Diploma in Fetal Medicine & ISUOG Educational Series

[11 - 14 weeks scan]

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REVIEWED
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Chapter 4 - DIAGNOSIS OF FETAL ABNORMALITIES

The early pregnancy scan was initially introduced with the primary intention of measuring the fetal crown–rump length to achieve accurate pregnancy dating. During the last decade, however, improvement in the resolution of ultrasound machines has made it possible to describe the normal anatomy of the fetus and diagnose or suspect the presence of a wide range of fetal defects in the first trimester of pregnancy. In some conditions, the sonographic features are similar to those described in the second and third trimesters of pregnancy, but in others there are characteristic sonographic features confined to the first trimester.

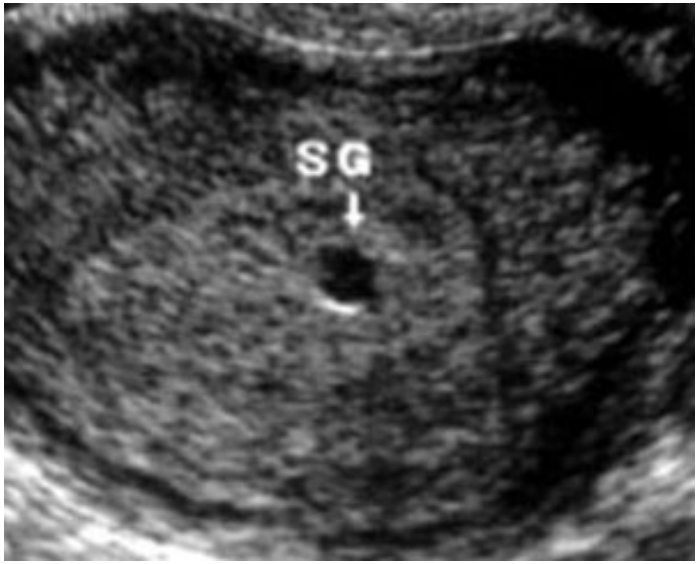
NORMAL FIRST-TRIMESTER ULTRASOUND FINDINGS

Normal human embryogenesis is a stereotyped sequence with little statistical variation, but menstrual data in individual cases may be unreliable in dating this sequence'[1]. An embryo of 10 postmenstrual weeks is less than half the length of an adult thumb, but already possesses several thousand named structures, practically any of which may be subject to developmental deviations[2]. Thus, the embryonic period proper is of particular importance because the majority of congenital anomalies make their appearance during that time[2]. These statements from embryological investigations have become highly relevant for those involved in first-trimester ultrasound scanning.

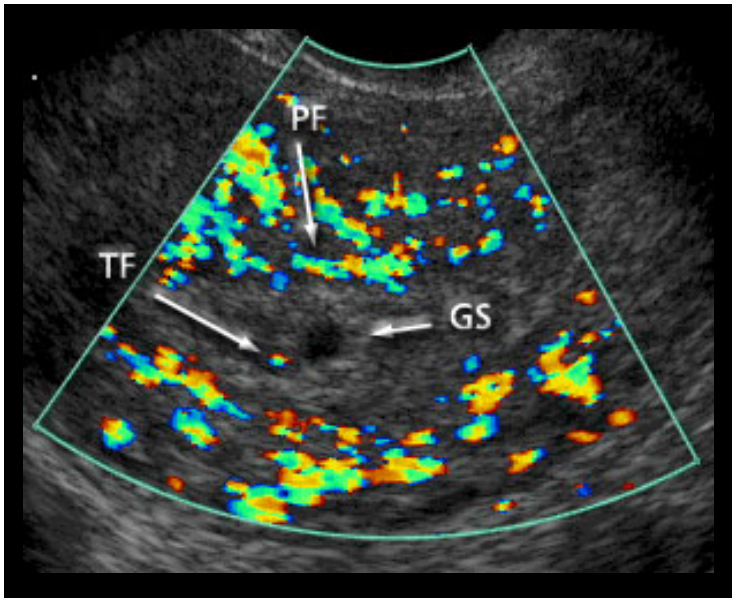
The term sonoembryology[3] designates the description of the embryonic anatomy, the normal anatomic relations and the development of abnormalities as visualized by ultrasound. To confirm the presence of normal anatomy or to make the diagnosis of an anomaly, we need knowledge of the normal embryonic development, including the appearance of the normal embryo. This section is based on data from sonoembryological and embryological studies[4–13]. For the ultrasound studies, 7.5-MHz transducers were used.

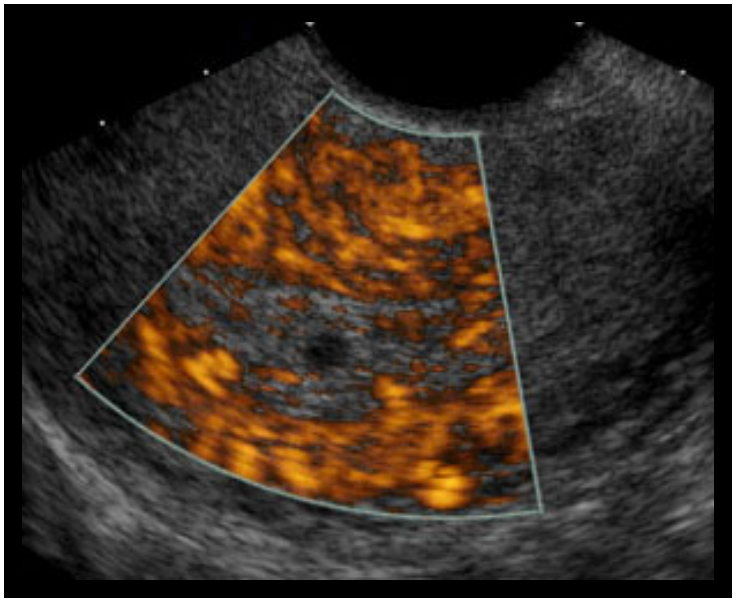
4 weeks

At 4 weeks and 3 days, a tiny gestational sac becomes visible within the decidua.



Uterus (transverse view); Gestational Sac (arrow) and the decidual reaction



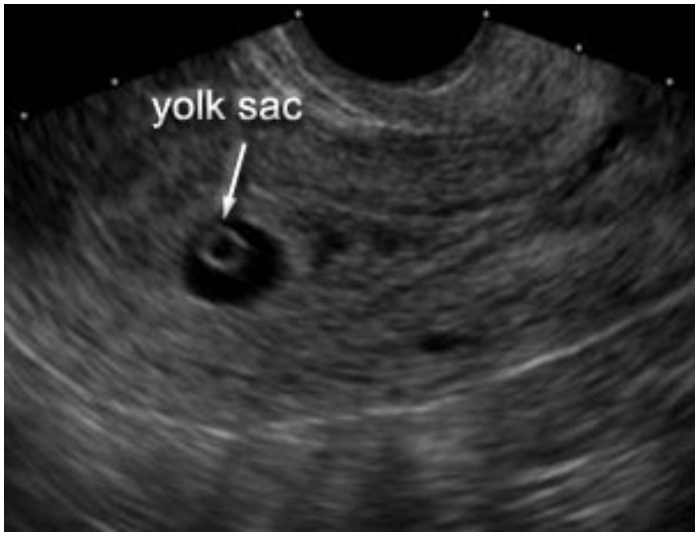


Uterus (longitudinal view) with identification of the Gestational Sac (5,0mm mean diameter) and color doppler maping of the uterine vessels, trophobastic flow (TF) and peri-endometrial flow.

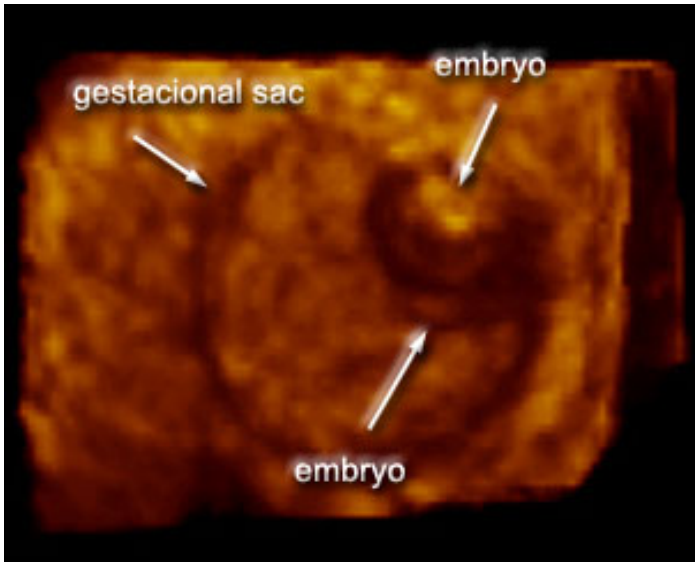
Uterus (longitudinal view) with identification of the Gestational Sac (5,0mm mean diameter) and color doppler energy maping of the uterine vessels

5 weeks

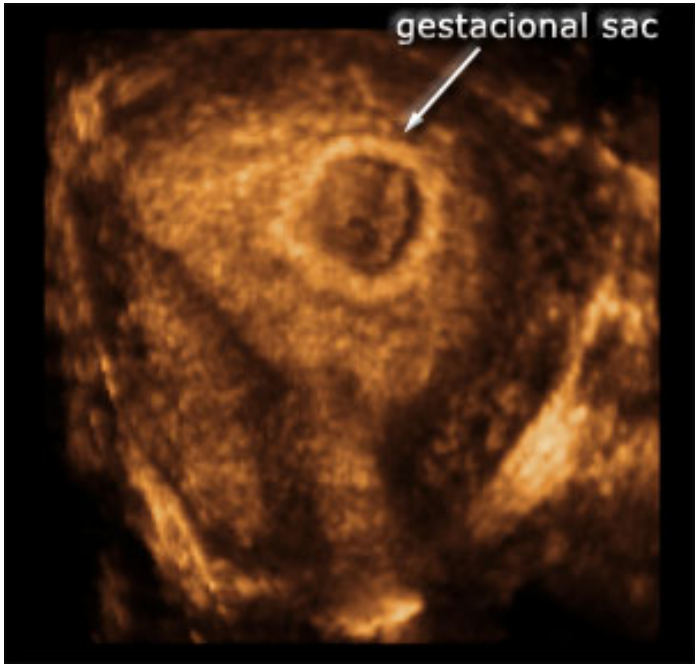
The yolk sac is first visible at 5 weeks and it is always present by 5 weeks and 4 days. There are lacunary structures at the site of implantation. The embryonic pole appears adjacent to the yolk sac, soon showing cardiac activity. Since the connecting stalk is short, the embryonic pole is found near the wall. At the end of week 5, the heart rate is about 100 bpm.



Longitudinal view of the uterus
Gestational Sac + Yolk Sac (embryionic pole not visible)



end of the week 5 and visualization of the embryo



Coronal section showing the implantation (fundus+left corno), normal decidual reaction

6 weeks (crown–rump length 4–8 mm)

The embryonic pole, yolk sac and heart activity are now always present. The heart rate increases to 130 bpm. At the end of week 6, the first sign of the rhombencephalic cavity appears as a tiny hypoechogenic area in the cranial pole of the embryo. The amniotic cavity can be seen surrounded by a thin membrane around the embryo.

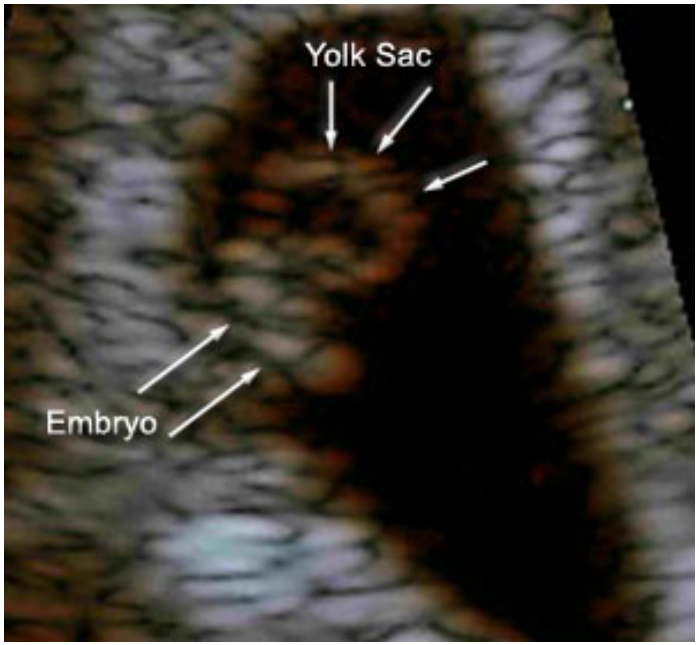


Figure 1a - Embryo at 6 weeks (crown–rump length 5 mm). Coronal section with arrows pointing to the embryo. The yolk sac lies adjacent to the embryo

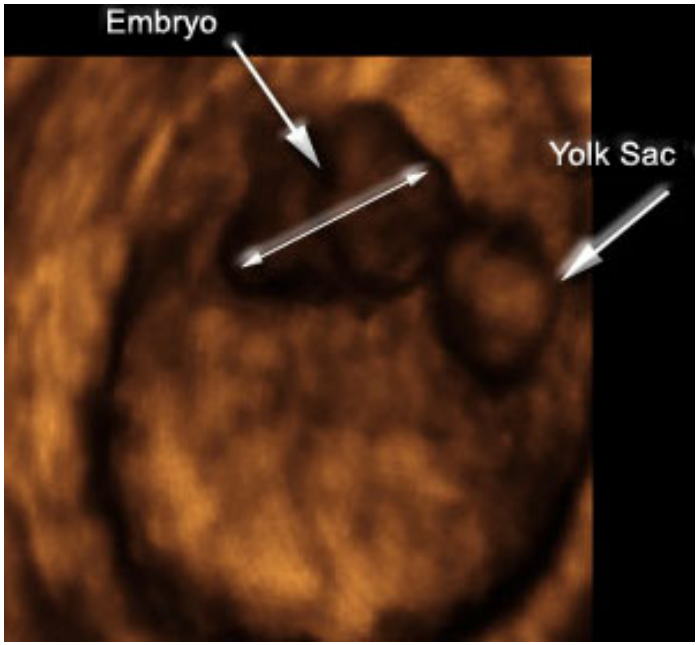


Figure 1b - Embryo at 6 weeks (crown–rump length 5 mm). 3D reconstruction with arrows pointing to the embryo (CRL). The yolk sac lies adjacent to the embryo

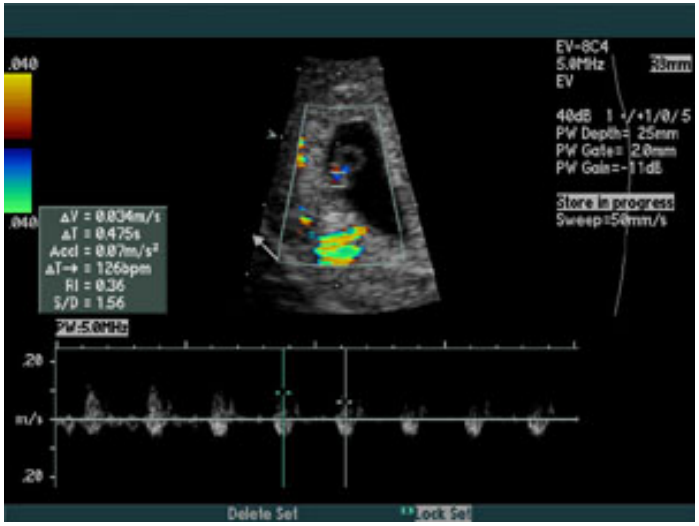


Figure 1c - Embryo at 6 weeks (crown–rump length 5 mm). Embryo cardiac ativity with a heart rate of 126 bpm.

7 weeks (crown–rump length 9–14 mm)

External form

The embryonic body appears as a triangle in the sagittal section. The sides consist of (1) the back, (2) the roof of the rhombencephalon, and (3) the frontal part of the head, the base of the umbilical cord, and the embryonic tail. The embryonic body is slender in the coronal plane. The limbs are short, paddle-shaped outgrowths.

Central nervous system

The hypoechogenic brain cavities can be identified, including the separated cerebral hemispheres. The lateral ventricles are shaped like small, round vesicles. The cavity of the diencephalon (future third ventricle) runs posteriorly. In the smallest embryos, the medial telencephalon forms a continuous cavity between the lateral ventricles. The future foramina of Monro are wide during week 7. In the sagittal plane, the height of the cavity of the diencephalon is slightly greater than that of the mesencephalon (future Sylvian aqueduct). Thus, the wide border between the cavities of the diencephalon and the mesencephalon is indicated. The curved tube-like mesencephalic cavity lies anteriorly, its rostral part pointing caudally. It straightens considerably during the following weeks. By week 8, it is regularly identified. The relatively broad and shallow rhombencephalic cavity is always visible from 7 weeks onwards. It then has a well-defined rhombic shape in the cranial pole of the embryo.

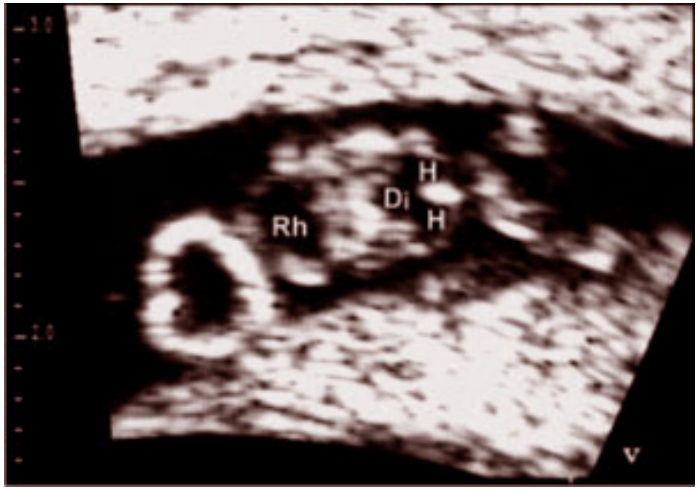
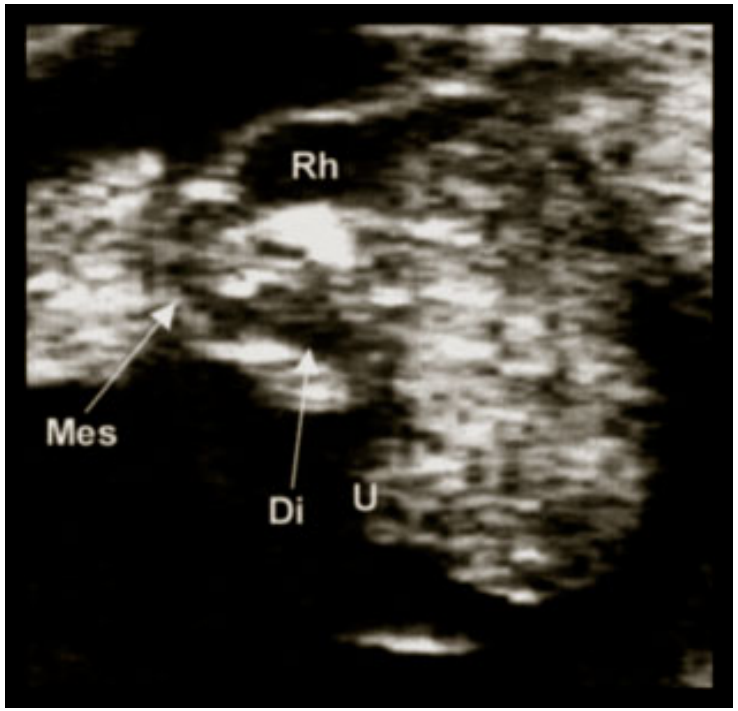


Figure 2 - Embryo at 7+2 weeks (crown–rump length 12 mm). Oblique transverse section through the head demonstrating the rhombencephalon (Rh), diencephalon (Di) and hemispheres (H). The connections between the lateral ventricles and third ventricle (foramina of Monro) are still wide. The echogenic ring to the left is the yolk sac



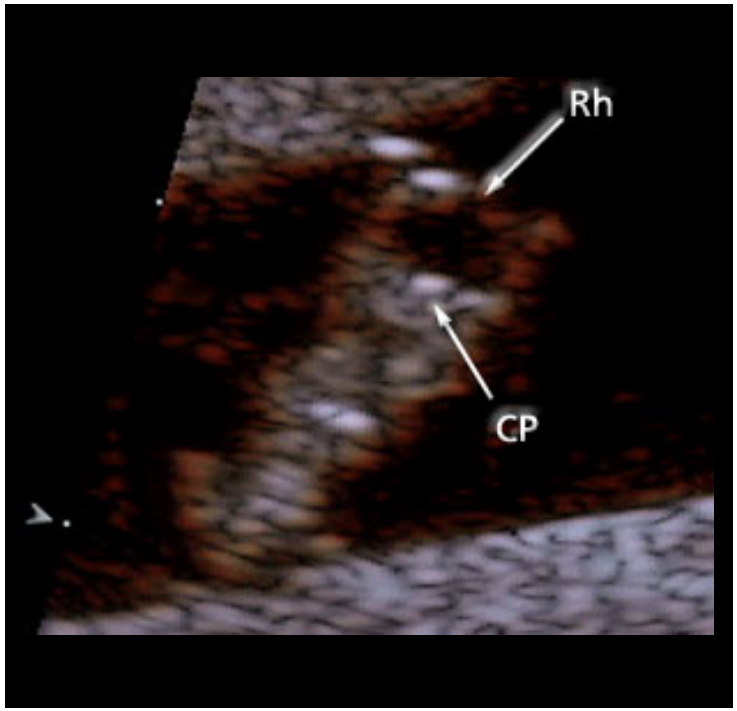


Figure 3a - Embryo at 7+5 weeks (crown–rump length 14 mm). Sagittal section through the 'triangular' body demonstrating the shallow cavity of the rhomben-cephalon (Rh), the curved tube-like mesencephalon (Mes), the diencephalon (Di) and the umbilical cord (U)

Figure 3b - Embryo at 7+5 weeks (crown–rump length 14 mm). Coronal section through the head and body demonstrating the shallow cavity of the rhomben-cephalon (Rh), choroid plexus (CP)

Heart

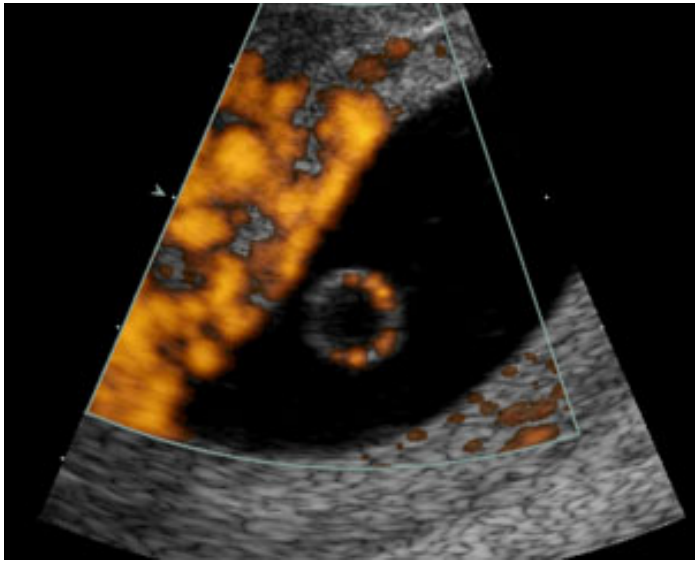
The heart can be recognized as a beating, large and bright structure below the embryonic head at 7 weeks. The heart rate increases from 130 bpm to 160 bpm. Details of the heart anatomy are not visible, but the atrial and ventricular compartments can sometimes be distinguished by the reciprocal movements of the walls.

Intestinal tract

The short umbilical cord shows a large celomic cavity at its insertion, where the primary intestinal loop can be identified. The first sign of herniation of the gut occurs during week 7 as a thickening of the cord and showing a slight echogenic area at the abdominal insertion. Within a few days, this echogenic structure becomes more distinct.

Extra-embryonic structures

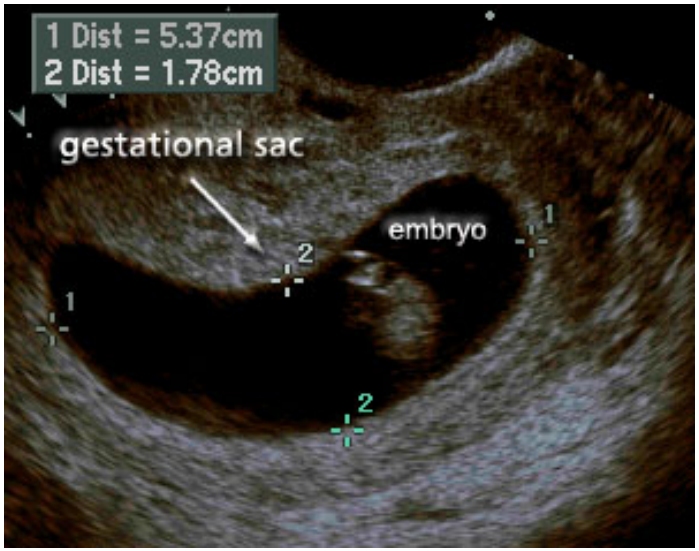
The amniotic cavity becomes visible at the beginning of week 7. The mean diameter of the amniotic cavity is almost the same as the corresponding crown–rump length.

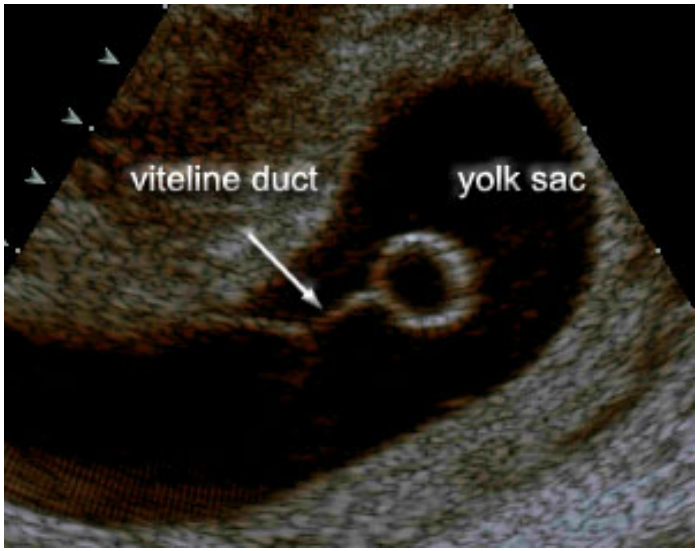


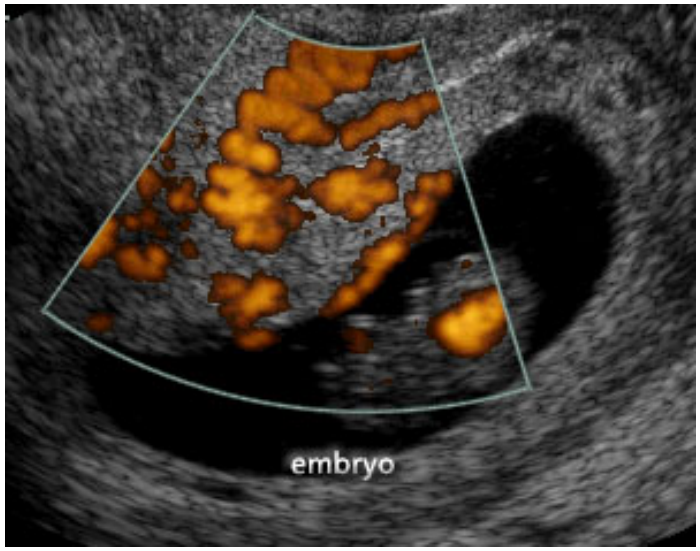
Identification of the yolk sac and the placenta vascularization and yolk sac

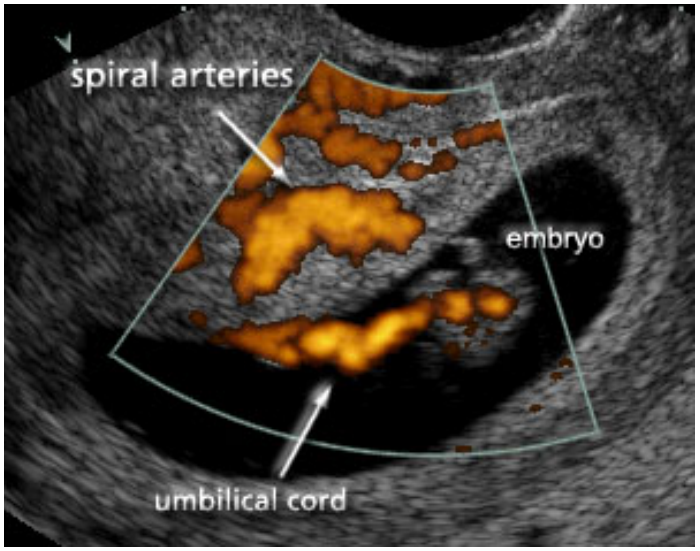
8 weeks (crown–rump length 15–22 mm)

Gestational Sac and Yolk Sac









External form

The body gradually grows thicker and becomes cuboidal. At the end of the week, the elbows become obvious, the hands angle from the sagittal plane and the fingers are distinguishable.

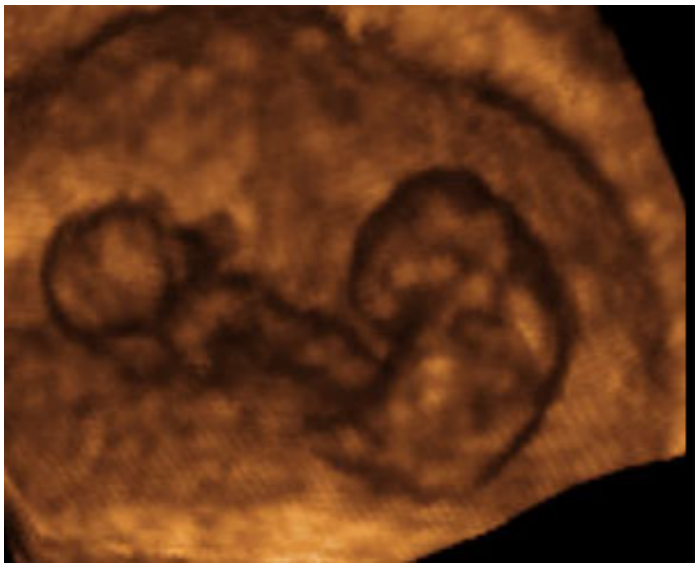


Figure 4 - 3D scan - the body grows, visualization the future upper and lower limbs.

Central nervous system

The brain cavities are easily seen as large 'holes' in the embryonic head. The hemispheres enlarge, developing via thick round slices originating antero-caudally from the third ventricle into a crescent shape. The choroid plexus in the lateral ventricles becomes visible as tiny echogenic areas. The future foramina of Monro become more accentuated during week 8. The third ventricle is still relatively wide, as is the mesencephalic cavity. At this stage, the mesencephalon lies at the top of the head. The increased growth of the rostral brain structures and the deepening of the pontine flexure leads to the deflection of the brain. The rhombencephalic cavity (future fourth ventricle) has a pyramid-like shape with the central deepening of the pontine flexure as the peak of the pyramid. The first signs of the bilateral choroid plexuses are lateral echogenic areas originating near the branches of the medulla oblongata caudal to the lateral recesses. Within a short time, the choroid plexuses traverse the roof of the fourth ventricle, meeting in the mid-line and dividing the roof into two portions, about two-thirds are located rostrally and one-third caudally. In the sagittal section, the choroid plexuses are identified as an echogenic fold of the roof.

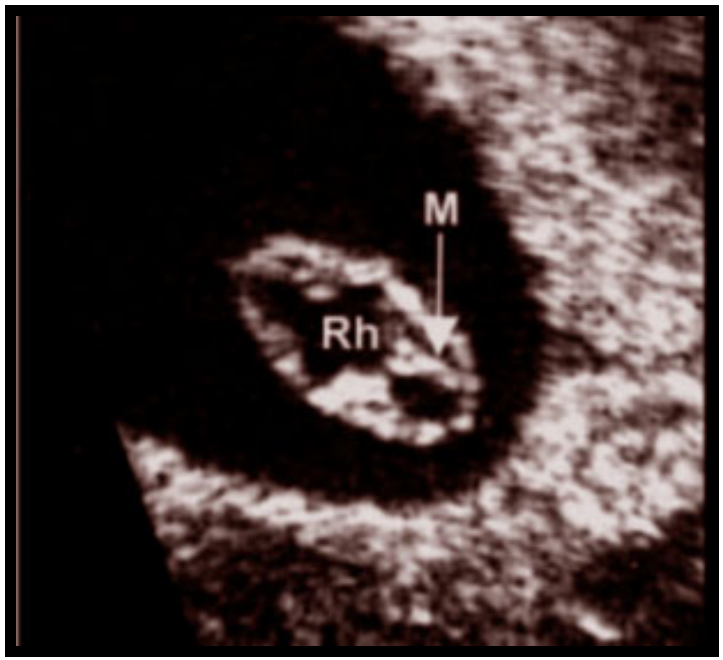


Figure 5 - Embryo at 8+1 weeks (crown–rump length 17 mm). Section through the rhomb-encephalon (Rh) and mesencephalon (arrow, M)

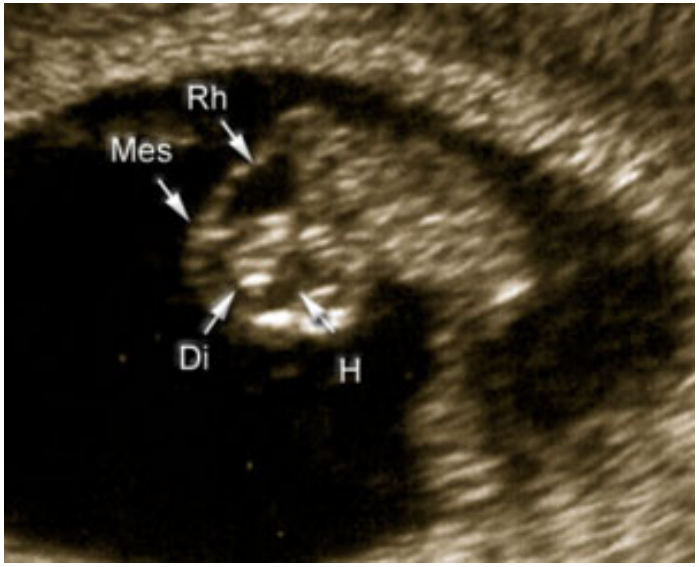


Figure 6 - Embryo at 8+5 weeks (crown–rump length 18 mm). Slightly parasagittal section demonstrating the ventricle of one hemisphere (H) leading through the foramen of Monro into the third ventricle, which is the cavity of the diencephalon (Di). The wide mesencephalic cavity (Mes) lies at the top of the head and the cavity of the rhombencephalon lies posteriorly. The arrow points at the choroid plexus of the rhombencephalon

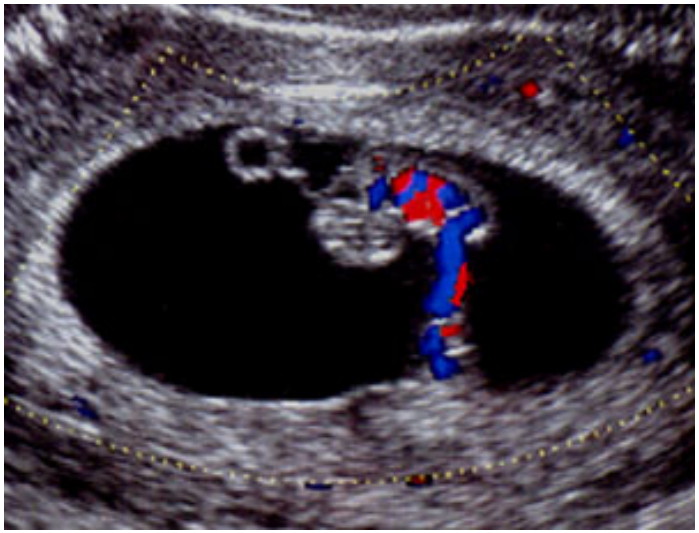


Figure 6a - Embryo at 8+5 weeks (crown–rump length 20 mm). Sagittal section vascularization and the umbilical cord.

Heart

The heart rate has increased to 160 bpm. Occasionally it is possible to identify the atrial and ventricular walls moving reciprocally as early as at the end of week 8. The atrial compartment appears wider than the ventricular compartment, and the heart covers about 50% of the transverse thoracic area. A kind of four-chamber view of the heart can then be obtained, where the atrial compartment is wider than the ventricular part.

Intestinal tract

There is no sign of the stomach during week 7. In some cases, it is possible to recognize the fluid-filled stomach as a small

hypoechogenic area on the left side of the upper abdomen below the heart at the end of week 8.

9 weeks (crown–rump length 23–31 mm)

External form

The body develops an ellipsoid shape with a large head. The soles of the feet touch in the mid-line at the end of the week. At the same time, it is possible to obtain acceptable images of the profile; thus, it should be possible to examine the mouth. The ventral body wall is well defined.

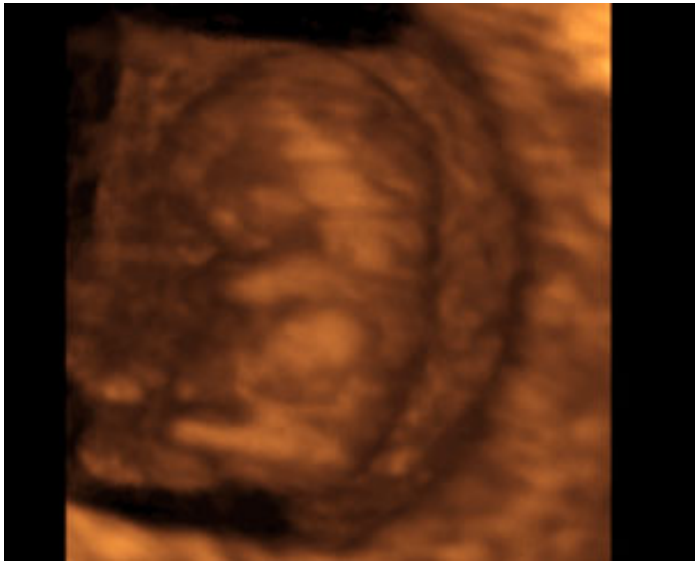


Figure 7 - Embryo at 9-10 weeks (crown–rump length 30 mm). 3D scan showing the external form of the fetal body (upper and lower limbs).

Central nervous system

The lateral ventricles are always visible. They are best seen in the parasagittal plane, where the C-shape becomes apparent. The cortex is smooth and hypoechogenic. The bright choroid plexuses of the lateral ventricles are regularly detectable at 9 weeks 4 days. They show rapid growth, similar to the hemispheres, and soon fill most of the ventricular cavities. The width of the diencephalic cavity narrows gradually, while the width of the mesencephalon remains wide. A distinct border (‘isthmus prosencephali’) has developed between the cavity of the mesencephalon and the third ventricle. The wall of the diencephalon, initially very thin, thickens considerably starting from week 8 to 9. The isthmus rhombencephali is always distinct. The cavity of

the mesencephalon remains relatively large, especially the posterior part. The height and the width are about the same size. During weeks 8 and 9, the rhombic fossa becomes deeper due to the progressive flexure of the pons. The lateral corners of the rhombencephalic cavity, called the lateral recesses, are easily identified at weeks 7 and 8. During this period, the distance between these recesses increases (rhombencephalon width). Later, during weeks 9 and 10, the lateral recesses often become covered by the enlarging cerebellar hemispheres. Thus, only the central part of the hypoechogenic fourth ventricle, which is divided by the choroid plexuses, is visible. The choroid plexuses of the fourth ventricle are bright landmarks, dividing the ventricle into rostral and caudal compartments. The cerebellar hemispheres are easily detectable. The primordia of cerebellar hemispheres are clearly separated in the mid-line during the embryonic period.

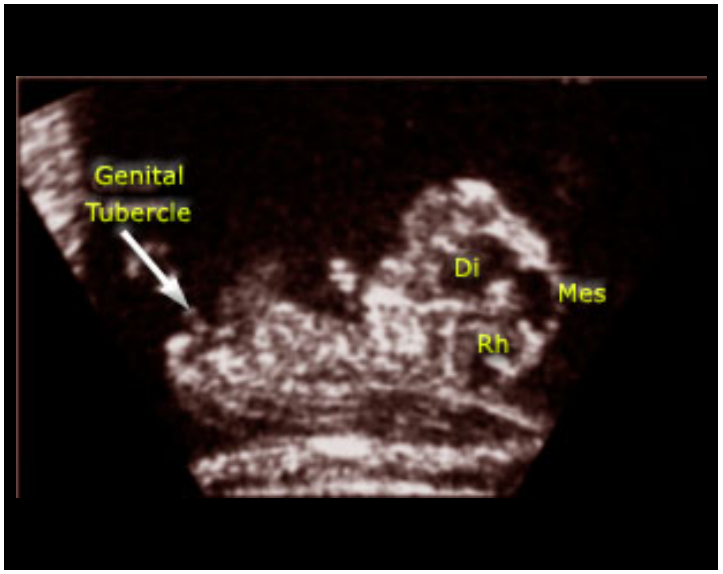


Figure 7a - Embryo at 9+4 weeks (crown–rump length 28 mm). Sagittal section demonstrating the relatively large head and the cavities of the diencephalon (Di), mesencephalon (Mes) and rhombencephalon (Rh). The arrow points at the genital tubercle, but at this stage it is not possible to differentiate between male and female gender

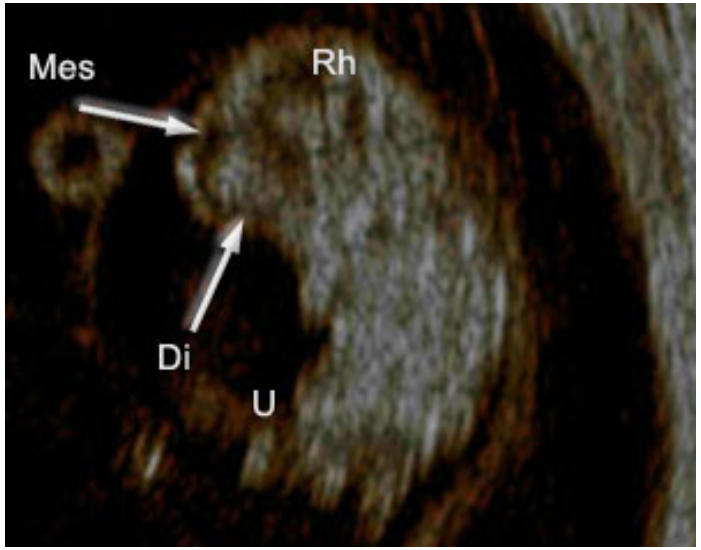


Figura 7b - Embryo at 9+4 weeks (crown–rump length 28 mm). Sagittal section demonstrating the relatively large head and the cavities of the diencephalon (Di), mesencephalon (Mes), rhombencephalon (Rh) and umbilical cord (U).

Heart

During week 9, the heart rate reaches a maximum of mean 175 bpm.

Intestinal tract

From 8 weeks 3 days to 10 weeks 4 days of gestational age, all embryos have herniation of the midgut, most distinctive during weeks 9 and 10. At this stage, the midgut herniation presents as a large hyperechogenic mass. The stomach can be detected in 75% of the embryos before 10 weeks.

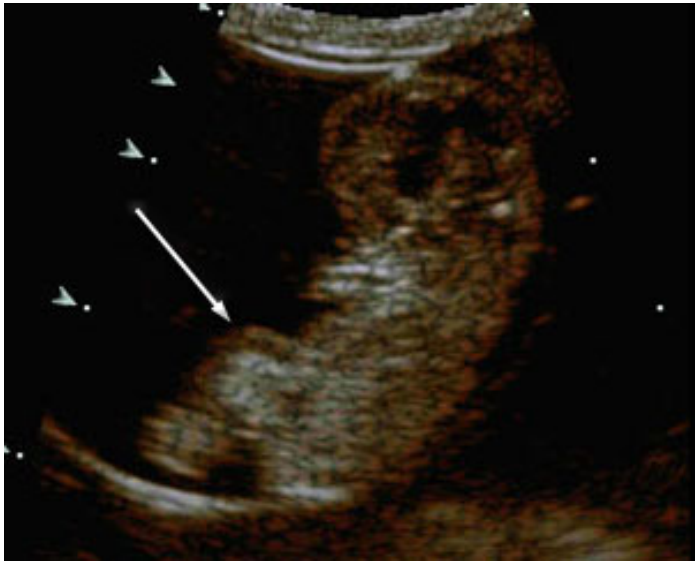
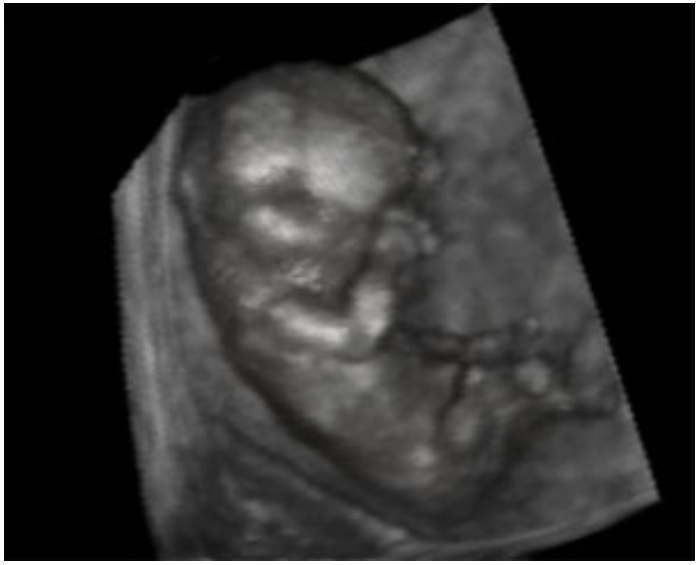


Figure 7c - Embryo at 9+4 weeks (crown–rump length 28 mm). Longitudinal section demonstrating the the physiological midgut herniation present as a large hyperechogenic mass.

Postembryonic period, weeks 10 and 11 (crown–rump length 32–54 mm)

External form

The human features of the fetus become clearer. The fetal body elongates, the arms and the legs develop into upper and lower arms and legs, the hands and fingers and the feet and toes. In the largest fetuses, the soles of the feet rotate from the sagittal plane. The head is still relatively large with a prominent forehead and a flat occiput. The future skull can be distinguished; ossification starts at about 11 weeks with the occipital bone[14].

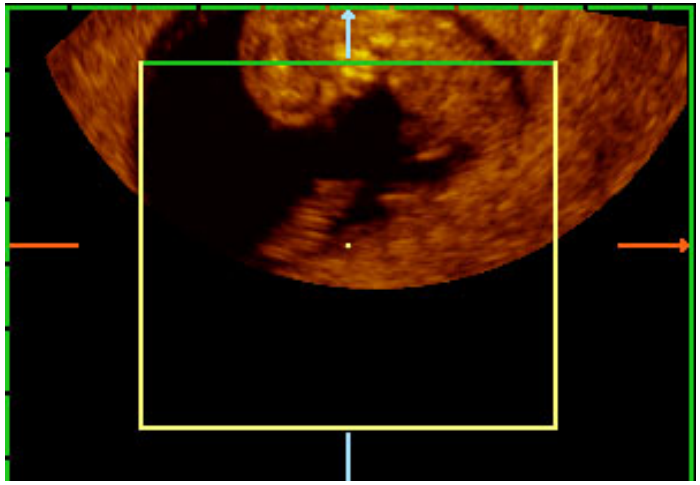


3D scan at 11-12 weeks

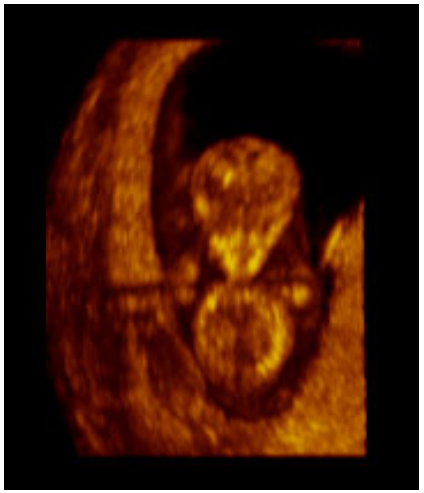
Central nervous system

The thick crescent-shaped lateral ventricles fill the anterior part of the head and conceal the diencephalic cavity. The thickness of the cortex is about 1 mm at the end of the first trimester. The diencephalon lies between the hemispheres, and the mesencephalon gradually moves towards the center of the head. After an initial increase, the width of the third ventricle becomes narrow towards the end of the first trimester. The cerebellar hemispheres seem to meet in the mid-line during weeks 11–12. After 10 weeks 3 days, the choroid plexuses of the fourth ventricle can always be visualized. The distance between the choroid plexuses and the cerebellum becomes shorter during weeks 9–11 because of cerebellar growth. The onset of ossification of the spine occurs at the end of the first trimester.

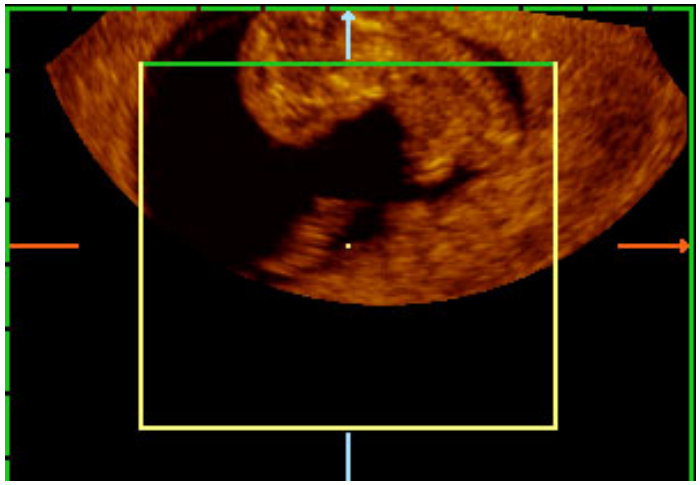
3D volume at 10 weeks - Central Nervous System Slices



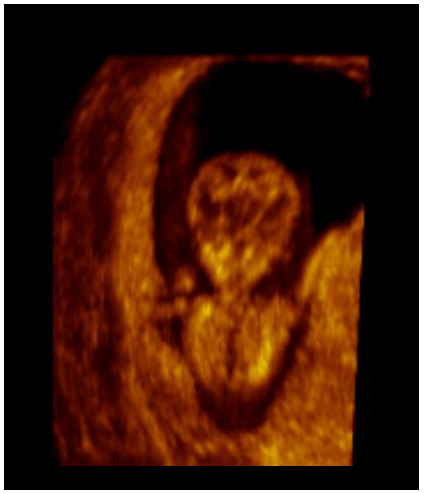
slice at frontal lobe level (sagital)



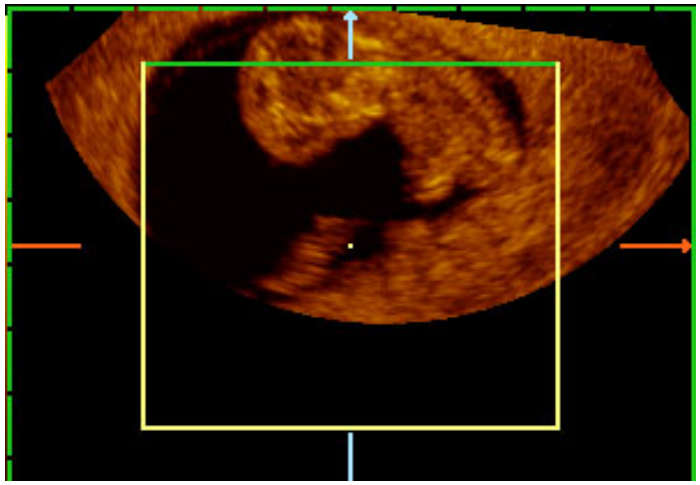
frontal lobe level (coronal)



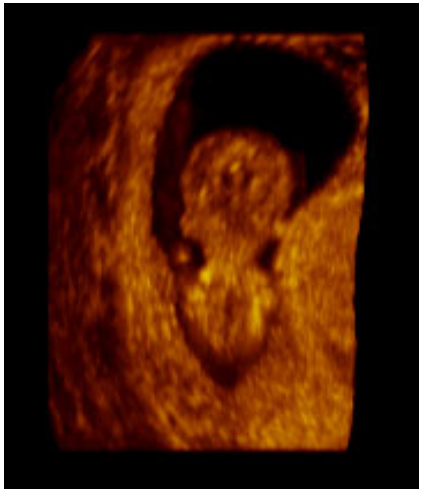
slice at midline level (sagital)



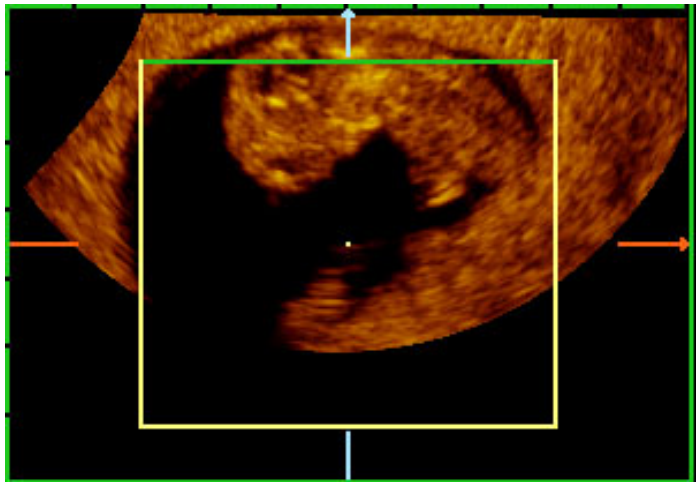
midline level (coronal)



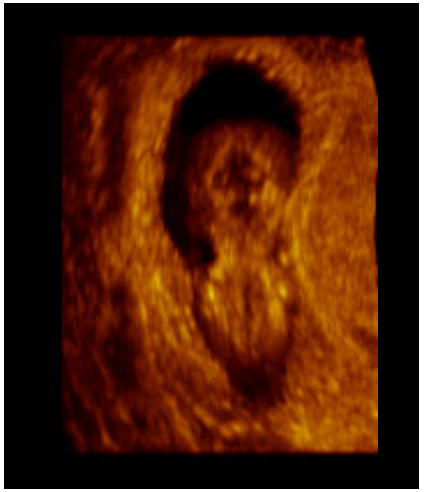
slice at thalamo level (sagital)



thalamo level (coronal)



slice at posterior fossalevel (sagital)



posterior fossa level (coronal)

Heart

At 10 weeks, the moving valves and the interventricular septum can be identified. The heart rate slows down to 165 bpm at the end of week 11. The ventricles, atria, septa, valves, veins and outflow tracts become identifiable.

Intestinal tract

Midgut herniation has its maximal extension at the beginning of week 10 and returns into the abdominal cavity during weeks 10–11. The gut retracts into the abdominal cavity between 10 weeks 4 days and 11 weeks 5 days. Fetuses which are older than 11 weeks 5 days usually do not demonstrate any sign of the herniation. The esophagus can be identified as an echogenic

double line anterior to the aorta, leading into the stomach. The stomach is visible in all specimens before 11 completed weeks.

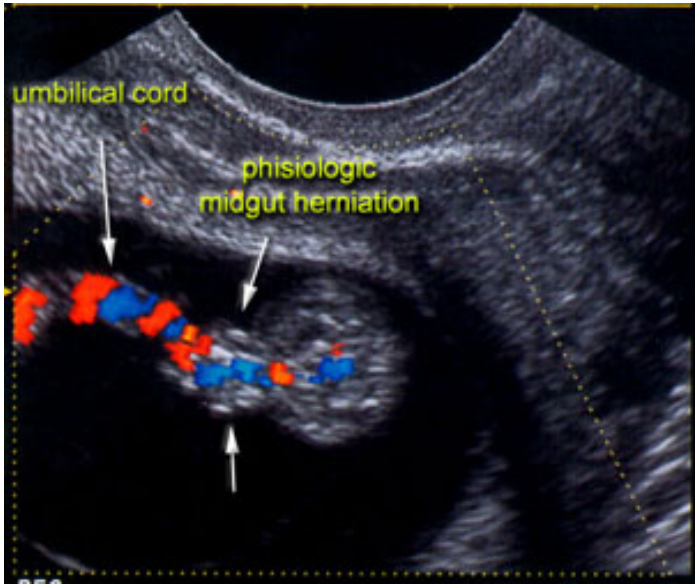
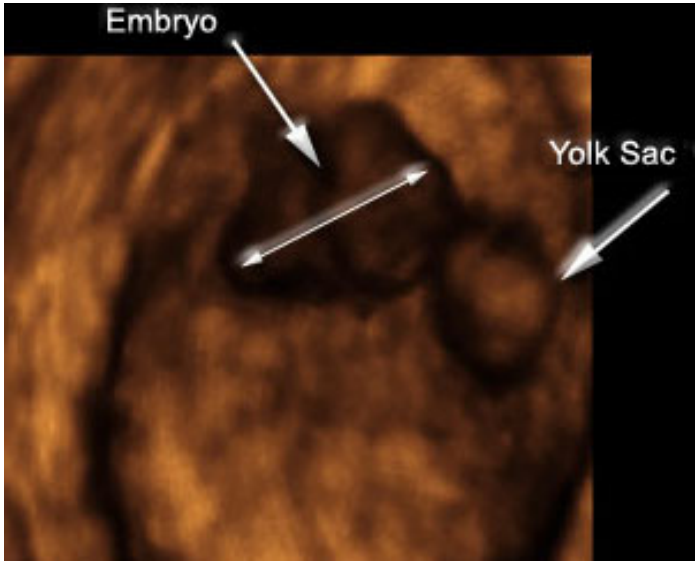


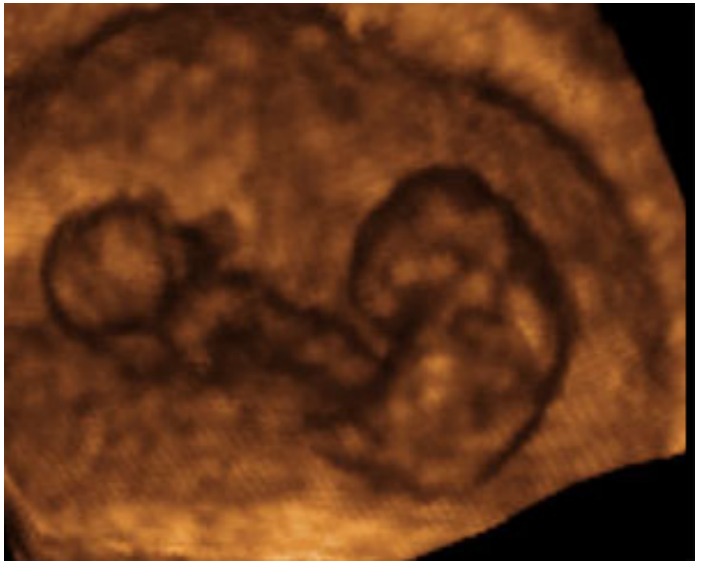
Figure 8a - Embryo at 10 weeks (crown–rump length 32 mm). Horizontal section through the abdomen demonstrating the umbilical cord. The arrows show the extension of the physiological midgut herniation

Fetal growth from 7 to 12 weeks

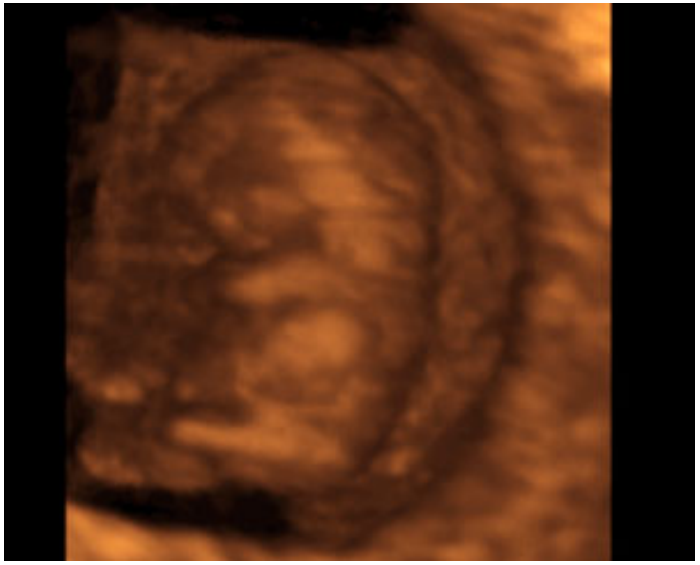
The longitudinal measurements of the biparietal diameter, occipito-frontal diameter, mean abdominal diameter, crown–rump length, amniotic cavity diameter and chorionic cavity diameter show a high degree of uniformity with virtually the same growth velocities. The yolk sac demonstrates uniform growth until week 10 only.



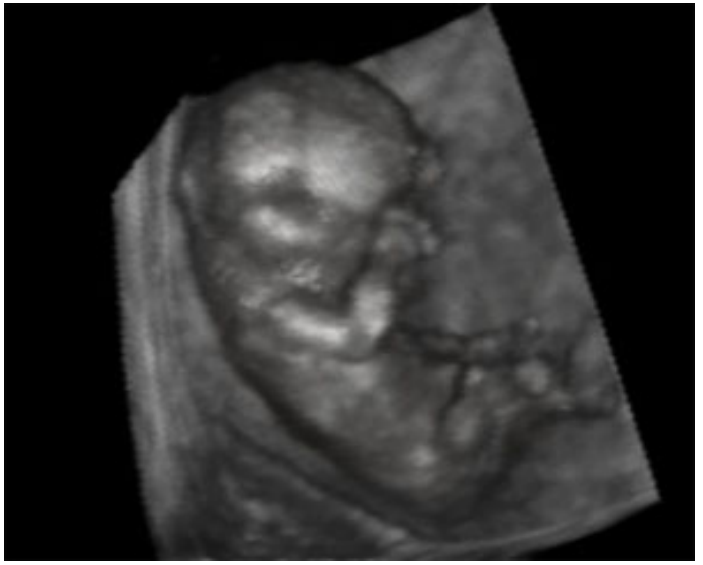
3D scan at 5-6 weeks



3D scan at 7-8 weeks



3D scan 9-10 weeks

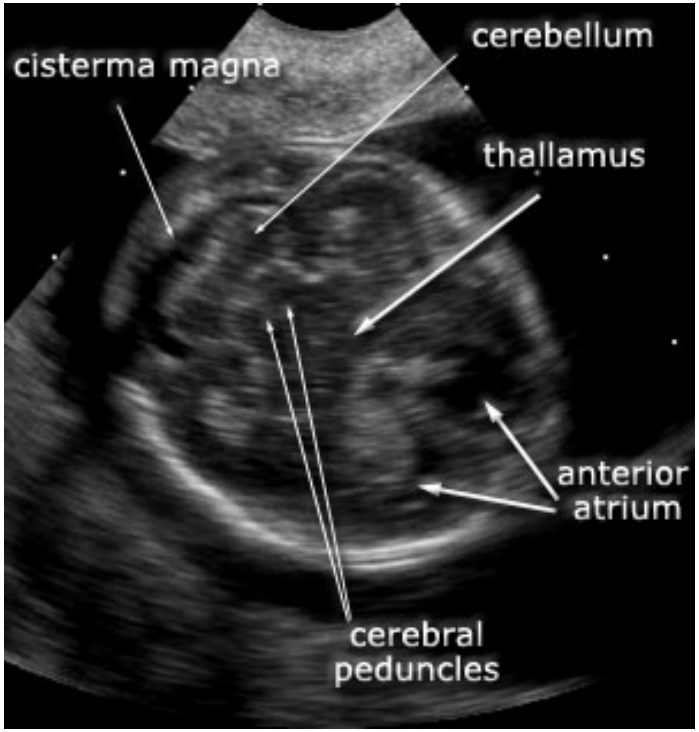


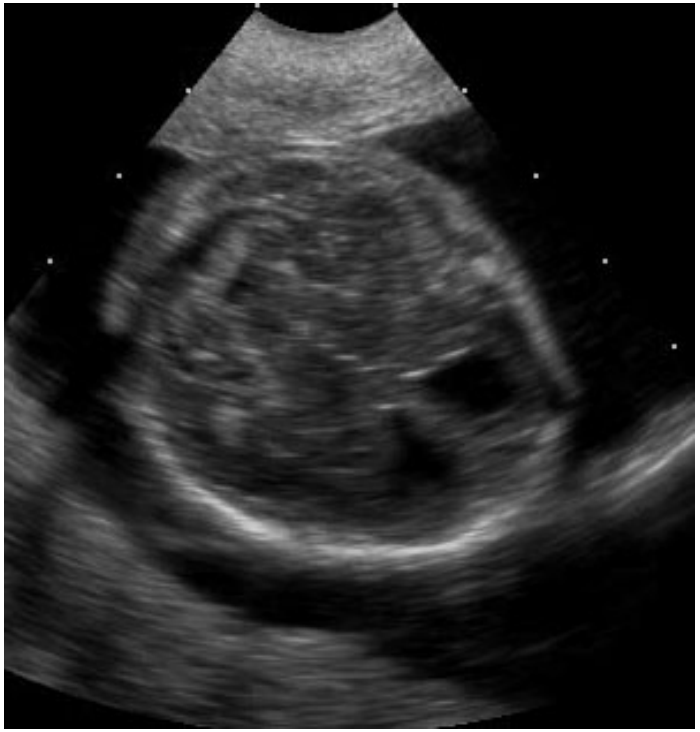
3D scan at 11-12 weeks

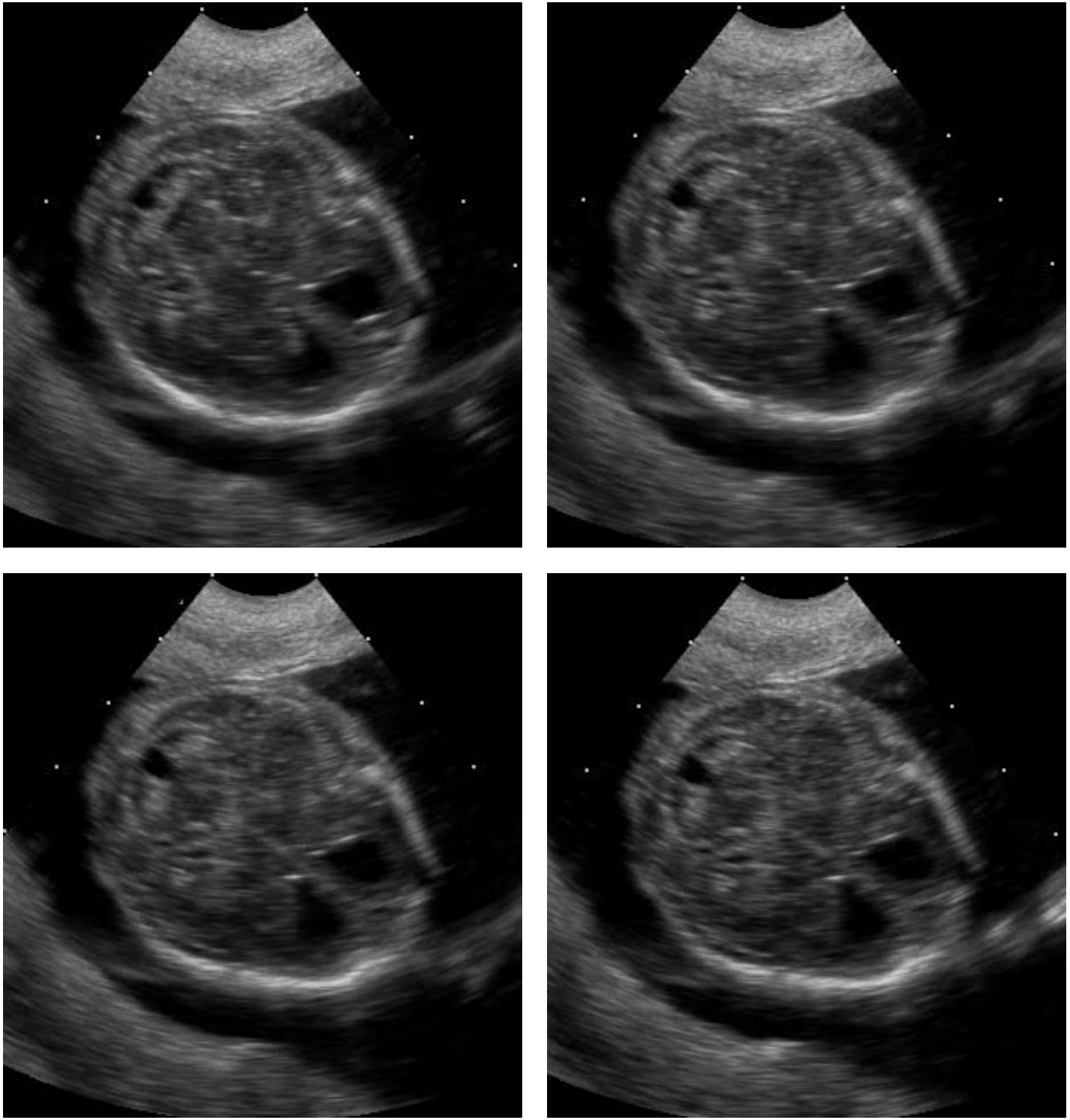
Fetal growth from 12 to 14 weeks

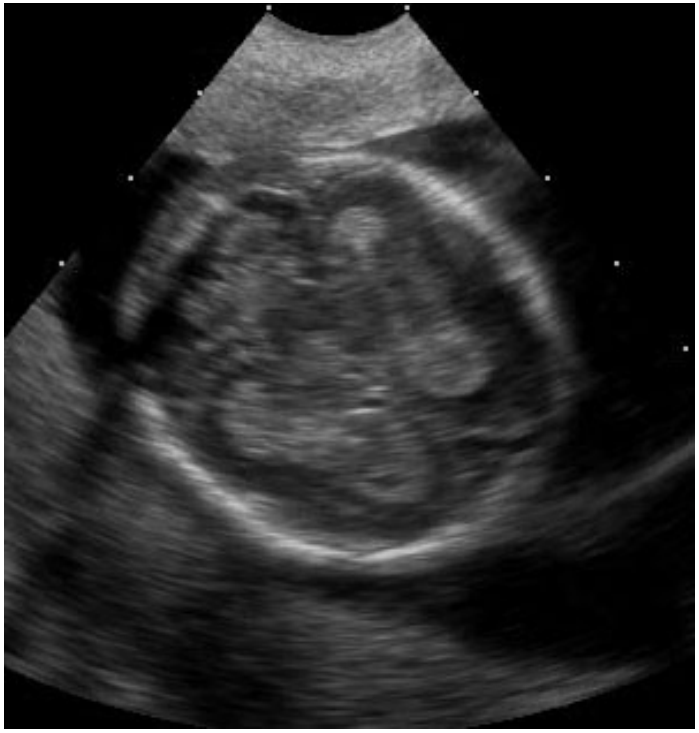
CNS

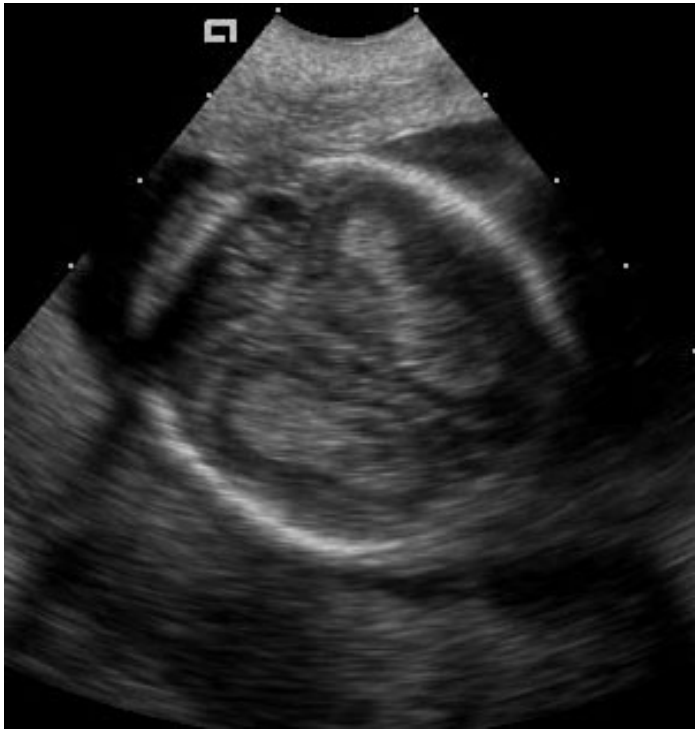
In this phase the development of the ventricular system, cerebellum, cisterna magna (the posterior fossa). At this time the vermis is not completely closed. The complete development of the cerebellum will be completed at 17 weeks gestation.











Clip: 14 weeks - middle cerebral artery

Clip: 13-14 weeks (brain+posterior fossa)

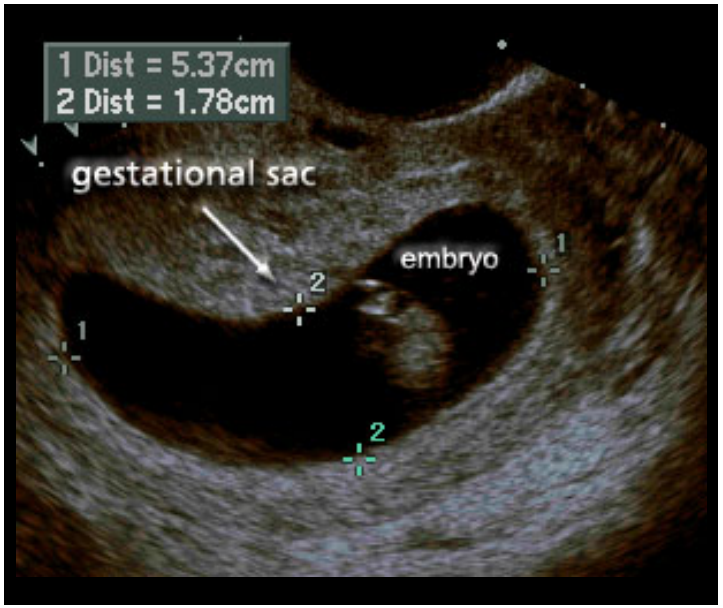
Clip: 13-14 weeks (choroid plexus)

Routine 11-14 weeks scan

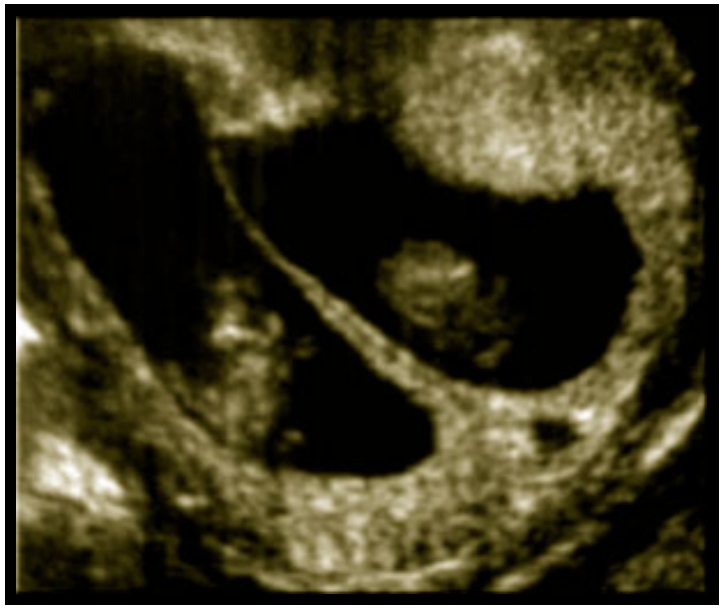
Routine ultrasound scans

11-14 weeks

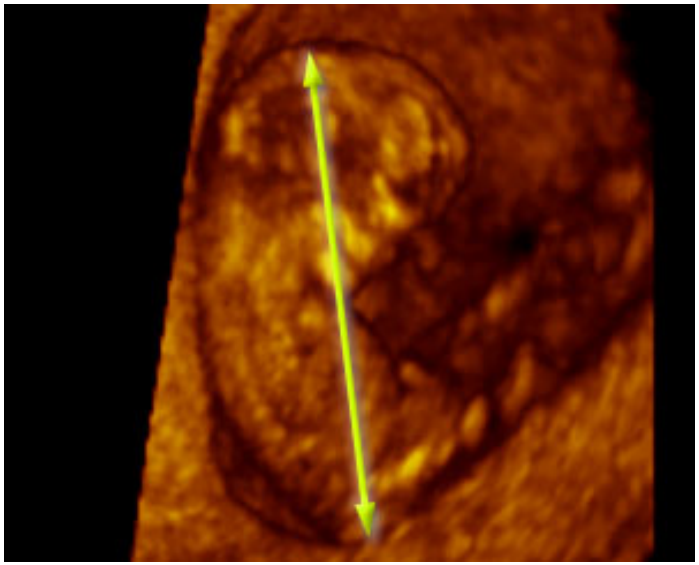
- viability, number & size
- Nucal Trnaslucency
- Anatomy
  - Brain
  - Nucal Translucency
  - Torax
  - Cardiac
  - Abdome (stomach, bowell)
  - Urinary (bladder, kidneys)
  - Lims
- cervical lengh

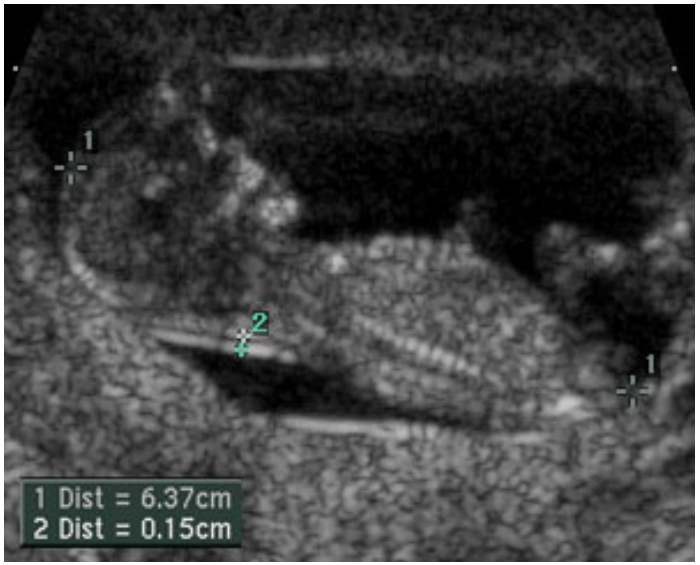


Gestational Sac (number of sacs)



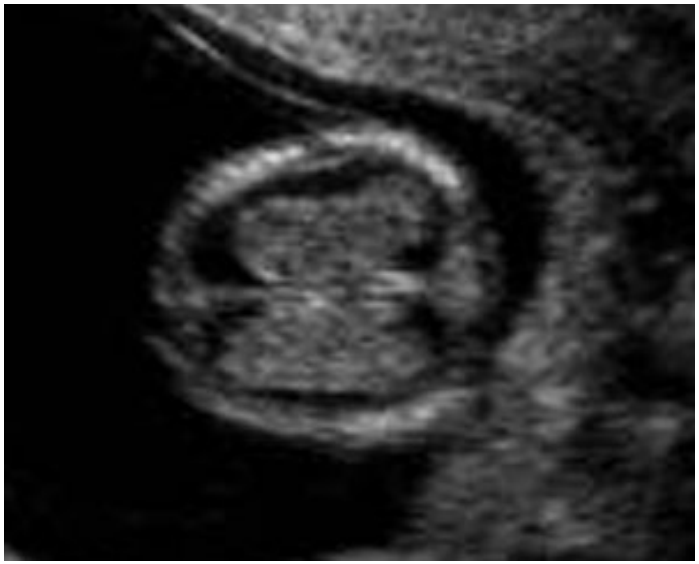
Number of Amnios and chorions

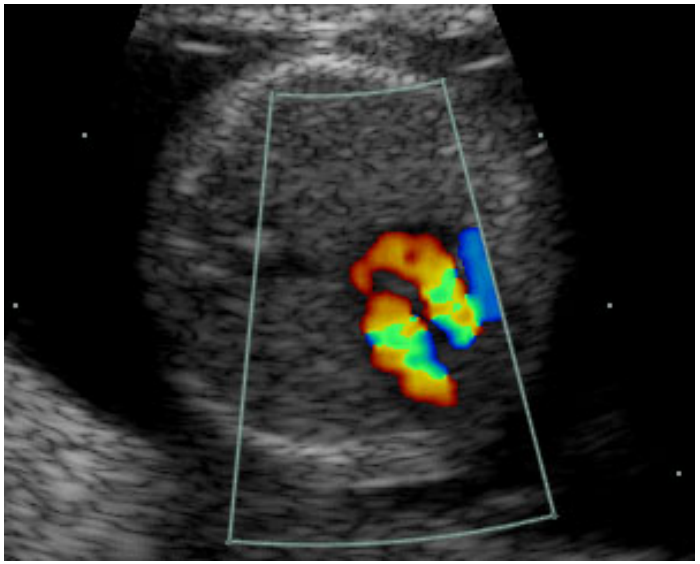




CRL: measurement of Crown-Rump-Lenght.

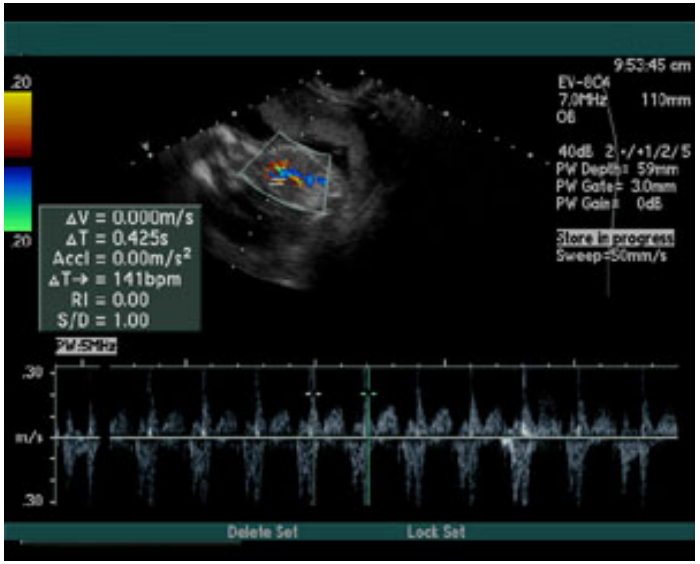
Nucal Translucency : measurement of the Nucal Translucency in association of the CRL.

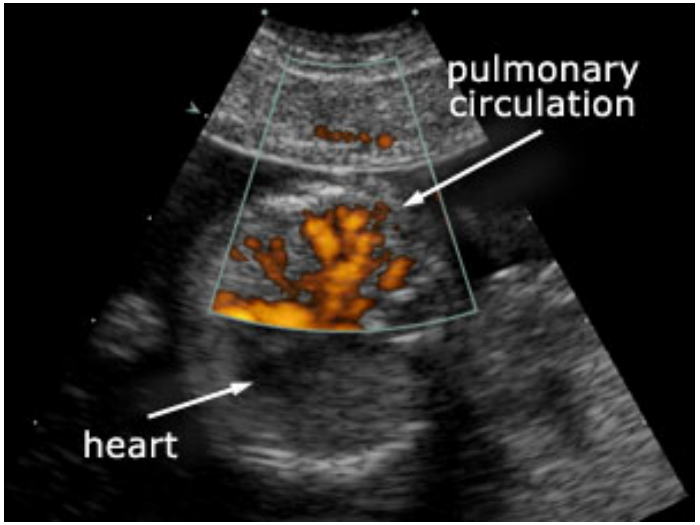




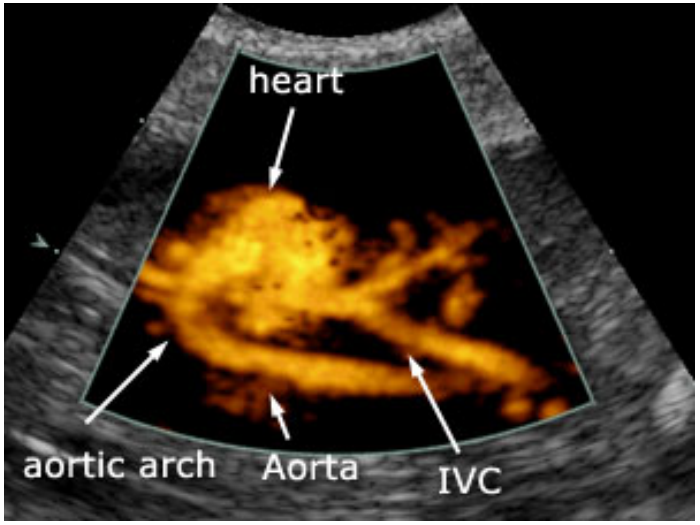
Brain: calvarium, ossification, measurements (BPD, OFD, BPD/OFD), choroid plexus, interhemispheric line (foice).

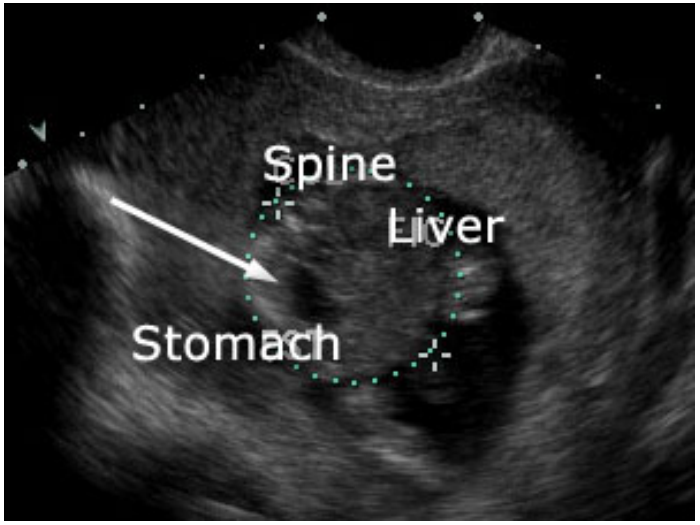
- **Torax & Heart**
- cardiac axis
- chambers size and proporcion
- estrutures identification
- RV, LV, RA, LA and Forame ovale



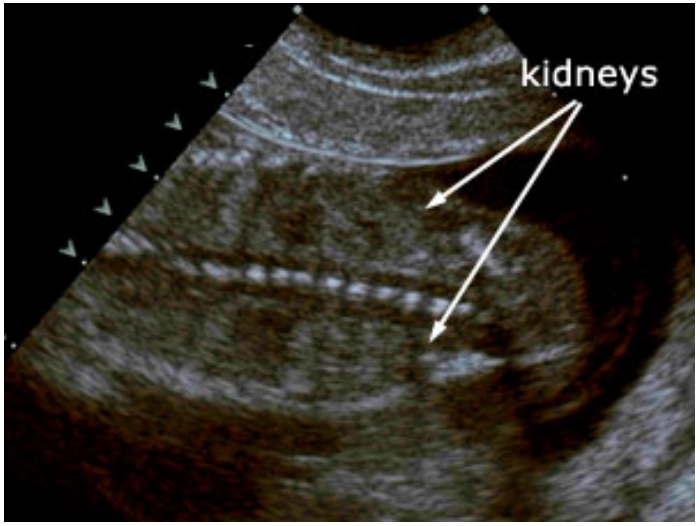


Fetal Heart Rate: evaluation of the fetal cardiac activity and the heart rate.



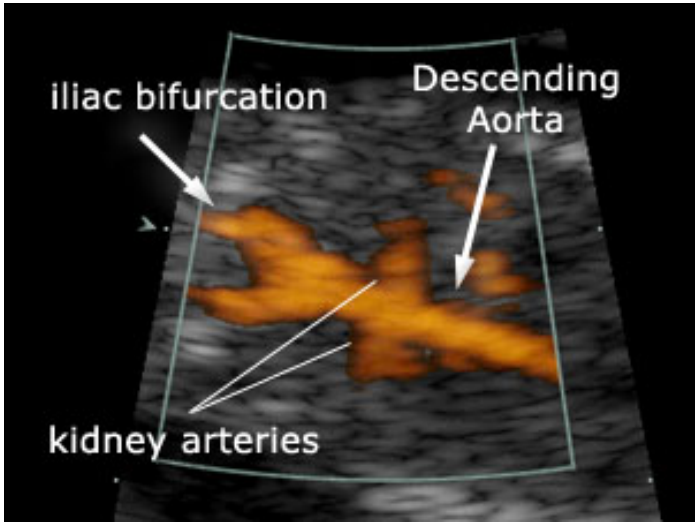


Descending Aorta, kidneys arteries, iliac bifurcation

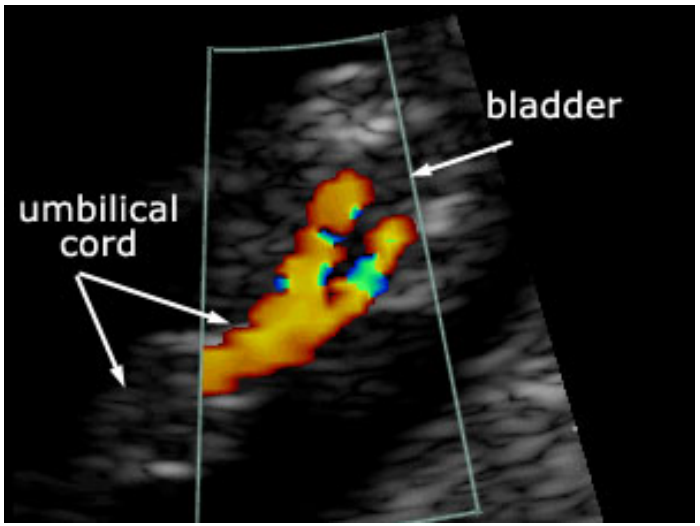


Kidneys: coronal section showing the 2 kidnets, spine and iliac wings

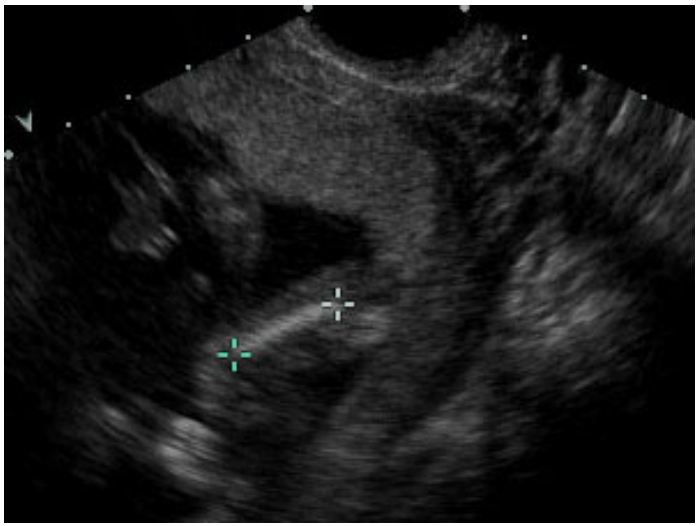
Abdome: Abdome Circunference, estomach, liver and spine.



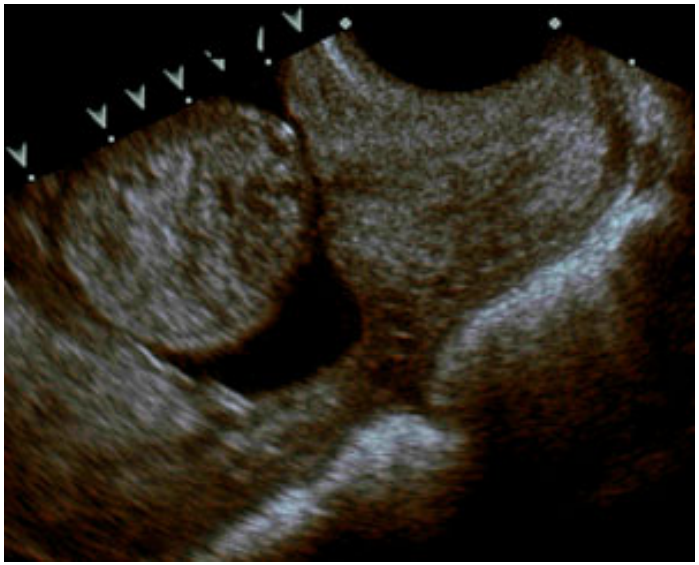
Descending Aorta, kidneys arteries, iliac bifurcation



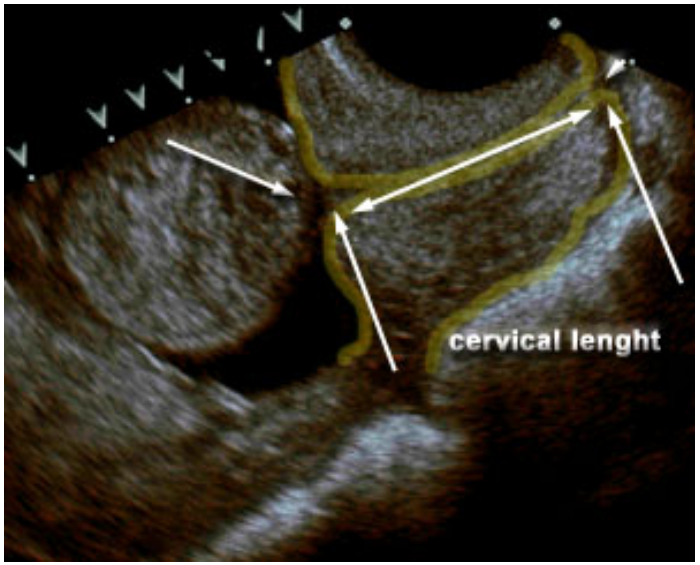
Umbilical insertion, bladder, umbilical arteries (2 arteries)



Limbs: evaluation of the upper and lower limbs. Measurement of the femur.



Cervical Length



Cervical Length

Clip: cervical lenght

CENTRAL NERVOUS SYSTEM DEFECTS

Acrania / exencephaly / anencephaly

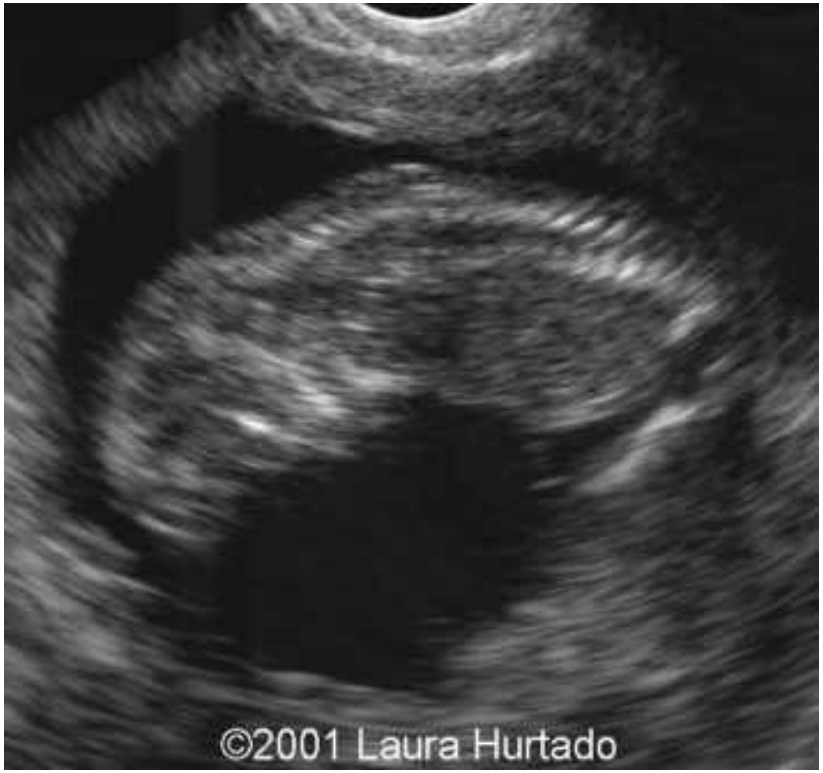
Prenatal ultrasonographic diagnosis of anencephaly during the second and third trimesters of pregnancy is based on the demonstration of an absent cranial vault and cerebral hemispheres[15]. Animal studies have shown that, in the absence of the cranial vault, there is progressive degeneration of the exposed cerebral tissue to anencephaly[16].

In normal human fetuses, there is histological evidence that the onset of ossification of the cranial vault is at 10 weeks of gestation[17] and that, ultrasonographically by 11 weeks, there is hyperechogenicity of the skull in comparison to the underlying tissues[18]. Ultrasound reports have demonstrated that in the human, as in animal studies, there is progression from acrania to exencephaly and finally anencephaly (Table 1)[19–23]. In the first trimester, the pathognomonic feature is acrania, the brain being either entirely normal or at varying degrees of distortion and disruption.

Table 1 - Case reports on the prenatal diagnosis of anencephaly at 11–14 weeks of gestation

Author	Case	Gestational (weeks)	12 weeks 13 and 14 weeks
Schidt and Kubli 1982 [19]	1	13	anencephaly
Johnson et al., 1985 [20]	2	11	anencephaly
Rottem et al. 1989 [21]	3	9 11	abnormal cephalic pole anencephaly
Kennedy et al. 1990 [22]	4	10	exencephaly
Bronshtein and Ornoyet al. 1991 [23]	5	9 11 12 14	normal normal acrania anencephaly

Goldstein *et al*. reported the difficulties with early diagnosis of anencephaly; the 12-week scan showed no defects but repeat examination at 26 weeks demonstrated anencephaly[24]. Rottem *et al*. reported a fetus at 9 weeks with an abnormal shape of the cephalic pole and cervical spine; at 11 weeks, the diagnosis of anencephaly and open cervical spina bifida was made[21]. Kennedy *et al*. described a case of acrania at 10 weeks in which the brain was of normal volume but appeared echogenic and disorganized; at 14 weeks, the fragmented and degenerating brain was visualized[22]. Bronshtein and Ornoy reported a case with no abnormal findings at 9 and 11 weeks, but at 12 weeks there was acrania and at 14 weeks there was anencephaly[23].



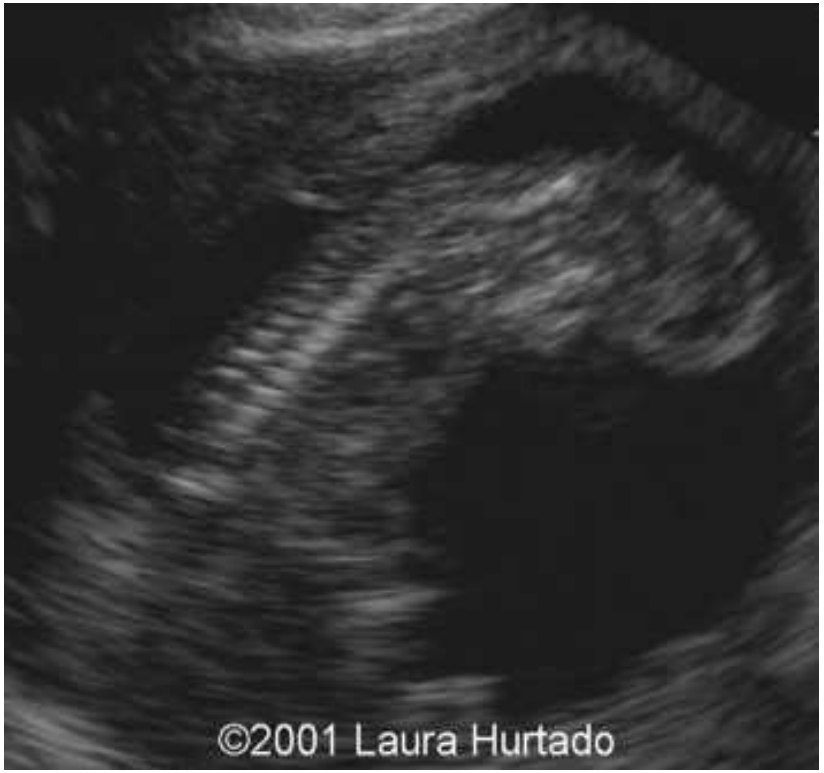
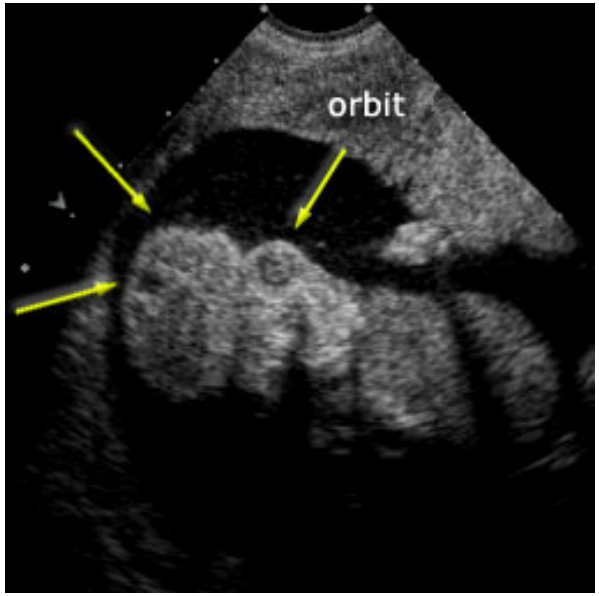
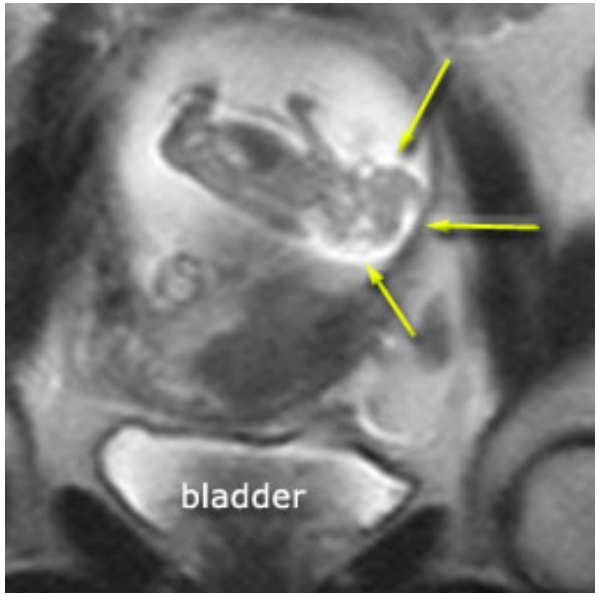


Figure 9 - Acrania in an 13-14 week fetus

Courtesy from Dr. Laura Hurtado (www.thefetus.net)



13 weeks - cephalic pole, absence of the calvarium. yellow arrows pointing the encephalic tissue and the orbit



MRI - yellow arrows pointing the encephalic tissue.

Courtesy Prof Dr. Jacob Szenjfeld - CURA & Radiology UNIFESP© 2001

Screening studies

In an ultrasound screening study of 622 high-risk pregnancies at 10–13 weeks and 16–18 weeks of gestation, all three fetuses with acrania/anencephaly were correctly identified at the first scan[25]. Another screening study examined 3991 patients by ultrasound at 11–14 weeks and again at 18–20 weeks; there were two cases of exencephaly (one associated with spina bifida and another with inienceph aly) and they were both diagnosed at the early scan[26]. Two screening studies for chromosomal abnormalities by fetal nuchal translucency at 10–14 weeks in a total of 6861 pregnancies correctly diagnosed all seven cases of anencephaly in the first-trimester scan[27,28].

In a multicenter study of screening for chromosomal abnormalities, by assessment of fetal nuchal translucency thickness at 10–14 weeks of gestation, there were 53 435 singleton and 901 twin pregnancies[29]. There were 47 fetuses with anencephaly, including three from twin pregnancies. The diagnosis of anencephaly was made at the early scan in 39 cases and at the 16–22-week scan in a further eight cases. During the first phase of the study, 34 830 fetuses were examined. In this group, there were 31 cases of anencephaly but the diagnosis was made at the early scan in only 23 (74%) of the cases[29]. Subsequently, the sonographers from the participating centers were informed of the different diagnostic features of anencephaly in the first

compared to the second trimester and they were instructed to specifically look for and record the presence or absence of acrania at the early scan. In the second phase of the study, 20 407 fetuses were examined and all 16 cases of anencephaly were diagnosed at the early scan[29].

These findings demonstrate that anencephaly can be reliably diagnosed at the routine 11–14-week ultrasound scan, provided the sonographic features for this condition are specifically searched for.

Encephalocele

This is a cranial defect with protrusion of meninges (meningocele) and brain (encephalocele). In about 75% of cases, the lesion is occipital but alternative sites include the frontoethmoidal and parietal regions. It is often associated with microcephaly, hydrocephaly, spina bifida and Meckel–Gruber syndrome.

A prerequisite for the diagnosis of encephalocele (in contrast to nuchal cystic hygroma) is the demonstration of an associated bony defect in the skull and, therefore, the diagnosis may not be possible before the onset of cranial ossification at about 10 weeks of gestation. However, van Zalen-Sprock *et al*. have reported that, at least in some cases, the first sign for possible encephalocele is enlargement of the rhombencephalic cavity from about 9 weeks[30].

Bronshtein and Zimmer described a case of occipital encephalocele that was first seen at 13 weeks as an empty occipital sac measuring 8 x 9 mm[31]. At 14 weeks, the sac remained of the same size and was filled with brain tissue. At 15 and 16 weeks, repeated examinations demonstrated complete resolution of the defect and the maternal serum a-fetoprotein was normal. At 19 weeks, there was recurrence of the encephalocele and this persisted until 24 weeks when the pregnancy was terminated; pathological examination confirmed the diagnosis of encephalocele.

van Zalen-Sprock *et al*. described a fetus at 11 weeks of gestation with two translucent areas in the occipital region[32]. A repeat scan at 13 weeks demonstrated a bony defect and protrusion of the brain. The diagnosis of occipital encephalocele was made and this was confirmed by pathological examination after termination of the pregnancy.

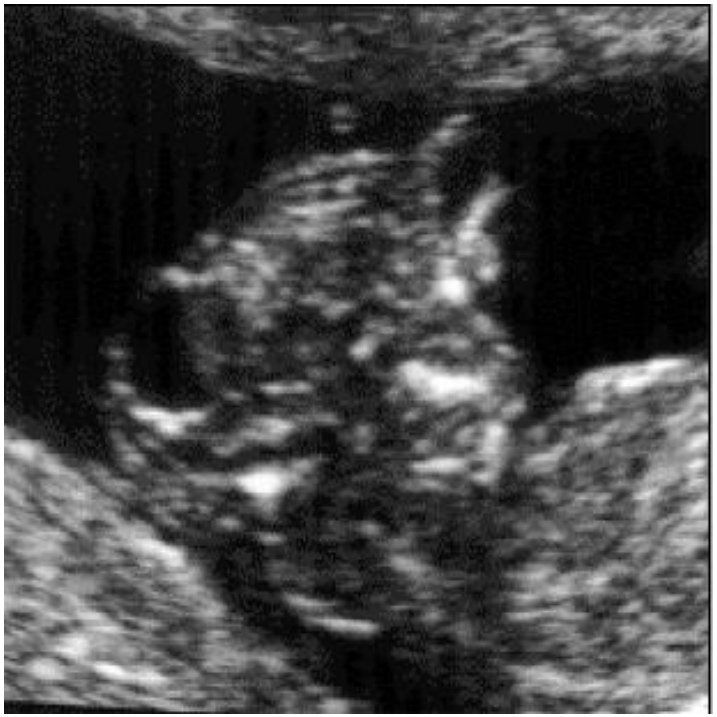
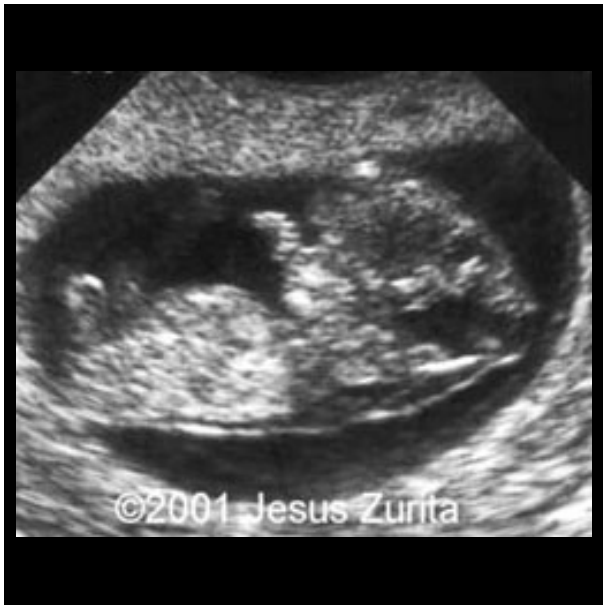


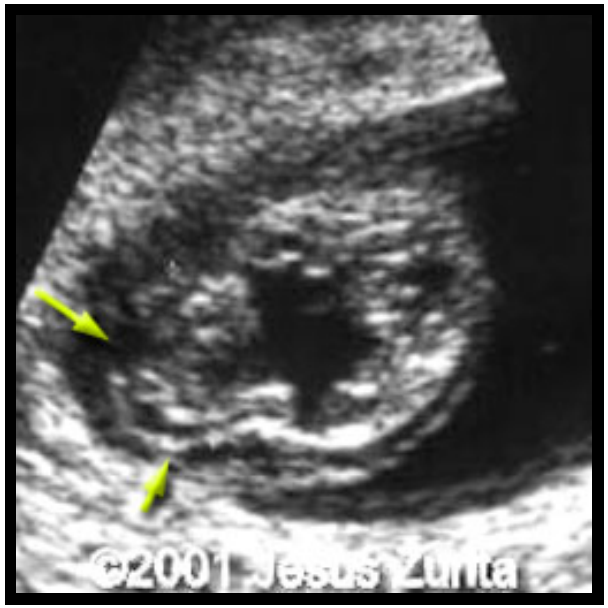
Figure 10 - Encephalocele in a 12-week fetus

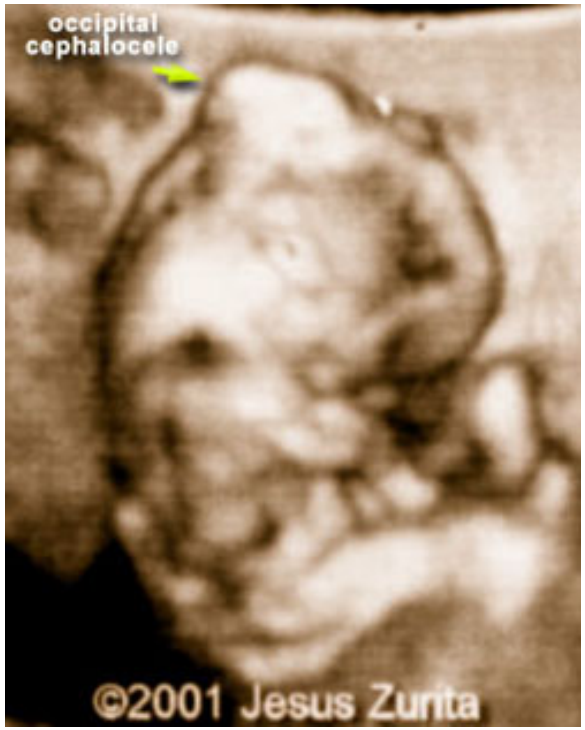
Meckel–Gruber syndrome

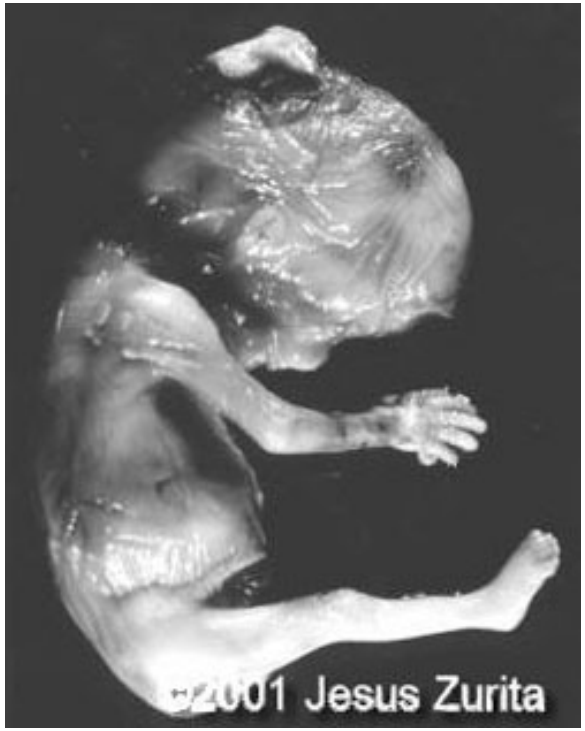
This is a lethal, autosomal recessive condition characterized by the triad of encephalocele, bilateral polycystic kidneys and polydactyly.

Pachi *et al*. described the sonographic features of the syndrome in a high-risk pregnancy at 13 weeks of gestation[33]. There was an occipital bony defect accompanied by encephalocele and abnormally enlarged kidneys. Pathological examination, after termination at 13 weeks, detected all three features of the syndrome. Sepulveda *et al*. examined nine high-risk pregnancies at 11–13 weeks and correctly diagnosed the four affected fetuses by the presence of the characteristic triad of the syndrome[34]. Similarly, van Zalen-Sprock *et al*. examined five high-risk pregnancies and correctly identified the three affected fetuses at 11–14 weeks[30].









Courtesy form Zurita © 2001 - www.thefetus.net

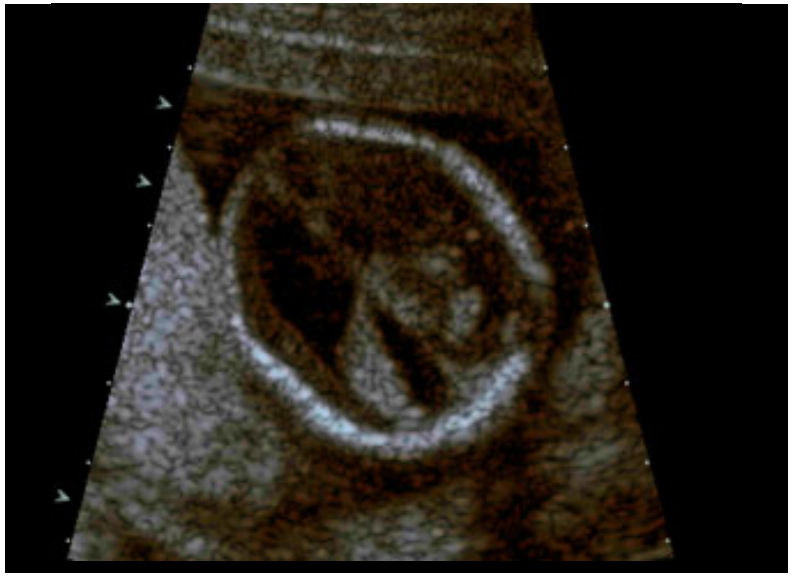
Screening studies

An ultrasound screening study for fetal abnormalities at 12–14 weeks of gestation, involving 1632 pregnancies correctly identified the one case of Meckel–Gruber syndrome; there was an occipital bony defect with a small encephalocele at 12 weeks and enlarged cystic kidneys at 13 weeks[35]. The parents chose to continue with the pregnancy and at 15 weeks there was enlargement of the encephalocele. Serial scans from 18 weeks demonstrated the presence of anhydramnios, making visualization of the fetal abnormalities difficult. The diagnosis was confirmed after delivery at 37 weeks and neonatal death[36]. Sepulveda *et al*. detected the triad of the syndrome in a 13-week fetus during screening for chromosomal abnormalities by measurement of fetal nuchal translucency thickness in 21 477 pregnancies[34].

These findings suggest that the phenotypic expression of the syndrome is evident from at least 11 weeks of gestation. Consequently, all affected cases could potentially be diagnosed by the early scan, provided that systematic examination of both the skull/brain and the renal fossae is carried out routinely. Indeed, the diagnosis is likely to be easier at 11–14 weeks, when the amniotic fluid is normal, than during the second trimester when the presence of the associated oligohydramnios could easily cause encephalocele and certainly polydactyly to be missed. Additionally, at 11–14 weeks, the fingers are easier to examine because they are invariably extended, whereas in the second trimester the hands are often clenched.

Hydrocephalus

Congenital hydrocephalus has a birth prevalence of about 2 per 1000. Although the underlying cause may be chromosomal abnormalities, genetic syndromes, fetal infection or brain hemorrhage, many cases have no clear-cut etiology and are probably due to a combination of genetic and environmental factors. Antenatal sonographic diagnosis is based on the demonstration of dilated lateral cerebral ventricles.



Dilated lateral cerebral ventricules 13+2 wees

In normal fetuses, the outline of the lateral ventricles, the echogenic choroid plexi and the mid-line echo are visible by ultrasound from 9 weeks of gestation; at 10–11 weeks, the third and fourth ventricles become visible and, at 12 weeks, the cerebellum and thalamii can be seen[18,37]. The transverse diameter of the choroid plexus increases from 2 mm at 10 weeks to about 5 mm at 13 weeks[7]. The lateral ventricle diameter to hemisphere diameter ratio decreases with gestation from 72% at 12 weeks, 67% at 13 weeks and 61% at 14 weeks[38]. The transverse cerebellar diameter increases linearly with gestation from about 6 mm at 10 weeks to 12 mm at 14 weeks[7,10].

Screening studies

Ventriculomegaly usually develops after the 14th week of gestation. In a screening study involving ultrasound examinations at 11–14 weeks of gestation and again at 18–20 weeks in 3991 patients, there were eight cases of ventriculomegaly (two were associated with spina bifida); only two were diagnosed at the early scan and the other six at 18–20 weeks[26].

Dandy–Walker malformation

This condition, which complicates about 10% of cases with hydrocephalus, is characterized by complete or partial absence of the cerebellar vermis and cystic dilatation of the fourth ventricle. The Dandy–Walker complex is a non-specific end-point of chromosomal abnormalities (usually trisomy 18 or 13 and triploidy), more than 50 genetic syndromes, congenital infection or teratogens such as warfarin, but it can also be an isolated finding.

Ulm *et al*. reported a 14-week fetus with an apparently isolated Dandy–Walker malformation but fetal karyotyping demonstrated triploidy[39].

Screening studies

In a screening study involving ultrasound examinations at 11–14 weeks of gestation and again at 18–20 weeks in 3991 patients, there was one case of the Dandy–Walker malformation and this was not diagnosed in the first-trimester scan[26]. In another screening study for chromosomal abnormalities by fetal nuchal translucency in 1473 pregnancies, there was one case of Dandy-Walker malformation and this was correctly diagnosed in the first-trimester scan[27].

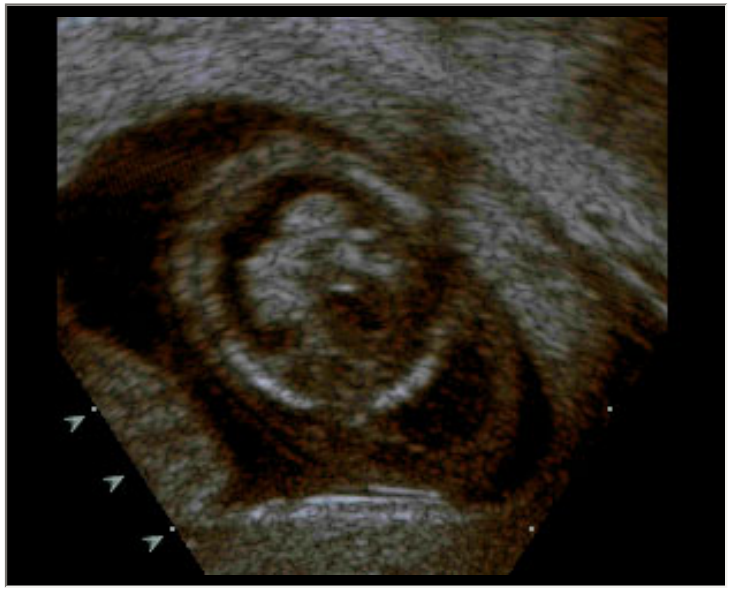
Hydranencephaly

This is a lethal, sporadic condition characterized by absence of the cerebral hemispheres with preservation of the mid-brain and cerebellum. It is thought to result from widespread vascular occlusion of the internal carotid arteries or their branches, prolonged severe hydrocephalus, an overwhelming infection, or defects in embryogenesis. About 1% of infants thought to have hydrocephalus are later found to have hydranencephaly.

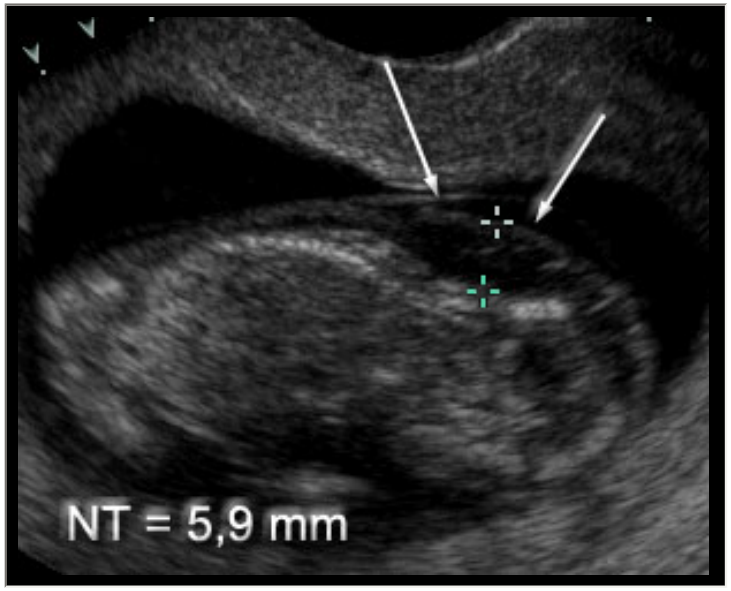
Lin *et al*. reported a 12-week fetus with a large head, small hemispheres and a fluid-filled intracranial cavity with no mid-line echo[40]. A repeat scan at 18 weeks demonstrated a cystic fetal head with no cerebral hemispheres and falx; the brain could be seen protruding into the cystic cavity. Unlike alobar holoprosencephaly, there was no rim of cortex present. The pregnancy was terminated and pathological examination confirmed the diagnosis.

Holoprosencephaly

Holoprosencephaly, with a birth prevalence of about 1 in 10 000, is characterized by a spectrum of cerebral abnormalities resulting from incomplete cleavage of the forebrain. There are three types according to the degree of forebrain cleavage. The ~~alobar type,~~ which is the most severe, is characterized by a monoventricular cavity and fusion of the thalami. In the ~~semilobar type~~, there is partial segmentation of the ventricles and cerebral hemispheres posteriorly with incomplete fusion of the thalami. In ~~lobar holoprosencephaly,~~ there is normal separation of the ventricles and thalami but absence of the septum pellucidum. The first two types are often accompanied by facial abnormalities.



Alobar type -monoventricular cavity and fusion of the thalami at 11+2 weeks



Increased Nucal Transluncency (white arrows) at 11+2 weeks - trissomy 13.

Toth *et al*. observed a floating membranous structure in place of the skull of an 11-week fetus[41]. At 12 weeks, they noted acrania and a floating, balloon-like, membranous brain substance. At 16 weeks, the diagnosis of acrania and holoprosencephaly with cyclops was made and these findings were confirmed at postmortem examination after termination at 18 weeks[41]. Bronshtein and Weiner described a case of alobar holoprosencephaly during routine ultrasound examination at 14 weeks; there were a single cerebral ventricle, fused thalami and a crescent-shaped frontal cortex[42]. The fetal karyotype was normal. Gonzalez-Gomez *et al*. described a 10-week fetus with a single ventricular cavity, absence of the orbits and mid-facial cleft[43]. The karyotype was normal. Pathological examination after termination at 11 weeks demonstrated alobar holoprosencephaly, anophthalmia, arrhinia and facial cleft[43]. Sakala and Gaio diagnosed alobar holoprosencephaly in a 13-week fetus with absent falx, large single ventricle and fused thalami; the karyotype was 69,XXY[44]. Turner *et al*. reported a case of alobar holoprosencephaly (single ventricle and fused thalami), exomphalos and increased nuchal translucency at 10 weeks; the

karyotype was trisomy 18[45]. Wong *et al*. reported three cases of alobar holoprocencephaly (single ventricle and fused thalami) at 10–13 weeks; there was one case each of trisomy 18, triploidy and mosaic 18p deletion and duplication[46].

Snijders *et al*. reported on the sonographic features of 46 trisomy 13 fetuses at 10–14 weeks of gestation[47]. In 76% there was increased nuchal translucency thickness, 64% were tachycardic, 24% had holoprosencephaly and 10% had exomphalos. There was no significant difference in nuchal translucency thickness between those with and those without holoprosencephaly or exomphalos[47].

Screening studies

In a screening study involving ultrasound examinations at 11–14 weeks of gestation and again at 18–20 weeks in 3991 patients, there was one case of holoprosencephaly and this was not diagnosed in the first-trimester scan[26]. Another screening study for fetal abnormalities at 12–14 weeks of gestation, involving 1632 pregnancies, correctly identified the one case of holoprosencephaly[35].

Iniencephaly

This is a rare malformation of unknown etiology, characterized by cervical dysraphism and occipital (inion) defect with or without an encephalocele.

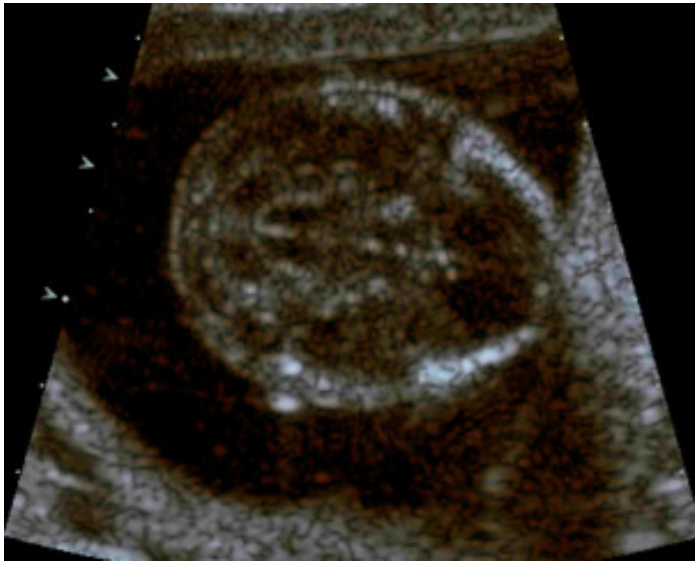
Sherer *et al*. reported the diagnosis of iniencephaly in a 13-week fetus; there was acrania, persistently hyperextended head and spinal dysraphism[48]. After termination, pathological examination demonstrated complete craniorachischisis with hyperextended cervical vertebrae.

Spina bifida

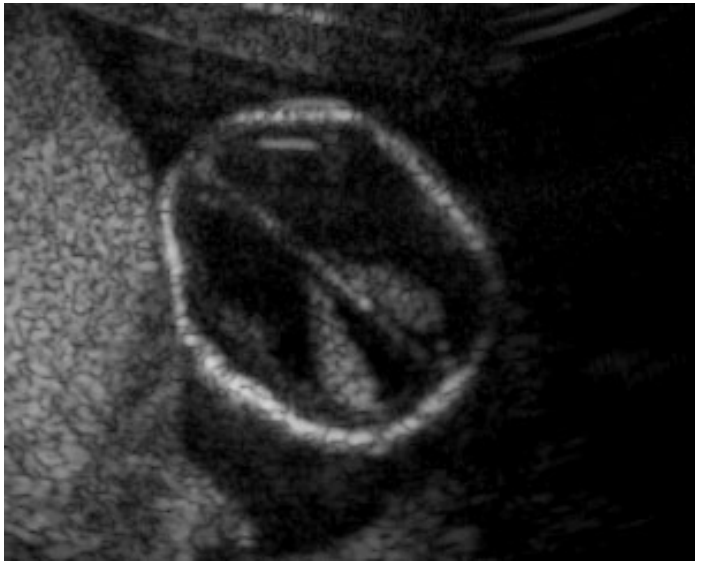
In spina bifida, there is failure of closure of the neural tube, which normally occurs by the 6th week of gestation. In the spine of normal fetuses, there are three ossification centers, two pedicles and the spinal body, and these are present from the 10th week of gestation, allowing ultrasonographic visualization of the neural canal from this gestation. Braithwaite *et al*. assessed the fetal anatomy at 12–13 weeks of gestation, by a combination of transabdominal and transvaginal sonography, and they reported successful examination of the vertebrae and overlying skin in both the transverse and coronal planes in all cases[49].

In the 1980s, the main method of screening for open spina bifida was by maternal serum a-fetoprotein at around 16 weeks of gestation and the method of diagnosis was amniocentesis and measurement of amniotic fluid a-fetoprotein and acetyl cholinesterase. Although it was possible to diagnose the condition by ultrasonographic examination of the spine[50], the sensitivity of this test was low[51]. However, the observation, that spina bifida was associated with scalloping of the frontal bones (the ‘lemon’ sign) (Figure 11), and caudal displacement of the cerebellum (the ‘banana’ sign)[52], has led to the replacement of

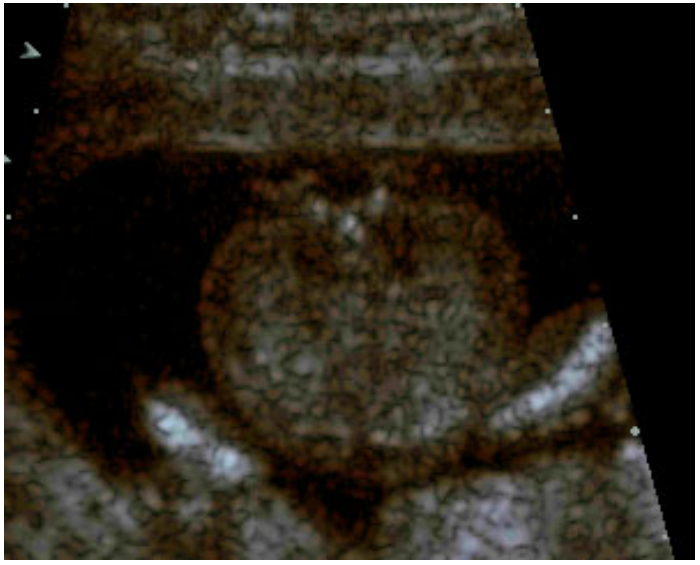
biochemical assessment with ultrasonography, both for screening and for diagnosis of this abnormality.



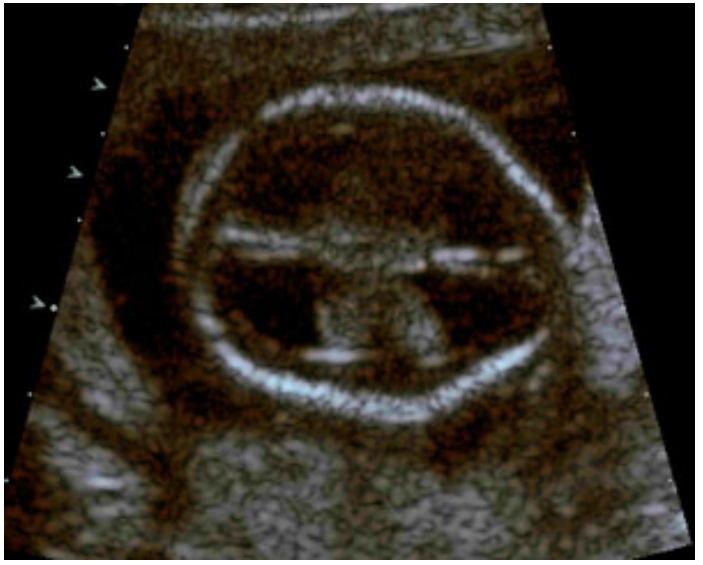
Banana sign and cisterna magna < 2,0mm



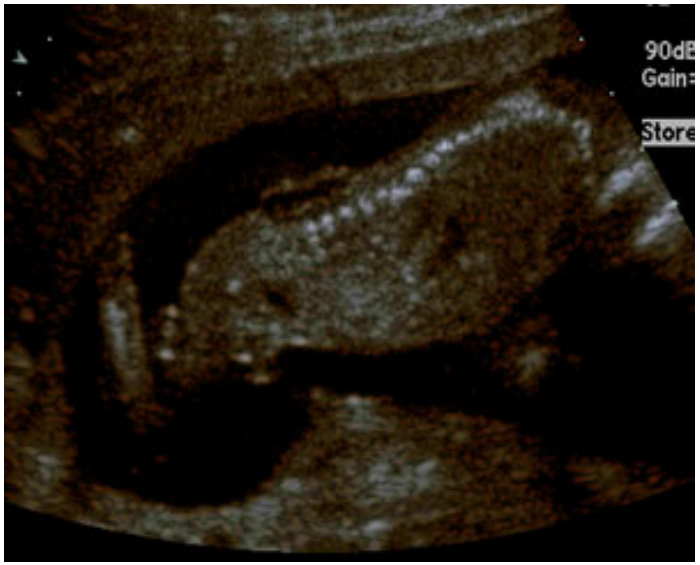
Lemon sign



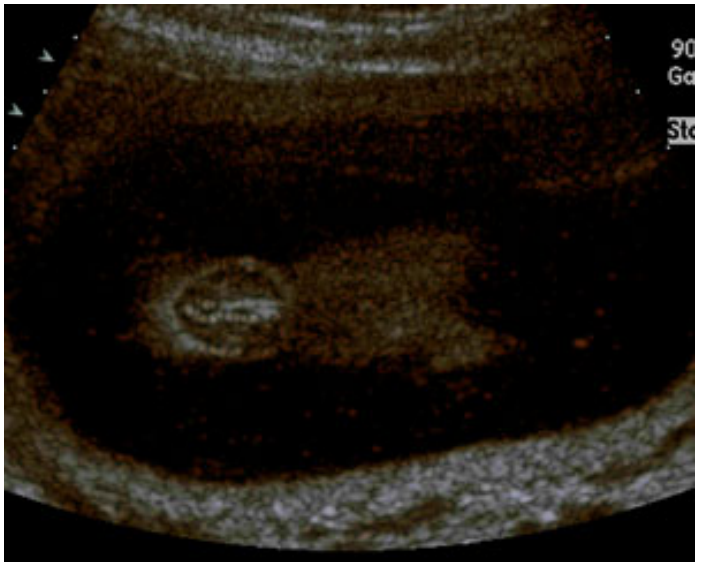
U-shaped spine (transverse)



early dilatation of the ventricules



spine lombar sacral defect (longitudinal)



mielomeningocele (coronal)

Figure 11 - Case Spina bifida + lemmon sign - 13 + 6 weeks

In the 1990s, improvements in the quality of ultrasound equipment have led to the diagnosis of spina bifida during the first trimester of pregnancy. Blumenfeld *et al*. described the evolution of the cranial and cerebellar signs of spina bifida in an affected fetus that was scanned at 10, 12 and 15 weeks of gestation[53]. In the first scan, there was a sacral irregularity but the cerebellum appeared normal; at 12 weeks, the banana sign was detected and, at 15 weeks, when the diagnosis of sacral meningocele was made, the lemon sign was identified. Sebire *et al*. described that, in three cases of lumbosacral spina bifida diagnosed at 12–14 weeks of gestation, there was an associated lemon sign[54]. Similarly, Bernard and colleagues reported the diagnosis of spina bifida in a 12-week fetus with narrowing of the frontal bones and flattening of the occiput[55].

These findings demonstrate that, at least in some cases of spina bifida, the characteristic lemon and banana signs are present from the first trimester of pregnancy. However, the prevalence of these signs at the 11–14-week scan remains to be determined.

Screening studies

In a screening study involving ultrasound examinations at 11–14 weeks of gestation and 18–20 weeks in 3991 patients, there were six cases of spina bifida (including one with associated exencephaly) and five of these were diagnosed at the early scan[26]. In two other screening studies involving 1632 pregnancies at 12–14 weeks[35] and 1473 pregnancies at 10–14 weeks[27],

respectively, there were two cases of spina bifida (one in each) and these were not diagnosed in the first-trimester scan.

CARDIAC DEFECTS

Abnormalities of the heart and great arteries are the most common congenital defects and the birth prevalence is 5–10 per 1000. In general, about half are either lethal or require surgery and half are asymptomatic. The first two groups are referred to as major. Specialist echocardiography at around 20 weeks of gestation can identify most of the major cardiac defects, but the main challenge in prenatal diagnosis is to identify the high-risk group for referral to specialist centers. Currently, screening is based on examination of the four-chamber view of the heart at the 20-week scan, but this identifies only 26% of the major cardiac defects[56].

Examination of the four-chamber view of the heart can now be carried out at the 11–14-week scan (Table 2)[57–60]. At 12–13 weeks of gestation, the four-chamber view can be examined successfully by transabdominal ultrasound in 76% of the cases and transvaginally in 95%[49]. Bronshtein *et al*. reported that the diameters of the two ventricles were similar and increased linearly with gestation from about 1.5 mm at 11 weeks to 3 mm at 14 weeks; the diameter of the heart was about one-third that of the chest and the ratio did not change with gestation[58]. In contrast, Blaas *et al*. examined the ratio of the heart diameter to that of the abdomen and reported a decrease with gestation from 51% at 8 weeks to 42% at 12 weeks[11].

Table 2 - Studies reporting on the proportion of cases where the four-chamber view of the heart was successfully visualized by ultrasonography at 10–14 weeks of gestation

Author	10 weeks	11 weeks	12 weeks	13 and 14 weeks
Dolkart & Reimers 1991 [57]	0/8	3/10 (30%)	9/10 (90%)	24/24 (100%)
Bronshetein et.al, 1992 [58]	-----	3/18 (16%)	9/25 (36%)	66/72 (90%)
Johnson et al. 1992 [59]	7/26 (27%)	19/33 (58%)	36/51 (71%)	73/100 (73%)
Gembruch et al. 1993[60]	-----	12/15 (80%)	28/30 (93%)	66/66 (100%)

Dolkart and Reimers reported that the earliest defined cardiac structures visible were the mitral and tricuspid valves; at 10 weeks, they were seen in 25% of the cases, at 12 weeks in 90% and at 13–14 weeks in all cases[57]. The five-chamber, aortic arch and ductus arteriosus views were first seen in some fetuses from 12 weeks but, in the majority, only at 14 weeks. The aortic root in short-axis projection and the left ventricle in long-axis view could be imaged in 70% and 40% of fetuses, respectively by 12 weeks. Aortic and pulmonary valves were first visualized at 12 weeks in 20% of the cases[57]. Johnson *et al*.

reported that the proportion of cases in which a full cardiac anatomic survey (four-chamber, aorta, pulmonary artery and pulmonary veins) was possible was 0% at 10–11 weeks, 31% at 12 weeks, 43% at 13 weeks and 46% at 14 weeks[59]. Gembruch *et al*. visualized the four-chamber view as well as the origin and double crossing of the aorta and pulmonary trunk in 67% of cases at 11 weeks, 80% at 12 weeks and 100% at 13–14 weeks[60].

There are several case reports on the sonographic diagnosis of cardiac defects at 11–14 weeks of gestation. Gembruch *et al*. reported an 11-week fetus with persistent bradycardia (60 bpm), increased nuchal translucency, complete atrioventricular canal defect and complete heart block; the pregnancy was terminated and pathological examination demonstrated situs inversus visceralis totalis and confirmed the septal defect[61]. DeVore *et al*. examined a 14-week fetus with persistent bradycardia (70 bpm) and found ventricular septal defect, ventricular wall hypertrophy, dilated aortic root, pericardial effusion, ascites and situs inversus of the stomach; pathological examination after intrauterine death at 16 weeks confirmed the ultrasound findings[62]. Bronshtein *et al*. reported the ultrasound findings in a 13-week fetus with ventricular septal defect and overriding aorta, suggesting the diagnosis of tetralogy of Fallot[63]. In addition, there was increased nuchal translucency thickness and exomphalos, and cytogenetic analysis demonstrated trisomy 18. Pathological examination after intrauterine death at 17 weeks confirmed the diagnosis of tetralogy of Fallot. In another case of exomphalos at 13 weeks, pericardial effusion and ventricular septal defect were identified; the fetal karyotype was normal. At 18 weeks, hydrocephalus and oligohydramnios were also noted and pathological examination after intrauterine death at 21 weeks confirmed the ultrasound findings and in addition, there was a double-outlet right ventricle and absence of the ductus arteriosus[63].

Achiron *et al*. reported the sonographic findings in eight fetuses with cardiac defects diagnosed at 10–12 weeks of gestation[64]. In seven of the cases, there was increased nuchal translucency thickness and pericardial effusion; the fetal karyotype was normal in seven and one had Turner syndrome. There was one case of tachycardia, one of ectopia cordis in association with exomphalos, one with a giant right atrium that, in subsequent pathological examination after termination of pregnancy, was diagnosed as Uhl disease, two cases with atrioventricular septal defects and three cases with ventricular septal defects; pathological examination in the latter group showed tetralogy of Fallot in two and persistent truncus arteriosus in the third[64].

Bronshtein *et al*. reported the results of an ultrasound screening study involving 81 fetuses at 12 weeks, 341 at 13 weeks and 980 at 14 weeks[65]. Five fetuses with cardiac defects were identified, including one with a small left ventricle and pericardial effusion at 11 weeks, one with ventricular septal defect, dilated left ventricle and pericardial effusion at 12 weeks that was subsequently diagnosed as tetralogy of Fallot, one with ventricular septal defect and overriding aorta at 13 weeks, one with dextrocardia at 14 weeks that was subsequently found to also have a ventricular septal defect, and another with a single atrium and single ventricle at 14 weeks.

Gembruch *et al*. reported the results of ultrasound screening in 15 fetuses at 11 weeks, 30 at 12 weeks, 51 at 13 weeks and 11 at 14 weeks[60]. There were ten fetuses with cardiac anomalies and, in nine of these, the diagnosis was correctly made at the 11–14-week scan; in one case, complete atrioventricular septal defect with double- outlet right ventricle was not detected at 12 weeks but was correctly diagnosed at 21 weeks. The defects identified were: five cases with complete atrioventricular septal defect, including one with dextrocardia and two with atrioventricular heart block; there was one case of single ventricle and

Gembruch *et al*. reported the results of ultrasound screening in 15 fetuses at 11 weeks, 30 at 12 weeks, 51 at 13 weeks and 11 at 14 weeks[60]. There were ten fetuses with cardiac anomalies and, in nine of these, the diagnosis was correctly made at the 11–14-week scan; in one case, complete atrioventricular septal defect with double- outlet right ventricle was not detected at 12 weeks but was correctly diagnosed at 21 weeks. The defects identified were: five cases with complete atrioventricular septal defect, including one with dextrocardia and two with atrioventricular heart block; there was one case of single ventricle and common atrium that was subsequently, at the 20-week scan, also found to have dextrocardia, malposition of the great arteries and situs inversus visceralis; one case of perimembranous ventricular septal defect; one case with suspected single ventricle and hypoplasia of the aorta that was subsequently found at postmortem examination to have hypoplastic left heart, hypoplasia of the ascending aorta and the aortic arch, right-sided isomerism of the atria and asplenia; one case of hypoplastic left heart, hypoplastic aorta and left ventricular endocardial fibroelastosis. In eight of the ten cases with cardiac defects, there was increased nuchal translucency thickness; the fetal karyotype was normal in six cases, trisomy 21 in two, trisomy 18 in one and Turner syndrome in one[60].

In a study of 29 154 chromosomally normal, singleton pregnancies, 56% of major abnormalities of the heart and great arteries were found in the subgroup with nuchal translucency above the 95th centile[66]. Therefore, measurement of nuchal translucency thickness at 11–14 weeks may constitute the most effective method of screening for cardiac defects.

In patients with increased nuchal translucency, it is now possible to undertake detailed cardiac scanning in early pregnancy. A specialist scan from 14 weeks can effectively reassure the majority of parents that there is no major cardiac defect. In the cases with a major defect, the early scan can either lead to the correct diagnosis or at least raise suspicions so that follow-up scans are carried out. The scans can be performed either transvaginally or transabdominally. However, more important than the actual route for such a scan is the need to use high-quality equipment and, in particular, with facilities for color Doppler examination. At 14 weeks, the gray scale alone is not sufficient for accurate examination of the heart and it is necessary also to use color Doppler to confirm normal forward flow to both ventricles and to identify the outflow tracts.

Screening studies – relation to nuchal translucency thickness

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examination. At 14 weeks, the gray scale alone is not sufficient for accurate examination of the heart and it is necessary also to use color Doppler to confirm normal forward flow to both ventricles and to identify the outflow tracts.

ABDOMINAL WALL DEFECTS

Sonographically, the stomach is identified as a sonolucent cystic structure in the upper left quadrant of the abdomen. It is first visualized at 8–9 weeks and it is seen in all cases by 12–13 weeks[11,18,49]. At 8–10 weeks, of gestation, all fetuses demonstrate herniation of the midgut that is visualized as a hyperechogenic mass in the base of the umbilical cord; retraction into the abdominal cavity occurs at 10–12 weeks and it is completed by 11 weeks and 5 days[11,67,68].

Exomphalos

This is a sporadic abnormality with a birth prevalence of about 1 in 4000. Prenatal diagnosis by ultrasound is based on the demonstration of the mid-line anterior abdominal wall defect, the herniated sac with its visceral contents and the umbilical cord insertion at the apex of the sac (Figure 12). Occasionally, there is an associated failure in the cephalic embryonic fold, resulting in the pentalogy of Cantrell (omphalocele, anterior diaphragmatic hernia, sternal cleft, ectopia cordis and cardiac defects) or failure of the caudal fold, in which case the omphalocele may be associated with exstrophy of the bladder or cloaca, imperforate anus, colonic atresia and sacral vertebral defects. Fetal exomphalos is associated with chromosomal defects, usually trisomy 18, in about 30% of cases at mid-gestation and in 15% of neonates.

Schmidt and Kubli described a case of exomphalos at 13 weeks as an echogenic tumor at the umbilicus; the fetus was subsequently found to have trisomy 18[19]. Brown *et al*. reported the diagnosis of exomphalos containing liver at 10 weeks, but retrospective examinations of the sonograms obtained at 6–9 weeks did not reveal any abnormality; the diagnosis was confirmed after delivery[69]. Similarly, Pagliano *et al*. reported the diagnosis of exomphalos containing liver and bowel in a 10-week fetus; the pregnancy was terminated and the diagnosis was confirmed[70]. Heydanus *et al*. reported the diagnosis of exomphalos in three fetuses at 12–14 weeks; in one there was an associated ectopia cordis and hydrops and the pregnancy was terminated, in the second there was an associated two-vessel cord and intrauterine death occurred and, in the third with isolated exomphalos, there was an infant death[71].

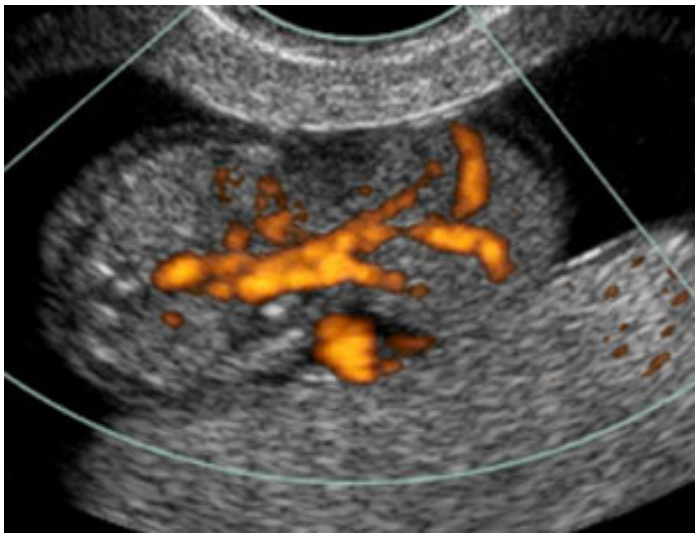


Figure 12 - Exomphalos in a 13-week fetus

van Zalen-Sprock *et al*. reported the findings of 14 cases with exomphalos diagnosed at 11–14 weeks of gestation[68]. In eight cases, there was increased nuchal translucency thickness (3.5–10 mm) and seven of these had chromosomal abnormalities, mainly trisomy 18. The contents of the exomphalos were bowel only in the chromosomally abnormal group and liver as well as bowel in those with a normal karyotype. In the chromosomally normal group, there were four with other defects, such as tetralogy of Fallot and Meckel–Gruber syndrome; only three infants were liveborn.

Screening studies

An ultrasound screening study of 622 high-risk pregnancies at 10–13 weeks correctly diagnosed the two cases of exomphalos[25]. In two other screening studies of low-risk patients, involving 1632 pregnancies at 12–14 weeks[35] and 1473 pregnancies at 10–14 weeks[27], respectively, there were four cases of exomphalos (two in each) and they were all diagnosed in the first-trimester scan.

In a screening study for chromosomal abnormalities by assessment of fetal nuchal translucency thickness at 10–14 weeks of gestation, there were 15 726 pregnancies with a minimum gestation of 11 weeks and 4 days and, in this group, there were 18 cases of exomphalos[72]. In seven cases, the karyotype was normal, in nine there was trisomy 18, in one trisomy 13 and in one triploidy. Furthermore, in the total group, the prevalence of exomphalos in fetuses with trisomy 18 was 23%, in those with trisomy 13 it was 9%, in those with triploidy it was 13% and in those with no evidence of these chromosomal defects it was 0.045%. This study demonstrated that both the prevalence of exomphalos and the associated risk for chromosomal defects increase with maternal age and decrease with gestational age[72].

Gastroschisis

This is a sporadic defect with a birth prevalence of about 1 in 4000. Evisceration of the intestine occurs through a small abdominal wall defect located just lateral and usually to the right of an intact umbilical cord. Prenatal diagnosis by ultrasound is based on the demonstration of the normally situated umbilicus and the herniated loops of intestine, which are free-floating. Associated chromosomal abnormalities are rare.

Surprisingly, although the incidence of gastroschisis in ultrasound studies during the second trimester of pregnancy is similar to that of exomphalos, there is a sparsity of reports on first-trimester diagnosis. Kushnir *et al*. reported a 13-week fetus with a free-floating cauliflower-shaped mass protruding through the fetal abdomen and to the right of a normally inserted umbilical cord; the diagnosis was confirmed after delivery at term[73]. Similarly, Guzman reported a 12-week fetus with gastroschisis; there was spontaneous rupture of membranes and intrauterine death at 22 weeks[74].

Screening studies

In an ultrasound screening study of 622 high-risk pregnancies at 10–13 weeks, there was one 11-week fetus with gastroschisis, encephalocele and kyphoscoliosis; the pregnancy was terminated[25].

URINARY TRACT DEFECTS

The fetal kidneys and adrenals can first be visualized by transabdominal ultrasound at 9 weeks and they are seen in all cases from 12 weeks[18]. The renal echogenicity is high at 9 weeks but decreases with gestation; the adrenals appear as translucent structures with an echodense cortex[18]. The fetal bladder can be visualized in about 80% of fetuses at 11 weeks and in more than 90% by 13 weeks[75]. At 12–13 weeks, the fetal kidneys can be visualized in 99% of the cases, by using both transabdominal and transvaginal sonography[49].

Bilateral Renal Agenesis

This sporadic condition, with a birth prevalence of about 1 in 4000, is usually diagnosed in the second trimester of pregnancy by the findings of anhydramnios, absence of the urinary bladder and failure to identify the fetal kidneys; the differential diagnosis is preterm prelabor rupture of membranes and severe uteroplacental insufficiency that may also present with oligohydramnios.

Bronshtein *et al*. reported the prenatal diagnosis of bilateral renal agenesis at 14 weeks of gestation in five fetuses; in all cases, there were hypoechogenic masses in the renal beds, that were subsequently found at pathological examination to be enlarged adrenals[76]. The amniotic fluid volume was normal in all cases at 14 weeks. In two cases, a cystic structure suggestive of the fetal bladder was temporarily detected in the fetal pelvis but this disappeared by 16–17 weeks.

Infantile polycystic kidney disease

This an autosomal recessive condition with a birth prevalence of about 1 in 50 000. It is subdivided into perinatal, neonatal, infantile and juvenile types, on the basis of the age of onset of the clinical presentation and the degree of renal involvement. Prenatal diagnosis by ultrasound is confined to the perinatal and probably the neonatal types and is based on the demonstration of bilaterally enlarged and homogeneously hyperechogenic kidneys. While there is often associated oligohydramnios, this is not found invariably. These sonographic appearances, however, may not become apparent until 26 weeks of gestation, and therefore serial scans should be performed for exclusion of the diagnosis.

Bronshtein *et al*. reported a case of infantile polycystic kidney disease; at 11 and 15 weeks, the kidneys and bladder looked normal, but at 28 weeks there was oligohydramnios with bilaterally enlarged and diffusely hyperechogenic kidneys[77]. Retrospective examination of the videotapes taken from the early scans demonstrated that the kidneys were of increased echogenicity and increased length from as early as 12 weeks.

Multicystic dysplastic kidney disease

In this sporadic condition, which may be unilateral or bilateral, the collecting tubules and nephrons are dysplastic. The collecting tubules become cystic and the diameter of the cysts determines the size of the kidneys, which may be large and multicystic or small, shrunken and hyperechogenic. Occasionally, only one of a small number of adjacent collecting tubules is involved so that only a segment of the kidney is abnormal. With bilateral involvement, there is associated absence of the bladder and oligohydramnios.

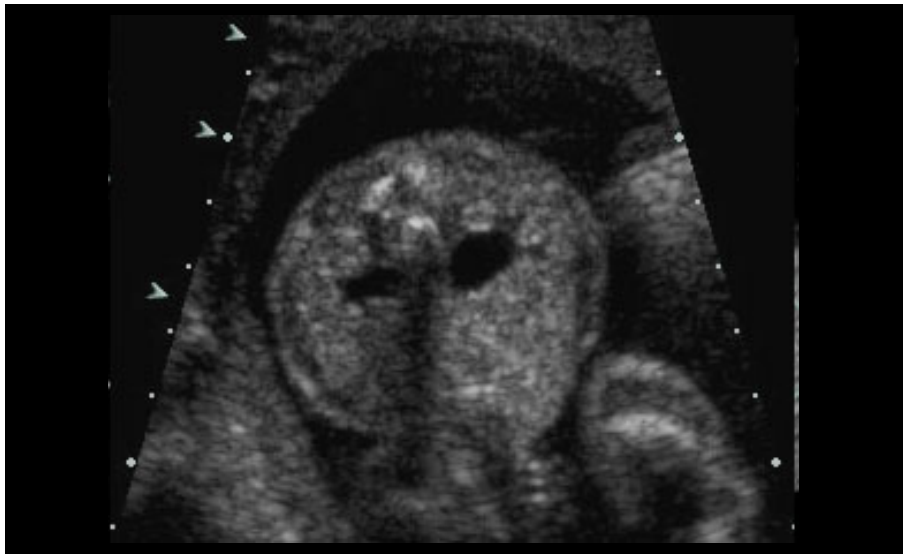
Cullen *et al*. reported a case that at 11 weeks demonstrated hyperechoic kidneys with no obvious dilatation of the bladder; ultrasound examination in the newborn, after delivery at term, confirmed the diagnosis of cystic dysplastic kidneys[25]. Bronshtein *et al*. reported a case with a unilateral multicystic kidney diagnosed at 12 weeks during routine ultrasound examination; the fetal karyotype was normal[78]. Ultrasound examination of the newborn confirmed the antenatal diagnosis.

Screening studies

In a screening study involving ultrasound examinations at 11–14 weeks of gestation and at 18–20 weeks in 3991 patients, there were three cases of unilateral multicystic dysplastic kidneys and none was detected at the early scan; two were diagnosed at 18–20 weeks and the third was detected at 31 weeks[26]. In another screening study involving 1632 pregnancies at 12–14 weeks, there was one case with unilateral multicystic kidneys and this was correctly identified in the first-trimester scan[35].

Hydronephrosis

Varying degrees of pelvicalyceal dilatation are found in about 1% of fetuses. Mild hydronephrosis or pyelectasia may be due to relaxation of smooth muscle of the urinary tract by the high levels of circulating maternal hormones, or maternal–fetal overhydration. In the majority of cases, the condition remains stable or resolves in the neonatal period. In about 20% of cases, there may be an underlying ureteropelvic junction obstruction or vesicoureteric reflux that requires postnatal follow-up and possible surgery. Moderate or severe pelvicalyceal dilatation is usually progressive and, in more than 50% of cases, surgery is necessary during the first 2 years of life.



Mild hydronephrosis or pyelectasia at 13-14weeks

Screening studies

In an ultrasound screening study of 622 high-risk pregnancies at 10–13 weeks, there were two cases of hydronephrosis and exomphalos and they were both detected at the first scan; one pregnancy was terminated and the other resulted in a livebirth with cloacal defect as well as the exomphalos[25]. In a screening study involving ultrasound examinations at 11–14 weeks of gestation and at 18–20 weeks in 3991 low-risk patients, there were four cases of hydronephrosis and only one of these was diagnosed at the early scan[26].

Megacystis

Sebire *et al*. examined transabdominally 300 pregnancies at 10–14 weeks of gestation and reported a significant increase in bladder length with crown–rump length (Figure 13), but, within this gestational age range, none of the measurements was more than 6 mm[79]. The fetal bladder was always visualized if the crown–rump length was more than 67 mm, but not in 9% of those with a crown–rump length of 38–67 mm.

Bulic *et al*. described a 14-week fetus with megacystis (bladder length 50 mm) and oligohydramnios; pathological examination after termination at 15 weeks showed urethral atresia, hypertrophic bladder, dysplastic kidneys and absence of abdominal musculature[80]. In another 11-week fetus, there was megacystis (20 mm); at 14 weeks there was enlargement of the bladder and oligohydramnios. Pathological examination after termination demonstrated urethral atresia, severe megacystis but normal kidneys[80].

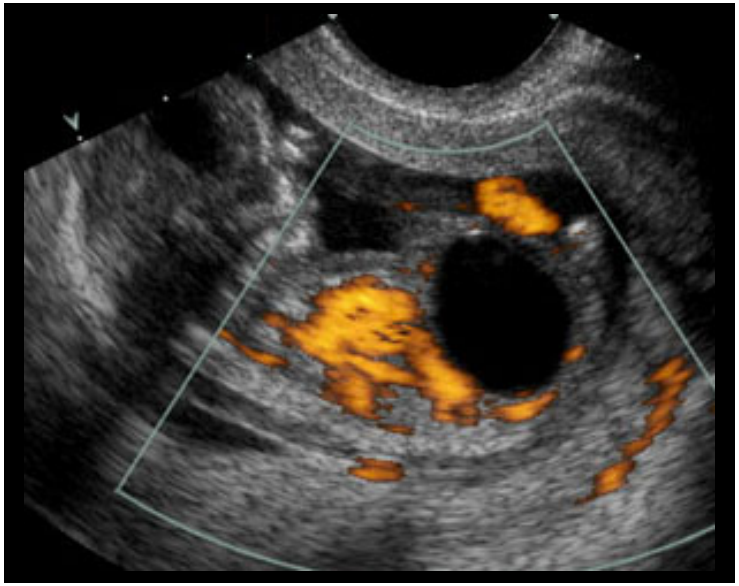


Figure 13a - Megacystis in a 12-13 week fetus (>18 mm diameter)

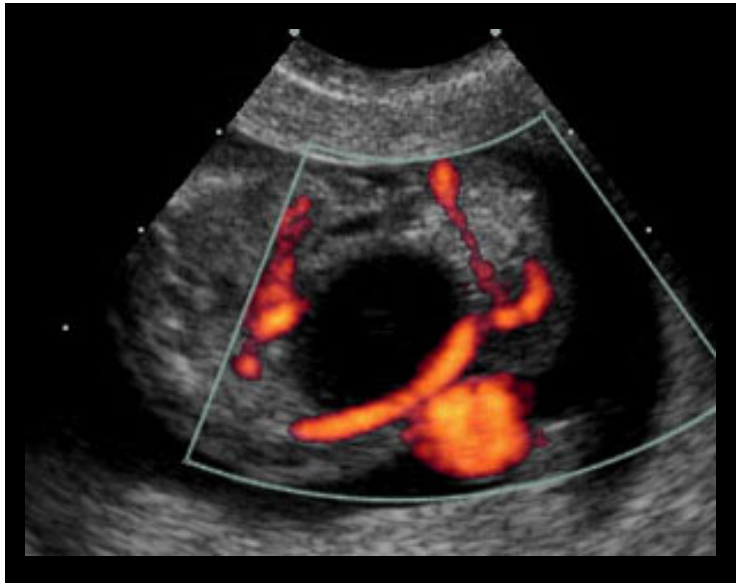


Figure 13b - Megacystis in a 12-13 week fetus + color doppler showing single umbilical artery

Stiller reported an 11-week fetus with megacystis (10 mm) but normal kidneys and amniotic fluid[81]. At 13 weeks, there was enlargement of the bladder (30 mm) and bilateral hydronephrosis with reduced amniotic fluid; the pregnancy was terminated.

Drugan *et al*. reported a 12-week fetus with megacystis (18 mm); at 14 weeks there was further enlargement of the bladder with normal kidneys but oligohydramnios[82]. Vesicoamniotic shunting was carried out and the pregnancy continued normally; a male infant with mild prune-belly and moderate renal function (40–50%) was born at 35 weeks.

Zimmer and Bronshtein reported an 11-week fetus with megacystis (13 mm) and two umbilical cord cysts[83]. At 12 weeks, the bladder increased (30 mm) and there was evidence of hydronephrosis; at 13 weeks there was intrauterine death. In another 12-

week fetus, there was megacystis (46 mm), bilateral hydronephrosis, increased nuchal translucency and talipes. Chorionic villus sampling showed Turner mosaicism and the pregnancy was terminated.

Yoshida *et al*. reported a 13-week fetus with megacystis (45 mm) and decreased amniotic fluid volume; follow-up scans demonstrated resolution of the megacystis and normalization of the amniotic fluid volume[84]. At 28 weeks, tetralogy of Fallot was diagnosed. Investigations after delivery at 38 weeks confirmed the cardiac defect and, in addition, demonstrated vaginal atresia, imperforate anus, recto-urethral fistula, bilateral vesicoureteral reflux, unilateral renal hypoplasia, hypoplasia of abdominal muscles, scoliosis and bilateral talipes. The karyotype was normal female. The suggested diagnosis was VACTERL-like association.

Fried *et al*. reported a 13-week fetus with megacystis (30 mm); a repeat scan 2 days later demonstrated urinary ascites with a thick-walled deflated bladder and the pregnancy was terminated[85]. The fetal karyotype was 46,XY.

Hoshino *et al*. reported a fetus with normal sonographic appearance at 10 weeks but, at 12 weeks, there was megacystis (40 mm) with normal amniotic fluid volume; at 13 weeks, the diameter of the bladder increased to 54 mm, there was bilateral hydronephrosis and the amniotic fluid volume was reduced[86].

Cazorla *et al*. reported a fetus with normal sonographic appearance at 8 weeks but, at 13 weeks, there was megacystis (33 mm) and reduced amniotic fluid volume; the fetal karyotype was 46,XY[87]. At 16 weeks, the fetus developed generalized edema and the pregnancy was terminated. Pathological examination revealed urethral atresia, megacystis, hydronephrosis and atrophied abdominal muscles.

Screening studies

In an ultrasound screening study of 622 high-risk pregnancies at 10–13 weeks, there were two cases with urethral obstruction presenting as megacystis at 11 and 13 weeks of gestation[25]. In a screening study for chromosomal abnormalities by assessment of fetal nuchal translucency thickness, 24 492 singleton pregnancies were examined[79]. Megacystis was present in 15 fetuses (prevalence of 1 in 1633) and, in these cases, the longitudinal bladder diameter was 8–32 mm. There were three cases with chromosomal abnormalities and two of these had increased nuchal translucency thickness. In the chromosomally normal group with mild-to-moderate megacystis (longitudinal bladder diameter of 8–12 mm), the majority of fetuses had ~~spontaneous resolution~~ without any obvious adverse effects on renal development and function. In those with severe megacystis (minimum longitudinal bladder diameter of 17 mm), ~~there was evolution to obstructive uropathy and renal dysplasia~~[79].

Extensive animal studies have demonstrated that obstructive uropathy causes renal dysplasia and the degree of renal damage is related both to the onset and duration of the obstruction[88,89]. Furthermore, such studies have shown that renal damage can be reduced by intrauterine surgery to by-pass the obstruction. However, the data from vesico–amniotic shunting in human fetuses with obstructive uropathy have not provided conclusive evidence that such interventions are beneficial, possibly

because, by mid-gestation, when surgery is usually undertaken, irreversible renal damage may have already occurred. The extent to which first-trimester diagnosis of megacystis and vesico–amniotic shunting could prevent the subsequent development of renal damage remains to be determined.

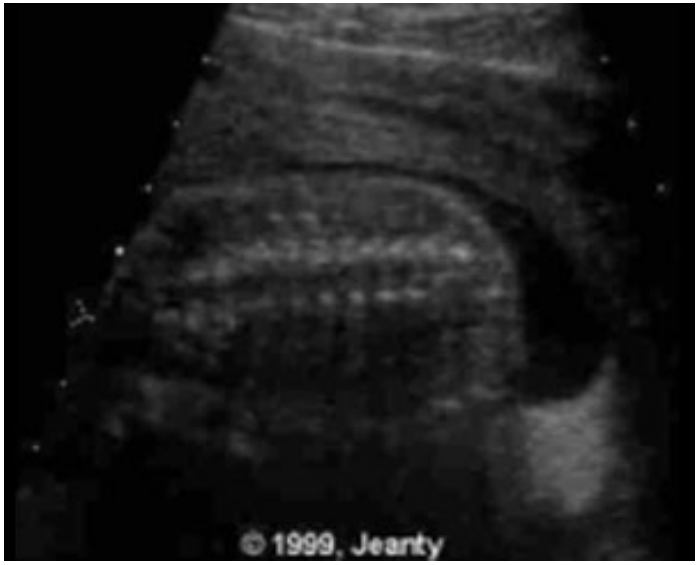
SKELETAL DEFECTS

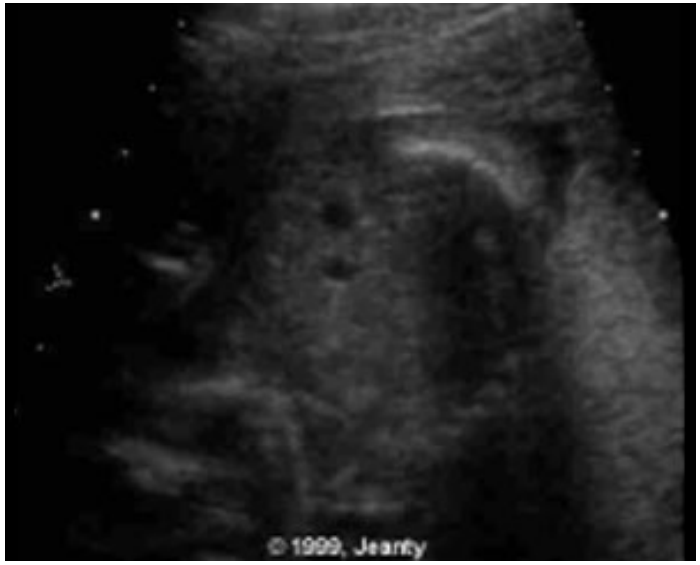
Limb buds are first seen by ultrasound at about the 8th week of gestation, the femur and humerus are seen from 9 weeks, tibia/fibula and radius/ulna from 10 weeks and digits of hands and feet from 11 weeks; all long bones are consistently seen from 11 weeks[14,18,90,91]. Body movements (wiggling) are seen at 9 weeks and, by 11 weeks, limbs move about readily[18,90]. The length of the humerus, radius/ulna, femur and tibia/fibula are similar at 11–14 weeks and increase linearly with gestation from about 6 mm at 11 weeks to 13 mm at 14 weeks; the femur to foot ratio is 0.85[92].

Skeletal dysplasias are found in about 1 per 4000 births; about 25% of affected fetuses are stillborn and about 30% die in the neonatal period. The most common dysplasias are thanatophoric dysplasia, osteogenesis imperfecta, achondroplasia, achondrogenesis and asphyxiating thoracic dysplasia. Several case reports have described the prenatal diagnosis of a wide range of skeletal defects in the first trimester of pregnancy and they are usually associated with increased nuchal translucency thickness (see Chapter 2).

Caudal regression syndrome

This rare, sporadic syndrome presents with varying degrees of vertebral anomalies from partial sacral agenesis to complete absence of the lumbosacral spine. Sirenomelia is the extreme form, with variable fusion and hypoplasia of the lower extremities and genitourinary, gastrointestinal, cardiovascular and central nervous system abnormalities. It is 250 times more common in poorly controlled diabetic mothers than in the general population.





Although on superficial examination this image might pass for normal, note that on the caudal side of the image (on the right, since the ribs can be seen on the left side of the image) the spine terminates without the usual landmark of the iliac wings and sacrum.

The lack of sacrum allows the iliac wings to be approximated, giving them a “shield” like appearance.

courtesy Phillipe Jeanty - www.thefetus.net

Baxi *et al*. performed serial ultrasound scans in a patient that originally presented in diabetic ketoacidotic coma[93]. At 9 weeks, the crown–rump length was shorter by a week than expected from the menstrual age. At 11 weeks, there was a protuberence of the lower spine and no normal movements of the thighs were seen. At 14 weeks, the femora were fixed in a ‘frog-leg’ position and were never seen moving independently from each other. At 17 weeks, shortening and kyphosis of the lower spine were observed. Pathological examination after termination of the pregnancy confirmed the diagnosis of caudal regression syndrome.

Chapter 4 - References

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