The ultrasound detection of chromosomal anomalies[1]

Werther Adrian Clavelli, MD[2], Silvia Susana Romaris de Clavelli, MD[2], Philippe Jeanty, MD, PhD[3]

Adapted from "The Ultrasound Detection of Chromosomal Anomalies—A multimedia Lecture" by Philippe Jeanty. ISBN (0-9667878-0-3) available at www.prenataldiagnosis.com and www.TheFetus.net

Second trimester findings.

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

Central nervous system

Ventriculomegaly is a common finding that occurs in 5 to 25 per 10,000 deliveries. The normal measurement of the atrium should be less than 10 mm at any time during gestation. When it is between 10 and 15 mm (the gray zone) it is suspicious for aneuploidy, when it is greater than 15 mm it is more likely to represent hydrocephalus.

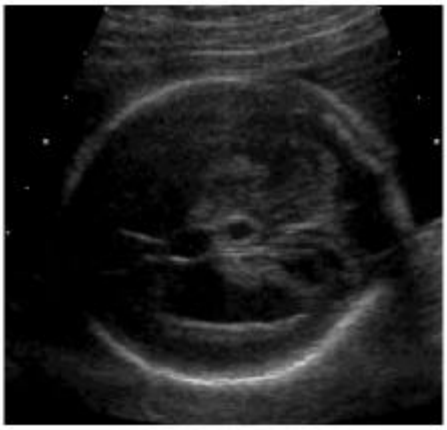

Figure 1: Mild ventriculomegaly can be a sign of aneuploidy.

About 15% of fetuses with ventriculomegaly will have an aneuploidy, only 2 percent if the hydrocephalus is isolated, but 17 percent if other findings are noted. And ventriculomegaly is not a predictor of a particular type of aneuploidy.

Choroid plexus cysts occur in one percent of the normal population. According to the literature about 30 to 60 percent of fetuses with trisomy 18 have choroid plexus cysts. Further, about 97 percent of fetuses that have trisomy 18 and choroid plexus cysts have associated anomalies.

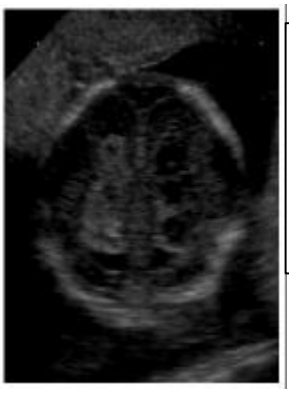

Figure 2 Choroid plexus cysts in a fetus with trisomy 18. The CPC are indistinguishable from those of normal fetuses.

The question of "Should we do in amniocentesis for fetuses that have a choroid plexus cyst" has come up many times. And this is one of the ways to answer the question[4]: let us assume a population of one million fetuses. Since the incidence of choroid plexus cyst is one percent in midtrimester fetuses, among one million fetuses 10,000 will have a choroid plexus cyst and be normal. Further since the incidence of trisomy 18 is three per 10,000, in that million fetuses 300 will have trisomy 18. And since the prevalence of choroid plexus cyst in trisomy 18 is 30 percent, the fetuses with trisomy 18 in this million fetuses will be contributing 100 cases of choroid plexus cysts to the pool of choroid plexus cysts. Further since the sensitivity of ultrasound in detecting trisomy 18 is 75 percent, of those 100 fetuses that have trisomy 18 and a choroid plexus cysts, 25 would be missed by a normal ultrasound alone. Therefore altogether, 25 fetuses with trisomy 18 and a choroid plexus cyst would be missed out of 10,075 fetuses that have a choroid plexus cyst and are correctly identified either as normal or as having trisomy 18. This is roughly a miss of one in four hundred fetuses with only a choroid plexus cyst and trisomy 18. This is the reason why doing amniocentesis in fetuses that have only a choroid plexus cyst and no other finding is probably not worthwhile, because in order to detect that fetus with trisomy 18, one would have to do four hundred amniocentesis in normal fetuses. If one assumes that the risk of miscarriage after amniocentesis is 1:200 or even 1:400 this would risk the lives of one to two normal fetuses to detect one fetus with trisomy 18 whose outcome is dismal anyway.

Dysgenesis of the corpus callosum may be an isolated finding of little significance but may also be associated with trisomy 13 and 18 in which case it is rarely an isolated finding. The ultrasound finding include widening of the interhemispheric fissure, the teardrop shaped lateral ventricles and colpocephaly.

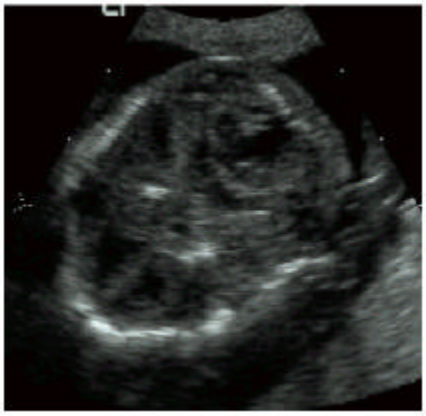

Figure 3: Dandy-Walker variant in trisomy 13.

The presence of an enlarged cisterna magna or a **Dandy Walker malformation**, either with a blocked fourth ventricle or a communicating fourth ventricle may also be an indicator of aneuploidy. Isolated Dandy Walker cysts is not at much risk, however when associated anomalies are present the risk is about 50% and is predominantly for trisomy 13 and trisomy 18.

Holoprosencephaly occurs in one per 10,000 deliveries. Fetuses with holoprosencephaly have a higher risk of aneuploidies than those with simple ventriculomegaly. About a third will have an aneuploidy, if holoprosencephaly is isolated while if other anomalies are noted almost 40 percent will have an aneuploidy. This is thus a very significant finding. and trisomy 13 and 18 are the most likely aneuploidies.

Microcephaly occurs in 10 per 10,000 deliveries. This is a difficult diagnosis to make. The commonly used criteria include a BPD less than the first percentile or a head perimeter over femur length less than the 2.5 percentile[5],[6]. The BPD is a difficult criterion to use the BPD is not very much affected by microcephaly. What is affected is the size of cranial vault compared to the size of the face, something that is easier to see in a sagittal section of the head. 20 percent of fetuses with microcephaly have an aneuploidy.

Head and neck

Facial clefts occur in 14 per 10,000 delivery, and they are associated with several aneuploidies such as trisomy 13 and 18, but others such as 4p- syndrome may also have clefts.

Micrognathia to is a nonspecific finding but it can be associated with trisomy 18, trisomy 13 and triploidy. This is easier to see in a sagittal section of the face.
These are two normal sagittal views of the profile, and notice the position of the chin, compared with the middle section, which is that of a fetus with trisomy 18, both the ultrasound image and the image after delivery.

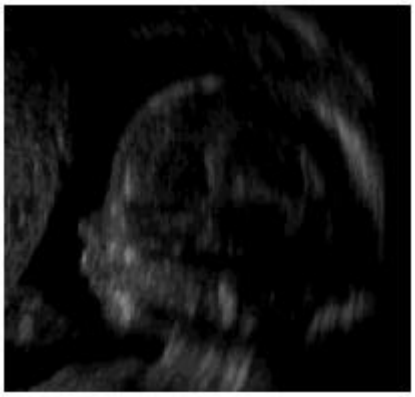

Figure 4: Micrognathia. Note the small chin and compare to the postnatal appearance in this trisomy 18 fetus.

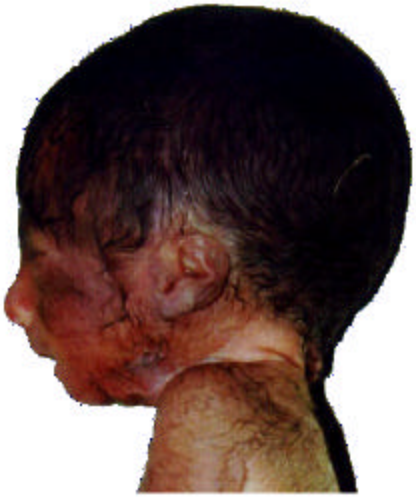

Figure 5: Micrognathia. Note the small chin and compare to the ultrasound appearance in this trisomy 18 fetus.

Macroglossia is the presence of a too large tongue and it is typical of trisomy 21 and the Beckwith-Wiedeman syndrome. Normally the tongue should not pass the alveolar ridge of the teeth. But in cases of macroglossia the tongue extends pass the teeth buds.

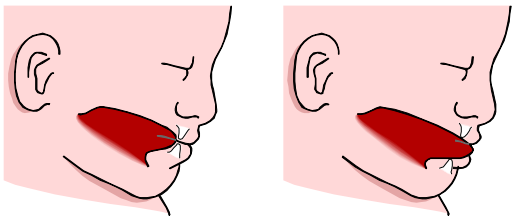

Figure 6: In macroglossia the tongue extends pass the teeth buds.

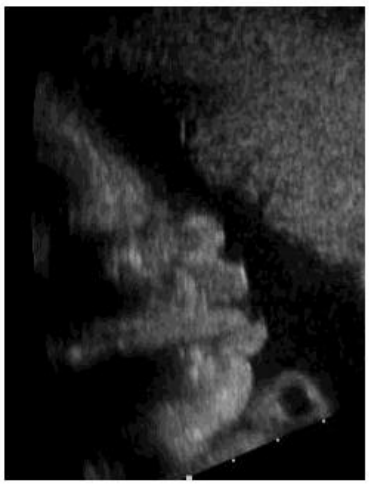

Figure 7: Macroglossia.

A **nuchal fold** is usually considers abnormal if it is greater than 6 mm between 15 and 22 weeks. Although the measurement can be obtained in sagittal section of the head and neck, it is more typically obtained in the axial section of the head going through the cerebellum. Even an isolated a nuchal fold is a significant finding, mainly a predicting factor for trisomy 21.

Cystic hygroma is a very common finding, it occurs in 0.5 percent of all the spontaneous abortion. It is also associated with hydrops in 40-100%, congenital heart defect in 0-92% of the cases, and with aneuploidy in about 46-90% of the cases. Cystic hygroma can be localized in the back of the neck, or may extend further down the back of the embryo or fetus.

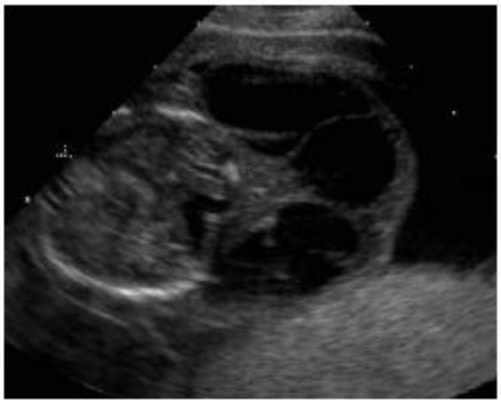

Figure 8: This is a large cystic hygroma in a fetus with monosomy X "Turner's syndrome", and all what appears to be amniotic fluid behind the neck of fetus is in fact a large cystic hygroma. Observe not only the large cysts, but also to the large septations that separate the cysts. Those septations help differentiate the condition from cephaloceles.

Ears that are too small, too round or have a malformed helix may be associated with trisomy 13, 18, 21 monosomy X and several other translocations. Therefore in the proper context the finding of an abnormal ear may suggest the need for a karyotype.

Microphtalmia are eyes that too small and is often associated with hypotelorism. Microphtalmia is associated with several aneuploidies. Notice that in the image the eyes are also a bit more echogenic and then they would normally appear.

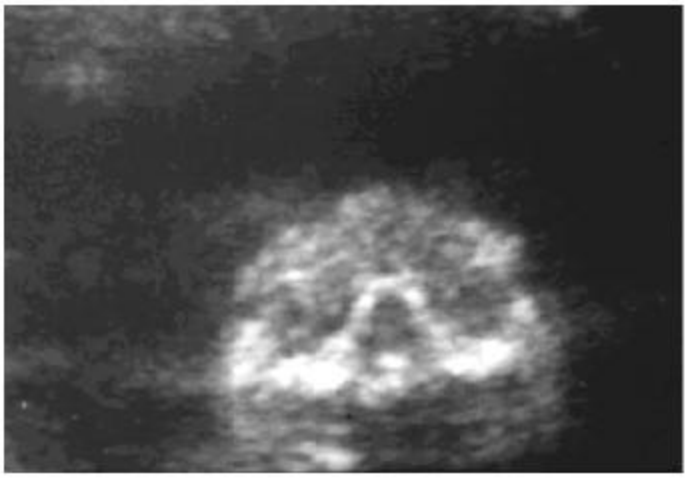

Figure 9: Microphtalmia is associated with several aneuploidies. Notice that in the image the eyes are also a bit more echogenic and then they would normally appear

The finding of **hypotelorism** should suggest that the fetus might have cyclopia and proboscis, which are typical of holoprosencephaly and thus associated with trisomy 13. Hypotelorism is a decrease of the interocular distance, and fetuses will have an inter-ocular distance less than a third of the binocular distance.

A **cataract**, which is an opacification of the lens of the eye, is a finding that may be associated with aneuploidy. It is associated with other conditions such as the TORCH infections but it may also be associated with aneuploidy. The way to observe it is to make a section through the eye and observes echoes of low level intensity inside the lens.

Wormian bones, described by a Dr. Olaus Worm, a Danish anatomist from the 16-century, are little bones that occur in the fontanels and sutures. They are also called Inca bones. They may occur in several

disorders including trisomy 21, cleido-cranial dysplasia, osteogenesis imperfecta, hypothyroidism, pycknodysostosis and progeria.

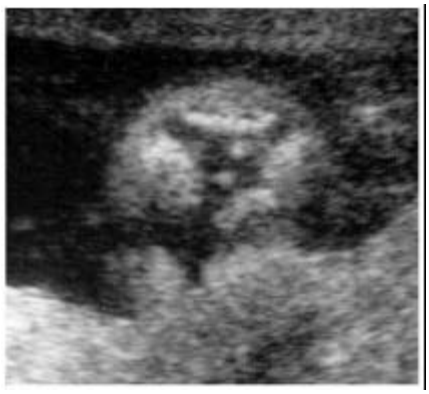

Figure 10: Two small wormian bones in the posterior fontanel.

Hypoplasia of the nose is a typical finding of trisomy 18.

A **low nasal bridge** is a common finding to many aneuploidies, but it is also common in other conditions such as the skeletal dysplasias. The portion that is hypoplastic is the nasal spine, and when it is too small it appears as if the nose base is too low. This is seen by ultrasound as a continuous dark echo between the eyes of the fetus.

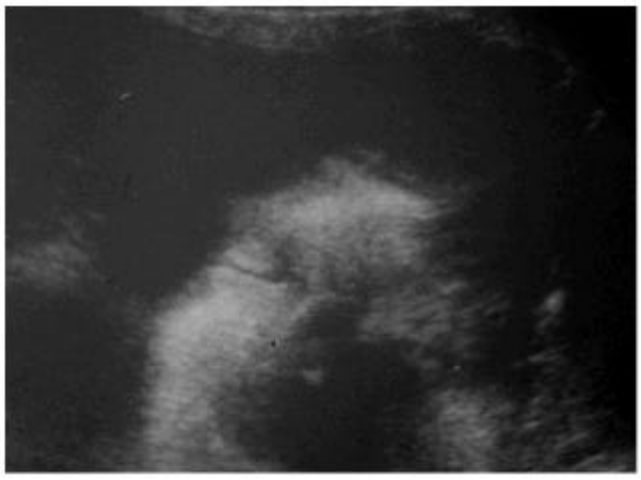

Figure 11 Low nasal bridge in a fetus with trisomy 21.

References

[1] Adapted from "The Ultrasound Detection of Chromosomal Anomalies—A multimedia Lecture" by Philippe Jeanty. ISBN (0-9667878-0-3) available at www.prenataldiagnosis.com and www.TheFetus.net

[2] Diagnostico Maipú, Buenos Aires, Argentina clavelli@arnet.com.ar

[3] Women's Health Alliance, Nashville, TN

[4] Benacerraf BR, Harlow B, Frigoletto FD Jr: Are choroid plexus cysts an indication for second-trimester amniocentesis? Am J Obstet Gynecol 1990 162(4):1001-1006

[5] Chervenak FA, Jeanty P, Cantraine F, Chitkara U, Venus I, Berkowitz RL, Hobbins JC: The diagnosis of fetal microcephaly. Am J Obstet Gynecol 1984 Jul 1;149(5):512-517

[6] Chervenak FA, Rosenberg J, Brightman RC, Chitkara U, Jeanty P: A prospective study of the accuracy of ultrasound in predicting fetal microcephaly. Obstet Gynecol 1987 Jun;69(6):908-910