Anatomical study of the proximal femur in the fetus

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Two angles effectively describe the upper femur geometry: The neck shaft angle (NSA) and anteversion (AV). AV and NSA decrease from birth until they reach their adult values, but little work has focused on in-utero life. Our aim was to determine if and how AV and NSA change through the fetal life. Eighty-seven femurs from 44 formalin preserved fetuses were sampled to achieve a biometry. Correlation tests and linear regression showed that AV was highly correlated with age: AV increases during the second half of gestation. No conclusion can be given concerning NSA. It is speculated that these changes may be caused by mechanical stresses. *J Pediatr Orthop B* 14:105–110

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Introduction

The three-dimensional shape of the proximal femur changes a lot throughout growth. It is known that in normal subjects, femoral anteversion (AV) and the femoral neck shaft angle (NSA) decrease from birth to the end of the growth until these angles reach their adult values, when the growth is completed [1,2]. It is also known that several pathological features are associated with the shape of the proximal femur, in newborns, infants, children and adults, such as lower limb rotational problems that may lead to gait abnormalities and early osteoarthritis. The geometry of the hip is also certainly involved in congenital dislocation of the hip.

The evolution of the geometry of the proximal femur during the fetal stage is poorly known. An acute biometry in the fetus may provide sufficient material to establish pre-birth variations of AV and NSA over time using statistics (Pearson's correlation test).

Our aim was to achieve this acute biometry of the proximal femur, using an anatomical method, to assess if there was some kind of correlation between angles measured and age, and to determine if and how AV and NSA change over time through the fetal stage.

Materials and methods

The aim of the present work was to achieve a biometry of the proximal femur in the fetus and to assess NSA and AV variations over time.

Materials

The anatomical work was performed on formalin preserved fetuses first examined in order to determine the cause of the fetal death. Criteria for inclusion were absence of external malformation, absence of malformation of the viscera, absence of bone abnormality on entire body radiograph (including no delay in the skeletal ossification), a normal karyotype, absence of maternal personal or familial history of congenital disease, absence of maternal pathology such as diabetes or high blood pressure. Fetal age was assessed using both last menstruation date and early ultrasonography. When data were not consistent, age was not mentioned (three cases). Age was expressed in weeks after conception. Forty-five foetuses were included, all of them were considered as free of orthopaedic disease. Ages ranged from 13 to 36 weeks. There were 16 females and 28 males.

Methods

Anatomical dissections were performed. Each time, the two femurs were fully dissected and removed. On each specimen, a mark was painted on the top of the great trochanter (in order to ease its location). Two pictures of each femur were shot, according to the method described by Wanner [3]. The femur was laid down on a hard desk, the lower epiphysis laying on the posterior side of the condyles, and the upper extremity lying on the intertrochanteric crest. The first picture was shot perpendicular to the plan on which the femur lay, in order to have the marked top of the great trochanter standing right in the middle of the screen. The second picture was shot vertically from above, the femur still lying in the same position, in order to get an anterior view of the sample. For each installation, parallax errors were controlled. The camera used was an Olympus E-10 (Olympus, Tokyo, Japan) with four megapixel CCD. The computer used was a PC with a Pentium 4 (Intel, Santa Clara, California, USA) 2.66 MHz processor powered by Windows XP (Microsoft, Redmond, Washington, USA). The software used for biometry was Photoshop 7.0 (Adobe Systems, San Jose, California, USA). The statistical evaluation was performed using SPSS 11.0 (SPSS, Chicago, Illinois, USA).

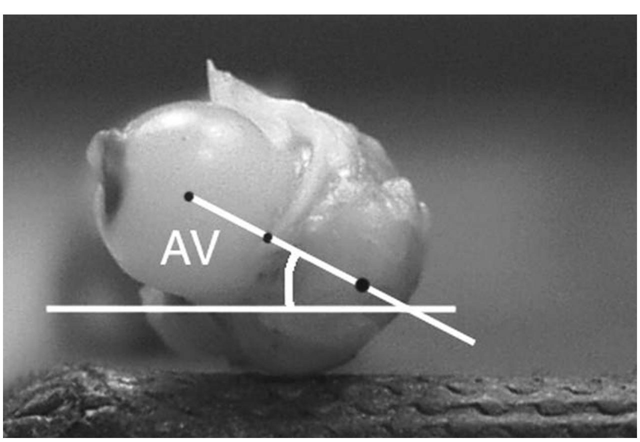
In three fetuses (six femurs), we were unable to determine the age with accuracy because of discrepancy between last menstruation date and early ultrasonography. Additionally, one femur (left-hand side) was damaged during the dissection. Eventually, the statistical analysis was performed on 83 femurs (42 on the right side and 41 on the left side).

It is commonly assumed that the axis of the femoral neck is a straight line connecting the centre of the femoral head, the centre of the femoral neck and the axis of the femoral shaft [4]. It is also commonly assumed that the axis of the femoral shaft is a straight line passing through the centre of the femoral shaft [4].

Angle measurements were recorded as follows: The AV is the angle formed by the intersection of the axis of the femoral neck and horizontal when the femur is shot by its upper extremity, placed as described by Wanner [3] (Fig. 1). In this position, the axis of the femoral shaft is represented by a single point assimilated to the top of the great trochanter (that was previously marked).

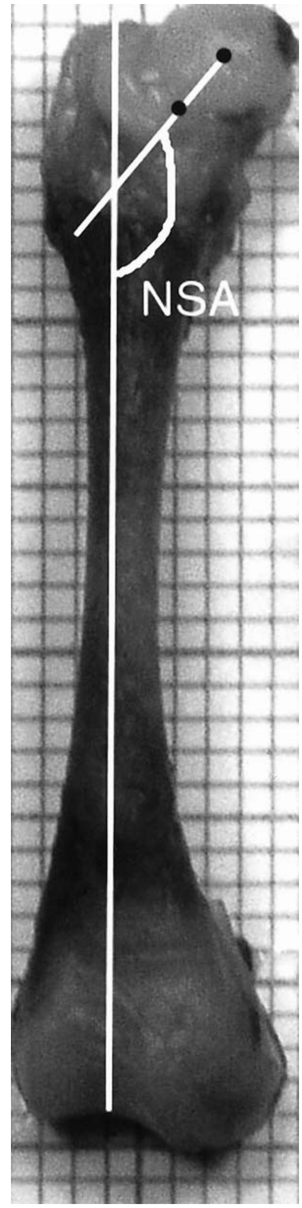
The NSA is the angle formed by the intersection of the axis of the femoral neck and the axis of the femoral shaft when the femur is shot from above (Fig. 2). In this position, the axis of the femoral shaft is assimilated to a line connecting the top of the great trochanter and the inter-condylar notch.

Fig. 1



Anteversion (AV) angle.

Fig. 2



Neck-shaft angle (NSA).

Validation of the method

The angle measurement method was based on the Adobe Photoshop angle measurement tool applied on digital photographs of each specimen. The measurement method was validated as follows: 50 different metallic devices (standard office paper-clips) were manually modelled, with a shaft-like branch, and a neck-like branch, defining NSA-like angle and AV-like angle on each device. Measurements of these 100 angles (50 AV-like and 50 NSA-like) were performed with a classical method, using a protractor. Two pictures of each device were shot according to the protocol described above. Computerized measurements using Photoshop 7.0 (Adobe Systems) of these 100 angles (50 AV-like and 50 NSA-like) were performed. A paired samples t test was performed to compare classical and computerized measurements of both AV-like and NSA-like angles.

The intra-observer repeatability of the experiment was checked as follows: a randomized selection of 45 different femurs from our collection was done. A first biometry (measuring AV angle and NSA of each femur) according to the protocol described above was performed. For each femur, at this first time, the value of AV angle was noted as the t1 AV angle and the value of the NSA as t1 NSA. Three weeks later, a second biometry (measuring AV angle and NSA of each femur) was performed in the same conditions by the same observer without any indication of the first results. For each femur, at this second time, the value of the AV angle was noted as the t2 AV angle and the value of the NSA as the t2 NSA. A paired samples t test was performed to compare these two measurements from the same observer.

The inter-observer repeatability of the experience was checked as follows: using the same selection of femurs, a first biometry was performed by a first observer (measuring AV angle and NSA of each femur according to the protocol described above. For each femur, the value of the AV angle was noted as the ob1 AV angle and the value of the NSA as ob1 NSA. A second biometry (measuring AV angle and NSA of each femur) was performed in the same conditions by a second observer without any indication of the first results. For each femur, with this second observer, the value of the AV angle was noted as ob2 AV angle and the value of the NSA as ob2 NSA angle. A paired samples t test was performed to compare the two measurements from two different observers.

Biometry

After method validation, the biometry itself was performed. For each specimen, age, sex and side were noted, and AV and NSA were measured using the previously described method. A Pearson's correlation test was performed, matching each angle (AV and NSA) with age and sex. Scatterplots with linear regression matching AV and age, and NSA and age were also proposed.

Control for confounders

In a cross-sectional study, a control for confounders is necessary. The main confounder factor is thought to be the size of the specimens (the younger the fetus the smaller are the proximal femur and the femoral neck). In the presence of a short femoral neck, minor alterations in the way the neck axis is delineated, could have significant impact on the AV and NSA measured). A sub-population was selected in order to minimize size-related confounder factors: all of the 19 fetuses from 24–36 weeks (third trimester of pregnancy) from the initial population were included. This represented only 37 femurs because one was damaged during the dissection. Pearson's correlation tests matching AV and NSA matched with age were performed in this sub-population of 19 fetuses.

Results

Validation of the method

The paired samples t test, comparing classical angle measurements (using a protractor) and computerized measurements (using Adobe Photoshop) showed no significant difference at the 95% level between the two methods for both NSA-like ($t = 0.465$) and AV-like ($t = -0.136$) angles.

Intra-observer repeatability

The paired samples t test comparing two measurements performed by the same operator at two different times showed no significant difference at the 95% level between the two series for both NSA ($t = -1.112$) and AV ($t = -1.814$).

Inter-observer repeatability

The paired samples t test comparing two measurements performed by two different observers at the same time showed no significant difference at the 95% level between the two series for both NSA ($t = 1.544$) and AV ($t = -1.238$).

Biometry results

A synthesis of the results of Pearson's correlation test and a linear regression analysis of the relationship between AV, NSA and age is given in Table 1. Scatterplots with linear regressions are shown in Figures 3 and 4. Pearson's correlation tests showed that AV and NSA were both correlated with age (AV increases with age; NSA decreases with age). There was no correlation between AV or NSA and sex. A box-plot showing AV mean values and the range of anteversion for each age is given in Figure 5.

Control for size-related confounders

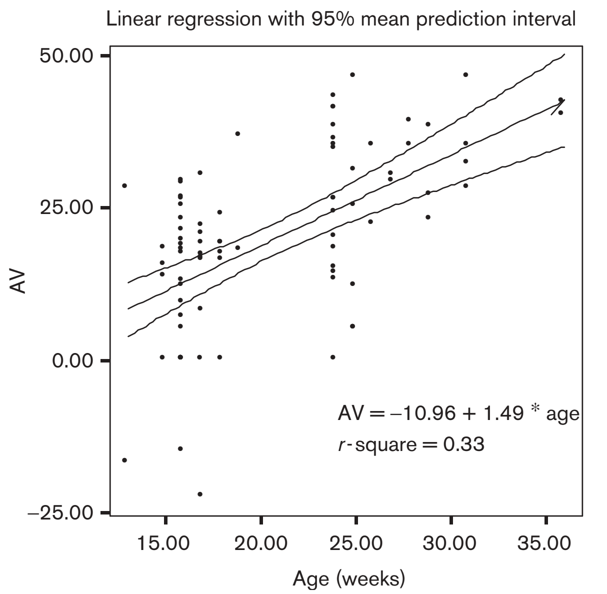
In the sub-population of 19 fetuses (only 37 femurs because one was damaged during the dissection) from 24–36 weeks, there was a correlation between AV and age

Table 1 Results of Pearson's correlation and regression analysis of the relationship between anteversion, neck shaft angle and age

Angle	Pearson correlation coefficient (r)	Linear regression
AV	0.575 ($P<0.01$)	$AV = -13.94 + (1.49 \times age)$ $r^2 = 0.33$
NSA	−0.528 ($P<0.01$)	$NSA = 158.71 - (0.77 \times age)$ $r^2 = 0.28$

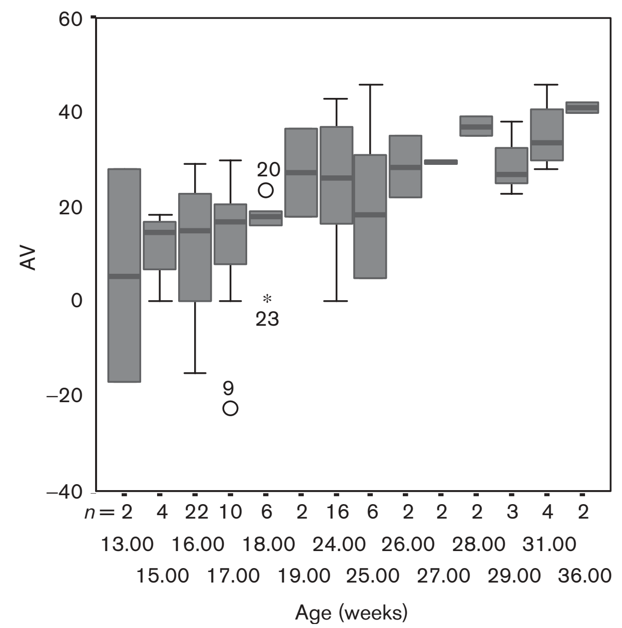
AV, anteversion; NSA, neck shaft angle.

Fig. 3



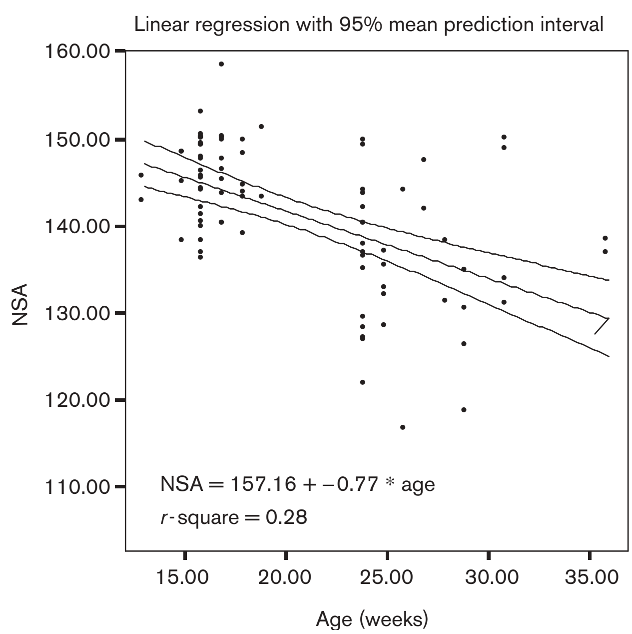
Linear regression scatter plot of anteversion (AV) angles with 95% mean prediction interval.

Fig. 5



Boxplot showing the range and the mean values of the anteversion (AV) angle for each age.

Fig. 4



Linear regression scatter plot of neck-shaft angles (NSA) with 95% mean prediction interval.

(Pearson correlation coefficient (r) 0.377; $P < 0.05$) and there was no evidence of correlation between NSA and age ($r = 0.037$; NS).

Discussion

Few works can be found in the literature focusing on fetal hip joint geometry and especially its femoral part. It has been known that femoral AV and NSA are specific neither of human beings nor biped walking [1]. It was known that AV and NSA change during childhood, until growth is completed [1,2]. Both AV and NSA decrease.

In 1925 Murray and Huxley [5] with their experiments on graft and limbs showed that the shape of a limb segment is given independently from the function of the limb, suggesting a genetic determination in the primary shape of the epiphysis, that could be later remodelled by a mechanical stress.

The role of the mechanical stress has been assessed by several authors. In 1987 a survey showed that AV decreases faster in case of obesity [6]. It has been known for a long time that in cases of cerebral palsy AV and NSA do not decrease over time during the growth (or at least decrease less than in healthy children), especially in non-ambulatory cerebral palsy patients [7,8]. In 1995, two cases of progressive coxa valga after excision for tumour of the hip abductor muscles in children were reported [9], pointing out the role of the mechanical stress factor in the global shape of the proximal epiphysis of the femur. In the literature there are biomechanical models that can explain why both AV and NSA decrease over time during the growth in healthy (and walking) children. In 1993 a work showed that the great trochanter growth is stimulated by a resultant force that has a craniolateral direction; this oblique growth explains why NSA decreases over time during the growth [10]. In 2002 further work showed that the physiological value of AV at the end of growth is theoretically the ideal value to obtain a perpendicular relation between the orientation of the capital epiphyseal growth plate and the projection of the resultant force, on the transversal or horizontal plane, during walking [11].

These two angles (AV and NSA) are associated with pathology in newborns, children and adults. The most common femoral torsion abnormality is known as coxa antetorsa (excessive anteversion). Coxa antetorsa may be associated with many clinical features ranging from intoeing gait in children to osteoarthritis of the hip joint [12] and femoropatellar instability in adults [13,14]. The spontaneous regression of excessive femoral anteversion in children is usual and occurs in most cases [15]. It is in cases lacking spontaneous correction that pathological features appear in adults. Less frequently, a reduced femoral anteversion (or even a real retroversion) may be observed. In this case, the clinical expression appears to be a posterior instability of the hip joint. In 1985, a survey compared femoral anteversion in two groups of adults, one group consisting of patients who had previously suffered from traumatic posterior dislocation of the hip, and the other group composed of normal adult volunteers. Femoral anteversion on both the injured and uninjured side was significantly reduced in the patients compared with the volunteers [16]. In 1989 a case was reported about a recurrent posterior traumatic dislocation of the hip associated with a reduced anteversion of the femoral neck [17]. NSA is increased in 70% of cases of congenital dislocation of the hip [18], but it is now well known that this is a minor factor in the pathological cause of this disease. Nevertheless, in case of congenital dislocation of the hip, after reduction, it is known that bony changes may occur, such as excessive femoral valgus and anteversion [12,19,20].

Few works focus on what happens during the fetal period. It would be helpful, in order to understand pathologies that could occur later, to better know how the fetal hip develops. We conducted a cross-sectional study in order to determine if and how the upper femur geometry changes during the fetal stage. Clearly, a longitudinal study is not feasible unless done by sequential intrauterine imaging to measure change over time. Although ultrasonography has been used to measure femoral anteversion in newborns and infants [21], it was not feasible for our purpose because the specimens were too young and too small to be acutely measured by intrauterine classical imaging methods. Only an anatomical method (and so a cross-sectional study) fitted an acute biometry of such small specimens. For a cross-sectional study to be of value, an analysis that controls for confounders is necessary. The main potential confounder is the size of specimens (that might influence AV and NSA rather than or in addition to age). It was postulated that our primary outcomes (correlation between AV or NSA and age in fetus from 13 to 38 weeks) may have resulted from the difficulties to accurately define where axes were located in the smallest and therefore the youngest specimens. To eliminate this confounding factor, we gathered a sub-population made of the oldest fetuses (19 fetuses ranging from 24 to 36 weeks), and the statistical analysis was conducted in this sub-population. Concerning AV, the same result (a positive correlation between AV and age) was found; we concluded that the size was not responsible for the observed variation in this sub-population. Concerning NSA, there was a discrepancy (no correlation between NSA and age was found). We concluded that the observed variation over time in the initial population may have resulted from size variations. Our work showed that AV seemed to increase over time at least during the period from 24 to 36 weeks. Concerning the period from 13 to 24 weeks, no conclusion could be given because of the possibility of size-related confounders. In the same way, in a cross-sectional study like ours, no conclusion about NSA changes over time could be given, because of the possibility of size-related confounders.

It may be suggested from a genetically determined pattern of the hip that mechanical stress remodels the shape of the epiphysis (as it is assessed in children). Mechanical features that lead to increased AV (and perhaps to decreased NSA) during the second half of gestation (and perhaps the entire gestational period) must be studied.

It is remarkable that during growth, fetuses become more and more contained in the uterus, and the space available to extend hips becomes more and more reduced: hips are flexed in the fetal position. In such flexed position, the femur is upside down and therefore, a positive AV angle means that the femoral head is 'looking' backwards. It is also remarkable that while the AV angle changes through the second half of gestation, and maybe through the entire gestational period, the acetabulum seems to have a fixed anteversion. (In 1992, 47 hips from embryo and fetus, from 6 to 20 weeks of age, were studied, and no significant variation in the acetabular anteversion through the embryonic and early foetal stages was found [22].) It can be suggested that a femoral head that looks backward is more and better contained in an acetabulum that looks forward.

The proximal femur greatly changes through growth. During the fetal period AV seems to increase and after birth, until growth is over, both AV and NSA decrease.

These changes could be caused by mechanical stress factors that are able to modify a primary anatomical shape that could have been genetically determined.

References

1 Castiaux P. Torsion abnormalities of the legs [in French]. *Acta Orthop Belg* 1977; **43**:410–415.

2 Lerat JL. Rotation abnormalities of the lower limbs [in French]. *Rev Chir Orthop Reparatrice Appar Mot* 1982; **68**:1–74.

3 Wanner JA. Variations in the anterior patellar groove of the human femur. *Am J Phys Anthrop* 1977; **47**:99–102.

4 Hoiseth A, Reikeras O, Fonstelien E. Basic concepts of femoral neck anteversion: comparison of two definitions. *Br J Radiol* 1989; **62**:114–116.

5 Murray PDF, Huxley JS. Self differentiation in the grafted limb bud of the chick. *J Anat* 1925; **59**:379.

6 Galbraith RT, Gelberman RH, Hajek PC, Baker LA, Sartoris DJ, Rab GT, *et al.* Obesity and decreased femoral anteversion in adolescence. *J Orthop Res* 1987; **5**:523–528.

7 Bobroff ED, Chambers HG, Sartoris DJ, Wyatt MP, Sutherland DH. Femoral anteversion and neck-shaft angle in children with cerebral palsy. *Clin Orthop* 1999; **364**:194–204.

8 Laplaza FJ, Root L, Tassanawipas A, Glasser DB. Femoral torsion and neck-shaft angles in cerebral palsy. *J Pediatr Orthop* 1993; **13**:192–199.

9 Brien EW, Lane JM, Healey J. Progressive coxa valga after childhood excision of the hip abductor muscles. *J Pediatr Orthop* 1995; **15**:95–97.

10 Heimkes B, Posel P, Plitz W, Jansson V. Forces acting on the juvenile hip joint in the one legged stance. *J Pediatr Orthop* 1993; **13**:431–436.

11 Fabeck L, Tolley M, Rooze M, Burny F. Theoretical study of the decrease in the femoral neck anteversion during growth. *Cells Tissues Organs* 2002; **171**:269–275.

12 Tegnander A, Holen KJ, Anda S, Terjesen T. Good results after treatment with the Frejka pillow for hip dysplasia in newborns: a 3-years to 6-years follow up study. *J Pediatr Orthop B* 2001; **10**:173–179.

13 Hvid I, Andersen LI. The quadriceps angle and its relation to femoral torsion. *Acta Orthop Scand* 1982; **53**:577–579.

14 Grijalvo PH, Laville JM, Cahuzac JP, Bonnevialle P, Lebarbier P, Pasquie M. Patellar syndromes in children [in French]. *Acta Orthop Belg* 1983; **49**: 447–456.

15 Svenningsen S, Apalset K, Terjesen T, Anda S. Regression of femoral anteversion. A prospective study of intoeing children. *Acta Orthop Scand* 1989; **60**:170–173.

16 Upadhyay SS, Moulton A, Burwell RG. Biological factors predisposing to traumatic dislocation of the hip. A selection process in the mechanism of injury. *J Bone Joint Surg Br* 1985; **67B**:232–236.

17 De La Caffiniere JY, Ould Ouali A. Recurrent posterior traumatic luxation of the hip and anteversion defect of the femoral neck in adults. About one case, general review of the literature. *Rev Chir Orthop* 1989; **75**:48–52.

18 Le Damany P. *La Luxation Congénitale de Hanche*. Paris: Felix Alcan; 1912.

19 Sherk HH, Pasquariello PS, Watters WC 3rd. Congenital dislocation of the hip. A review. *Clin Pediatr (Phila)* 1981; **20**:513–520.

20 Doyle SM, Bowen JR. Types of persistant dysplasia in congenital dislocation of the hip. *Acta Orthop Belg* 1999; **65**:266–276.

21 Prasad SS, Bruce C, Crawford S, Higham J, Garg N. Femoral anteversion in infants: a method using ultrasound. *Skeletal Radiol* 2003; **32**:462–467.

22 Lee J, Jarvis J, Uhthoff HK, Avruch L. The fetal acetabulum. A histomorphometric study of acetabulum anteversion and femoral head coverage. *Clin Orthop* 1992; **281**:48–55.