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Histological Study of the Fetal Development of the Human Acetabulum and Labrum: Significance in Congenital Hip Disease

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Seventy-four acetabula from a total of 140 normal human fetuses, obtained from abortions and deaths in the prenatal period, were used. The fetuses ranged from 9.1 to 40 cm in crown-rump length and are believed to be between 12 weeks and term. Acetabula were decalcified, embedded in paraffin or celloidin, sectioned, and stained using conventional histologic techniques. Sections from the superior one-quarter of the acetabulum were examined for the initial appearance and later spread of osseous tissue.

Throughout the fetal period bone was present only in the floor of the acetabulum and did not extend into the socket walls. Ossification was detected initially more posteriorly in the socket floor, and at all ages, ossification was more prominent on the ischial side of the socket. Despite the lack of osseous tissue a well-formed hyaline cartilage socket was present. The fetal labrum was composed of fibrous tissue with the density of fibers increasing with age. Typical-appearing chondrocytes were detected at only the inner articular margin of the labrum. Contributing from one-fifth to one-half of the socket depth, the labrum may play a greater role in containing the femoral head at birth than it does in the mature joint.

In seven acetabula, from joints that were neither subluxated nor dislocated, an area of areolar tissue with capillaries was detected at the hyaline cartilage-labrum junction. Such defects may weaken the labrum and contribute to neonatal hip instability.

This paper presents a histological study of the prenatal development of the human acetabulum and labrum in fetuses and neonates between 9.1 and 40.0 cm crown-rump length, about 12 to 42 weeks of gestational age.

At birth the skeletal components of the human hip joint are largely cartilaginous, and the joint is underdeveloped and potentially unstable. Abnormality of joint structures in infants with congenital hip disease (CHD), however, may be minimal at birth [1,2]. In the established case of CHD, the following characteristics are frequently observed: a small, nonspherical femoral head, abnormal angles of the proximal femur, a shallow, noncircular socket, and an excessively long ligament of the head of the femur.

The embryonic development of the hip joint has been well documented [3-13]. However, it is not completely settled whether the depth of the socket increases at a constant rate throughout fetal life, or whether, in relation to the socket diameter, depth increases at a slower rate resulting in a shallow socket at birth, as noted by Le Damany [14] and Rális and McKibbin [11]. Laurenson [15], in a limited sample, observed, histologically, uneven osseous development within the acetabulum with

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greater growth at term of the medial perichondral region, compared with the lateral perichondral region of the socket. No other studies were found that indicated differences in the rate of bone growth in different areas of the socket, a factor that may contribute to neonatal hip instability.

Whereas the role of the labrum in increasing the overall depth of the socket and stability of the hip joint is recognized [16], there is controversy concerning its composition. The fetal labrum is described as composed of fibrocartilage [11,2,17] or as hyaline cartilage [7,18]. Both Gardner and Gray [7] and Sawada [19] noted that fetal labrum is not similar to adult fibrocartilage. Matles [20], however, concluded from a study of non-formalin-fixed term labra that differences in histological findings were due to techniques of preparation, rather than histodifferentiation.

Because of the above controversies concerning aspects of the development of the hip joint a comprehensive study of this joint in the human fetus was conducted; only the histological study of the acetabulum and the labrum are reported herein. Analysis of the growth patterns of the joint will be reported separately. This study may contribute to our understanding of the factors in the growth process that may contribute to the development of congenital hip disease.

METHODS

The sources of the 140 normal human fetuses, criteria for inclusion in the study, number and sex by age group with mean values and range of crown-rump lengths (CRL) have been previously reported [21].

Since many specimens were received already fixed in formaldehyde (10 percent) it was necessary, therefore, to accept the formalin state as a basis for the group as a whole. To improve fixation in larger fetuses, the hip joints were immediately dissected down the level of the capsule.

Histology

Seventy-four paired acetabula were decalcified in 5 percent formic acid [22], then embedded in paraffin wax (Paraplast) or celloidin (Parlodion). The embedded blocks were serially sectioned at 10–25 μm (Fig. 1) and the sections were stained with Alcian blue and van Gieson in the routine manner. A number of acetabula were cleared in methyl salicylate to reveal the osseous development.

Measurement of the Labrum

The percentage of the socket formed by the labrum was calculated from measurements made on histological sections from the superior quarter level of the acetabulum (Fig. 2). No mathematical adjustment was made for the concavity of the labrum in these calculations.

RESULTS

Ossification

When the whole acetabula from the early fetal period were cleared with methyl salicylate, almost no ossification was apparent in the socket (Fig. 3). This observation was confirmed by examination of sections of acetabula (Fig. 4). In fetuses of 9.1 to 15.3 cm CRL, the socket was composed entirely of hyaline cartilage with round chondrocytes evenly spaced within a homogeneous matrix. On the inner articular surface of the socket, chondrocytes were more closely packed and somewhat flattened. This inner margin stained more intensely than the remainder of the

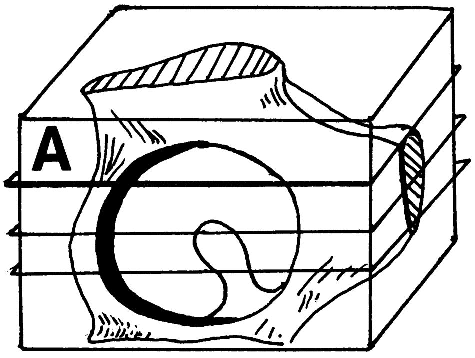


FIG. 1. Positioning of acetabula in blocks. The face of the acetabulum is vertical. Sections were taken from the marked 1/4, 1/2, and 3/4 levels of the acetabulum. A = anterior aspect.

cartilaginous socket. The majority of vascular canals were present at the outer edge of the acetabular sections in specimens less than 12 cm CRL. The vessels appeared to penetrate the acetabular cartilage from the perichondrium. In fetuses over 13 cm CRL, there was an increased number of blood vessels in the cartilaginous matrix close to the perichondrium. The vascular canals appeared randomly distributed throughout the socket. Vessels were observed to enter the cartilage from the acetabular fossal depression in sections from 20 cm CRL fetuses.

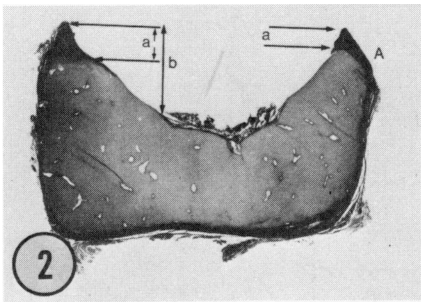
In whole acetabula, cleared in methyl salicylate, from fetuses of 20 cm CRL (about 20 weeks), extensions of the iliac and ischial primary ossification centers were visible in the floor of the socket (Fig. 5). Extension of the iliac ossification center into the socket, in sections from the superior quarter level, was first observed in an 18.1 cm CRL fetus. The zone of early ossification was located at the rear of the acetabular fossa, more to the ischial side, and did not extend to the floor of the socket or to the posterior margin of the socket. By 21.8 cm CRL a thin layer of periosteal bone was present on the posterior border, mainly on the ischial side (Fig. 6). The central region of the socket was composed of bone surrounded by a zone of hypertrophic chondrocytes that did not reach the floor of the acetabular fossa.

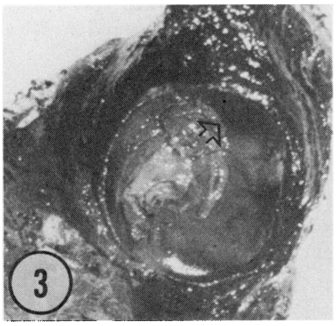
The amount of osseous tissue present in sections from the superior quarter level of the socket gradually increased with further growth. However, in a 30.0 cm CRL fetus, while endochondral bone had reached the floor of the acetabular fossa centrally, this zone had not extended beyond the floor into the walls of the socket (Fig. 7).

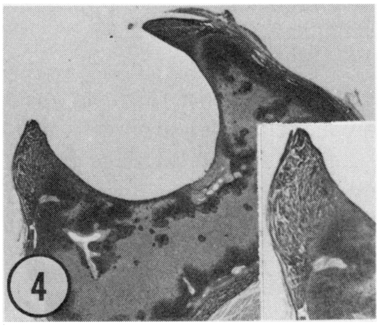
Whereas bone from iliac, ischial, and pubic ossification centers was visible in a 36-week acetabulum cleared in methyl salicylate, osseous tissue had not extended into the walls of the socket (Fig. 8). Examination of histological sections from two neonatal specimens confirmed this observation. Neither endochondral bone nor hypertrophic chondrocytes were visible in the walls of the socket. Little change was observed in the extent of osseous tissue at the superior quarter level of the acetabulum in one older specimen studied, a 48 cm CRL stillborn infant with an estimated gestational age of 50 weeks (Fig. 9).

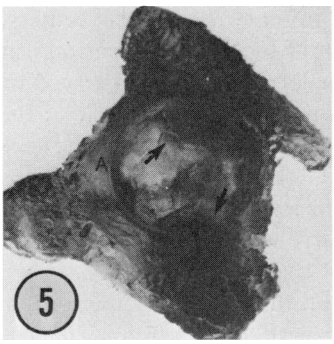
Acetabular Labrum

The most distinctive change in the labrum observed with growth of the fetuses was in the density of the collagenous fibers. In younger specimens the labra were typically composed of matrix, fibroblasts, and loosely arranged parallel bundles of collagenous fibers (Fig. 10A). Labra from term fetuses, however, were composed of thick, dense bundles of collagenous fibers, resembling a ligament in appearance and having no apparent matrix. Cells with the typical morphology of chondrocytes, lying in









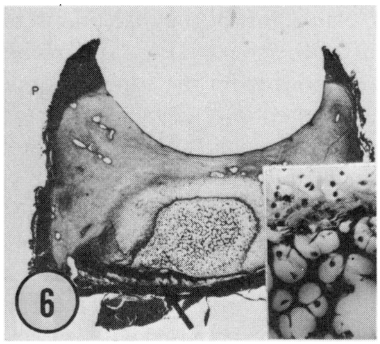


PLATE 1 · EXPLANATION OF FIGURES

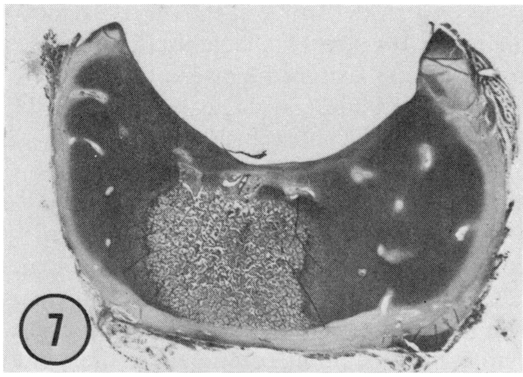
FIG. 2. Calculation of the percentage of the socket formed by the labrum. The height of the labrum (a) was measured on both sides and the mean of the two measurements × 100 was divided by the socket depth (b). The depth measurement did not include the acetabular fossa. A typical side difference in rim labra is shown. Sections from the superior one-quarter of the acetabula were measured. No adjustment was made for the curvature of the socket wall.

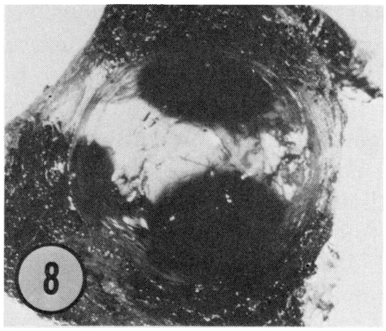
FIG. 3. A 12-week (9.8 cm CRL) methyl salicylate cleared socket showing that bone is only visible on the sacral side of the superior pole (*arrow*) × 7.

FIG. 4. A typical section from the superior one-quarter level of acetabula from fetuses with CRL values between 8.7 and 16.0 cm, here from a 15.3 cm CRL fetus. Alcian blue and van Gieson, × 11. The distinction between the predominantly fibrous labrum and hyaline cartilage of the socket proper is shown in the inset. (× 22, 10 μm).

FIG. 5. The socket, cleared in methyl salicylate, is still cartilaginous in this about 20-week fetus. Bone is visible in the floor from the iliac and ischial centers (*arrows*). Compare with Figs. 3 and 8. 19.5 cm CRL, × 1.8, Anterior border (A).

FIG. 6. Section from the superior one-quarter level from a 21.8 cm CRL fetus. A thin layer of bone (*arrow*) is present to the rear of the socket floor, more to the posterior side. The ossific center is surrounded by a zone of hypertrophic chondrocytes (*see inset*) but this region does not reach the socket floor. Hematoxylin and eosin, × 9, 10 μm.





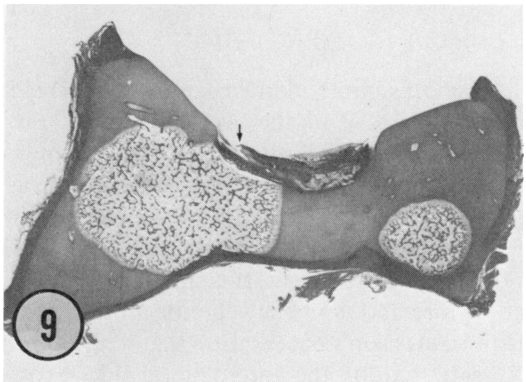


PLATE 2 EXPLANATION OF FIGURES

FIG. 7. Section from the superior one-quarter level, from a 30 cm CRL fetus. The central region of endochondral bone almost reaches the socket floor and is situated toward the posterior side. Alcian blue and van Gieson, × 5, 20 μm.

FIG. 8. Socket, cleared in methyl salicylate, from a 32-week, 30.0 cm CRL fetus. All three centers of ossification, iliac, ischial, and pubic, are present. × 2.3.

FIG. 9. Section from the lower limit of the superior one-quarter level, from a 48 cm CRL postmature "term" fetus. Bone, from the iliac ossific center, has reached the lateral wall on the posterior or ischial side of the socket but has not extended into the walls of the socket beyond the level of the acetabular fossa (*arrow*). Alcian blue and van Gieson, × 3.5, 20 μm.

lacunae, were observed only in the labra, at the inner articular margin of the socket (Fig. 10B). Cells in the substance of the labra had the typical morphology of fibrocytes, being elongated and flattened between the collagen bundles.

In the youngest specimens studied histologically (9.1 cm CRL), blood vessels were observed in the labrum close to the outer covering of fibrous tissue which is continous with the perichondrium. In older fetuses, blood vessels were seen at the inner articular margin of the labrum. There was an apparent decrease in the number, or density per unit volume, of blood vessels in labra from third trimester fetuses.

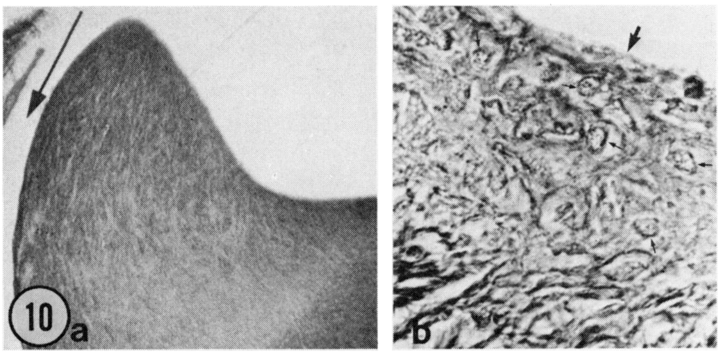
In seven acetabula (13.7 percent of those studied histologically) from fetuses of CRL from 10.5 to 28.5 cm, areolar tissue with several capillaries was observed at the inner margin of the junction between the cartilaginous socket and the labrum (Figs. 11A,B). This area had a lighter staining reaction than the labra proper or the hyaline cartilage portion of the acetabulum. In serial sections, vessels at this junction could be traced from the perichondrium to the articular surface of the labrum. No vessels were traced from the socket proper into the labrum. In all seven specimens, the areolar tissue at this junction was observed on the anterosuperior portion of the socket labrum (socket orientated in the anatomical position). In three specimens, this area was present for the entire length of the anterior rim of the socket. In four specimens, this area had disappeared by the midpoint of the anterior rim length. The areolar tissue in another four specimens was replaced in later sections by a distinct cleft. In one specimen (Fig. 11C) the cleft was present for 26 percent of the total socket circumference. On macroscopic examination of these acetabula, and under a dissecting microscope, the labra had appeared normal.

DISCUSSION

Laurenson [15], in a small sample of arthrograms, concurred with Morville's [23] observation that the osseous roof of the acetabulum was flat, but also noted on histological sections that the medial or posterior perichondral border was more prominent than the lateral or anterior spur. His observation supports Badgley's [24] finding of greater growth posteriorly. In the present study, sections from the superior quarter level of the acetabulum were studied because this area corresponds to the region which forms the roof of the socket. It is this area that will receive and transmit forces in the upright posture and limit the superior motion of the head of the femur. These findings confirm Laurenson's observation that development is more prominent on the posteromedial side than on the anterolateral side. From the first instance in which signs of ossification can be detected in the floor of the socket, osseous tissue was more prominent on the medial or ischial side. As also noted by Badgley [24], ossification in this study was not observed to occur in the sides of the socket, even in sections from term fetuses. The detailed observations made by Gardner and Gray [7] on the relative development of the three primary centers have been corroborated in this study. The iliac primary center appears first close to the lesser sciatic notch and spreads outward in a triangular manner. It is therefore not surprising that, in sections from the superior quarter level of the acetabulum, ossification was detected initially more posteriorly in the socket.

It is well known that pressure is an important stimulus to bone development. The typical fetal posture of flexion and abduction may direct forces along the long axis of the femur to the acetabulum, providing a stimulus for greater development of the socket floor in relation to the socket wall, the pattern seen in this series.

The present examination of sections from young fetuses has confirmed previous reports [5,7,8,12] that the cartilaginous anlage of the acetabulum resembles in form



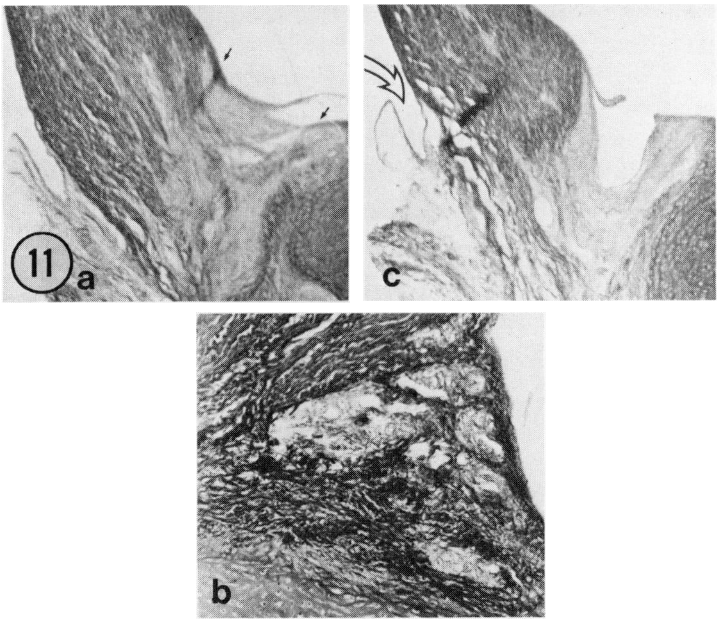


PLATE 3 EXPLANATION OF FIGURES

FIG. 10A. The typical appearance of the labrum, with loosely packed but parallel arranged fibers, here from a 13.7 cm CRL fetus (about 14 weeks). The articular surface is on the right; an arrow indicates the capsular sulcus. Alcian blue and van Gieson, × 2, 15 μm.

FIG. 10B. Articular surface of the labrum shown in Fig. 10A. Typical chondrocytes, in lacuna (*arrows*) were only observed in a narrow, basophiliac staining strip, on the inner articular margin; elsewhere the cells resembled fibrocytes and the labrum stained acidophiliac. × 200, 15 μm.

FIG. 11. Defects at the cartilage-labrum junction. A typical junction is seen in Fig. 10A. These defects were only observed on the anterior side of the socket. Sections shown are from a 13.7 cm CRL fetus (about 14 weeks), 15 μm.

FIG. 11A. The area immediately adjacent to the cartilage of the socket proper (*arrows*) contains disorganized collagenous fibers and many capillaries. Alcian blue and van Gieson, × 16, 15 μm.

FIG. 11B. The disorganized arrangement of tissue at the junctional defect is shown at higher magnification (× 20). Hyaline cartilage is inferior, the joint surface is on the right, and the labrum is superior. Alcian blue and van Gieson.

FIG. 11C. A cleft is present in the region of the defect. This section is 600 μm from the section shown in Fig. 11A. Note that the fiber separation in the labrum above the defect, seen here and in Fig. 11A, is an artifact. The capsule sulcus is shown (*arrow*). Alcian blue and van Gieson, × 16, 15 μm.

the adult socket, and appears to be a deep hemispherical concavity. Further study is necessary to determine whether differential growth rates exist, within the socket during the fetal period, that may account for frequent observations of a shallow socket at term [5,7–9,12]. It is not established whether underdevelopment of the osseous acetabulum, as shown in radiographs of infants with congenital hip disease, is associated with underdevelopment of the cartilaginous portion of the acetabulum. Of interest is the finding that variant features were primarily located on the anterior rim and wall of the acetabulum [25], the same side that shows slower spread of osseous tissue.

Kobayashi and Mizuno [16], from measurements on radiographs of the angular values of the socket and the labrum, also concluded that the socket is shallower at term, and commented that the labrum plays a role in neonatal hip stability. The present series confirms the impressions of this and other investigators that the labrum does contribute significantly to femoral head coverage, by forming from one-fifth to one-half of the total socket depth. Whereas the percentage of the socket formed by the labrum was shown to decrease with fetal growth, the labrum still appears to form a greater proportion of the socket at birth than it does in a mature hip.

Composition of the labrum is of interest because fibrocartilage may be expected to provide greater support to the femoral head than would a rim of regular, dense fibrous tissue. Sawada [19], in the only study published on the labrum at all ages, maintained that this structure is composed of fibrous tissue. He observed chondrocytes only at the articular margin. Most investigators, however, refer to the fibrocartilaginous labrum in the fetus [24,20,11] and in adult [26–28] while others have described a hyaline cartilage labrum in fetuses, newborns, and in an infant [7,18,20,29,30].

Observations made in the present study support Sawada's thesis. Typical round chondrocytes lying in lacunae, were found only at the inner articular margin of the labrum. At all ages the junction between the hyaline cartilage of the socket proper and the labrum was distinct. The staining reaction in the labrum was similar to that in the perichondrium or periosteum, both fibrous tissue structures predominantly composed of collagenous fibers. All the specimens in the present study, and in Sawada's study, were fixed in formalin. Matles [20] considered that the method of fixation was responsible for differences in histological appearance, because he noted in frozen sections not fixed in formalin that the labrum more closely resembled adult fibrocartilage. Further studies are indicated; however, there is no evidence to support the observations that the bulk of the labrum is hyaline cartilage.

The significance of the defects, observed in the labrum of seven acetabula and reported for the first time, with regard to the strength of the labrum is unknown. The areolar tissue with capillaries, which filled the area or surrounded a cleft, detectable by light microscopy, was observed only on the anterosuperior margin of the labrum. Sawada (personal communication) made similar observations, but did not comment on their possible significance in congenital hip disease. If these defects are artifacts of tissue preparation, it is reasonable to expect to observe them in a greater number of specimens. This type of structure may weaken the labrum and permit the femoral head to subluxate in an anterosuperior direction, the reported modal direction of subluxation in congenital hip disease (Stanisavljevic, personal communication).

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