groups

Two-week groups ^b	Number			Crown-Rump Length (cm)		
	Male	Female	Total	Mean	Min.	Max.
12-14	8	8	16	10.5	8.7	11.9
14-16	5	13	18	12.9	12.0	13.9
16-18	10	8	18	14.9	14.1	15.9
18-20	10	9	19	17.7	16.0	18.7
20-22	4	11	15	19.9	19.0	20.8
22-24	6	6	12	21.7	21.0	22.5
24-26	6	3	9	23.8	23.0	24.7
26-28	5	3	8	25.1	25.0	25.5
28-30	1	0	1		27.5	27.5
30-32	2	5	7	28.3	28.0	28.9
32-34	1	1	2	30.0	30.0	30.0
34-36	0	3	3	32.5	32.0	33.0
36-38	0	1	1		34.0	34.0
38-40	2	0	2	36.0	36.0	36.0
40-42	2	3	5	37.8	37.5	38.0
42	4	0	4	39.3	38.5	40.0
	66	74	140			

*Adapted with permission of Yale J Biol Med 53, 1980.

^bEstimated gestational age based on CRL [26,28-30,70].

phology, while 46 fetuses exhibited one or more minor variations. Only 65 joints from these 46 fetuses showed variation from the expected morphology [33] but these joints showed no statistically significant differences from "normal joints" ($p \geq .1$). Therefore, from 140 fetuses, both hip joints (280) were studied for growth as one group.

Estimation of Age

Crown-rump lengths were measured with Vernier anthropometric calipers and the spine was straightened but not extended [26]. Birth weight and/or estimated gestational age was used to place the eight fetuses, for whom a crown-rump measurement was not obtained, in a specific age group. Scammon and Calkin's formula [30] was used to convert the supplied crown-heel lengths to CR lengths in two fetuses where only the hip joints were received. Thirteen fetuses when aged on CRL were placed in a younger age group than when aged on last menstrual period. Correlation between age and CRL ($r^2 = 0.98$, $p < .0001$) was highly significant because one variable was estimated from the other. (The change in age relative to change in CRL can be obtained from the equation: $\text{age} = 0.67252 + 1.01033 \times \text{CRL}$; SE est.¹ = 0.91461).

The CR measurement was selected as the standard for estimating the gestational age of specimens because it remains widely used and is, therefore, more frequently recorded. Use of CRL permits comparison of this study with previous reports of hip joint development. It is recognized, however, that estimated age based on CRL is a rough approximation [34]. Age estimates for fetuses less than 17 weeks are recog-

¹Standard error of the estimate.

nized as being in error by at least one week, and at term the error is up to four weeks [35]. Although, for this growth analysis, fetuses have been grouped into two-week intervals, summary statistics presented in Table 1 permit conversion to mean CR measurements for each age interval.

Birth Weight

Birth weights were present for 87 of the 140 fetuses (62 percent). The possibility existed that fetuses that lacked birth weight data were a different group from fetuses with known weights. The former group was derived from anatomy department collections. Using the BMDP3F program [36], the best fit log-linear model was the mutual independence or complete independent model. The likelihood ratio chi-square for goodness of fit was $G^2 = 10.85$, $p = 0.1453$. Hence no two factor interactions were needed to explain the age by sex by birth weight frequency table. The interaction for age (in three groups) by birth weight (known, unknown) was $G^2 = 4.42$, $p = 0.1097$, and the interaction for sex by birth weight was $G^2 = 0.12$, $p = 0.7290$. This indicates that the presence or absence of birth weight is unrelated to the age or the sex of the fetus.

METHODS

Fixation

Approximately 90 percent of fetuses were received prefixed in neutral 10 percent formaldehyde and were transferred to neutral formalin buffered to pH 7.0 [37]. Because so many specimens were received already fixed in formaldehyde, it was necessary, therefore, to accept the formalin state as a basis for the group as a whole. Measurements were taken after at least two weeks in fixative as there is a small increase in crown-rump length immediately after simple preservation in formalin [26,38]. Schultz [38] noted that fixative changes affect external circumferences more than total length, and soft tissue more than hard tissue dimensions, and that these changes are most rapid in the initial period of fixation. After a period of time the specimen tends to return to its original size and weight [26,38,30]. Hammond and Charnley [39] and Blowers et al. [40] investigated whether or not the effects of formalin preservation may alter the shape of the femoral head cartilage and concluded that no significant alteration occurred. Differences in the period of time in formaldehyde may contribute to variability demonstrated in hip dimensions measured. To improve fixation in larger fetuses, the hip joints were immediately dissected down to the level of the capsule.

Observations

The presence or absence of limb crossing and the level of crossing (toes, foot, leg) was noted in 118 intact fetuses.

Measurements

All measurements were repeated three times and the means of these measurements were recorded. Measurements taken with the dissecting microscope had high reproducibility (range in sets of three measurements equalled 0.4 mm). Femoral angle measurements were less precise and reproducible, due to difficulty in locating the neck axis on the underdeveloped neck of femur. The maximum difference be-

tween all angle measurements was 7° . Mean deviations for torsion and the neck-shaft angle were 3.5° and 2.3° , respectively.

Acetabular diameter, femoral head diameter, ligament of the head of femur (LHF): A stereoscope, with a ten-power wide-field measuring eyepiece and graticule (120 divisions, 0.1 mm apart), both calibrated with a stage micrometer, was used to measure the maximum transverse diameter of the acetabulum and of the femoral head, and the maximum free length and width of the LHF. In some acetabula the oblique and vertical diameters of the acetabulum were also measured (Fig. 1). LHF measurements were taken immediately after detachment of the ligament from the acetabular fossa to reduce shrinkage effects; the moist state of the ligament, present when the capsule was opened in all joints, was maintained during measurement [41].

Acetabular depth: Depth was measured directly using a pointer attached to the stereoscope (Fig. 2). After the socket was levelled, the pointer was aligned with the acetabular rim and then the lowest point of the cartilage of the socket. These measurements were read off a vernier side scale mounted to the mechanical stage of the stereoscope. Depth equalled the difference between the first and second measurement.

Femoral torsion angle: Methods described for measurement of this angle in the adult femur [42,43] proved to be unreliable for the fetal femur. Each femur was positioned so that it rested on the posterior surfaces of the condyles and greater trochanter. A transparent circular protractor was mounted with the zero-to- 180° line coincident with the surface on which the femur rested. A drafting triangle was aligned so that the shorter edge was coincident with the transverse axis of the femoral neck; then the opposite orthogonal edge, parallel with the long axis of the femoral neck, was used to provide direct reading on the protractor. The angle between the long axis of the neck and the surface on which the femur rested was recorded. When a femur did not naturally rest on the greater trochanter, celluloid blocks were placed under each end of the femur and the circular protractor, to ensure all femora were measured in an identical manner (Fig. 3). Because the femoral head does not always sit symmetrically on the neck, but may be tilted anteriorly or posteriorly, care is required to align the drafting triangle with the long axis of the neck and not that of the head. Therefore, India ink dots were made to mark the junction of the head and the very short fetal femoral neck to ensure correct alignment. When a negative angle was present (retroversion), the drafting triangle was in-

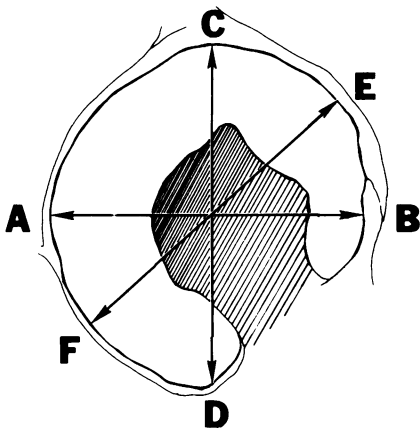


FIG. 1. Acetabular diameter measurements. The acetabulum was levelled and the maximum transverse diameter (A-B) was measured on all specimens. Where discrepancy in diameters was obvious, measurements also were made of the maximum vertical (C-D) and oblique (E-F) diameters.



FIG. 2. Acetabular depth measurement. The rim of the acetabulum was levelled by ensuring the pointer made contact on both sides. The adjustable pointer, attached to the microscope head, was contacted first with the rim of the socket (*shown*) then with the lowest level of the acetabular cartilage. Both positions were read off a vernier side scale mounted to the mechanical stage of the microscope. The difference between the rim and the socket floor readings was the depth recorded.

verted. The angle was not measured in 7 fetuses (13 femora, one right femur missing) because only the proximal portion of femora were received, and no reliability could be placed on positioning the shaft in the absence of the condyles.

Neck-shaft angle: Femora were supported in the mid-shaft with both extremities free. A protractor was placed over the proximal end of the femur, the vertical axis was aligned with the long axis of the femur, and then the angle formed between the neck and shaft was measured (Fig. 4).

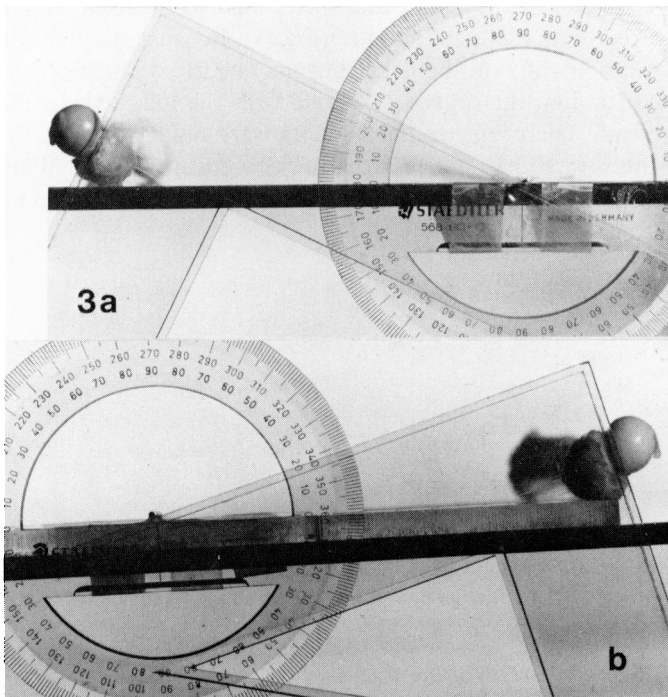


FIG. 3. Torsion measurement. Femora were positioned so that the proximal point of contact was the greater trochanter (**a**). When a femur naturally rested on the lesser trochanter, perspex blocks were placed under both femoral extremities and the circular protractor (**b**). The drafting triangle was aligned with the shorter edge coincident to the transverse axis of the femoral neck. The opposite orthogonal edge, parallel with the long axis of the femoral neck, was used to provide a direct reading on the protractor.

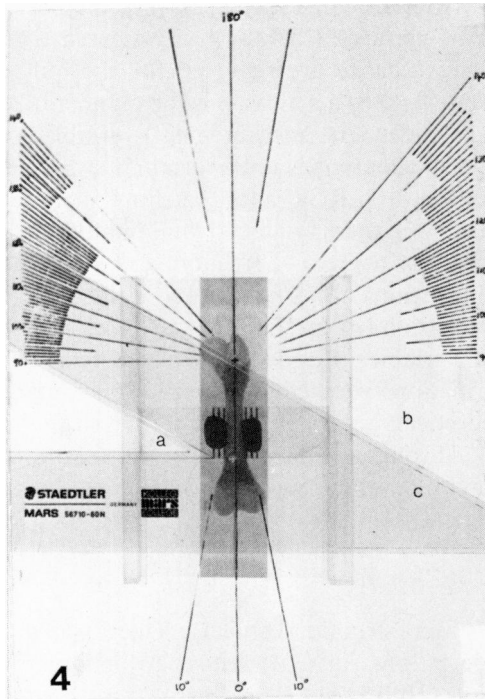


FIG. 4. Neck-shaft angle measurement. Femora were positioned with perspex blocks (a) to ensure both extremities were free. A protractor (b) was placed on the frame and the long axis, 0°-180°, aligned with the long axis of the femoral shaft. A drafting triangle (c) was superimposed and aligned with the long axis of the femoral neck.

Indices

An acetabular index (depth \times 100/acetabular diameter), expressed as a percentage, was calculated to provide a measure of socket shallowness. In a hemispherical acetabulum, the ratio is greater than or equal to 50 percent, but where diameter exceeds depth, the index falls below 50 percent.

A diameter index (femoral head diameter \times 100/acetabular diameter), expressed as a percentage, was calculated to provide a measure of the extent that the two diameters were similar. When the diameters are equal, the index is 100 percent, but if the femoral head exceeds the acetabular diameter, the index will exceed 100 percent.

Analysis

The statistical analysis was done on a CDC 6400 computer at McMaster University. The SPSS (Statistical Package of Social Sciences) system of computer programs was used [44,45] as well as the BMDP3F program [36]. Where frequencies are given, the percentage follows in parentheses, and where means are given, the standard deviation (SD) follows in parentheses; standard error (SE) is given for the estimate (SE est.) and for the slope (SE). Range is used in its statistical sense (the difference between minimum and maximum values observed) and interval is used when minimum and maximum values observed are presented. Although an actual probability is given, the level of significance used (α) is five percent.

The method of Draper and Smith [46] was used in analyzing the mean square lack of fit which assesses adequacy of regression models. To express the relative amount of variation explained by the model, the raw coefficient of determination (R^2) and modified coefficient of determination corrected for the mean (Q_m^2) are reported since this latter statistic is more appropriate in assessment of explainable variation [47].

Since the seven measurements were obtained from the same specimen, they may be correlated. Therefore, multivariate analysis of variance (MANOVA) was used to analyze variables simultaneously. Tests of significance are reported for the null hypothesis: $H_0: \mathbf{B} = \mathbf{O}$, where \mathbf{B} and \mathbf{O} are $(p - 1) \times q$ matrices, p is the number of independent variables, and q is the number of dependent (measurement) variables. When $q = 1$, this is a univariate analysis and the analysis is multivariate if $q > 1$. The MANOVA test statistic, large root criterion (LRC), and Hotelling's trace criterion (HTC), are reported with parameters s , m , and n , where s (total number of eigen values) = $\text{Min}(n_h, q)$ where n_h = hypothesis degrees of freedom and q is the number of response variables; and m , n , are functions of n_h , n_e where n_e is the error degrees of freedom [45]. Product moment correlation (r) coefficients were calculated and chi-square tests were used for categorical variables. Residual analyses were also used to test regression models, and transformations were employed to correct any assumptions that were violated. The theoretical bases of statistical programs employed are given in SPSS manuals [44,45]. Throughout the paper, age in weeks is given but the equivalent crown-rump length can be obtained from Table 1.

RESULTS

Sex and Side

Of the 140 fetuses, 66 were male, and 74 were female (Table 1). There was a general trend for the means and standard deviations for male fetuses to be larger than that for female fetuses, regardless of side. Univariate F tests for sex, without controlling age, showed that all variables had significant F values ($p < 0.001$) except for the neck-shaft angle. All the variables measured, as expected, increased in value with age except the neck-shaft angle. Apparent differences between males and females were not due to sex or side (Table 2). In the multivariate analysis of effects, none of the F values was significant ($p \geq 0.1$). Also, none of the variables was statistically significant for the interaction of sex and side, and there were no significant differences due to side. However, in univariate tests for the effect of sex, controlling for age, the F value for torsion was significant ($p < 0.01$).

Because the more sensitive multivariate tests failed to provide any evidence of significant differences between the means of the sexes or sides, the sexes were pooled for the growth analysis.

Intra-Side and Between-Side Relationships

A strong relationship was present between the diameters of the acetabulum and

TABLE 2
Multivariate and Covariance* for Sex and Side
Using Age as a Covariate

Effect	HTC ^b	LRC ^c	F	$P (\geq F)$
Sex by side	0.1594	.01569	.61	.7455
Side	0.0119	.01176	.46	.8649
Sex	0.3540	.03421	1.36	.2220

*Parameters: $s = 1$, $m = 2\frac{1}{2}$, $n = 133\frac{1}{2}$ or $F(7,269)$ [71]
 S = total number of eigen values, m = function of hypothesis and error degrees of freedom

^bHTC, Hotelling's trace criterion

^cLRC, largest root criterion

TABLE 3
Coefficients of Determination between Diameters
and Depth by Side^a

Variable	R ²
R depth, R acediameter	.894
L depth, L acediameter	.884
R acediameter, R FH diameter	.982
L acediameter, L FH diameter	.986
R depth, R FH diameter	.889
L depth, L FH diameter	.880

^aR, right; L, left; acediameter, acetabular diameter; FH, femoral head; $n = 140$

the femoral head (Table 3). Raw coefficients of determination between the right and left sides for each of the measurements (Table 4), with the exception of the neck-shaft angle, were numerically high for this kind of data ($p < 0.001$). The analysis was, therefore, conducted on measurements of 140 fetuses.

The correlation coefficients between sides (Table 5) for acetabular depth, diameter, and femoral head diameter remained highly significant after adjustment for age. Correlation coefficients were lower than the former variables for the ligament length, width, and for torsion. The neck-shaft angle correlation coefficients were not significant after adjustment for age. These results indicate a strong effect by age alone on between-side similarity in the femoral angles. After adjustment for age, the highest correlation was that between acetabular and femoral head diameter ($r = 0.860$).

Effect of Age

Age group means, plus and minus one SD, for the sexes combined, by side (right then left, for each age group) for each variable are shown in Figs. 5-9.² These data for LHF variables have been reported separately [41]. When cases were plotted by CRL, a steady continuum of cases was seen [48].

Except for the neck-shaft angle (Fig. 8) the means for all variables increase steadily with age. The strongest linear trend in the variables mentioned was seen between 12 and 18 to 20 weeks. The increase in observed means from 12 weeks to term was greatest for LHF length which shows a fivefold increase, and was more than fourfold for LHF width, acetabular diameter, and femoral head diameter. Acetabular

²Tables presenting the means and SD by sex, side, and age group, for each variable, with the frequency of observations, may be obtained from J.M.W.

TABLE 4
Coefficients of Determination for Variables between Sides^{a,b}

Variable	R ²	n
R depth, L depth	.936*	140
R acediameter, L acediameter	.988*	140
R FH diameter, L FH diameter	.995*	140
R torsion, L torsion	.769*	133
R neck-shaft, L neck-shaft angle	.133	139
R LHF length, L LHF length	.862*	138
R LHF width, L LHF width	.845*	138

^aLHF, ligament of the head of femur

^b* $p < .001$

TABLE 5
Correlation Coefficients and Standard Deviations of Variables between Sides Adjusted for Age Covariate

Left down	Right across	Depth	Acediameter	FH Diameter	LHF Width	LHF Length	Neck-Shaft Angle	Torsion
Depth		.60**						
Acediameter		.637	.89*					
FH diameter		.618	.860	.85*				
LHF width		.222	.319	.343	1.01*			
LHF length		.242	.347	.407	.589	1.71*		
Neck-shaft angle		.103	.086	.088	.003	.041	8.20*	
Torsion		.340	.341	.431	.181	.273	-.032	9.61*

**Pooled standard deviations in mm or degrees are given on the diagonal.

FIGURE ABBREVIATIONS

R, right; L, left

Figures 5-9 display the mean plus and minus one standard deviation; the sample size is given above each age period. For purposes of clarity, only a single number (e.g., 12) is given for each two-week group.

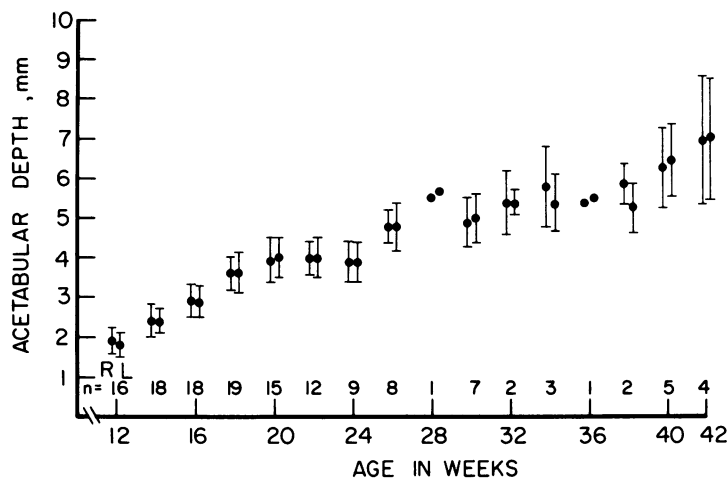


FIG. 5. Acetabular depth mean values and standard deviations, sexes combined, by side, for $n = 140$.

depth showed the slowest growth in the period studied, the increase being less than fourfold. Over all age groups a consistent linear growth trend was apparent in only acetabular and femoral head diameters. Overlapping in standard deviation intervals between age groups was most marked for the LHF variables and for the two femoral

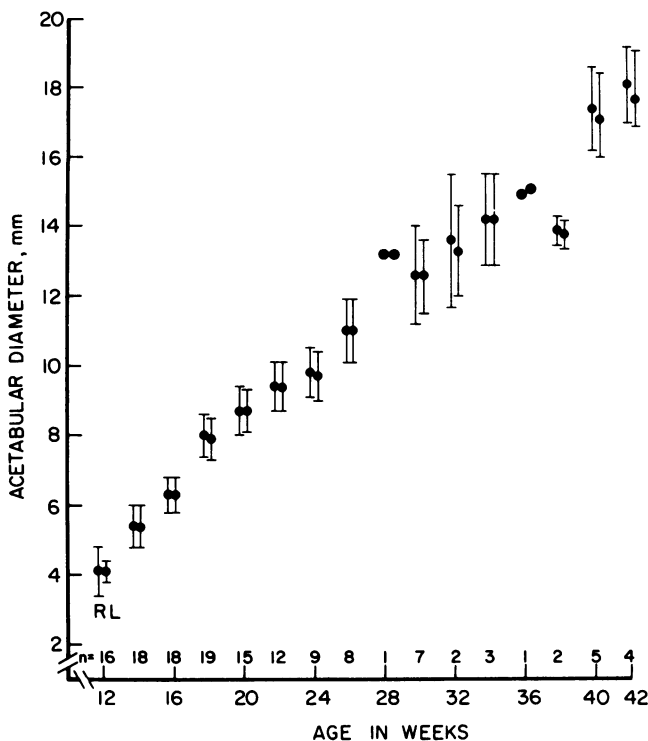


FIG. 6. Acetabular diameter mean values and standard deviations, sexes combined, by side, for $n = 140$.

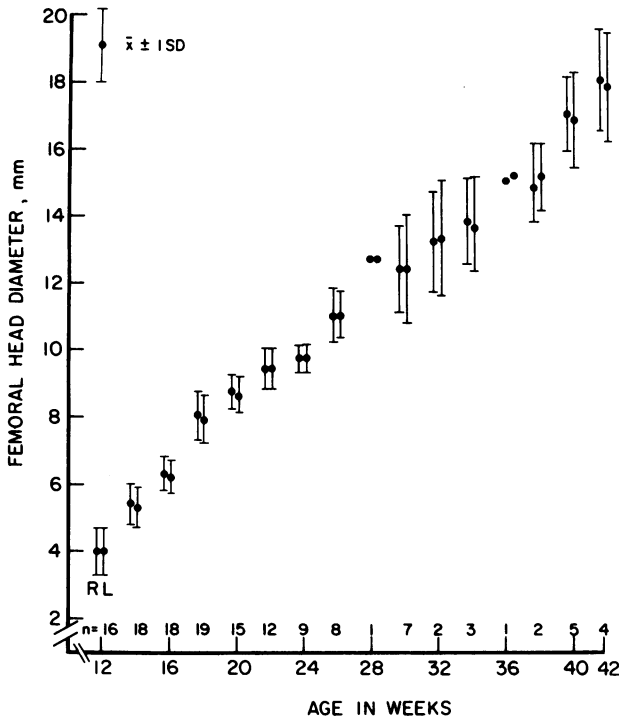


FIG. 7. Femoral head diameter mean values and standard deviations, sexes combined, by side, for $n = 140$.

angles. For both femoral angles, standard deviation intervals at term (38–42 weeks) overlap with those at 12 weeks and demonstrate considerable dispersion throughout the fetal period. Maximum values for torsion were not observed at term but at 32 weeks (30.0 cm CRL) as shown in Fig. 9. Another indicator of the greater

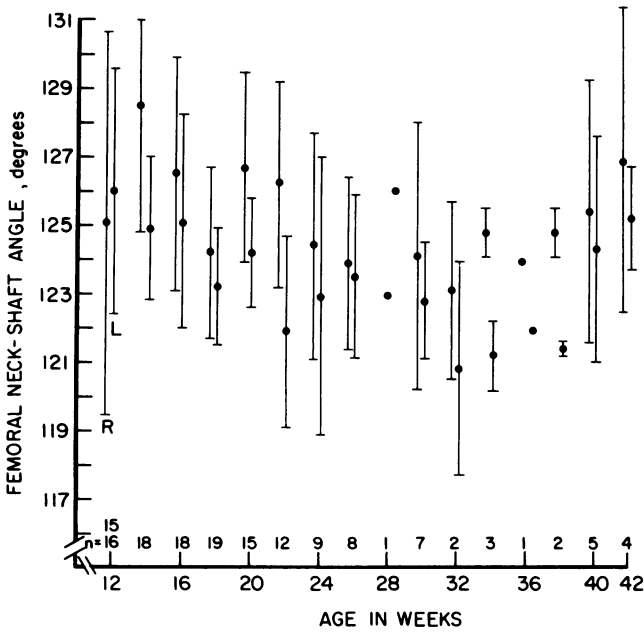


FIG. 8. Neck-shaft angle mean values and standard deviations, sexes combined, by side, for $n = 139$ right (R), 140 left (L).

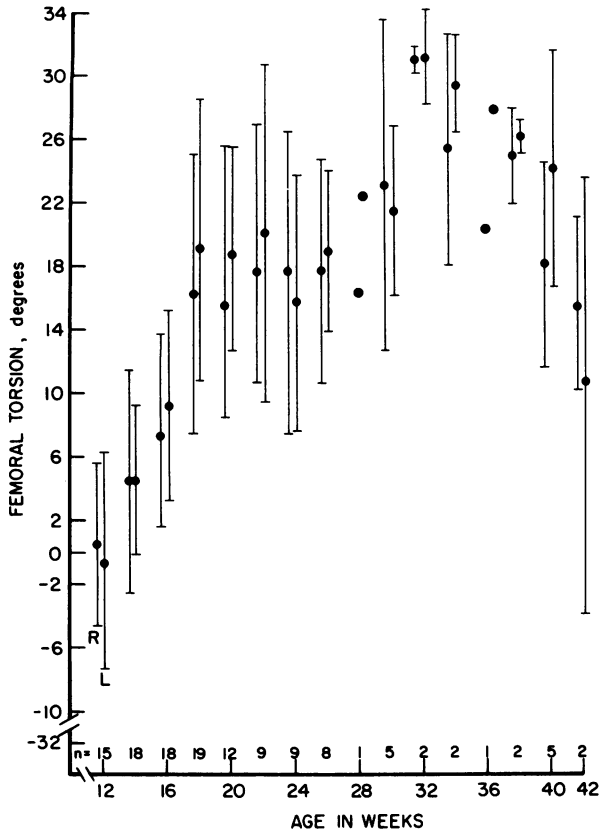


FIG. 9. Femoral torsion mean values and standard deviations, sexes combined, by side, for n = 133 right (R), 134 (L).

variability in angle values was revealed by the pooled sample standard errors which were smallest for depth and largest for torsion (Table 6).

Figures 10 and 11 show, in the same series of femora, the definite change over time in the torsion angle, but the lack of change over time in the neck-shaft angle.

Socket Shape and Joint Congruency

Although considerable variability in the acetabular index was evident in scatter plots (Fig. 12, left side only shown) there was a trend for this index to be smaller at term. None of the mean indices, for age grouped in two-week intervals, exceeded 50

TABLE 6
Sample Standard Errors for Variables by Side^a

Variable ^b	Right	Left
LHF width	0.147 ¹³⁸	0.141 ¹³⁹
LHF length	0.241 ¹³⁸	0.244 ¹³⁹
Depth	0.116	0.117
Acetabular diameter	0.309	0.305
Femoral head diameter	0.306	0.306
Neck-shaft angle	0.312 ¹³⁹	0.214
Torsion	0.893 ¹³³	0.936 ¹³⁴

^an = 140 unless denoted by superscript

^bIn mm except for angles which are in degrees

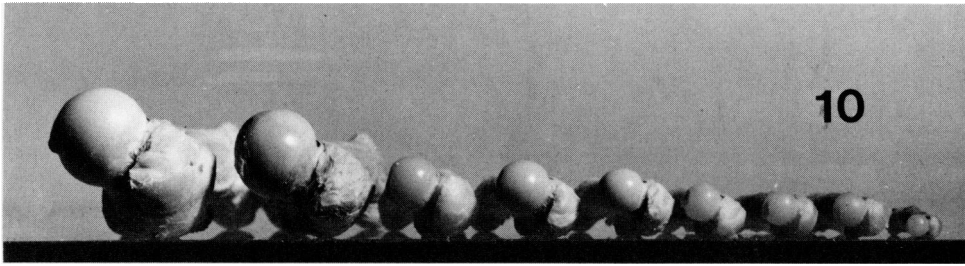


FIG. 10. Torsion angle in a series of right femora from 12 weeks (10.2 cm CRL) to term. Note also the variation in the proximal point of contact.

percent, and term indices of 35 percent indicate a shallow socket which resembles one-third of a sphere.

Maximum diameter indices exceeded 100 percent in individual cases, in all age categories except at 34 weeks ($n = 3$). Therefore, in a number of hips the femoral head diameter exceeded the acetabular diameter and may not be "seated" in the socket. No distinct trend was seen with age. Because mean diameter indices were less than 100 percent, these results indicate that the maximum width of the femoral head could be contained within the socket. These results support observations made during dissection when it was noted that in younger fetuses, after cutting the capsule, some force was required to distract the head from the socket. In older fetuses, however, division of the capsule produced immediate subluxation or dislocation of the femoral head from the hip socket. Furthermore, many joints clearly demonstrated a position of maximum congruency, when reciprocal coverage of articular cartilage surfaces was present with minimal motion between the two surfaces. This position corresponded with the presumed *in utero* posture, assessed post-delivery. Any movement of the femur out of this one position decreased the socket coverage of the articular surface of the femoral head.

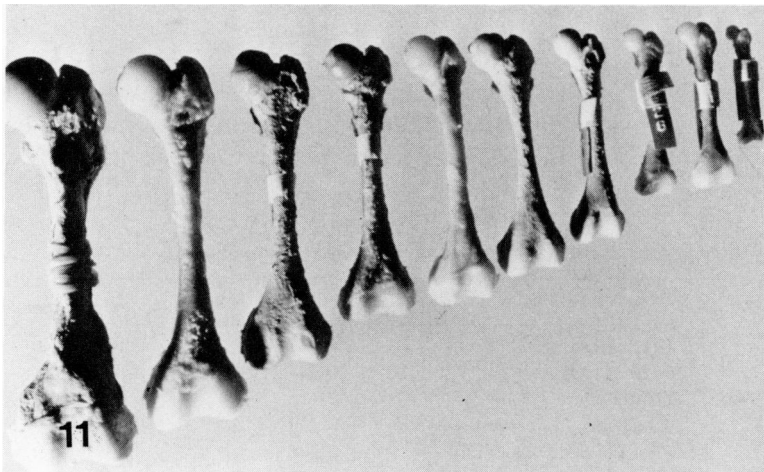


FIG. 11. Lack of change with age in the neck-shaft angle in a series of left femora from 12 weeks (10.2 cm CRL) to term. Note that the femoral neck still has no appreciable length in the 40-week femur.

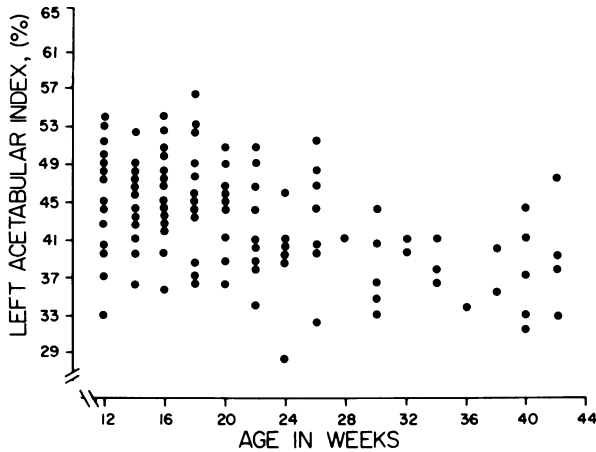


FIG. 12. Scatter plot of the left acetabular index by age, sexes combined, for $n = 140$. A single point may represent more than one case.

Leg Crossing

The legs were uncrossed in 46 percent of fetuses, while 30 percent of fetuses had the right leg crossed over the left, and in 24 percent the left leg was crossed over the right ($n = 118$). Leg crossing, with fetuses in three age groups, was random ($\chi^2 = 8.92$, $p = 0.0629$). No association was seen between leg crossing and torsion angle values. Crossing occurred at three levels, the toes, forefoot, or leg.

Morphology of the Proximal Femur

Variability in the proximal point of contact was observed when positioning femora for measurement (Fig. 13). In 56 percent of paired femora the lesser trochanter was more prominent than the greater trochanter. The lesser trochanter was prominent unilaterally in 11 percent. Where femora rested on the lesser trochanter, the latter was directed more posteriorly than medially. A significant relationship was shown between trochanter position (in four groups) and age (in three

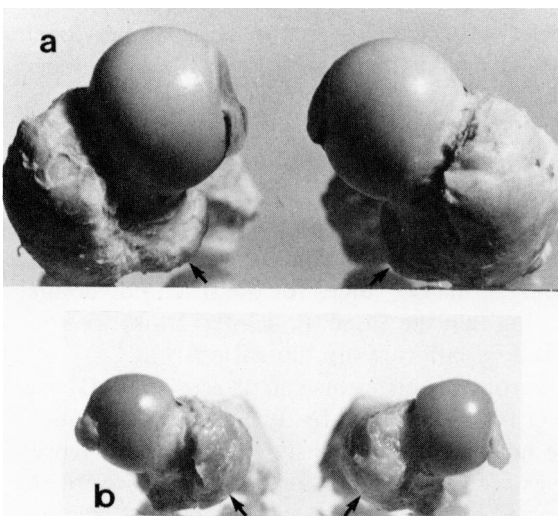


FIG. 13. Trochanter position. **a.** Both femora from a term fetus rest on the greater trochanter. $\times 2$ **b.** Both femora, from a 29.4 cm CRL fetus, rest on the lesser trochanter. Arrows indicate the greater trochanter. $\times 2$

groups; $\chi^2 = 42.72$, $p < 0.001$), but there was no difference between males and females overall when adjusted for age, or by age in two-week intervals.

In fetuses, less than 20 weeks of age (mean CRL = 14.58 cm), 58 (68.2 percent) femora bilaterally rested on the lesser trochanter whereas femora in 10 fetuses (71.4 percent), in the 32-to-40-week group (mean CRL = 37.36 cm), rested on the greater trochanter. An equal number of femora rested on either the greater or lesser trochanter in the 22-to-32-week group (mean CRL = 23.63 cm). There was no association between trochanter position and the neck-shaft angle, but a significant association of trochanter position with torsion angle was demonstrated (torsion in three groups: $< 0^\circ$, 0° - 20° , $> 20^\circ$; right $\chi^2 = 43.5$, left $\chi^2 = 41.9$, both $p < 0.0001$). A greater number of femora with a torsion angle less than 90° rested on the lesser trochanter. Of nineteen femora with a retroverted angle, none rested on the greater trochanter. Because 39 (57.4 percent) femora with a torsion angle greater than 20° rested on the lesser trochanter this may indicate that the presence and the amount of positive torsion are not the only factors involved in determination of trochanter position.

Fitting of Growth Curves

Regression models were devised to define a pattern of growth for the hip variables and to obtain predictive values for these variables with an estimation of age based on CRL. Analysis of residuals showed that variance increased with time for all variables except for the neck-shaft angle. This observation was supported by the correlation which was demonstrated when the means and standard deviations at each age group for each variable were plotted against one another. Models devised, therefore, included a natural logarithmic transformation, the use of logistic function, and the addition of a second- and third-degree polynomial to the independent variable age to determine which model best fitted the data. Adequate fit for the straight-line model was obtained for only two of the 14 variables, left LHF length and right LHF width (Table 7). With the exception of both acetabular diameters and left acetabular depth, adequate fit was obtained by fitting a model with a second-degree polynomial on age.

The relative amount of variation explained by the models is expressed by the Q_m^2 statistic (Table 7). Because little improvement in the explainable variation was obtained by fitting a cubic term model, we decided to fit the same model to all variables, and the model which appeared to make the most biological sense included a quadratic term. Addition of a cubic term noticeably improved the explainable variation, expressed by the Q_m^2 , only for right torsion. For depth, acetabular and femoral head diameters bilaterally, the partial F values indicated some lack of fit ($p < 0.05$), but none of these F values retained significance at the "four times level" [46]. (For example, left depth in the quadratic model has an F value of 1.89 which is significant at $p < 0.05$ but not at the "four times" level where $F_{0.05}(1,140) = 20.5$). With the exception of the neck-shaft angle, the Q_m^2 values for the fitted polynomial model are close to 100 percent, indicating that the fitted model performs a reasonable function in explaining the observed variation in hip dimensions.

The null hypothesis that the mean vector of coefficients equals zero ($\mathbf{B} = \mathbf{O}$) was rejected since the largest root criterion for all models greatly exceeded the critical values. Because the coefficients were not all simultaneously equal to zero, it was concluded that separate growth curves for the different hip dimensions were required. That is, the growth pattern varied between the seven hip variables studied.

TABLE 7
Lack of Fit and Coefficients of Determination for Linear and Quadratic Regression Models by Variables*

Variable	Linear Model			Quadratic Model		
	F**	P (≥ F)	Q _m ² %	F**	P (≥ F)	Q _m ² %
R depth	1.95	.0155	94.53	1.57	.0760	95.80
L depth	2.52	.0012	93.05	1.89	.0123##	95.05
R acediameter	2.71	.0005	97.83	2.41	.0022##	98.12
L acediameter	2.72	.0005	98.00	2.31	.0035##	98.38
R FH diameter	1.83	.0254	99.16	1.45	.1173	98.95
L FH diameter	1.92	.0173	98.57	1.64	.0592	98.87
R torsion	2.15	.0065	61.19	0.58	.9136	63.00
L torsion	3.87	.0000	55.05	1.59	.0719	82.51
R neck-shaft	1.00	.4700	6.68	0.85	.6455	24.51
L neck-shaft	1.60	.0645	18.45	0.98	.4875	52.52
R LHF length	2.03#	.0232	95.69	0.91#	.5413	98.20
L LHF length	1.50#	.1252	95.61	1.18#	.3014	96.80
R LHF width	1.31#	.2144	96.77	1.01#	.4467	97.69
L LHF width	2.58#	.0034	94.03	1.57#	.1018	96.62
	**df 20, 111R, 112L #df 14, 122			**df 19, 111R, 112L #df 13, 122		

*Increases in Q_m² % indicate improvement in the amount of variation explained by the model while significant F values indicate lack of fit between the model and the data.
##lack of fit < .05 but not at the “four times” level when F 0.05 (1,140) = 20.5 [46]

The predicted growth curves are displayed in Fig. 14. Table 8 presents the regression equations with the standard error of the estimate (square root mean square residual) used for the curves. The growth curves for femoral head and acetabular diameter coincide, as do the curves for right and left acetabular depth, except for a marginally lower predicted value for left depth at term (0.1 mm). The neck-shaft angle was the only variable in which the left side was consistently predicted to have lower values than the right side.

For all models, outliers were defined as those observations outside of the two-standard-deviation confidence band around the predicted model line. Examination of these specimens, however, provided no explanation for the difference between the observed and predicted values. Specimens whose LHF length was outside the band at a specific age did not always elicit comment at the macroscopic level. Specimens that varied in minor ways from the expected morphology of the joint outnumbered “normal” specimens in the frequency of outlier values for the variables right depth, right acetabular diameter, and femoral head diameter bilaterally. Although 95 percent confidence limits for the models were calculated, these are not shown. For models other than those for the femoral angles, these were very small.

Growth Rates

To compare the rate of growth in the dimensions studied we calculated the first derivative ($\hat{d}y/dt = \hat{\beta}_1 + 2\hat{\beta}_2t$, where t = age in weeks) of the regression equation of the fitted quadratic model with respect to time. The value of this derivative, for example, in right depth at 20 weeks is: $0.26366 + 2(-.00207)(20) = 0.18086$ mm/week. Examination of Fig. 15 demonstrates that depth bilaterally with the right LHF width shows the slowest rates of growth, while LHF length exhibits the fastest

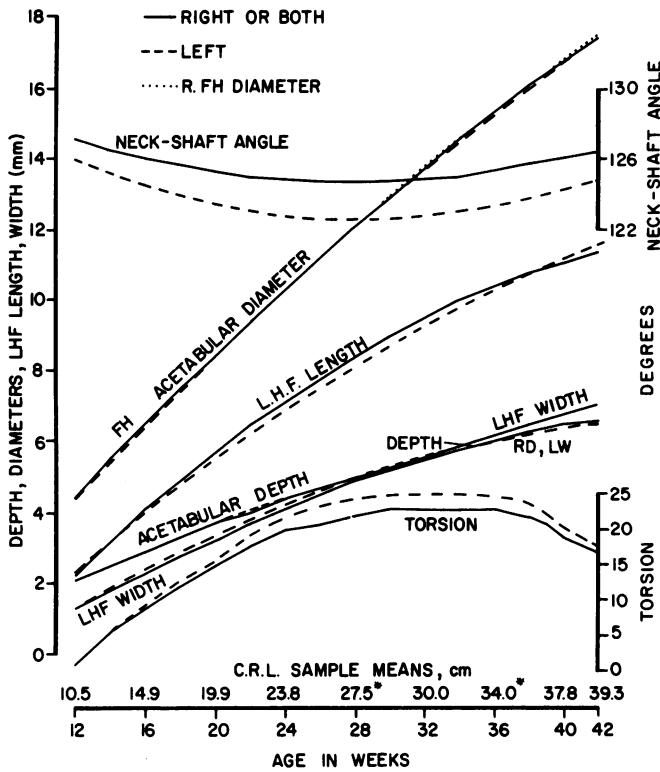


FIG. 14. Regression curves from the fitted quadratic model, for all variables, by side. C.R.L., crown-rump length; RD, right depth, LW, left ligament width; *n = 1.

rate of growth. Between sides, predicted growth rates differ most for the ligament variables. The growth rate for right length exceeds that of left length, but that for right width is less than that for left width. Rate of growth curves for acetabular and femoral head diameters are very similar with the latter predicted to grow at a slightly

TABLE 8
Regression Equations, by Side, for Quadratic Polynomials in Age, by Variable^{a,b}

Variable	$\hat{y} = \hat{B}_0$	+	\hat{B}_1x	+	\hat{B}_2x^2	SE est*
R depth	-0.77226		.26366		-.00207	.556
L depth	-1.10807		.29287		-.00263	.574
R acediameter	-2.29841		.59404		-.00292	.861
L acediameter	-2.45417		.60614		-.00314	.828
R FH diameter	-2.37984		.59923		-.00296	.791
L FH diameter	-2.62522		.61492		-.00343	.793
R torsion	-34.69084		3.65390		-.05775	7.703
L torsion	-38.85287		4.08782		-.06506	7.716
R neck-shaft angle	131.93882		-.51602		.00926	3.650
L neck shaft angle	132.65402		-.71103		.01254	2.680
R LHF length	-4.35858		.62019		-.00583	1.177
L LHF length	-3.36461		.52253		-.00397	1.386
R LHF width	-2.01329		.30592		-.00214	.772
L LHF width	-2.52949		.36261		-.00345	.739

^aPredicted growth curves from this model are displayed in Fig. 13.

^bRegression coefficient estimates: $\hat{B}_0, \hat{B}_1, \hat{B}_2$

*Standard error of the estimate (square root mean square residual)

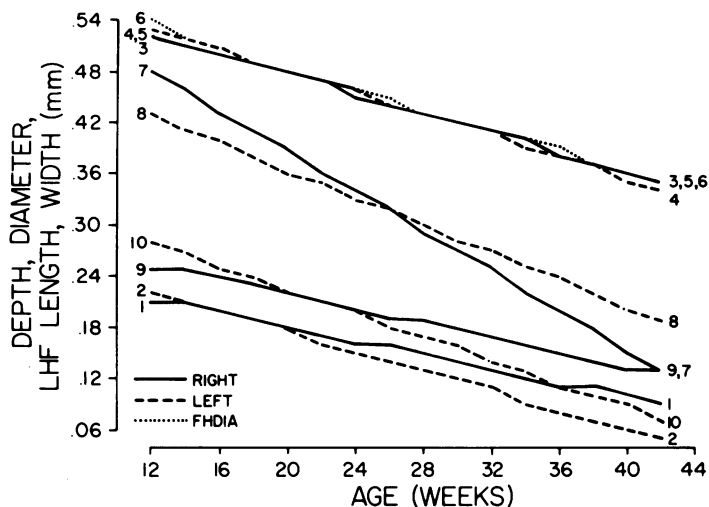


FIG. 15. Rate of growth curves from the fitted quadratic model, for variables measured in mm. 1, 2 = right, left depth 3, 4 = right, left acetabular diameter 5, 6 = right, left femoral head diameter 7, 8 = right, left ligament of the head of femur length 9, 10 = right, left ligament of the head of femur width

faster rate than the former (< 1 mm/week). The net effect of this disparity in the growth rates of these two dimensions would be a decreased stability of the joint with fetal aging.

DISCUSSION

Sex and Side

In congenital hip disease (CHD) a female preponderance and left-side involvement is commonly reported. Sex and side differences in the postnatal morphology of the acetabulum have been published [18–24]. The results presented here, however, show no difference in the fetal development of the hip joint, when all variables are examined simultaneously, either between males and females, or between the right and left sides. Sex and side were shown to have the least effect on acetabular depth. There is, however, a suggestion of difference between the sexes in the femoral angles, shown when the effect of sex on the angles was considered separately. Anatomical studies that have reported sex and side differences in the acetabulum considered variables separately, and the largest published study on the prenatal femur [6] did not separate data by sex or side.

Predicted growth curves herein suggest that left depth, acetabular and femoral head diameter increase in size during fetal development at a slightly faster rate than on the right side. This side difference, however, is probably accounted for by the small sample sizes of groups in the third trimester.

The lack of a significant effect for sex or side on growth of the fetal hip may give support to Dunn's [49,50] explanation for the greater female and left-side preponderance in CHD. Dunn considered that the female preponderance was due to greater influence of maternal sex hormones in female fetuses, and that the side involvement was related to the fetal position *in utero*. Whereas Watanabe [16] associated left leg involvement in CHD with the pattern of leg crossing, in the present study no association was shown between leg crossing and age, or with either of the femoral angles.

Socket Shape and Joint Congruency

Le Damany [18] and Ralis and McKibbin [11] from measurements showed that

the acetabulum became less of a hemisphere with increasing fetal age. However, the opinion based on macroscopic examination [5,49], or measurement on arthrograms [9], that there is little change in the relative acetabular depth or general morphology of the joint in the fetal period, has received some acceptance in orthopedic literature [51]. These results support previous reports that the socket is shallower at term than at any other period of fetal life. Whereas femoral head and acetabular diameter increased more than fourfold in the period studied, increase in depth of the acetabulum was less than fourfold, the smallest increase in size of the hip variables measured, except for the neck-shaft angle. That the velocity of growth for these dimensions was not constant was shown by fitting a straight-line model to these data. More growth occurred between 12 and 20 weeks than in the later period and only for depth did the two sides have different growth rates from an early age.

Mean acetabular indices, exceeding 50 percent, are similar to those reported by Ralis and McKibbin [11]. However, the latter investigators observed a maximum index value of 70 percent, whereas the maximum in the present study was less than 60 percent. The two studies differ in the aging of fetuses on CRL. Ralis and McKibbin's observation of higher acetabular indices, that implies deeper sockets in younger fetuses, may indicate that the slower growth rate of the depth dimension, as compared with that of diameter, commences very early in fetal life.

Because the best fitted model for age was quadratic, this may be interpreted as an adjustment for expressing growth of a three-dimensional structure, solely by linear dimensions. It can be expected that growth will proceed in all dimensions over time, and that when present, differences in growth rates, for example between length and breadth, will produce alteration in the shape of the socket. Although acetabular mean indices of 35 percent at term indicate a shallow socket, mean diameter indices less than 100 percent (except for the left hip at 24 weeks) indicate that the maximum diameter of the femoral head may be contained within the socket. Observations made during dissection of joints give justification to the viewpoint that soft tissue structures must play a role in stability of the hip joint in older fetuses because in older fetuses and neonates, the joint does not appear to be the secure ball and socket joint seen in the adult.

It is apparent that the ligament, a more robust collagenous structure than the capsule, must play a role in fetal and neonatal hip joint stability, as suggested by Crelin [13]. With the exception of the neck-shaft angle, however, the length of the ligament showed the lowest correlation with acetabular depth. The low correlations shown between both ligament length and width with other hip variables suggest that ligament shape and socket shape are not strongly related. Other aspects of the ligament have been reported [41].

Because femoral head and acetabular diameter were shown to be highly correlated, it seems reasonable to expect a strong relationship between head shape and socket shape. This relationship should be influenced by the degree to which the head is accurately centered in the socket. Although no specific measurements were made of the acetabular shape, minimum-maximum differences of 0.1 to 1.32 mm between the transverse, vertical, and oblique diameters of the socket (see Fig. 1) were observed. Many joints demonstrated a position of maximum fit or congruency in which there was maximum coverage of the femoral head by the socket and the least amount of play between the joint surfaces. This observation was more frequently made in third trimester fetuses and it is well established that neonates can be folded up more easily into one position that, it is assumed, is the *in utero* postural position [52-55,49,50]

When the joint surfaces are moved out of the position of maximum fit there is more "play" in the joint. In joints from older fetuses the femoral head easily separated from the socket when the capsule was opened. It is well established that many hip joints are unstable or subluxated in early postnatal life. After birth, the hip joint may not be in the *in utero* posture, and because of the shallow socket, the joint is less stable and thus more dependent on restraint by surrounding soft tissues.

When crown-rump lengths are compared, values for acetabular depth reported herein are similar to those reported by Le Damany [14] and Watanabe [16]. Watanabe, however, reported a CRL of 30 cm at 24 weeks of age, and in this series for the same age group, the mean CRL was 23.8 cm. Laurenson's [9] measurements of depth on arthrograms tend to be from one to two millimeters greater at any age than values in the present series. As the sample standard errors for depth are the smallest for any of the hip dimensions measured, values for depth reported herein may provide a reliable indicator of the population mean.

Racial Differences in Depth

An attempt was made to restrict the sample to the Caucasian race because Cheynel and Huet [8] have shown for acetabular depth and Trotter and Peterson [56] have shown for growth dimensions significant differences between Negroes and whites. However, the acetabular depth value of 3.5 mm reported for term whites by Cheynel and Huet is exceeded in the present series by both sexes after 26 weeks of gestational age. Further, mean values in the present study for males at term are similar to Cheynel and Huet's acetabular depth value for blacks of 7.1 mm. A recent study by Skirving and Scadden [17] confirmed Cheynel and Huet's finding of a deeper socket in African infants compared with white infants but did not find a racial difference for femoral torsion. Racial admixture may have contributed to higher values for depth and lower values for torsion at term because 39 percent of the present series was derived from sources where a high proportion of the population is Negroid. Anatomical differences present at birth may be genetically determined. African populations have a lower prevalence of congenital hip disease [57-60] but a higher prevalence of primary protusio acetabuli [61].

Angles of the Proximal Femur

Abnormal values of femoral angles with a "lengthened" ligament of the head are frequently reported in cases of CHD. Whereas a number of investigators have published values for the femoral angles, only Felts [6] and Watanabe [16] have published values from a reasonable sample size at different stages of fetal life. Watanabe's study extended only to 24 weeks of fetal life. Variation in values reported at specific age periods may be due to differences in measurement technique. This does not account, however, for the spread of values seen at any age point.

Neck-Shaft Angle

Stanisavljevic's [15] term values for the neck-shaft angle are accepted as the norm. Values calculated from radiographs, such as 137° at birth [62], and 150° at four-to-six months postnatal [63], are higher than values reported for any age period in the present series. Not only are the pooled mean values in the present study lower than those previously reported in infants and children, but also no apparent change in this angle was observed with age. Both Felts and Watanabe

demonstrated a similar lack of change in this angle over the period studied, although Felts did note a decrease of five degrees. Higher values observed in infants and children when the angle is evaluated on radiographs may be partially accounted for by differences in the attitude of the limb. Hamacher [64] observed on radiographs that medial rotation reduces the value of this angle, whereas lateral rotation increases its value.

Only minor differences from the accepted adult mean value of 125° are evident. The lack of variation in mean values at different prenatal ages may give support to the theory that the greatest decrease in this angle occurs early in fetal life. (It may be noted that it is easier to determine the neck-shaft angle from arthrograms than it is to determine acetabular depth.) However, the lack of correlation of this angle with the other hip variables means that the neck-shaft angle cannot be used to predict the approximate value of any of the other hip dimensions.

Because fitted regression models were not helpful in interpreting the explainable variation in neck-shaft angle values, prediction of the neck-shaft angle at any fetal age may be performed by taking the pooled sample mean values and standard deviations. Alternatively, the pooled mean values and standard deviations for sex and side could be used.

Femoral Torsion

The accepted mean value for femoral torsion at birth is about 35° [15,62]. However, neonatal values of 64° [42] and -2° [2] have been cited. As with the neck-shaft angle, variation in mean values for torsion may be partially explained by their own variation and lower reliability of measurement techniques. Felts, however, considered that there was insufficient variation in techniques to account for the wide dispersion of angle values.

Watanabe observed neutral values up to 24 weeks and with Kingsley and Olmsted [42] supported Le Damany's [14] theory that positive torsion develops in the second half of pregnancy. In the present study torsion showed the strongest linear trend between 12 and 18 weeks of gestation. Zero or negative values were rarely observed in fetuses older than 18 weeks. The present series is similar to that reported by Felts but differs from that of Watanabe perhaps because dysplastic cases were included in the latter's sample; differences may also be due to variation in the position of femora for measurement. In the present study an age difference in the morphology of the proximal femur was observed. Sixty-eight percent of young femora, with negative or low positive torsion angles, naturally rested on the lesser trochanter. Failure to ensure greater trochanter proximal support by the use of blocks in measurement will give a low torsion angle. This may account for the greater number of negative and neutral angles observed by Watanabe in fetuses up to 24 weeks of age, and in part for the range reported in a number of studies.

A highly significant relationship between trochanter support, considered equivalent to trochanter position, and age was demonstrated. Trochanter support was correlated with torsion with none of the femora with negative torsion values resting on the greater trochanter, whereas 57 percent of the femora with torsion greater than 20° did rest on the greater trochanter. Concomitant with an increase in the amount of positive torsion, there is a change in the morphology of the proximal femur that results in the lesser trochanter becoming directed more medially. This observation gives support to Le Damany's and Felts' opinions that torsion takes place in the femoral shaft, and not between the head and the neck. Because 43 percent of femora

with torsion greater than 20° did not naturally rest on the greater trochanter, there is evidence that torsion is not the only factor influencing the direction or position of the lesser trochanter in relation to the sagittal plane. Further explanation may lie in the development of the trochanters. The effect of abductor muscles crossing the hip joint on the developing greater trochanter may be small because of the limited mobility of the fetus within the uterus, and because of the flexed and abducted posture of the lower limbs in the third trimester.

The present series not only shows a wide range of values for torsion and overlap of standard deviation intervals amongst the 12- and 42-week groups, but also shows distinctly lower values at term than are reported from measurements made on radiographs. The mean adult value of 11.2° [65] was exceeded in the present study by 62 percent of femora and by 80 percent of Felts' fetal sample. The maximum length of fetuses in the present study that exceeded the mean adult value was considerably greater than that in Felts' study, which may be another expression of the individual variability exhibited by torsion.

Given the lack of a linear trend in torsion values throughout the entire period studied, it is not surprising that a straight-line model should explain less than 70 percent of the explainable variation in this angle. The better fit of the quadratic model may be related to Felts' observation that area, length, and breadth of the prenatal femur increase at unequal rates. Furthermore, torsion may be influenced by change in mass or volume of the femur, characteristics reflected by the cubic model. Torsion is recognized as a malleable characteristic influenced by environmental factors that are theorized to play a greater role in the third trimester of pregnancy [66]. Studies by Felts [6], Le Damany [14], Milch [67], Kingsley and Olmsted [42] and Watanabe [16] showed, in smaller or less complete samples, a steady increase in torsion values toward term. A similar change was not observed in the present study.

The present observations give support to statements by Le Damany and Felts, i.e., that because torsion is moderately correlated with the other hip joint dimensions, it should not be studied in isolation. With the exception of the neck-shaft angle, the side effect for torsion was the smallest observed, and was low after adjustment for age. The torsion angle appears to be more variable than the neck-shaft angle. Of greater consequence is the considerable dispersion of individual values shown for both angles that makes it difficult to determine clinically when these angles are indicative of pathology. Because only low to moderate correlation was shown between the femoral angles and other hip variables, abnormality of the angles alone may be a poor indicator of hip dysplasia.

Application of Growth Curves

There is general agreement that radiographs are of limited value in the diagnosis of CHD until the third postnatal month when ossification of the femoral head commences. At present, until ossification is well established, there is no clinical method available to obtain precise measurement of most of the hip joint dimensions measured in this study. Comparison of the present observations with Laurenson's small sample of values from arthrograms indicates that dimensions such as depth or diameter are overestimated when assessed on arthrograms, as would be expected. With the high correlation shown between depth, acetabular and femoral head diameter, these data could be useful to gain a quantitative measure of depth and acetabular diameter at a specific age or CRL. This would provide an assessment of how well formed the cartilaginous joint is, in infants with hip instability. Clinical ap-

plication of these data, within the age interval studied, must wait for further research in the field of radiology that devises a non-hazardous and non-invasive method of clearly visualizing the cartilaginous neonatal femoral head.

The regression equations established from these observations permit prediction of the value of a variable, such as depth (y) for a specific value of an independent variable, such as age, when the value of y cannot be directly assessed. The better fit of the quadratic model for these observations may be explained biologically in that measurement of hip joint dimensions all belong to structures which also possess area or surface, dimensions not assessed herein. Change in form or shape, as observed in the acetabulum, may reflect varying rates of growth of the different joint dimensions.

Limitations

The greater variability demonstrated by term fetuses may in part reflect incorrect age estimates. A possible error of four weeks in estimates of age at term is known [35]. It is recognized that length measurements of fetuses, as crown-rump or crown-heel, due to the flexed posture of the fetus, are less reliable than is assessment of weight or foot length [68,69]

Retardation in rate of growth after approximately 20 weeks was observed for all variables except for the femoral angles. Retardation in the rate occurs earlier than it does in overall fetal length seen in the third trimester when the fetus also shows an acceleration in overall mass, or weight. A possible explanation may lie in the sample composition. Fetuses less than 20 and 24 weeks of age (the latter interval spans age differences for declaration of a stillbirth in Canada and the USA) are the products of elective and therapeutic abortion. The sample older than 20 to 24 weeks comprises spontaneously aborted fetuses, stillbirths, and deaths in the perinatal period. The sample younger than 20 to 24 weeks may be more representative of normal growth and development. A higher frequency of growth problems, such as those producing small-for-dates or large-for-dates infants, the presence of placental insufficiency, and undetected maternal latent diabetes are known to occur in stillbirths.

It cannot be assumed, therefore, that this group is representative of normal growth patterns either in terms of total length measurements, birth weight, or in the growth of regions such as the hip joint. Development of the human fetal hip joint, however, as with any fetal growth study, can only be performed on the products of elective or spontaneous abortions, stillbirths, and deaths in the perinatal period. Such samples may be a biased sample of the population. Estimated age based on the CRL is a rough approximation [34]. Use of inclusion criteria should limit the degree of error.

With recognition of these limitations, the present study provides a measure of growth trends with a range of variability, and may improve our ability to detect deviation from average patterns of development.

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