CHAPTER 1

Fetal Anatomy

First Trimester Assessment

SUMMARY BOX

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HEAD AND NECK

ANATOMY ASSESSMENT

- Head
  - Cranial bones, midline falx
  - Ventricles filled with choroid plexus – 'butterfly' sign (Fig. 1.1)
  - Intracranial translucency/posterior fossa
- Face
  - Eyes with lenses (Fig. 1.2)
  - Normal profile with nasal bone
  - Intact lips (Fig. 1.3)
- Neck
  - Normal appearance
  - Nuchal translucency (Fig. 1.4)

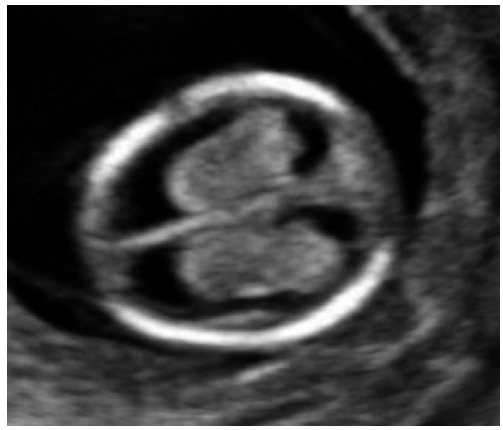

Fig. 1.1 Transverse view of the head. The appearance of the normal choroid plexus is called the 'butterfly sign'. Note that there is no space between the choroid plexus and the walls of the lateral ventricle.

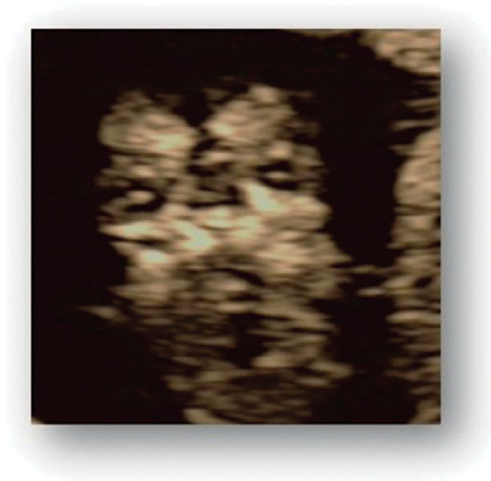

Fig. 1.2 Posterior coronal view of a normal face with large anterior fontanelle. The orbits are seen with the white dot indicating the lenses.

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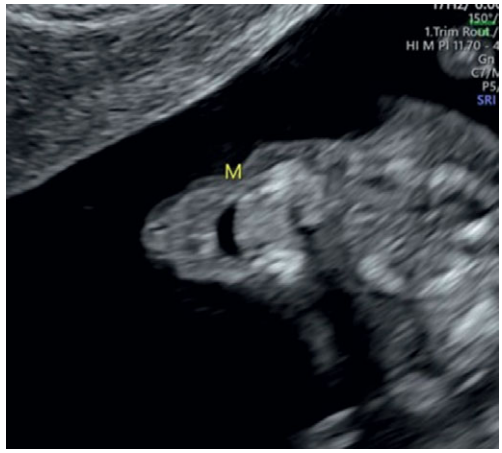

Fig. 1.3 Anterior coronal view of a normal fetal face with open mouth and intact lips.

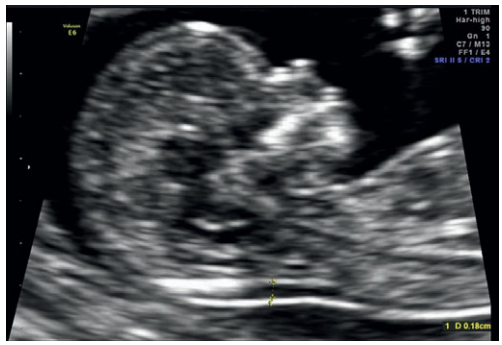

Fig. 1.4 Normal fetal profile with visible nasal bone and normal nuchal translucency (1.8 mm).

ABNORMAL SKULL

Acrania–Exencephaly–Anencephaly Sequence (Fig. 1.5)

Definitions and Characteristics

- Absent cranium – acrania
- Amorphous brain mass – exencephaly (Fig. 1.6)
- No recognisable brain tissue – anencephaly
- Commonly associated with neural tube abnormalities (craniorachischisis, spina bifida, iniencephaly) and facial, cardiac, renal and gastrointestinal malformations

Ultrasound Assessment

- Use transvaginal scan to exclude the presence of amniotic band sequence

Investigations

- Karyotyping may reveal an aneuploidy which would alter the risk for future pregnancy

Counselling and Management

- Offer termination of pregnancy
- Offer palliative care and discuss organ donation programme, if available
- Recurrence is ~3–4%
- Amniotic band sequence is sporadic with no increased risk for future pregnancies
- Advise folic acid supplementation (5 mg/day) in all future pregnancies

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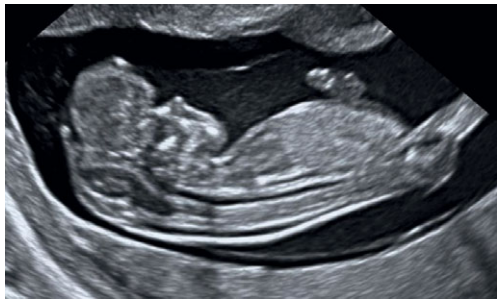

Fig. 1.5 Acrania–exencephaly–anencephaly sequence. Note the absent cranium and free-floating amorphous brain tissue. If first seen later in pregnancy, as the brain tissue is destroyed, this would present as a classic anencephaly.

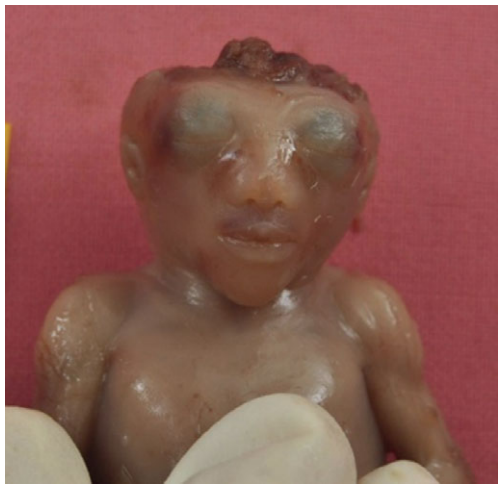

Fig. 1.6 Fetus with acrania. Only a small amount of amorphous brain tissue is still visible.

Skull Defects

Definitions and Characteristics

- Defects are most commonly occipital (85%) and may contain:
  - only meninges (meningocele) (Fig. 1.7)
  - brain tissue (encephalocele) (Figs. 1.8 and 1.9)
  - brain and part of the lateral ventricles (encephalocystocele)
- The clear distinction may not be accurate in the first trimester as contents of a defect may vary at later gestations

Ultrasound Assessment

- Look for *Meckel–Gruber syndrome* (occipital encephalocele with large cystic kidneys and polydactyly)
- Look for *amniotic band sequence* when defects are lateral or parietal

Investigations

- Offer invasive testing for karyotyping and microarray
- Exome sequencing can detect associated autosomal recessive ciliopathies including *Walker–Warburg syndrome* and *Joubert syndrome-related disorders*

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Counselling and Management

Isolated Meningocele

- Good prognosis; >90% survival without sequelae

Encephalocele

- Counselling is complex and should involve neurosurgeons
- Sac size and the amount of brain tissue will determine prognosis
- Mortality approaches 30% despite appropriate treatment
- The long-term outcome of milder forms remains uncertain as most had termination of pregnancy

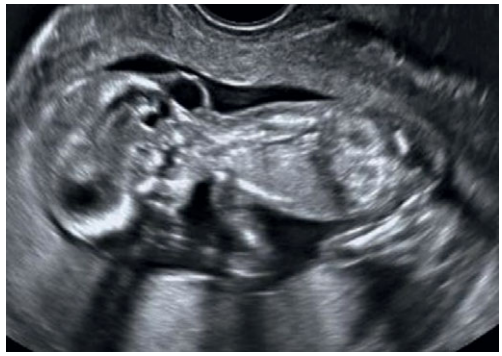

Fig. 1.7 Cystic swelling behind the occipital bone communicating with the posterior fossa through a small calvarial defect suggestive of occipital meningocele. This has to be differentiated from cystic hygroma or lymph cysts, wherein there will be no communication with intracranial structures.

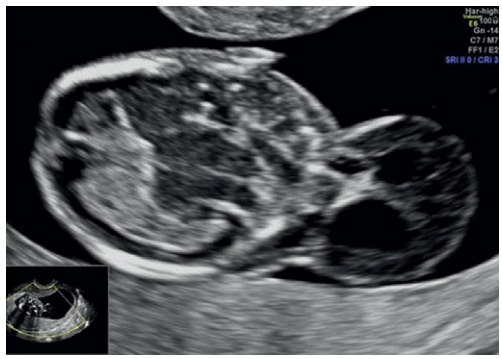

Fig. 1.8 Transverse view of an occipital encephalocele. Note the presence of the brain matter, calvarial defect and altered intracranial anatomy.

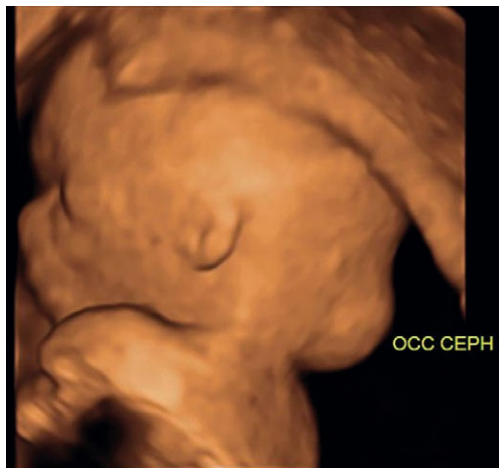

Fig. 1.9 3D view of an occipital encephalocele.

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'BUTTERFLY SIGN' IS ABSENT

Definition and Characteristics

- 'Butterfly sign' describes the normal appearance of the choroid plexuses on transverse imaging of the fetal brain in the first trimester

Ultrasound Assessment

- Look for signs of *alobar holoprosencephaly* (single ventricle, fused thalami, absent falx) (Fig. 1.10)
- Less severe forms of *holoprosencephaly* are unlikely to be detectable in the first trimester
- Early *ventriculomegaly* presents as choroid plexus filling less than half of the ventricular space and not touching the medial and lateral ventricular walls (Fig. 1.11)
- Check for facial clefts and proboscis (a trunk-like nose)

Investigations

- Offer invasive testing

Counselling

- *Alobar holoprosencephaly* is usually lethal in early childhood; up to 80% of fetuses will have abnormal karyotype, mainly trisomy 13 (60%), but also trisomy 18, triploidy and deletions
- *Ventriculomegaly* in the first trimester is often associated with chromosomal and posterior fossa abnormalities, but can also be 'isolated' or transient, with good long-term prognosis

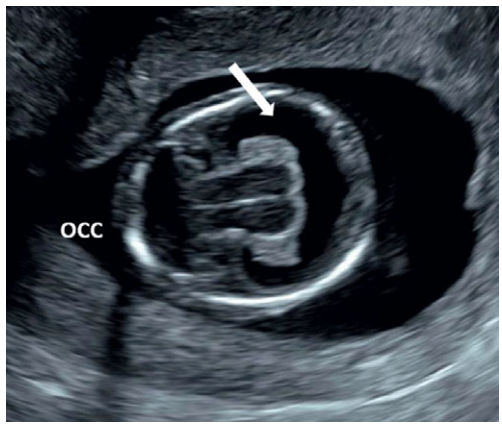

Fig. 1.10 Note the single ventricle (arrow) with absent midline falx and fused thalamus. The 'butterfly' sign is absent. Occ, Occiput.

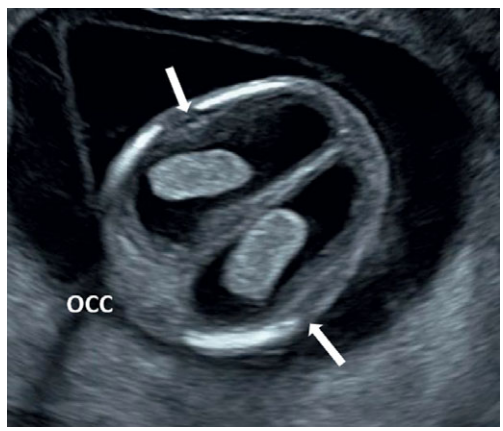

Fig. 1.11 Dilated lateral ventricles (arrows) are suspected in the first trimester when there is a visible space between the choroid plexus and the lateral wall of the lateral ventricles.
Occ, Occiput.

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INTRACRANIAL TRANSLUCENCY IS ABSENT

Definition and Characteristics

- Intracranial translucency (IT) is the fourth ventricle which is seen in the mid-sagittal view of the head
- The IT is parallel to the nuchal translucency and appears between two echogenic borders – brainstem anteriorly and choroid plexus of fourth ventricle posteriorly (Fig. 1.12)
- Immediately below the fourth ventricle is a small translucent area representing the cerebromedullary cistern, which later forms the cisterna magna
- The IT increases from 1.5 mm at a CRL of 45 mm to 2.5 mm at a CRL of 84 mm

Ultrasound Assessment

- Absent or small IT in sagittal section (Fig. 1.13)
- In axial sections the choroid plexus appears to 'fill' the hemisphere and is often referred to as the 'dried up brain' (Fig. 1.14), or the 'crash' sign in the transverse plane (Fig. 1.15)
- Look for spinal defect – it may not be obvious even when using the transvaginal approach
- Absence of lemon and banana signs is not reassuring enough – these signs are not typically present before 14 weeks

Investigations

- Offer invasive testing

Counselling

- Absent IT as a sign of spina bifida or other pathology has a relatively high false-positive rate; therefore, a normal follow-up scan should be sufficiently reassuring

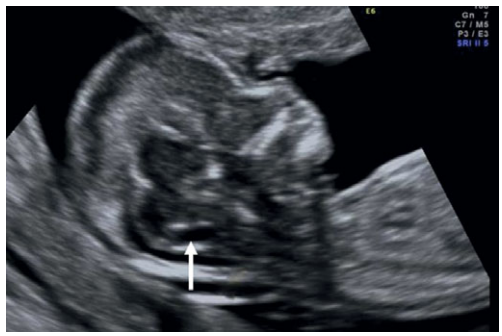

Fig. 1.12 Sagittal plane of the face with normal IT (arrow) which represents the fourth ventricle which lies between the brain stem (above) and the cisterna magna (below).

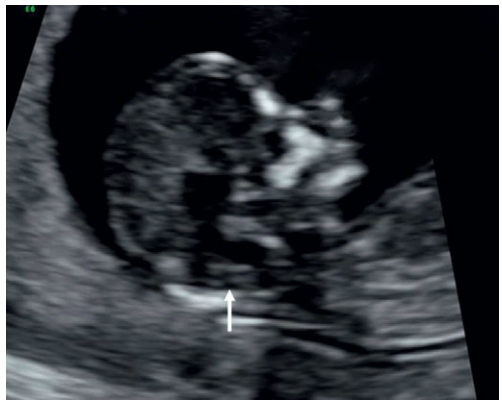

Fig. 1.13 Sagittal plane of the face in a fetus with an open neural tube defect. IT is absent due to the descent of the medulla oblongata through the foramen magnum and compression of the fourth ventricle (arrow).

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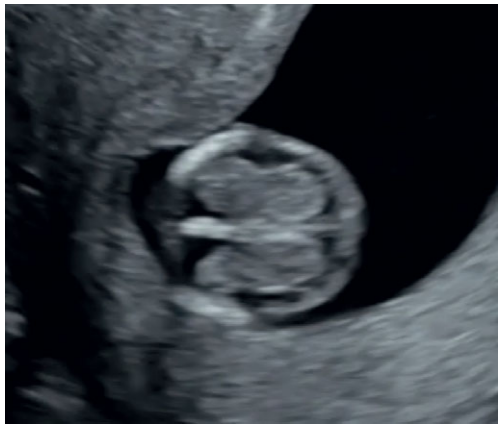

Fig. 1.14 Transverse section of the head in a fetus with spina bifida. The choroid plexus appears to fill up the entire hemisphere. This is referred to as the 'dried up brain'.

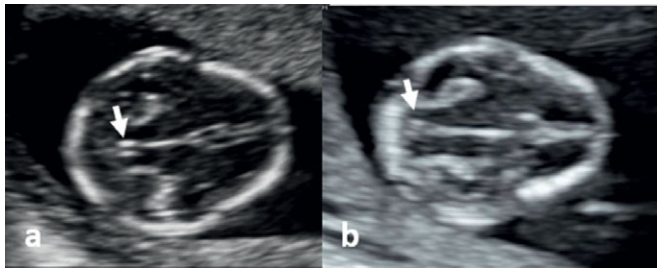

Fig. 1.15 (a) Transverse section of a normal fetal head, showing the thalami, cerebral peduncles and posterior fossa. The aqueduct is seen as a small slit (arrow) at a distance from the occiput. (b) Transverse section of the head in a fetus with spina bifida. The aqueduct is very close to the occiput (arrow) and is referred to as the 'crash sign'.

INTRACRANIAL TRANSLUCENCY IS ENLARGED

Definition and Characteristics

- 99th centile for IT ranges from 3.0 mm (CRL 45–54 mm) to 3.4 mm (CRL 75–84 mm)

Ultrasound Assessment

- Look for absent dividing septum between the IT (future fourth ventricle) and the cisterna magna
- There is a high chance of posterior fossa abnormalities (Dandy–Walker malformation, inferior vermian hypoplasia/Blake's pouch cyst) (Fig. 1.16)
- Arachnoid cysts may look similar

Investigations

- Offer invasive testing for aneuploidies and genetic syndromes (e.g. Walker–Warburg syndrome)

Counselling

- It is best to repeat a scan at 16–18 weeks to re-evaluate intracranial anatomy before discussing prognosis

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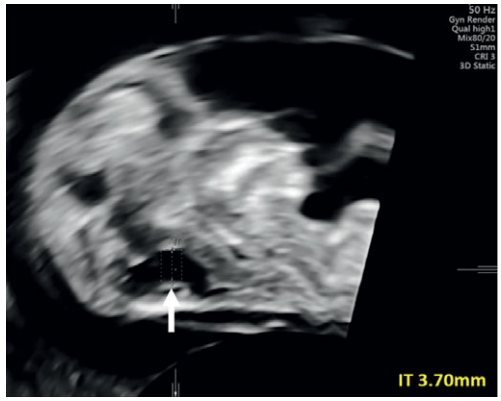

Fig. 1.16 Increased IT (arrow). A targeted scan at 16 weeks revealed a 'classic' Dandy–Walker malformation.

NASAL BONE IS 'ABSENT'

Definition and Characteristics

- The 'absence' describes lack of sonographic echogenicity, rather than absence of the bone/nose
- Prevalence in unselected population is 1–2% in the first trimester, <1% in the second trimester
- 65% of fetuses with trisomy 21 have an 'absent' nasal bone in the first trimester

Ultrasound Assessment

- Relies on comparison to overlying skin (Fig. 1.17)
- 'Absent' (unossified) nasal bone is less echogenic than skin and therefore only two dots are seen (Fig. 1.18)

Investigations

- If absent nasal bone has not been already included in the first trimester screening result, NIPT testing or karyotyping should be offered
- If absent nasal bone has been included in the first trimester screening and the result is low risk, the risk is not recalculated in the second trimester

Counselling

- When nuchal translucency and NIPT or karyotype are normal, interpret as a normal variant
- The couple can be informed that there is no risk of cosmetic problems after birth

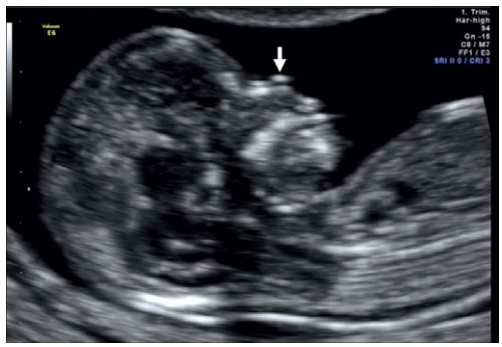

Fig. 1.17 Mid-sagittal view of the face showing an ossified nasal bone. Three 'dots' are visible – the brightest one is the nasal bone. Above the nasal bone is the skin; together they resemble = (equal sign). The third dot lying anteriorly is the tip of the nose (arrow). Note that the ultrasound beam is perpendicular to the nasal bone.

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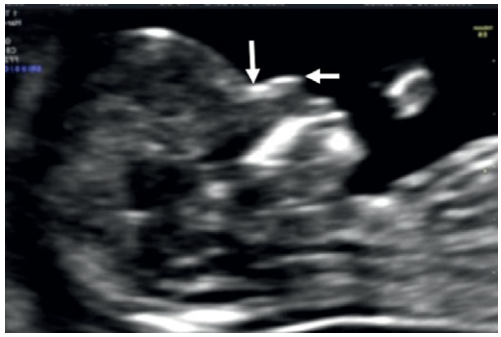

Fig. 1.18 Mid-sagittal view of the face showing 'absent' (unossified) nasal bone. Only two echogenic dots are seen, representing the skin and the tip of the nose (arrows).

MICROGNATHIA IS SUSPECTED

Definition and Characteristics

- Clinically significant facial abnormality should be suspected when the retronasal triangle is abnormal or the mandibular gap is absent

Ultrasound Assessment

- Visualise the retronasal triangle and mandibular gap on coronal section (Figs. 1.19 and 1.20)

Investigations

- Offer CVS when the retronasal triangle looks abnormal or mandibular gap is absent

Counselling

- As false positives are relatively common, detailed ultrasound assessment should be repeated around 16–18 weeks

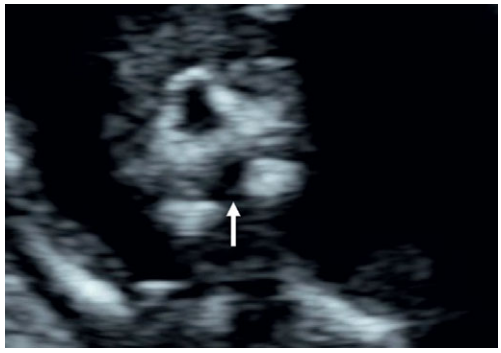

Fig. 1.19 Coronal view of the face with retronasal triangle and characteristic gap between mandibular bones (arrow). This mandibular gap is a normal finding. In cases of micrognathia the chin is still visible but this mandibular gap can be absent.

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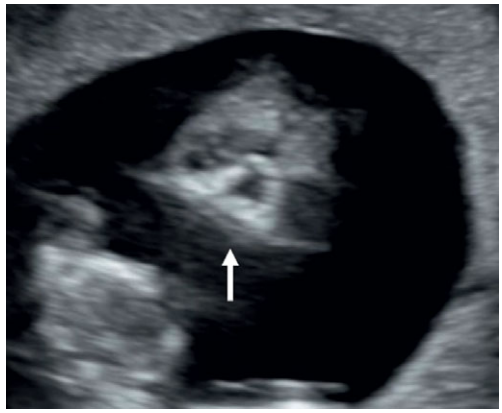

Fig. 1.20 In agnathia, no mandibular echogenicity is seen (arrow).

CLEFT LIP AND PALATE ARE SUSPECTED

Definition and Characteristics

- Cleft lip and palate are relatively common anomalies that are rarely suspected or detected during the first trimester scan
- The incidence of cleft lip and palate is around 1 in 1,250, although it is more common in some countries (e.g. 1 in 500 in Japan)

Ultrasound Assessment

- A cleft lip is recognised by lack of continuity of the upper lip in a coronal view (Fig. 1.21)
- Maxillary gap in the mid-sagittal view of the fetal face suggests that significant cleft palate is also present (Fig. 1.22)
- Assessment of the retronasal triangle may reveal its abnormal shape or defects in the base of the triangle when cleft palate is present (Fig. 1.23)

Investigations

- Offer CVS when facial clefts are detected

Counselling

- Detailed ultrasound assessment should be repeated around 16–18 weeks

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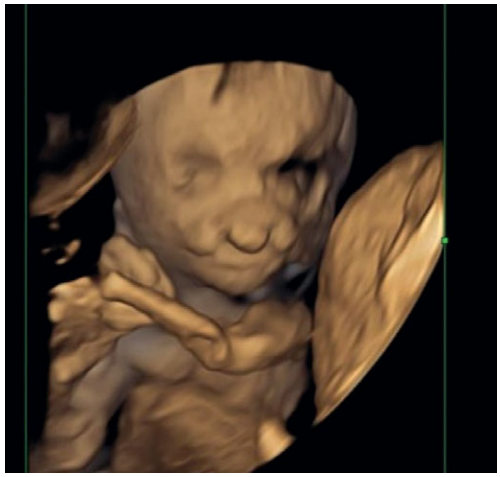

Fig. 1.21 3D picture of the face showing bilateral cleft lip.

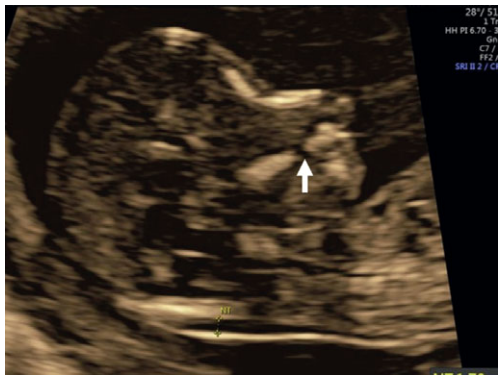

Fig. 1.22 Mid-sagittal view of the face showing a 'gap' in the maxilla which is indicative of cleft palate (arrow).

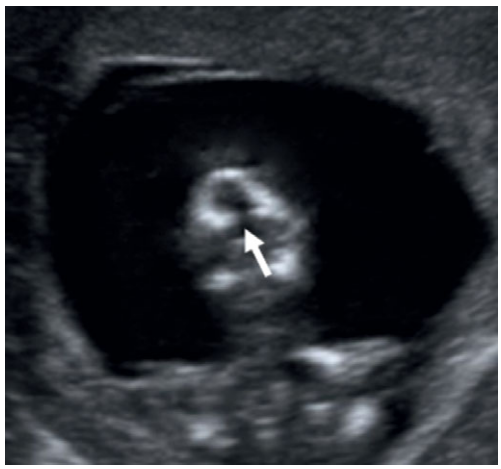

Fig. 1.23 Coronal view of the face of a fetus with cleft palate showing the retronasal triangle. The arrow points to the defect in the base of the triangle.

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LARGE NUCHAL TRANSLUCENCY

Definition and Characteristics

- Nuchal translucency (NT) is the subcutaneous accumulation of fluid behind the fetal neck (Fig. 1.24)
- Typically identified during aneuploidy screening between 11^{+0} and 13^{+6} weeks of gestation (CRL 45–84 mm), it may also be identified before 11 weeks during pre-NIPT scans
- Increased NT before 11 weeks is usually defined as >2.2 mm, corresponding to the 95th centile at 10 weeks
- Raised NT before 11 weeks is best described as nuchal oedema to avoid confusion with 'classic' NT seen in a fetus with CRL > 45 mm after 11 weeks
- NT ≥ 3.5 mm between $11+^{0}$ and 13^{+6} weeks, corresponding to the 99th centile, is associated with chromosomal abnormalities, genetic syndromes and a wide range of structural defects commonly involving cardiac, skeletal and lymphatic systems

Ultrasound Assessment

- Identify correct sagittal plane and position callipers correctly
- Use colour Doppler to exclude nuchal cord (Fig. 1.25)
- If views are suboptimal, transvaginal scan is recommended to exclude the presence of generalised subcutaneous oedema, mild ascites and pleural/pericardial effusions

Investigations

- Offer chromosomal microarray analysis
- Large NT may also be an indication for exome sequencing – various cut-offs in terms of NT size have been proposed depending on local circumstances and availability of clinical geneticists to interpret variants of unknown significance

Counselling

- Normal NIPT test may provide false reassurance by missing atypical aneuploidies
- Structural abnormalities including hydrops may become apparent later in pregnancy (e.g. Noonan syndrome)
- If karyotype and 20 weeks scan are normal, long-term outcome is comparable to the general population
- Offer fetal echocardiography in the second trimester and a third trimester follow-up scan
- Nuchal oedema seen before 11 weeks will resolve in ~80% of cases when reviewed again between 11 and 13^{+6} weeks, but the risk of an adverse outcome (chromosomal abnormality, major structural defect or miscarriage) remains relatively high (~10%)

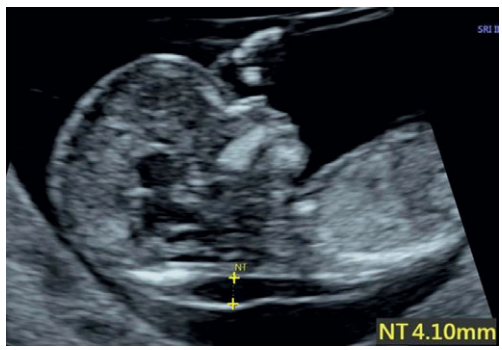

Fig. 1.24 Increased NT, no septa.

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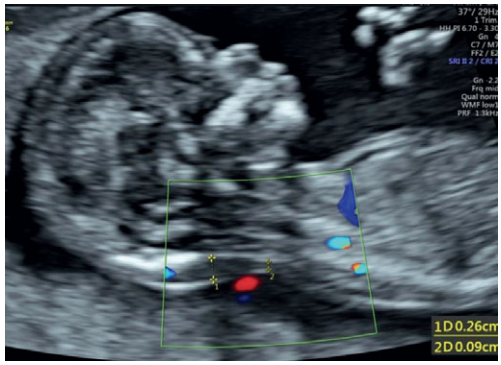

Fig. 1.25 NT with nuchal cord. Accurate measurement of the NT is compromised by the presence of nuchal cord. The measurements should be taken above and below the nuchal cord and the average used for risk calculation.

JUGULAR LYMPHATIC SACS

Definition and Characteristics

- Jugular lymphatic sacs (JLS) are accumulations of lymphatic fluid in the anterolateral region of the fetal neck
- Typically identified during anatomical survey of the neck in transverse section

Ultrasound Assessment

- Use both sagittal and transverse plane and colour Doppler to distinguish from increased NT, septated cystic hygroma or nuchal cord
- JLS will appear as spheroid echolucent 'cysts' in the anterolateral part of the neck (Fig. 1.26)
- The sacs do not cross the midline posteriorly

Investigations

- Offer invasive testing

Counselling

- If microarray and NT are normal, it is likely to be a normal variant
- If NT is increased but microarray analysis is normal, consider further testing for RASopathies (Noonan syndrome panel)

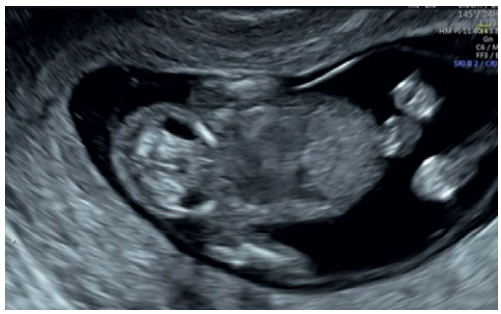

Fig. 1.26 Jugular lymphatic sacs are seen as small bilateral cystic areas on the sides of the neck.

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CYSTIC HYGROMA

Definition and Characteristics

- Cystic hygroma have cystic areas by the side of the neck, while increased NT is strictly confined to the back of the neck (Figs. 1.27 and 1.28)
- The distinction between cystic hygroma and large NT is subjective – internal echoic structures are invariably present in both. Many experts will not attempt to make this distinction in the first trimester

Ultrasound Assessment

- Septation should be visible in the transverse plane
- Fetal echocardiography should be performed as early as possible

Investigations

- Offer microarray testing and, if available, testing for RASopathies (Noonan syndrome)

Counselling

- Very high risk (~50%) of chromosomal abnormalities
- Turner syndrome is the most common, but trisomies 21 and 18 and atypical chromosomal abnormalities are also represented
- Turner syndrome with large hygroma and generalised oedema has very low survival rate (<5%)
- Repeat fetal echocardiography in the second trimester and offer growth and wellbeing scans in the third trimester
- ~15–20% will have a good outcome with normal karyotype and normal paediatric follow-up

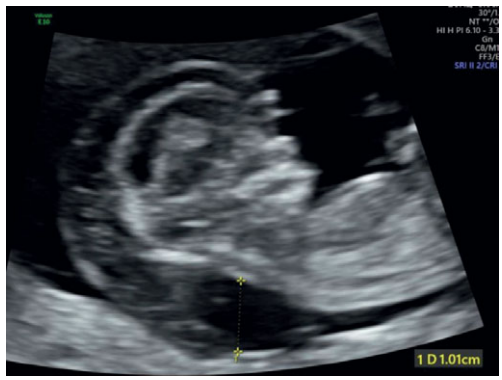

Fig. 1.27 Mid-sagittal view of the head and chest showing a large cystic hygroma. Generalised oedema is also present.

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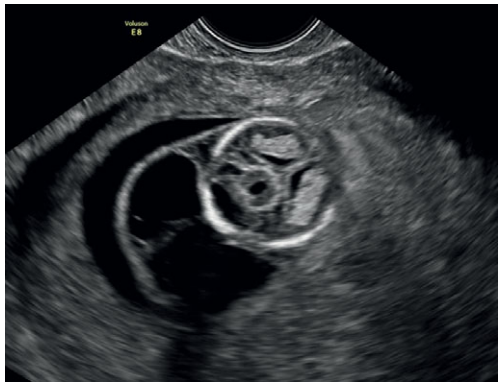

Fig. 1.28 Transverse view of the head with a septated cystic hygroma. Note that there is no communication with intracranial structures.

HEART

ANATOMY ASSESSMENT

Ultrasound Assessment

- Normal heart position with apex pointing to the left side of the chest (levocardia) (Fig. 1.29)
- Normal four-chamber view (Fig. 1.30)
- Normal three-vessel view/three vessels and trachea (3VV/3VT) view (Fig. 1.31)

Significant Heart Abnormality Should Be Suspected If

- Cardiac axis is abnormal
- NT is enlarged
- Tricuspid regurgitation is present (Figs. 1.32 and 1.33)
- Ductus venosus flow is abnormal (Figs 1.34 and 1.35)

Investigations

- If significant cardiac anomaly is suspected, CVS for chromosomal microarray testing should be offered

Counselling

- In most cases with normal microarray, the definitive diagnosis is best delayed until the second trimester

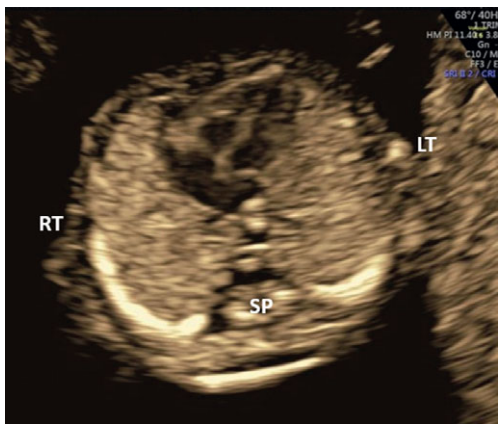

Fig. 1.29 Normal four-chamber view with the apex pointing to the left.

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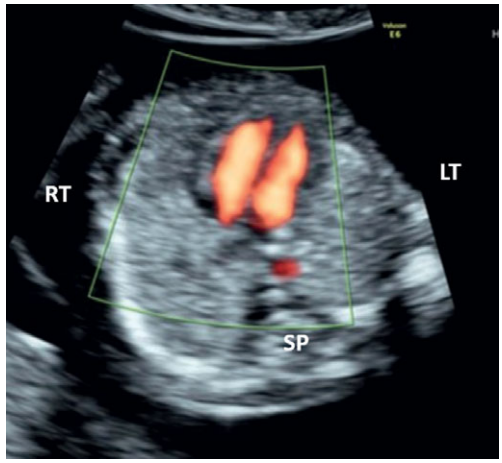

Fig. 1.30 Colour Doppler of the normal four-chamber view with blood flow reaching the apex of both ventricles.

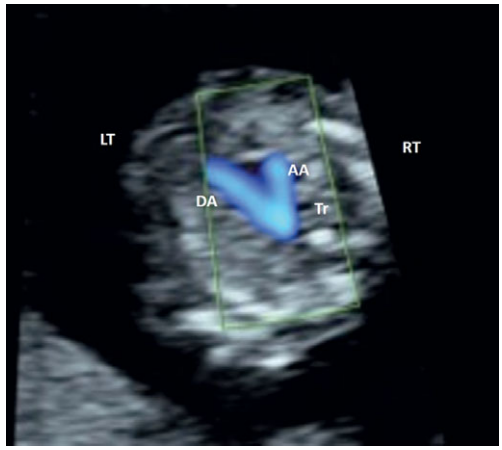

Fig. 1.31 Colour Doppler of the arches. Note that blood flow is towards the spine with both arches pointing to the left of the spine. AA, aortic arch; DA, ductal arch; Tr, trachea.

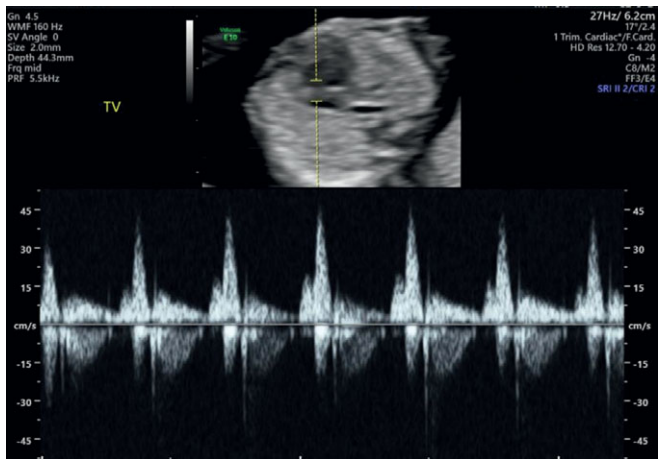

Fig. 1.32 Pulse wave Doppler showing normal flow across the tricuspid valve. Note that the sample volume is 3 mm and is placed across the whole tricuspid valve in an apical four-chamber view.

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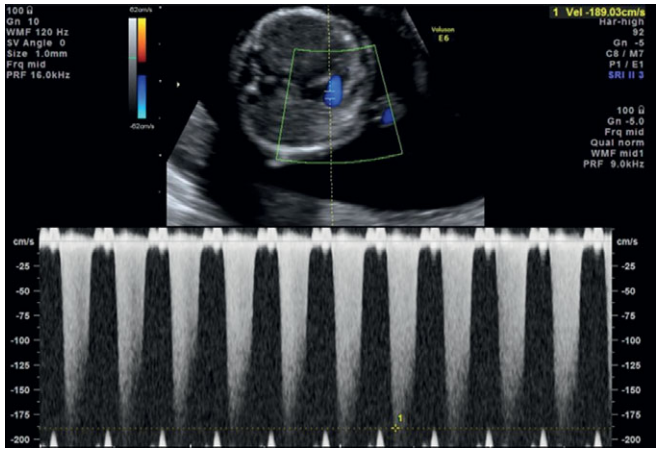

Fig. 1.33 Pulse wave Doppler showing tricuspid regurgitation. The regurgitant flow should reach at least 60 cm/s lasting at least two-thirds of the systole.

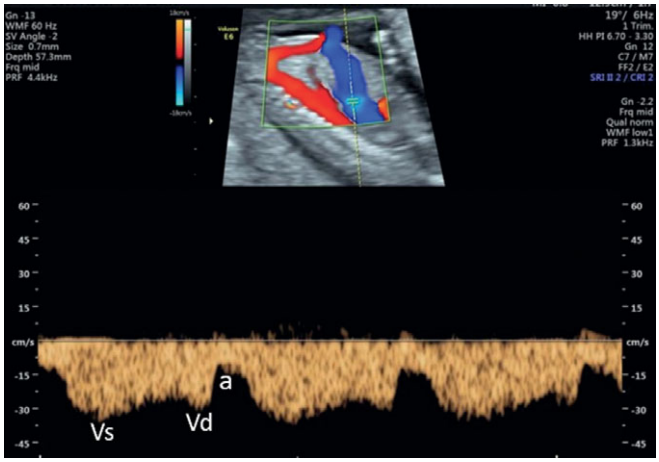

Fig. 1.34 Normal ductus venosus Doppler in the first trimester. The angle of the Doppler should be $<20^{\circ}$ in an adequately zoomed image with a sample volume of 0.5 mm placed at the colour aliasing point. In the typical 'M' waveform pattern the 'a' wave shows positive flow, which is normal. a, atrial systole; Vd, ventricular diastole; Vs, ventricular systole.

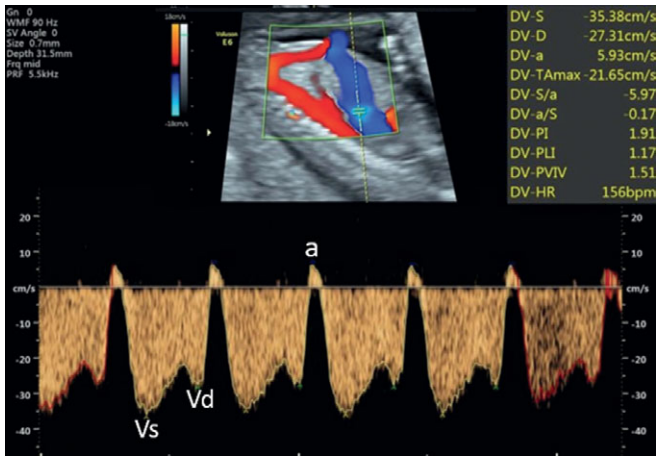

Fig. 1.35 Abnormal ductus venosus flow with reversal of the 'a' wave. a, atrial systole; Vd, ventricular diastole; Vs, ventricular systole.

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ABNORMAL FOUR-CHAMBER VIEW

Table 1.1 Abnormal Four-Chamber View

Ultrasound presentation	Differential diagnosis
Single ventricle	Univentricular heart; hypoplastic left heart syndrome (HLHS), tricuspid atresia, mitral atresia, severe coarctation Large atrioventricular septal defect
Ventricular disproportion	
• Small left ventricle with unequal ventricular filling on colour Doppler (Figs. 1.36 and 1.37). Reversal of flow may be seen in the aortic arch (Fig. 1.38)	HLHS (Fig. 1.36), coarctation
• Hypoplastic, hypokinetic right ventricle	Pulmonary atresia
• Hypoplastic right ventricle, large left ventricle	Tricuspid atresia with ventricular septal defect
Single channel of blood entering both ventricles	Atrioventricular septal defect (Figs. 1.39 and 1.40)

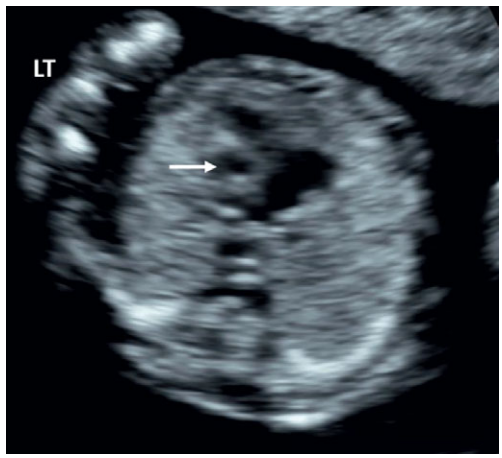

Fig. 1.36 Hypoplastic left heart syndrome (HLHS). Four-chamber view shows small left ventricle (arrow) and normal-sized right ventricle.

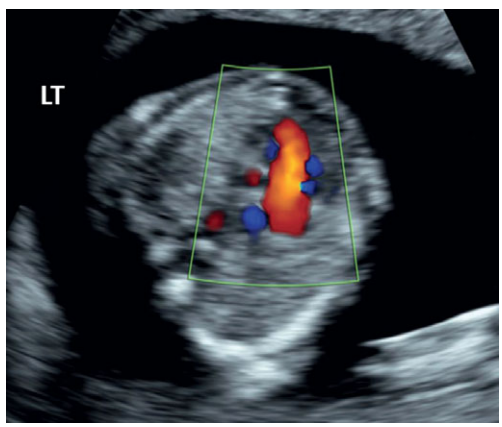

Fig. 1.37 Colour Doppler in HLHS shows single inflow filling on the right side and no filling on the left side.

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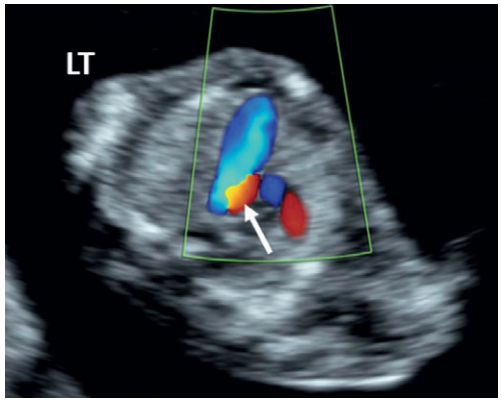

Fig. 1.38 Colour Doppler of the 3VT view in HLHS shows large pulmonary artery and reversal of flow in the aortic arch, shown in red (arrow).

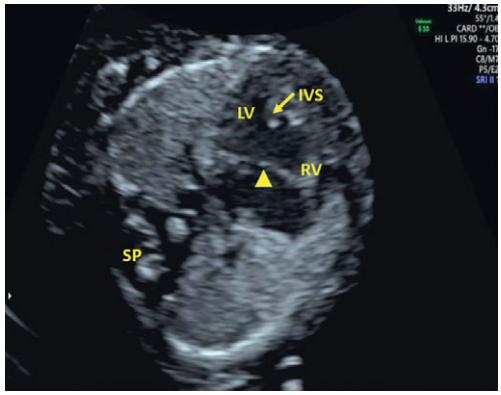

Fig. 1.39 Atrioventricular septal defect (AVSD). Note absence of crux and common AV valve (arrowhead). A small portion of the interventricular system is seen near the apex (arrow). LV, left ventricle; RV, right ventricle; SP, spine.

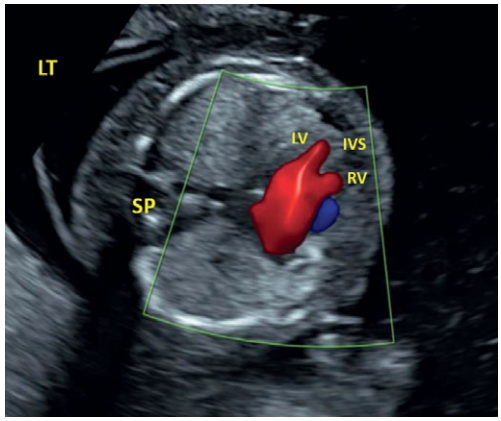

Fig. 1.40 Colour doppler in AVSD showing common atrioventricular flow. IVS, intraventricular septum; LV, left ventricle; RV, right ventricle; SP, spine.

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ABNORMAL THREE-VESSEL VIEW

Table 1.2 Abnormal three-vessel view

Large pulmonary artery, small aortic arch with reversed colour flow	Hypoplastic left heart syndrome
Small aortic arch with antegrade flow	Coarctation
Reverse flow in pulmonary artery and ductus venosus	Pulmonary atresia with intact septum
Small pulmonary artery with antegrade flow	Tricuspid atresia with ventricular septal defect
Single great vessel	Transposition of great arteries (Figs. 1.41–1.44)

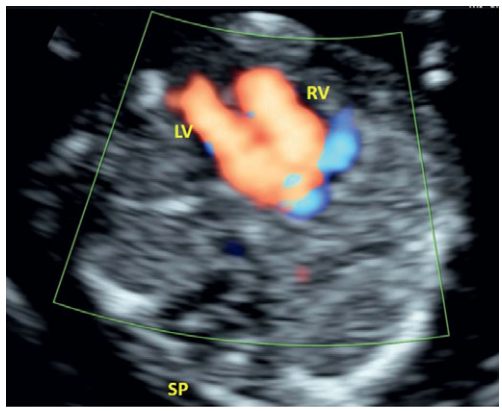

Fig. 1.41 Transposition of the great arteries (TGA). Colour Doppler in four-chamber view shows normal inflow into symmetrical ventricles. LV, left ventricle; RV, right ventricle; SP, spine.

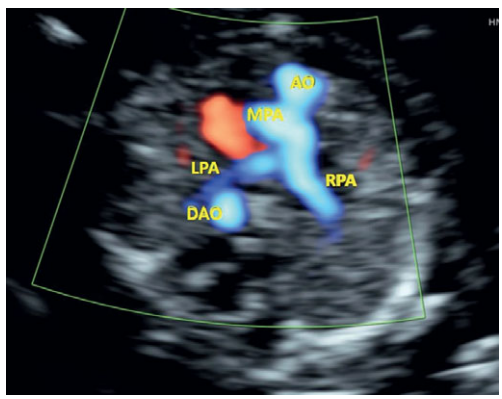

Fig. 1.42 Three-vessel view in TGA shows a cross section of the aorta anteriorly and the branching pulmonary artery posteriorly. In a normal fetus the anterior branching vessel is the pulmonary artery. AO, aorta; DAO, descending aorta; LPA, left pulmonary artery; MPA, main pulmonary artery; RPA, right pulmonary artery.

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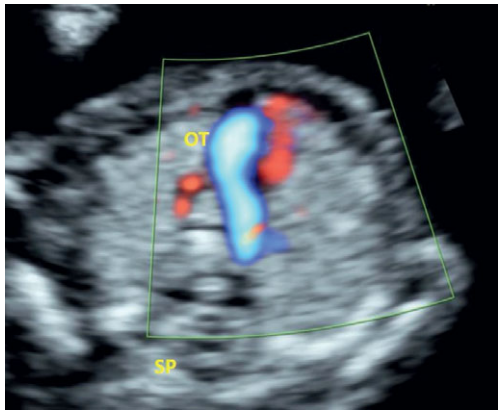

Fig. 1.43 Three-vessel trachea view in TGA shows a single outflow tract. The aorta is posterior and behind the PA and cannot be not seen at this level. OT, outflow tract; SP, spine.

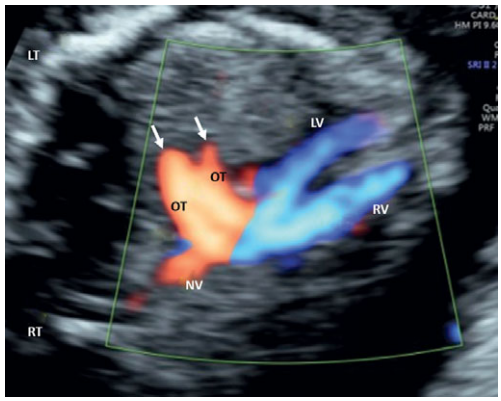

Fig. 1.44 Colour Doppler in sagittal view of TGA. Arrows show parallel outflow tracts (red colour) and ventricular blood flow (blue colour). LV, left ventricle; NV, neck vessel; OT, outflow tract; RV, right ventricle.

ABERRANT RIGHT SUBCLAVIAN ARTERY (ARSA)

Definition and Characteristics

- Arises most distally from the aortic arch, goes behind the oesophagus and trachea to the right upper arm (Fig. 1.45)
- The most common abnormality of the aortic arch

Ultrasound Assessment

- Measure NT
- Examine fetal heart in standard planes
- Exclude tricuspid regurgitation and abnormal ductus venosus
- Colour Doppler PRF set to 0.9–1.8 KHz
- Identify arches and aortic arch crossing trachea anterior and to the left of the spine (3VT view) (Fig. 1.46)
- Move the probe cranially to identify clavicles
- Normal subclavian artery is seen as a tortuous vessel going towards the clavicle and right arm
- Aberrant right subclavian artery is seen coursing behind the trachea

Counselling

- Isolated ARSA is not associated with an increased risk of aneuploidy
- Fetal karyotyping including 22q11 deletion is advisable, if the background risk is higher or additional markers are present

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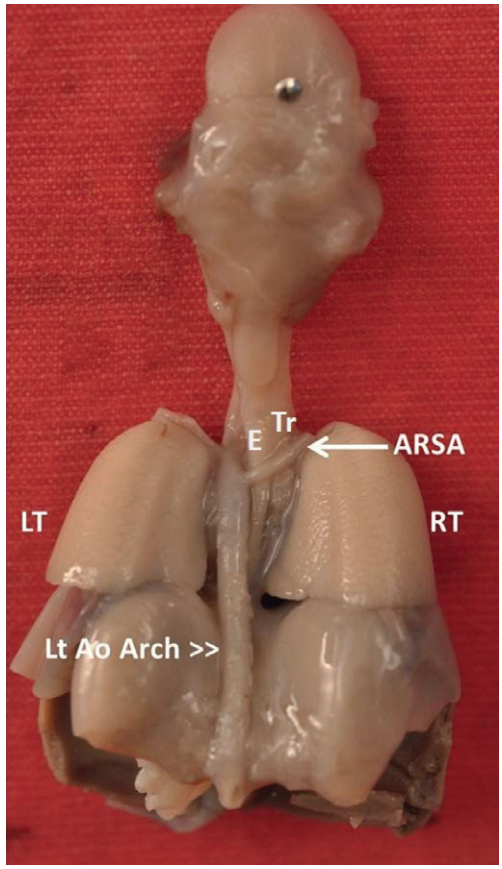

Fig. 1.45 Post mortem specimen viewed from the back showing the aberrant origin of the right subclavian artery (ARSA) from the aortic arch and traversing posterior to the oesophagus (E) and trachea (Tr).

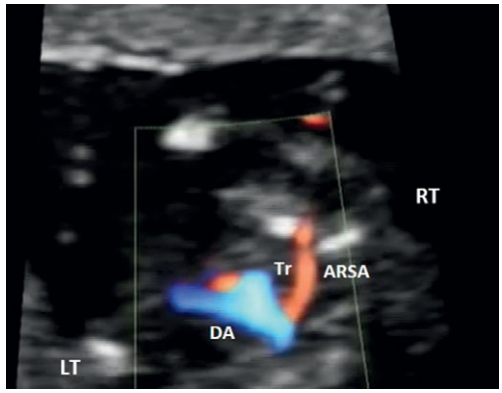

Fig. 1.46 Aberrant right subclavian artery (ARSA) seen in the 3VT view. DA, ductal arch; Tr, trachea.

CHEST

ANATOMY ASSESSMENT

- Homogeneous lung echogenicity should be seen on both sides without pleural effusions or cystic or solid masses (Fig. 1.47)
- Lungs are slightly more echogenic than cardiac muscles and fetal liver
- Diaphragmatic continuity with normal position of stomach and liver (Fig. 1.48)

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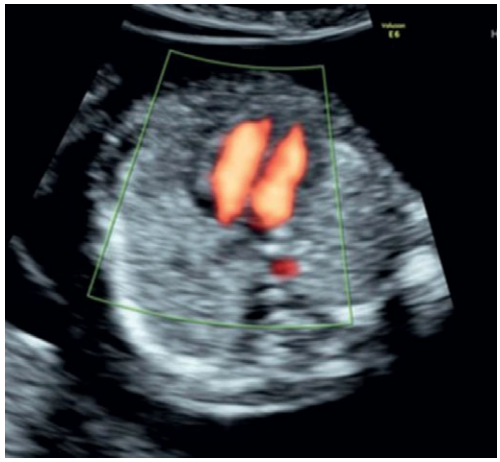

Fig. 1.47 Transverse section of the thorax at the four-chamber view with normal symmetrical lungs.

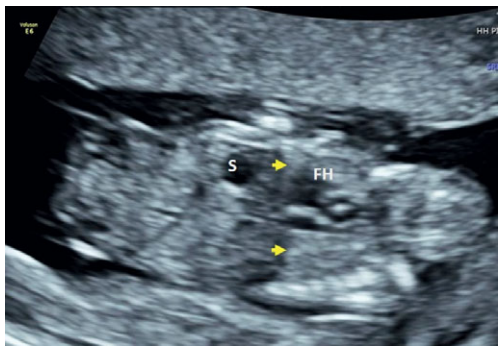

Fig. 1.48 Coronal view of the abdomen and thorax showing normal diaphragm (arrows). The stomach is seen below the diaphragm. FH, fetal heart; S, stomach.

MEDIASTINAL SHIFT

Ultrasound Assessment

- Mediastinal shift is diagnosed on a transverse four-chamber view plane by drawing an imaginary line connecting the spine and sternum, with the fetal heart lying on either side of the line
- Congenital diaphragmatic hernia (CDH) should be suspected in the presence of mediastinal shift, abnormal cardiac axis or herniated stomach (Figs. 1.49 and 1.50)
- Unilateral lung agenesis is also a (much rarer) possibility.
- In the sagittal sections of the abdomen an abnormal course of the ductus venosus and 'upturned' course of the superior mesenteric artery are pointers point to CDH (Fig. 1.51)
- In the coronal view the abdominal aorta is deviated

Investigations

- If CDH is suspected, offer invasive testing even if NT is normal; associated syndromes include trisomy 18, tetrasomy 12p (Pallister–Killian syndrome) and Cornelia de Lange syndrome

Counselling

- Definitive diagnosis of intrathoracic pathology, including diaphragmatic hernia, is best delayed until the second trimester

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- Isolated unilateral lung agenesis may have a good outcome, but is more likely to be associated with congenital heart defects, including Scimitar syndrome (anomalous venous return from the right lung) with very high mortality rate

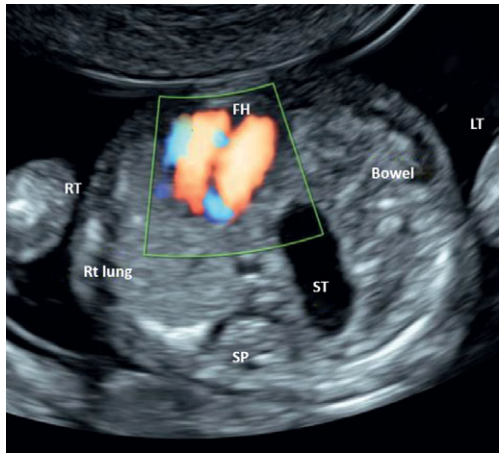

Fig. 1.49 Transverse section of the thorax showing left-sided diaphragmatic hernia. There is a mediastinal shift to the right. Stomach and small bowel are seen on the left side. FH, fetal heart; ST, stomach.

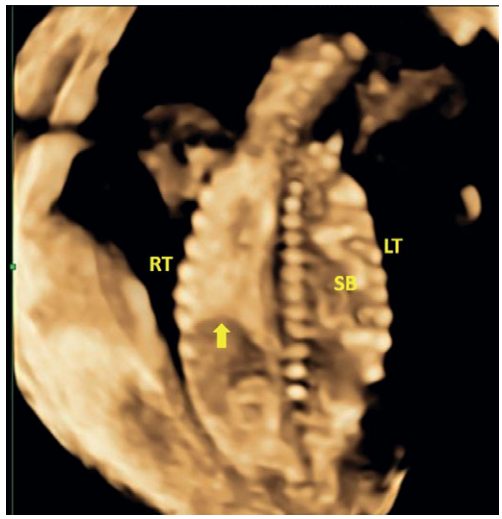

Fig. 1.50 Coronal 3D image of left diaphragmatic hernia with small bowel in the left hemithorax. The arrow points to the right hemidiaphragm. SB, small bowel.

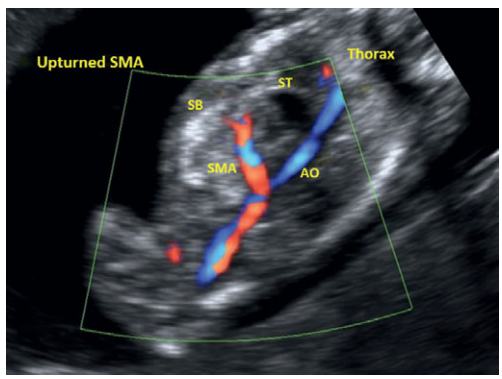

Fig. 1.51 Colour Doppler in a case of left-sided diaphragmatic hernia showing the upturned superior mesenteric artery. AO, aorta; SB, small bowel; SMA, superior mesenteric artery; ST, stomach.

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PLEURAL EFFUSION

Definitions and Characteristics

- In pleural effusions an abnormal collection of fluid lies between the layers of pleura within the chest cavity
- Incidence of non-hydropic pleural effusions is around 1 in 10,000.
- Most isolated pleural effusions will present before 24 weeks, but rarely in the first trimester

Ultrasound Assessment

- Look for other evidence of hydrops (skin oedema, slight ascites)
- Pericardial effusion can be mistakenly described as pleural effusion – the fluid in pericardial effusion surrounds the heart and is, therefore, seen on the medial aspect of the lung
- Diagnosis should be confirmed on transvaginal scan
- Unilateral effusions are very rarely seen in the first trimester

Investigations

- Offer invasive testing (microarray)

Counselling

- Most babies with pleural effusions associated with hydrops and/or chromosomal anomalies are likely to die before 20 weeks (>80%).
- Non-hydropic unilateral effusions are likely to resolve spontaneously

SPINE

ANATOMY ASSESSMENT

- Normal vertebral alignment in longitudinal, coronal and transverse views (Figs. 1.52–1.54)
- Intact overlying skin
- Particular effort should be made to confirm normal appearance of the spine when
  - IT is absent
  - biparietal diameter is <5th centile

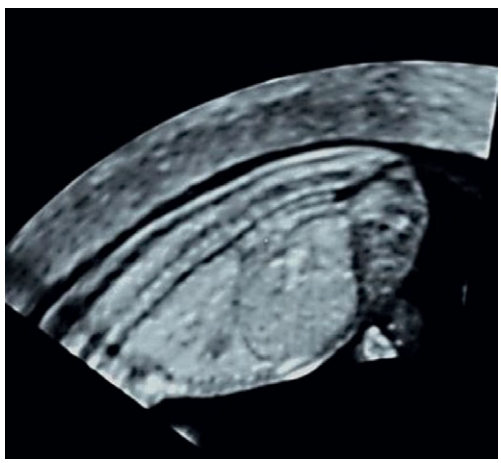

Fig. 1.52 Normal spine with intact skin posterior to the vertebrae from neck to sacrum in a mid-sagittal view. Note that vertebral bodies show ossification, but arches, which are still cartilaginous, are isoechoic or hypoechoic.

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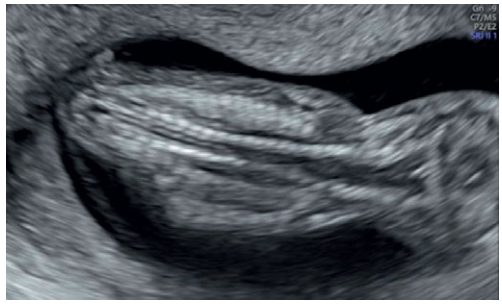

Fig. 1.53 Coronal view of the normal fetal spine at 13 weeks, showing normal cervical widening; the rest of the spine is parallel.

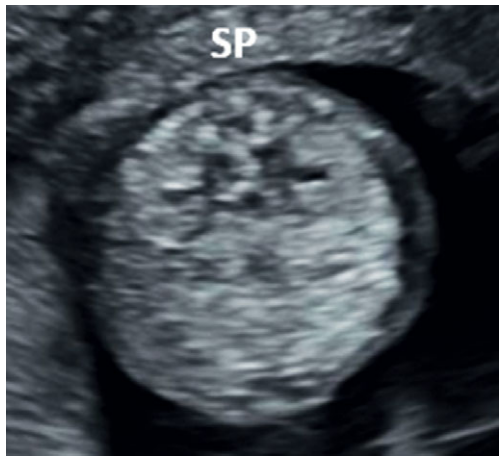

Fig. 1.54 Transverse view of the normal fetal lumbar spine of the same fetus (SP) showing the three ossification centres with intact overlying skin.

MENINGOMYELOCELE, MENINGOCELE

Ultrasound Assessment

- It is difficult to differentiate between meningocele and meningomyelocele as most first trimester defects are 'flat'
- Every effort should be made to determine whether the lesion is skin-covered (Fig. 1.55)

Investigations

- Offer invasive testing if spinal abnormality is detected

Counselling

- The outcome for open spina bifida is largely dependent on presence/absence of associated structural and chromosomal abnormalities, brain imaging later in pregnancy and the size and type of the lesion
- In apparently isolated meningocele, it is best to delay the definitive diagnosis until second trimester
- Even a large, thoracic skin-covered meningocele (limited dorsal myeloschisis) is associated with a very good long-term neurological outcome

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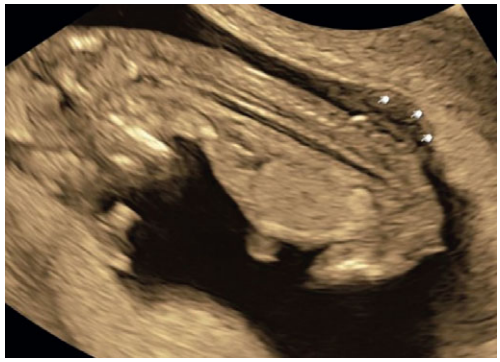

Fig. 1.55 Lumbosacral meningomyelocele. Note disruption of the skin line (small arrows) in the lumbosacral region.

ABDOMEN

ANATOMY ASSESSMENT

- A normal stomach filled with anechogenic gastric secretions is positioned in the left upper abdomen and is less echogenic than liver (on the right) (Fig. 1.56)
- The empty fetal stomach has no clinical significance in the first trimester as most fetuses don't swallow amniotic fluid before 14 weeks
- The gall bladder is almost always seen by 14 weeks' gestation, but non-visualisation in the first trimester has no clinical significance
- With normal situs, the inferior vena cava is anterior and to the right of the descending aorta
- Normal insertion of the umbilical cord should be documented after 12 weeks, together with the number of umbilical arteries
- Signs of gastrointestinal obstruction have been reported in the first trimester (e.g. double bubble); however, definitive diagnosis should be delayed until the second trimester

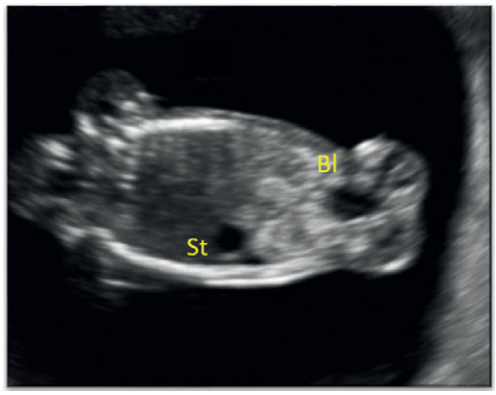

Fig. 1.56 Coronal view of fetal abdomen at 13 weeks, showing the stomach (St) and bladder (Bl).

EXOMPHALOS

Definition and Characteristics

- Exomphalos (*outside the navel* in Greek) and omphalocele (omphalos – umbilicus and cele – cavity) are synonyms
- Prevalence of exomphalos is around 1 in 5,000 births

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- Small bowel herniation into a midline sac measuring <7 mm and seen before 13 weeks is likely to be a physiological midgut herniation

Ultrasound Assessment

- Abdominal defect is membrane-covered (Figs. 1.57 and 1.58).
- The umbilical cord arises from the dome of the sac
- Large defects can include liver and stomach as well as bowel
- Patent urachal cyst can be quite large and easily mistaken for an exomphalos

Investigation

- Invasive testing is indicated as exomphalos is associated with chromosomal abnormalities in 50% of cases (trisomy 18 is the most common)

Counselling

- Small, isolated exomphalos with normal NT and normal karyotype will often resolve spontaneously in the late second trimester
- If there is an isolated exomphalos with normal chromosomes, consider a possibility of Beckwith–Wiedemann syndrome; CVS material can be used for prenatal diagnosis by methylation analysis

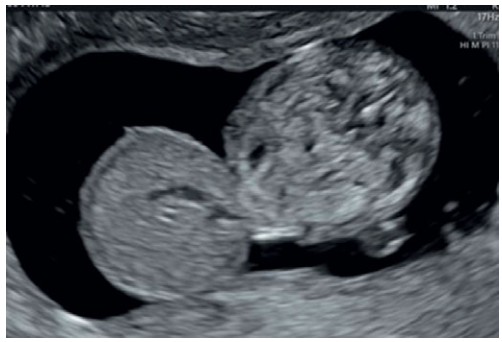

Fig. 1.57 Transverse view of the fetal abdomen showing a large anterior abdominal wall defect filled with liver. Note the covering membrane.

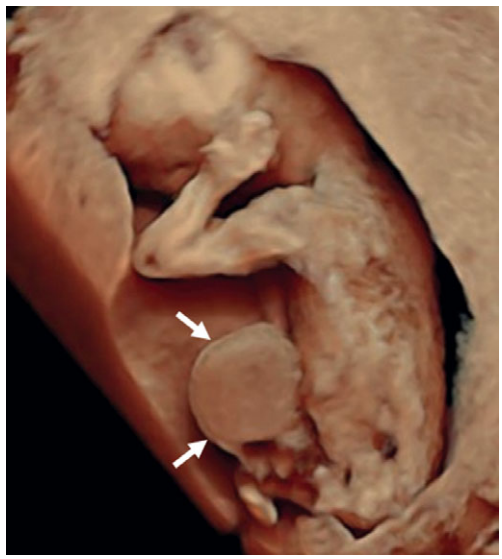

Fig. 1.58 3D image of the same fetus with exomphalos (arrows).

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GASTROSCHISIS

Definition and Characteristics

- A full-thickness paraumbilical abdominal wall defect to the right of the umbilicus
- Prevalence of gastroschisis is rising, especially in young mothers where the prevalence has risen to 1 in 500

Ultrasound Assessment

- The defect has no covering membrane (Fig. 1.59)
- The defect is to the right of the normal cord insertion

Counselling

- Apparently isolated gastroschisis is rarely associated with chromosomal and structural abnormalities and is, therefore, not an indication for invasive testing in the first trimester

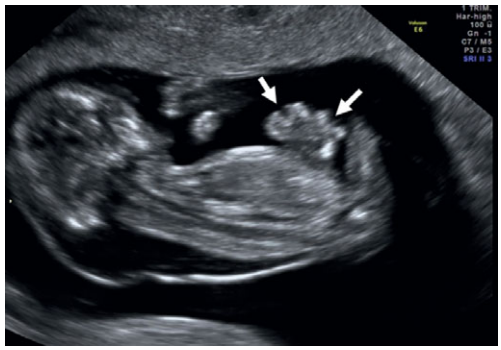

Fig. 1.59 Parasagittal longitudinal view of the fetus with an abdominal wall defect. Note the free-floating loops of bowel with no covering membrane (arrows).

ECTOPIA CORDIS, PENTALOGY OF CANTRELL OR BODY STALK ANOMALY?

Definitions and Characteristics

- The original description by Cantrell includes five parts (pentalogy):
  1. Deficiency of the anterior diaphragm
  2. Midline suprapubic abdominal wall defect
  3. Defect in the diaphragmatic pericardium
  4. Cardiac abnormalities
  5. Defect of the lower sternum
- In ectopia cordis the heart is either partly or completely protruding through the sternal defect
- Body stalk anomaly includes a large chest and abdominal wall defect with a very short or absent umbilical cord

Ultrasound Assessment

- A combination of ectopia cordis with supraumbilical omphalocele points to the pentalogy of Cantrell – a complete Cantrell pentalogy has been rarely reported (Fig. 1.60)
- In a body stalk anomaly, liver and bowel are often seen in the celomic cavity while an apparently intact amniotic sac contains the rest of the fetus. Umbilical cord is absent or

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very short with a baby in very close proximity to the placenta. Some degree of kyphoscoliosis is almost always present (Fig. 1.61)
- Isolated ectopia cordis is very rare; therefore, the diagnosis should be confirmed in the second trimester

Counselling

- Body stalk anomaly is uniformly fatal, but fetal karyotype is usually normal
- Pentalogy of Cantrell and ectopia cordis have a very high mortality even if chromosomes are normal

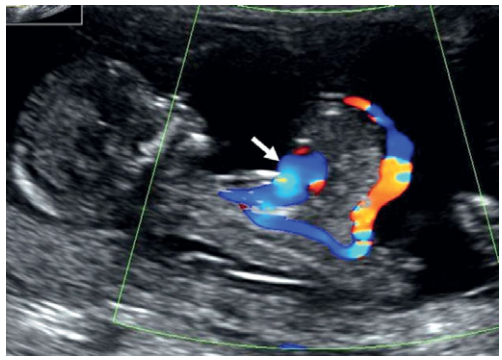

Fig. 1.60 Sagittal section of the fetus showing an abdominal wall defect with ectopia cordis (arrow).

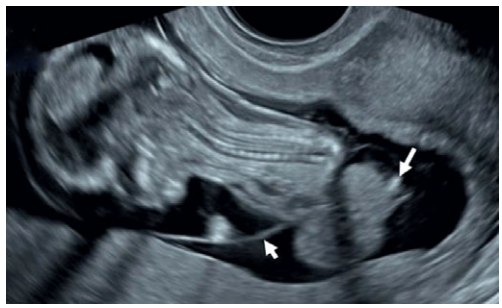

Fig. 1.61 Body stalk anomaly. The fetus is lying within the amniotic cavity, but the inferior abdominal wall defects (long arrow) is seen in the celomic cavity, which is beyond the amniotic membrane (short arrow). The umbilical cord is very short in body stalk anomaly.

GENITOURINARY SYSTEM

ANATOMY ASSESSMENT

- The fetal kidneys should be seen in a paraspinal location as bean-shaped, slightly echogenic structures with hypoechoic central renal pelvis
- In the first trimester kidneys are better visualised in the coronal plane (Fig. 1.62)
- Normal kidneys may appear hyperechoic
- Colour doppler helps to identify renal arteries and the location of the kidneys (Fig. 1.63)
- By 12 weeks' gestation, the fetal bladder should be visible as a median hypoechoic round structure in the lower abdomen and measures <7 mm in longitudinal diameter
- Colour Doppler can be used to confirm normal position of the bladder by identifying two umbilical arteries surrounding the bladder (Fig. 1.64)
- Absence of bladder filling may be indicative of renal agenesis

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- Sex determination is 85% accurate and can be used in conjunction with cffDNA (cell-free fetal DNA) to ascertain the need for invasive prenatal diagnosis of X-linked conditions and management of congenital adrenal hyperplasia

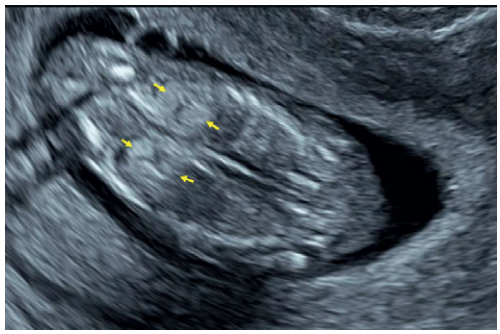

Fig. 1.62 Normal kidneys. Coronal view of the fetal abdomen showing normal kidneys, which are quite echogenic in the first trimester. Better visualisation can be achieved by increasing the dynamic range and by using 'chroma' colour.

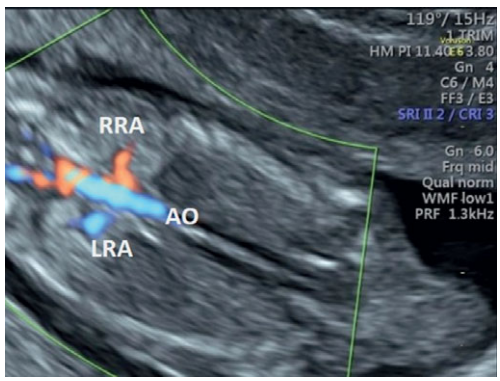

Fig. 1.63 Normal renal arteries. Coronal view of the fetal abdomen with colour Doppler showing both renal arteries. Ao, aorta; LRA, left renal artery; RRA, right renal artery.

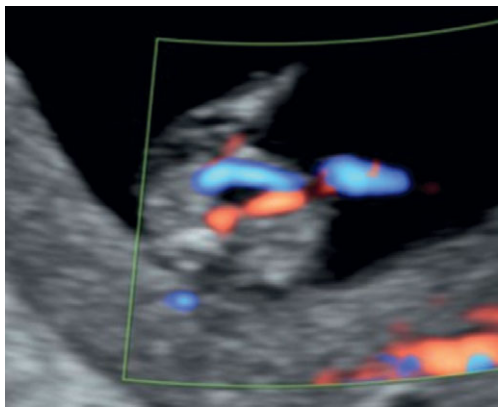

Fig. 1.64 Umbilical arteries. Colour Doppler of the lower abdomen showing a normal bladder surrounded by two umbilical arteries.

BLADDER IS LARGE (MEGACYSTIS)

Definition and Characteristics

- Usually defined as $\geq$7 mm in a longitudinal bladder diameter (LBD) (Fig. 1.65)
- Prevalence in the first trimester is around 1 in 1,500–2,000

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- Around 40% of cases will be complex (chromosomal abnormalities, anorectal malformations or multiple anomalies)
- 40% will have a lower urinary tract obstruction (urethral atresia, stenosis or posterior urethral valve)
- 20% will resolve spontaneously

Ultrasound Assessment

- Measure NT
- Look for umbilical cord cysts
- A large urachal cyst can be easily mistaken for a megacystis/bladder extrophy when a communication between the bladder and an extra-abdominal cystic structure surrounded by umbilical arteries is visible

Investigations

- Offer invasive testing

Counselling

- Megacystis when NT is >95th centile:
  - high risk of complex pathology (chromosomal, anorectal or multiple abnormalities)
  - isolated posterior urethral valve is very unlikely
- Umbilical cord cyst is also present:
  - High risk of a urethral atresia in both female and male fetuses
- LBD < 12 mm with normal karyotype, normal NT and no cord cyst:
  - spontaneous resolution is likely
  - offer follow-up at 16, 20 and 28 weeks for reassurance
- LBD > 12 mm, normal karyotype and NT, no cord cyst, male fetus:
  - isolated posterior urethral valve is the most likely diagnosis
  - Survival is around 50% and 25–30% of survivors will develop end-stage renal disease requiring dialysis and renal transplant by the age of 5

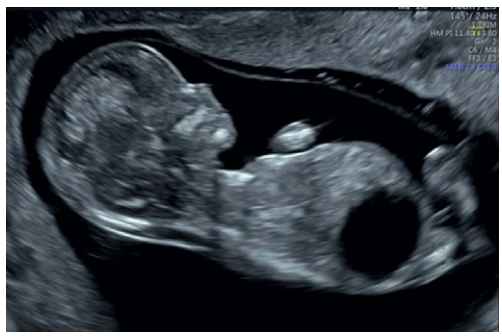

Fig. 1.65 Megacystis. Sagittal view of the fetus showing an abnormally large bladder.

SKELETAL SYSTEM

ANATOMY ASSESSMENT

- The presence of each bony segment of the upper and lower limbs and presence and normal orientation of the two hands and feet should be noted

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LIMB ABNORMALITIES

Definition and Characteristics

- Limb abnormalities detected in the first trimester can be isolated, but are more likely caused by chromosomal abnormality or a genetic syndrome (Table 1.3)
- Terminal transverse defects are more common in the upper limbs; most of them are caused by a vascular injury or amniotic band sequence

Table 1.3 Limb abnormalities that can be detected in the first trimester

Talipes equinovarous or clubfeet	In most cases the foot is twisted downward and inward
Clinodactyly	Abnormally bent finger due to abnormal bone development of the small bones of that finger
Clenched hand	Adducted thumb; second and fifth finger overlapping third and fourth
Polydactyly	Extra digits (Fig. 1.66)
Syndactyly	Two or more digits fused together
Ectrodactyly	Split hand or foot deformity with a deep central cleft (Fig. 1.67)
Phocomelia	Hands or feet attached close to the trunk
Sirenomelia	Fused lower limbs (Figs. 1.68 and 1.69)

Ultrasound Assessment

- Use transvaginal ultrasound to look for other abnormalities
- Look for signs of amnion disruption

Investigation

- Offer karyotyping/microarray

Counselling

- The definitive diagnosis is best delayed until the second trimester

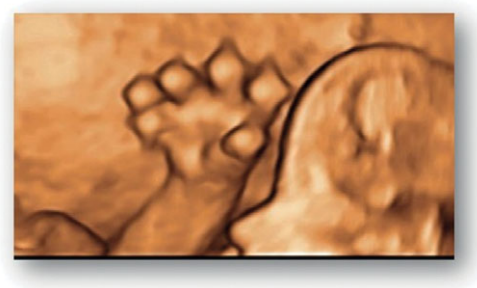

Fig. 1.66 Polydactyly. 3D image of a hand with post-axial polydactyly.

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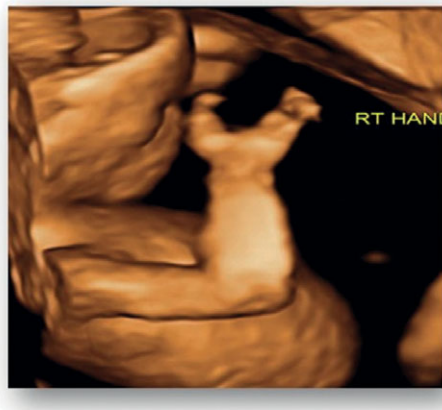

Fig. 1.67 Ectrodactyly. 3D image of a hand showing ectrodactyly (cleft hand).

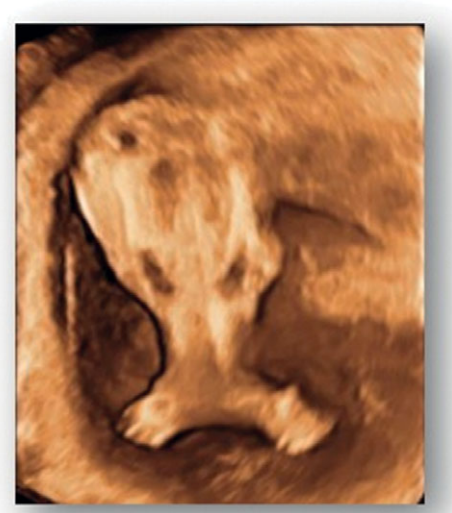

Fig. 1.68 3D image of fused lower limbs in sirenomelia (mermaid syndrome).

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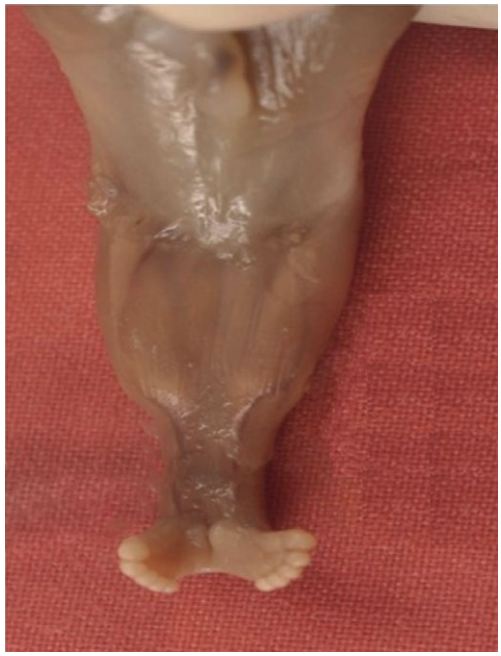

Fig. 1.69 Autopsy image of sirenomelia.

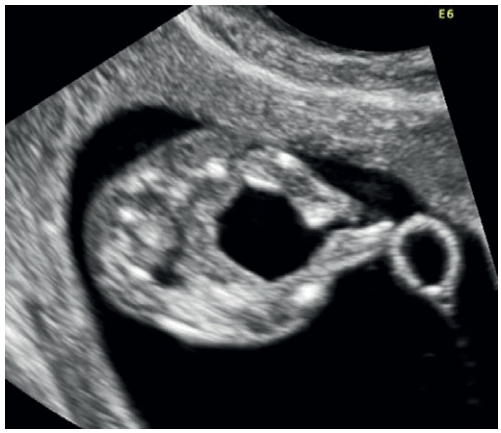

Fig. 1.70 2D image of both lower limbs showing short long bones in a fetus affected by achondrogenesis.

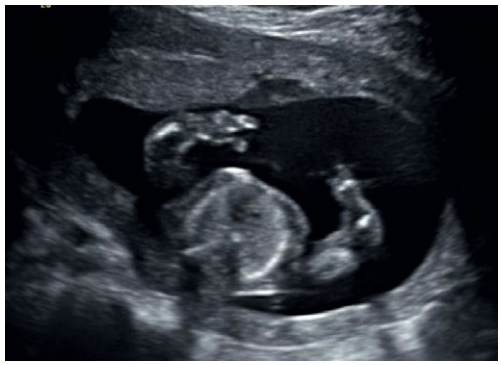

Fig. 1.71 2D image of the same fetus showing short upper limbs.

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Fig. 1.72 Autopsy picture of the same fetus showing short limbs.

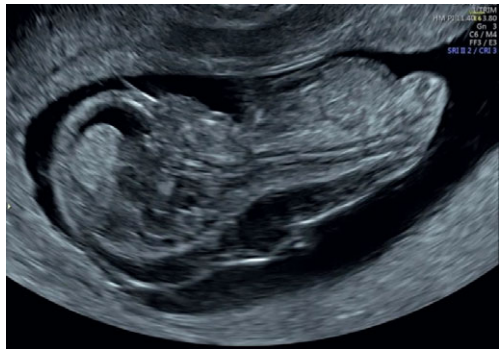

Fig. 1.73 Achondrogenesis at 13 weeks, showing significant oedema and poor mineralisation of the spine and skull.

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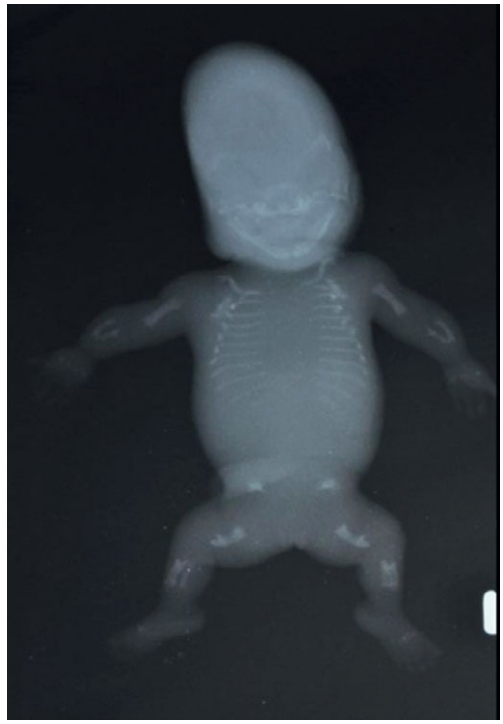

Fig. 1.74 X-ray of the same baby confirming poor ossification of the spine and skull.

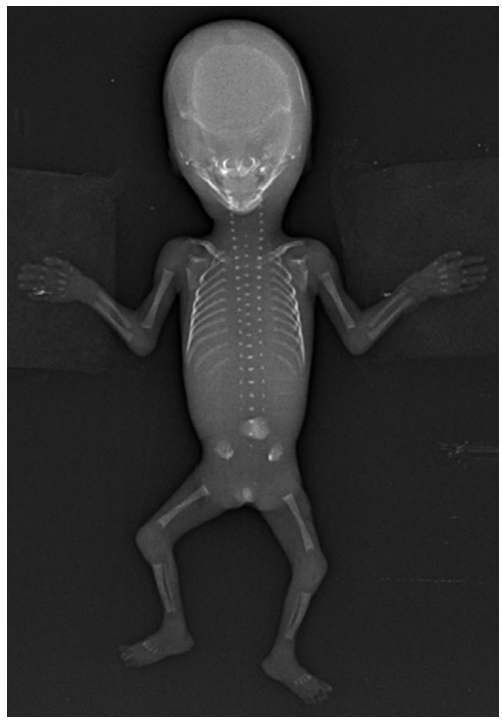

Fig. 1.75 Normal fetogram at 13 weeks. Note the distinct ossification of the spine and the normal long bones at this gestation.

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SHORT FEMUR

Definition and Characteristics

- Femur length <5th centile

Ultrasound Assessment

- A combination of short femur (<5th centile) and increased NT should prompt a detailed skeletal survey including transvaginal scan using the same principles as in the second trimester assessment (Table 1.4)

Table 1.4 Differential diagnosis when a short femur (<5th centile) is seen in combination with increased NT in the first trimester

Additional phenotype	Differential diagnosis
Generalised oedema, hydrops	Achondrogenesis (Figs. 1.70–1.75), short rib polydactyly syndrome, Noonan syndrome
Poor skull ossification	Achondrogenesis, osteogenesis imperfecta, hypophosphatasia, boomerang dysplasia, Roberts syndrome
Small thorax	Achondrogenesis, Ellis-van Creveld syndrome, osteogenesis imperfecta, thantophoric dysplasia, campomelic dysplasia, hypophosphatasia, boomerang dysplasia, Jeune syndrome, short rib polydactyly syndrome
Polydactyly	Short rib polydactyly syndrome, Jeune syndrome, Ellis-van Creveld syndrome, acrocallosal syndrome
Oligodactyly	Roberts syndrome
Missing long bones	Boomerang dysplasia, Roberts syndrome, femoral facial syndrome
Hitchhiker's thumb/toe	Atelosteogenesis, diastrophic dysplasia
Talipes	Campomelic dysplasia, hypophosphatasia, atelosteogenesis, diastrophic dysplasia, Roberts syndrome
Cardiac anomaly	Ellis-van Creveld syndrome, Meckel–Gruber syndrome, Noonan syndrome
Posterior fossa cyst	Ellis-van Creveld, Meckel–Gruber syndromes

Investigations

- Short femur in combination with increased NT, or phenotype suggestive of skeletal dysplasia or genetic syndrome, is an indication for invasive testing

Counselling

- If skeletal dysplasia is suspected, a definitive diagnosis based on the first trimester ultrasound appearances is best avoided and should be delayed until the second trimester
- Increasingly, the definitive diagnosis can be made by targeted genetic testing (e.g. FGFR3 for suspected thanatophoric dysplasia)

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HYDROPS

Definition and Characteristics

- Rather than using the umbrella term 'hydrops', it is more informative to be specific and describe a presenting phenotype more precisely; for example: pleural effusion, pericardial effusion, ascites, skin oedema, or a combination of these conditions (Fig. 1.76)
- Virtually all cases presenting in the first trimester are non-immune; immune hydrops due to feto-maternal blood group incompatibility occurs after 15 weeks
- Around 25% of cases presenting in the first trimester will have chromosomal abnormalities detected either by conventional karyotyping (20%) or microarray (additional 5%)
- Exome sequencing can identify pathogenic genetic variants in up to 30% of otherwise unexplained cases

Ultrasound Assessment

- Detailed structural survey
- Offer follow-up scan at 16 weeks to reassess anatomy with particular emphasis on fetal echocardiography and any changes in the amount of accumulated fluid

Investigations

- Offer invasive testing, including exome sequencing if available
- Maternal serology to exclude congenital viral infections (parvovirus B19, cytomegalovirus)

Counselling

- Significant, progressive hydrops has poor prognosis; termination of pregnancy should be considered
- Counselling for pathogenic genetic variants, if found, is complex and should involve clinical geneticists
- Unexplained cases should be followed regularly during pregnancy, even when the 20-weeks scan looks entirely normal as reappearance in the third trimester is relatively common (e.g. undiagnosed Noonan syndrome)
- In some cases of complete resolution in the second trimester, the definitive diagnosis has been established in early childhood (e.g. hereditary spherocytosis)

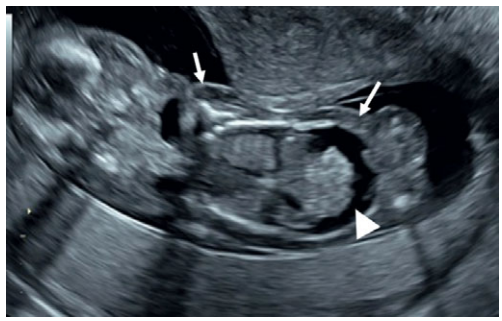

Fig. 1.76 Coronal section of fetus showing ascites (arrow head) and skin oedema (arrows).

PLACENTA AND UMBILICAL CORD

ANATOMY ASSESSMENT

- A three-vessel cord, cord insertion at the umbilicus and presence of cord cysts should be noted
- Evaluation of the placental size, thickness and localisation in the first trimester is of little clinical value

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SINGLE UMBILICAL ARTERY

Definition and Characteristics

- Prevalence of single umbilical artery (SUA) is around 0.5%
- Aplasia/atrophy has been suggested as the underlying cause
- Laterality is of no clinical importance
- Around 80% will be 'isolated'

Ultrasound Assessment

- Use a transverse plane at the level of the fetal bladder
- Use colour Doppler mode to confirm the diagnosis (Fig. 1.77)
- Use the transvaginal approach to assess anatomy
- It is important to exclude renal agenesis
- Measure NT

Counselling

- If SUA appears to be isolated and NT is normal, invasive testing is not indicated
- Perinatal mortality is not increased
- Detailed structural survey should be arranged in the second and third trimesters because of an increased risk of gastrointestinal atresias/stenosis and heart defects
- If a third trimester scan (30–32 weeks) has confirmed that SUA is isolated, follow-up scans should be arranged to exclude fetal growth restriction
- If there is no evidence of fetal growth restriction, early delivery is not indicated

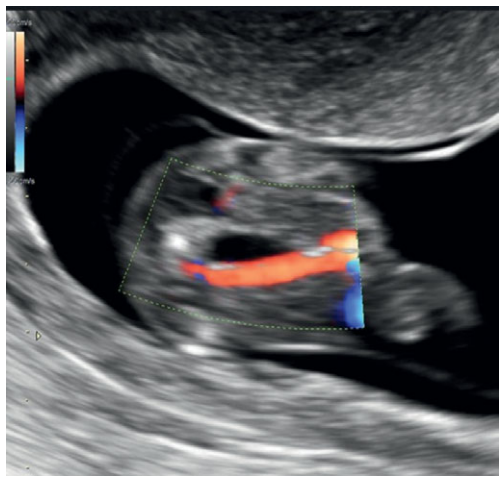

Fig. 1.77 Transverse section of fetal bladder. Colour Doppler shows an SUA.

UMBILICAL CYSTS

Definition and Characteristics

- Reported prevalence is higher (up to 3%) when transvaginal scans are used in the first trimester
- Differentiation between true cysts and 'pseudocysts' with no epithelial lining (*Wharton jelly cysts*) is of little clinical value

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Ultrasound Assessment

- It is important not to describe the yolk sac (extra-amniotic cyst with echogenic borders) as an umbilical cyst
- Urachal cyst should be suspected when there is a communication between bladder and extra-abdominal cystic structure surrounded by umbilical arteries (Fig. 1.78)

Counselling

- Isolated umbilical cord cysts seen in the first trimester have no clinical significance, regardless of their size or location (Fig. 1.79)
- Even multiple umbilical cysts seen before 10 weeks are likely to disappear by 14 weeks
- Detailed anatomy scan should be arranged around 16 weeks
- In the absence of structural abnormalities, fetal karyotyping is not indicated
- Extra-abdominal urachal cysts can be quite large and should not be mistaken for exomphalos or bladder exstrophy. If karyotype is normal, the prognosis after surgery is very good

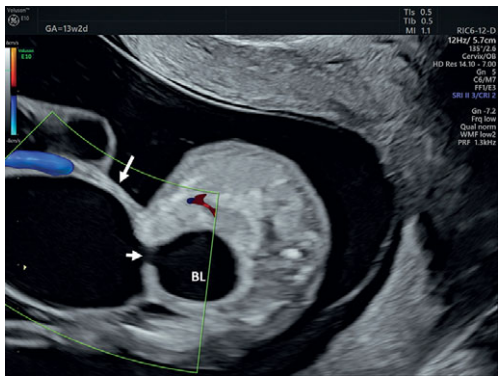

Fig. 1.78 Transverse section of the lower abdomen showing the bladder and a large urachal cyst in a fetus with trisomy 18. Note the communication (small arrow) between the bladder (BL) and a cyst (arrow).

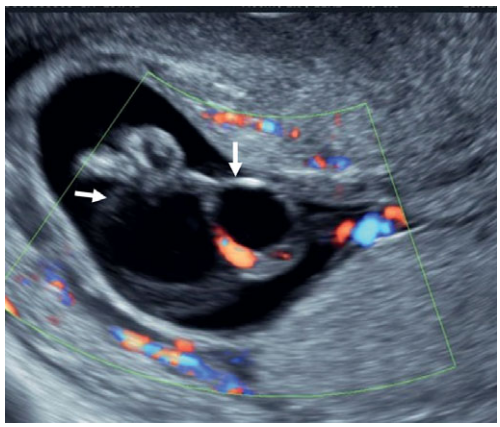

Fig. 1.79 Transverse section of the umbilical cord with two small umbilical cord cysts (arrows). If isolated, they have a good outcome.

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SUGGESTED READING

PRIMARY RESEARCH

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