

The ultrasound detection of chromosomal anomalies¹

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Second trimester findings.

In this section we will review the sonographic markers that can be used in second and third trimester fetuses.

Skeletal findings

In this section we will review the many skeletal findings that could be markers for aneuploidies. These include shortening of the limbs, clinodactyly, syndactyly, simian crease, radial ray aplasia, club foot, rocker bottom foot and sandal gap. Finally we will review other skeletal findings such as 11 pairs of ribs, hypoplasia of the clavicle, double ossification center of the manubrium and wide angle of the iliac wings.

Limb shortening

It has long been known that children with Down syndrome have shorter limbs than normal children. Beryl Benacceraf observed that in her population, a cut-off limit of 91% of the expected size of the femur compared to the BPD, had a sensitivity of 68% and a specificity of 98% in detecting fetuses with trisomy 21⁴. These specific numbers were not confirmed in other studies^{5,6}, although, clearly the trend has been, and it also has been extended to the finding of a short humerus⁷.

Brachymesophalangia of the fifth digit results from a too small middle phalanx of the fifth digit, which occurs in 68 percent of trisomy 21. Beryl Benacceraf studied the predictive value of this finding and found that if the middle phalanx of the fifth digit, is less than 70% of the middle phalanx of the fourth digit, there is a 70 percent chance of trisomy 21^{8,9}. Although few would make major clinical decisions on this finding, a hypoplastic middle phalanx is an important observation. Another anomaly commonly associated with brachymesophalangia is **clinodactyly**, in which the distal end of the fifth finger is bent towards the hand because of the deformed and hypoplastic middle phalanx.



Figure 1: In this image the middle phalanx of the fifth digit is too short.

A **clenched fist** is a typical finding of triploidy and trisomy 18. The overlapping of the finger gives the impression of a clenched fist that doesn't change during the examination. The typical finding is the overlapping of the third digit by the second digit and the fourth digit by the fifth digit.



Figure 2 The hand is a typical clenched fist from a trisomy 18 fetus. One can see the overlapping of the third digit by the second digit and the fifth digit over the fourth.

Simian crease

There are two normal transverse palmar creases: the proximal palmar crease and the distal palmar crease. In fetuses that do not open and close their hand often enough in the early gestation, only one crease develops and it is called the simian crease¹⁰. Simian creases are present in 4% of the normal population, in one hand, and 1% of the normal population, in both hands. They are mainly interesting because they are present in 45% of the fetuses with trisomy 21^{11, 12}. They also occur in trisomy 18, trisomy 13 and many conditions associated with decreased flexion of the hands such as skeletal dysplasias. Although looking for simian crease prenatally might look very difficult, this is in fact fairly easy to do when the right conditions (amniotic fluid and semi-open hand) are present.



Figure 3 This fetus has a simian crease which is well visible.

What is the risk of trisomy 21 when a simian crease is found? To answer that question, let us assume a population of 10,000 fetuses. Since 4% of the normal population has a simian crease, they will contribute 400 cases from the 10,000 fetuses. Further since trisomy 21 occurs at a rate of 13:10,000 and since 45% of the fetuses with Trisomy 21 have a simian crease, out of those 13 fetuses, 6 will have a simian crease and will be added to our pool of simian creases from the 10,000 fetuses. Therefore the total number of simian creases that will be found will be 406 (400+6) and the likelihood of trisomy 21 when a simian crease is found is $6/406$, which is roughly 1.5%.

Radial ray aplasia is a typical finding of trisomy 18, with very few differential diagnosis such as the Holt Oram syndrome and the TAR syndrome (thrombocytopenia aplasia of the radius syndrome). The spectrum of radial ray aplasia includes absence of the radius, absence of the radius and thumb, or absence of the radius and the whole hand.



Figure 4 Radial ray aplasia with club hand in a trisomy 18 fetus at 19 weeks.

Another finding of trisomy 21 is **elevation of the first toe**. This can be seen by ultrasound because the first toe is no longer in the same plane as the other toes. In a sagittal section one can see the angle between the big toe and the rest of the foot.



Figure 5: Elevation of the first toe in a fetus with trisomy 21.

A **rocker-bottom foot** is a foot that has a convex sole, instead of a concave sole, due to a malposition of the calcaneus and talus. It is typically associated with trisomy 18.

A **sandal gap** is a slight interspace between the first and second toe, and this is a risk factor for trisomy 21¹³.

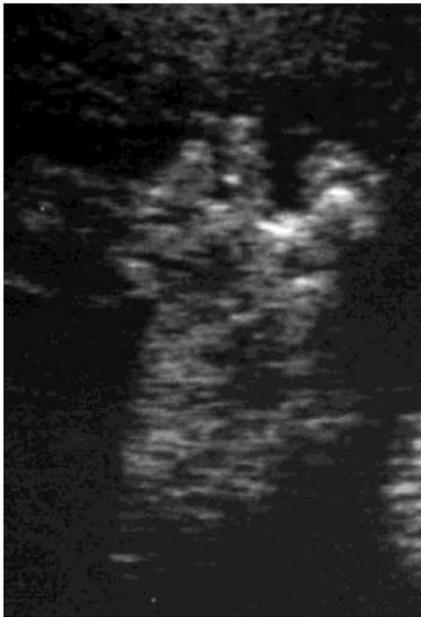


Figure 6 Scandal gap in a trisomy 21 fetus at 30 weeks.

Findings related to anomalies of the skull and skull shape.

Brachycephaly is a deformity of the head in which the skull appears to round, and this is manifested with a short occipitofrontal distance. This is measured by the cephalic index, which is the ratio of the biparietal diameter over the occipital frontal diameter, and normal values should be between 75 and 85 percent. If the cephalic index is greater than 85 percent, then fetus has brachycephaly. If the head is too flat side to side, the condition is referred to as “scaphocephaly”, something that we can find in fetuses that have in-utero crowding or premature rupture of the membranes for instance. This finding is not related to aneuploidy. Brachycephaly is a reliable indicator in children with trisomy 21 but it is a less reliable criterion in fetuses.

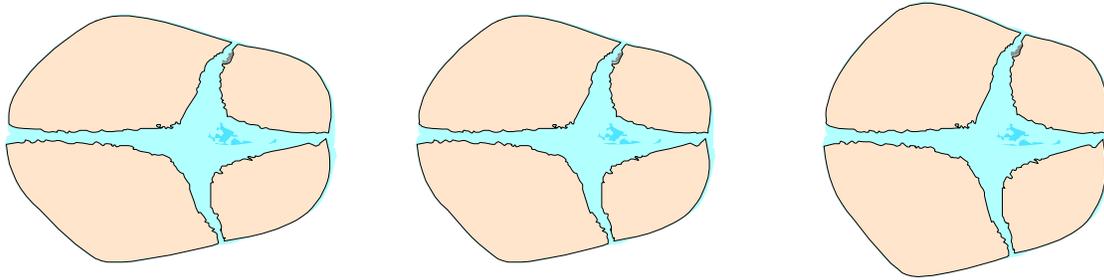


Figure 7: The first skull is too flat side to side, a condition referred to as “scaphocephaly”. This is not associated to aneuploidies. The middle skull is the normal one, while the right skull has brachycephaly.

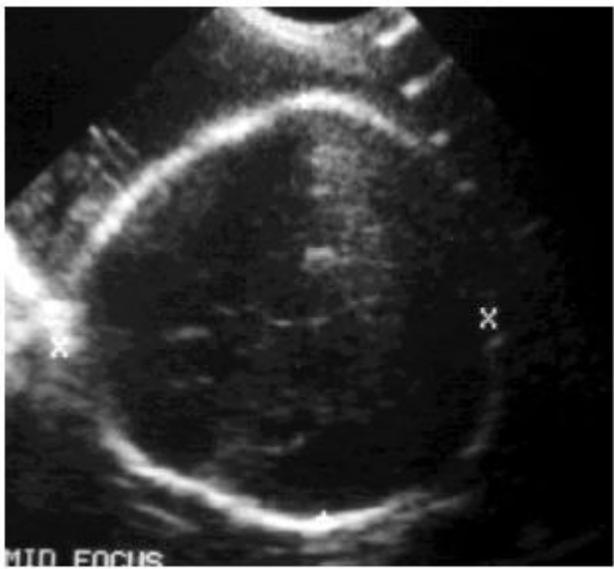


Figure 8: This is an example with obvious brachycephaly: the cephalic index does not need to be measured in such obvious cases.

A **strawberry head** is a head that has a deformity with narrowing of the frontal region and flattening of the occipital region. Strawberry heads are markers for trisomy 18 and they have not been found, at least yet, without other associated anomalies.

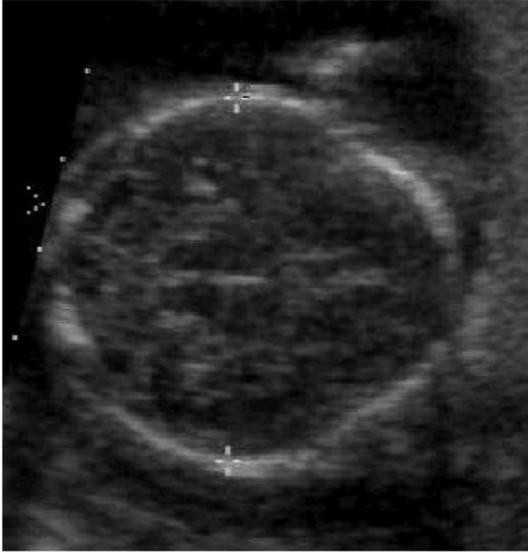


Figure 9: Typical images of “strawberry head” in a fetus with trisomy 18.

Eleven pairs of ribs

The presence of 11 pairs of ribs may be an indicator of aneuploidy. Five percent of the normal population has 11 pairs of ribs. The interest for this lecture is that it occurs in a third of fetuses with trisomy 21 and it also occurs in fetuses with trisomy 18. It is also present in some skeletal dysplasias such as camptomelic dysplasia and cleido-cranial dysplasia^{14, 15, 16}. Counting 11 pairs of ribs used to be very tedious: one used to have to take a single section that would include all pairs of ribs and not omit any. With the advent of cineloop it became easier to take a sweep through the rib cage, and then to go back and forth through the ribs on each individual frames. But now the problem has become much easier with use of 3-D ultrasound in which a single reconstruction demonstrates all the ribs.



Figure 10: 3D reconstruction of the spine and rib cage. By spinning the array around it is easier to identify all the ribs.

Hypoplasia of the clavicle is a common finding of trisomy 18. The length of the clavicle expressed in mm should be about equal to the gestational age expressed in weeks. Therefore, a 22 -week fetus should have a clavicle that measures about 22 mm.

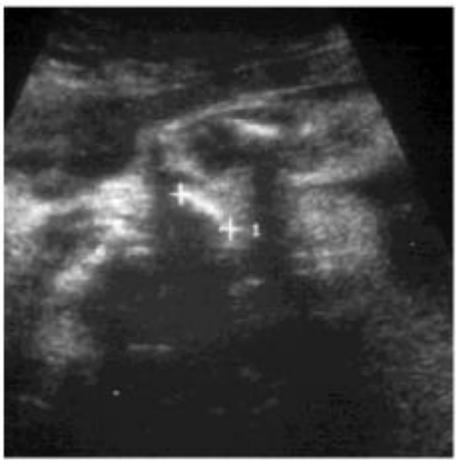


Figure 11: This clavicle belongs to a fetus with trisomy 18, and it is much shorter than the expected length for the gestational age.

Iliac wing angle

Borg has a recently demonstrated that the increase in the angle between the iliac wings, which has been a staple of the radiological diagnosis of trisomy 21 for many years, could also be recognized prenatally by

ultrasound¹⁷. In his nomogram, in an axial view of the pelvis, the angle between the iliac wings should be less than 70 degrees plus or minus 15 degrees. In his studies, fetuses with trisomy 21 had iliac wing angles > 100 degrees plus or minus 10 degrees.

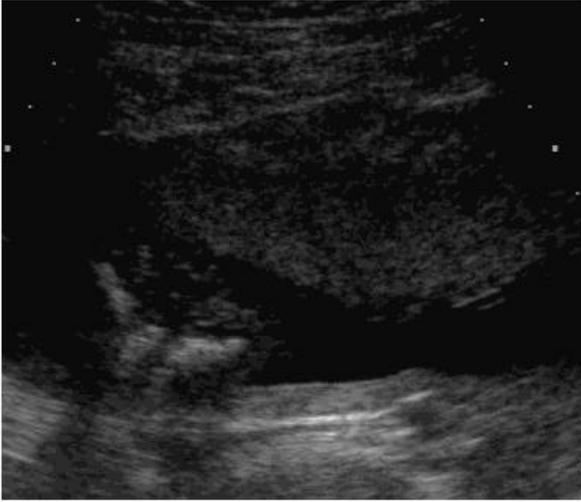


Figure 12 Widened iliac wing angle in a fetus with trisomy 21.

A **double ossification center of the manubrium** is another marker for aneuploidy. One would look for two ossification centers in a craniocaudal alignment, which distinguishes the ossification center of the manubrium from the ossification centers of the sternebrae, which are side-by-side. Ossification of the manubrium starts in the fifth month of the pregnancy. At first the manubrium appears as a hypoechoic center, then as it ossifies it becomes hyperechoic. A double ossification center of the manubrium is present in 10 percent of the normal population, but it is also present in 33 to 80 percent of trisomy 21, and 25 percent of monosomy X.

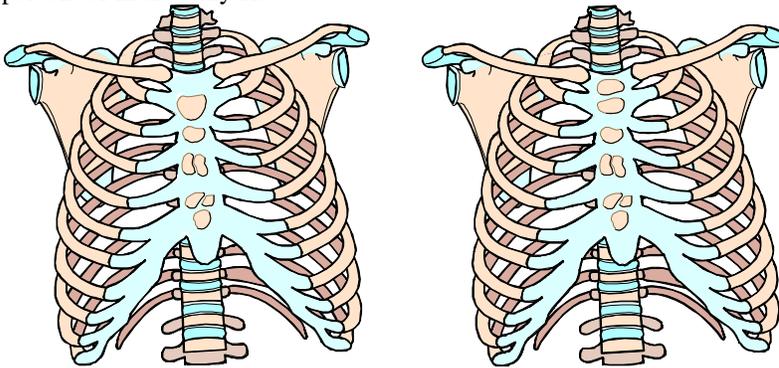


Figure 13 A double ossification center of the manubrium present as two ossification centers in a craniocaudal alignment, which distinguishes the ossification center of the manubrium from the ossification centers of the sternebrae, which are side-by-side (normal on the left, abnormal on the right).



Figure 14 This is a sagittal section of a trisomy 21 fetus in the third trimester (head to the left) and the double ossification center of manubrium (arrows), and the ossification centers of several of these sternbrae can be seen.

Growth restriction

Less than 1% of fetuses that suffer from growth restriction have an aneuploidy. Growth restriction is most typical of triploidy, trisomy 13 and trisomy 18. The association between IUGR and aneuploidy is more likely if the IUGR is already detected in the second trimester. A very typical finding of triploidy for instance is a very large head to abdomen disproportion, in which the abdomen is much smaller than the head size.

References

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