Ultrasound structural fetal anomaly screening: an update

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ABSTRACT

Screening for fetal anomalies by an ultrasound scan was introduced in many maternity units in the UK in the late 1970s and has become routine in most since then although there is little uniformity as to how the scan is performed and when it is offered.

Up to 5% of babies are born with a congenital abnormality. In this review article we will focus on what is already known about screening for the commonest and most serious structural fetal anomalies at the 11–14 and 18–23 week scans, and discuss new techniques that promise to improve the accuracy of screening and diagnosis. Chromosomal abnormalities, ''soft markers'' and biochemical screening are beyond the scope of this review.

Screening for fetal anomalies by an ultrasound scan was introduced in many maternity units in the UK in the late 1970s and has become routine in most since then. According to a national survey in 2002, 97% of units offer a routine 18–20 week scan,[1] though there remains little uniformity as to how the service is provided and at what gestation.

In an effort to standardise fetal anomaly screening, the UK National Screening Committee (NSC) has adopted the principle that screening programmes should allow each person to make an informed decision about screening based upon an appreciation of the risks and benefits.[2] The aims and objectives of the NHS Fetal Anomaly Ultrasound screening programme (FASP) are:

> ''…to offer all pregnant women in England a minimum of 2 ultrasound scans. The first is an early scan, undertaken after 8 weeks gestation and used mainly for dating the pregnancy and confirming viability. The second ultrasound scan is undertaken between 18–20 weeks of the pregnancy and screens for major structural anomalies.''

The National Institute for Health and Clinical Excellence (NICE) guideline, Antenatal Care: Routine care for the healthy pregnant woman (2003),[3] states the objectives of the 18–20 week ultrasound scan are to:

- offer choice to women and their partners about their screening options and pregnancy management,
- identify abnormalities associated with morbidity incompatible with life at a time when choice can operate about continuation of the pregnancy or termination,
- identify abnormalities that require early intervention following delivery,
- identify abnormalities that may benefit from interactive treatment.

STANDARDS AND REQUIREMENT

No internationally agreed standardised form for the 18–20 week scan exists. In 1993, a checklist for the detailed scan was put forward by Campbell and Chervenak, which formed the basis for the anomaly scan carried out in many units throughout Europe and the USA.[4] The subsequent Royal College of Obstetricians and Gynaecologists (RCOG) working party on ultrasound screening for fetal abnormalities[5] proposed a minimum standard for the 20-week anomaly scan (table 1) and the measurement of the bi-parietal diameter, head circumference and femur length with the abdominal circumference as optional.

The key requirements of NSC FASP and RCOG[5] also include the following recommendations:

> ''written information is given to parents prior to the scan; the scan should have 20 minutes allocated; a named midwife/counsellor with particular interest/expertise is available to women; discussion of the implications of a suspicious scan should occur with an obstetrician within 24 hours and/or referral to a tertiary centre with maternal fetal medicine specialists within 72 hours; women should receive written details about their scan result; scans should be archived and where abnormalities are found, hard copy or video recordings are recommended; all units should work towards developing computer-based records; every unit should audit its results for the detection of fetal abnormalities annually.''

Table 2 summarises the recommended specifications for the 20-week scan.

SCOPE OF THIS REVIEW

In this review article we will focus on what is already known about screening for the commonest and most serious structural fetal anomalies at the 11–14 and 18–23 week scans, and discuss new techniques to improve the accuracy of screening and diagnosis. Chromosomal abnormalities, ''soft markers'' and biochemical screening are not discussed.

WHEN IS THE OPTIMAL TIME TO SCREEN FOR STRUCTURAL ABNORMALITIES?

Second trimester ultrasound screening

The optimal time to be able to both obtain the required views on ultrasound and to be able to interpret the images and define normality has traditionally been taken to be around 20 weeks (ranging from 16–24 weeks). Very little evidence underpins the timing of the scan; however, a 1999 study investigating the percentage of scans that could be completed at 18, 20 and 22 weeks suggested that the optimal timing was 20–23 weeks (table 3).[6]

Table 1 Standards for the 20 week anomaly scan (Royal College of Obstetricians and Gynaecologists)[5]

Scan area	View/structures to visualise
Minimum standard	
Head	Shape, size and internal structures, cavum pellucidum, cerebellum, ventricular size at atrium <10 mm
Spine	Longitudinal and transverse view
Abdomen	Shape and content at level of stomach shape and content at level of kidneys and umbilicus
Renal pelvis	<5 mm anterior–posterior measurement
Diaphragm and bladder	Longitudinal axis abdominal–thoracic appearance
Thorax	At the level of a four-chamber cardiac view
Arms	Three bones and hand (not counting fingers)
Legs	Three bones and foot (not counting toes)
Optimal standard	
Head	Face and lips
Thorax	Cardiac outflow tracts

Most fetal organs are developed to allow detection of normality by 20 weeks except the fetal brain whose structural development continues into the neonatal period. The detection of major fetal anomalies by routine ultrasound screening in the second trimester also varies according to the anatomical system (table 4).

First trimester ultrasound screening

Early ultrasound is performed at 11–14 weeks of gestation for viability, gestation age estimation, twin pregnancy detection and twin chorionicity assessment. With increased sophistication of ultrasound technology and better training as a result of the introduction of first trimester nuchal translucency (NT) screening, it is now possible to detect structural anomalies in the first trimester.

There are clear advantages to recognising major abnormalities prior to the second trimester as early termination could be offered. An early anomaly scan, despite its lower sensitivity at an earlier gestation, may also offer reassurance for the "high risk", particularly where a previous pregnancy has been affected by an anomaly.

However, different fetal anomalies and syndromes present at varying gestations and the effectiveness of early anomaly scan depends upon their natural history, phenotypic expression[12] and operator skill.[13]

FETAL STRUCTURAL ABNORMALITIES AND NUCHAL TRANSLUCENCY MEASUREMENT

NT is a normal subcutaneous space between skin and soft tissue overlying the cervical spine; the optimal gestation for NT measurement is 11–13+ weeks.[7] NT thickness increases with fetal crown rump length. An association between increased NT and chromosomal defects, particularly trisomy 21, has been established since the early 1990s.[14–16]

The prevalence of major structural abnormalities, cardiac defects and genetic syndromes increases as the measurement of the NT increases, even with a normal karyotype. Ultrasound assessment at 16–18 weeks, including fetal echocardiography, is, therefore, frequently offered although there is no agreement as to what level of increased NT should prompt this. An outline of what is offered in our fetal medicine unit is shown in fig 1.

Table 2 Specifications for the 20-week scan

	Equipment	Timing of scan	Training required	Gestation age at which to scan
RCOG	Modern equipment Not more than 5 years old Should be of modest sophistication	About 20 minutes for the whole investigation, including introduction and documentation	Currently there is no statutory requirement for ultrasound practitioners to receive accredited training Medical staff should be specifically trained to undertake scans	First scan before 15 weeks Detailed scan 20 weeks
NSC	Use of modern equipment (not more than 5 years old) of modest sophistication	–	–	GA assessment before 13 weeks Detailed scan 18–20+6 weeks
NICE	Equipment should be of appropriate standard as outlined by NSC	–	Scan should be done by appropriately trained sonographer	First scan 10–13 weeks Detailed scan 18–20+6 weeks
ARC	–	–	–	For dating before 16 weeks Detailed scan 18–21 weeks
FMF	–	–	–	Dating + nuchal scan 12 weeks Anomaly scan 20–24 weeks

ARC, Antenatal Results and Choices; FMF, Fetal Medicine Foundation; GA, gestation age; NICE, National Institute for Health and Clinical Excellence; NSC, National Screening Committee; RCOG, Royal College of Obstetricians and Gynaecologists.

Table 3 Percentage of anomaly scans completed by gestation[6]

Gestation	18–18+6 weeks	20–20+6 weeks	22–22+6 weeks
% (n) anomaly scan completed	76.3% (306)	90% (371)	88.8% (393)

Table 4 Detection rate and incidence of the more common fetal abnormalities

System	Detection rate in second trimester (low risk population) (%)	Incidence
Central nervous system	76[7]	6.2:10 000[8]
Urinary tract	67[7]	1–5%[1]
Pulmonary	50[7]	Uncertain
Gastrointestinal tract	42[7]	0.8–3.9:10000[9] (omphalocele)
		0.4–2.3:10000[9] (gastroschisis)
Skeletal	24[7]	1:500[10]
Cardiac	17[7]–38.8	8:1000[11]

Which fetal abnormalities can be detected at 11–14 weeks?

Though abnormalities such as anencephaly, holoprosencephaly and conjoint twins are detectable early on, some with variable or late onset may not be irrespective of the quality of the ultrasound equipment and operator skill. These include ventriculomegaly, microcephaly, corpus callosum agenesis, diaphragmatic hernia, talipes and obstructive uropathy.

Ultrasound screening at 11–14 weeks in detecting structural fetal anomalies has been studied in low-risk[13 17–21] and high-risk[11] populations. Fetal anomaly detection is reported at 90% (100% on combining the early scan with an 18–20 week scan) in a high-risk population[12] and 59% in an unselected population (81% detection when 11–14 and 18–20 week scans are combined).[17] The gestation at which it is reasonable to expect that specific abnormalities are identified is shown in table 5.

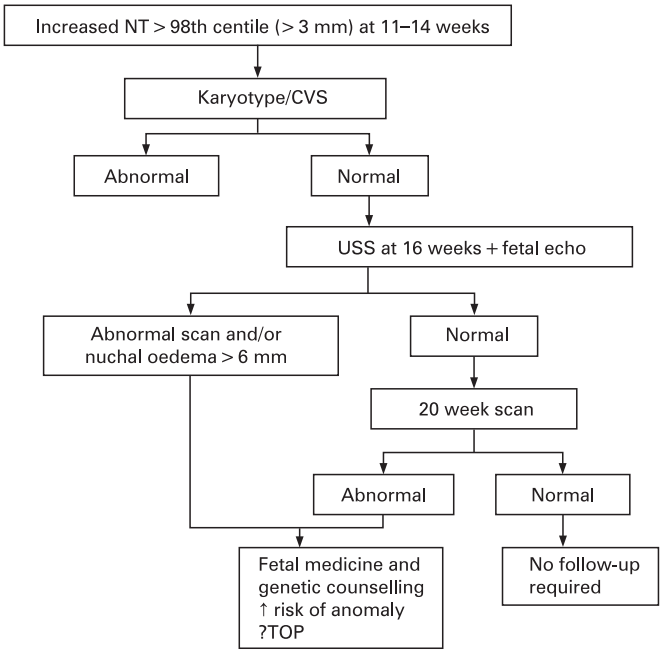

Figure 1 An outline of what is offered in our fetal medicine unit. CS, chorionic uillous sampling; NT, nuchal translucency; TOP, termination of pregnancy; USS, ultrasound.

Transvaginal ultrasound

High-resolution transvaginal probes allow malformations in first and early second trimester to be diagnosed as they provide better images as a result of the transducer's closer proximity to the uterus and the higher frequency used in the transducer array. A transvaginal ultrasound scan is particularly useful in women with high body mass index or cases where the part of interest is positioned low in the uterus—for example, in the assessment of fetal central nervous system (CNS) abnormality in the third trimester.[22] Maternal obesity increases the rate of suboptimal ultrasound visualisation for the fetal cardiac structures by 49.8% and for the craniospinal structures by 31%.[23]

MAJOR STRUCTURAL MALFORMATIONS BY SYSTEM

Central nervous system

Neural tube defects (NTD) are the commonest CNS malformation. Most are detected on a first trimester scan; almost all at the 20-week scan. The ultrasound sensitivity rate for open NTD is 81% with a tiny false-positive rate[24] and for anencephaly it is 96–100%.[1] Ultrasound demonstrates a characteristic lesion, usually in the lumbo-sacral spine showing a bony defect and pouch of dura/skin. In the fetal brain, the "lemon and banana sign" (lemon-shaped skull bones; banana shaped cerebellum) are characteristic.

Cerebral ventriculomegaly may be related to aneuploidy (particularly trisomy 21) and long-term neurological morbidity. Mild ventriculomegaly (posterior horn of lateral ventricle measuring 10–12 mm) can be a variant of normal, although in about 10% of "isolated" cases there is neurodevelopmental delay.[25] By contrast, severe ventriculomegaly (posterior horn of lateral ventricle >15 mm) is associated with a very high risk (around 90%) of poor perinatal outcome and abnormal neurological development.[26] Hydrocephalus, an extreme form of ventriculomegaly where the head circumference is greater that the 98th centile, is detected in 33–100% of cases on antenatal ultrasound, although it may not be apparent at the 20-week scan.[1]

Agenesis of corpus callosum (ACC) can either appear in isolation or be associated with neurological or other systemic, chromosomal or genetic malformations. Full development of corpus callosum occurs by 20 weeks and, therefore, the antenatal diagnosis of ACC cannot be made earlier. MRI is the preferred imaging modality, especially for the diagnosis of suspected partial agenesis and cerebral anomalies. Isolated ACC has an 85% chance of normal developmental outcome,[27]

Table 5 Earliest gestation at which ultrasound diagnoses can reasonably be made at

	Anomaly	11–14 weeks	18–22 weeks
CNS	Anencephaly	✓	
	Holoprosencephaly	✓	
	Corpus callosum agenesis		✓
	Microcephaly		✓
	Hydrocephalus	✓	
	Open spinal defects	✓	
CHEST	Diaphragmatic hernia		✓
	CCAM		✓
CVS	AVSD	✓	
GIT	Gastroschisis	✓	
	Omphalocele	✓	
Urinary system	Hydronephrosis		✓
	Bilateral renal agenesis	✓	
	Severe multicystic or polycystic kidney disease	✓	
	Megacystis	✓	
Neck/face	Cleft lip/palate		✓
	Cystic hygroma	✓	
Skeletal	Arthrogryposis	✓	
	Osteogenesis imperfect	✓	
	Achondroplasia		✓
Extremities	Talipes equinovarus		✓
Other	Ovarian cyst		✓

CNS, central nervous system; CVS, cardiovascular system; GIT, gastrointestrial tract; CCAM, congenital rystic adenomatoid malformation; AVSD, atrioventricular septal defect.

although 15% are associated with adverse neurological outcome, epilepsy or motor disturbances.

Posterior fossa anomalies are most frequently diagnosed by assessment of the cerebellum and cisterna magna. The cerebellar vermis is absent and cisterna enlarged in cases of Dandy-Walker syndrome. The cisterna magna is small in cases of Arnold-Chiari malformation[28] and the cerebellum is small and "banana" shaped.

Holoprosencephaly is a failure of separation of the forebrain frequently associated with other ultrasound findings such as hypotelorism, facial cleft and proboscis. It ranges most severely from alobar, through to semilobar and lobar forms that are all detectable on ultrasound, and the neurodevelopmental outcome ranges from very poor to poor. It is detectable in 86% of cases.[29]

Cardiovascular system

Congenital heart disease is the most common congenital disorder with a prevalence estimated at 8/1000 live births.[11] Its antenatal detection and evaluation of complexity, association with extra-cardiac malformations and fetal karyotype facilitates counselling of the parents for long-term outcomes, termination, deciding for the place for delivery and postnatal surgical options.

The "four chamber" view was first introduced into routine obstetric screening in the UK in 1986 as a method of identifying major cardiac malformations;[30 31] its sensitivity for detecting congenital heart defects varies from 5–60%.[32–34] The sensitivity for most congenital heart defects is higher by combining ventricular outlet views together with the four chamber view.[35 36]

Fetal heart assessment is usually performed at 16–22 weeks. Recently, the sensitivity of 12–14 week fetal echocardiography for cardiac abnormalities (isolated ventricular or great artery disproportion, tricuspid regurgitation, pulmonary stenosis and ventricular septal defect (VSD)), usually in specialist centres with high-risk patients, has been reported at 80–96%.[37–42]

Table 6 Detection rates for common cardiac conditions at the 20-week scan

	Antenatal detection rate %
Atrio-ventricular septal defect	29[43]
Ventricular septal defect	11.5[45]
Hypoplastic left heart syndrome	54.5[45]
Outflow tract anomalies	21.2[45]

Atrio-ventricular septal defect (AVSD) is the most common prenatally detected cardiac abnormality and is strongly associated with trisomy 21. It can easily be missed as the atrioventricular valve may appear normal even with a good four chamber view;[43] hence, the sensitivity of diagnosing AVSD is low (29%) in a low-risk population. Other more complex and obvious structural cardiac defects may be easier to detect (table 6).

A relatively new 3D technique, spatio-temporal image correlation, allows the fetal heart to be visualised with 2D and 3D cine sequences. A multiplanar reformatted cross-sectional display and/or a surface-rendered display can then be examined by re-slicing all the fetal cardiac images required for a comprehensive diagnosis of even complex cardiac defects.[44]

Genitourinary-renal anomalies

Renal lesions constitute about 20% of all congenital abnormalities[45 46] and approximately 60% are detected at the 18–20 week scan (table 7).[47]

Fetal kidneys can be visualised as early as 14 weeks and by 20 weeks their internal architecture can be assessed. Mild renal pelvic dilatation (5–10 mm) is diagnosed in 2–5% of scans at 18–23 weeks.[48 49] Over 80% resolve in utero; fewer than 5% require urinary tract surgery. More severe renal pelvic dilatation (usually taken as >10 mm) is infrequent and has an increased likelihood for postnatal surgery.[48 50] However, about 40% of children requiring postnatal surgery will have had a normal antenatal ultrasound examination.[47]

Thorax

Chest lesions often appear as an echogenic area in the thorax, sometimes containing cysts. Ultrasound may not differentiate between the different lesions; MRI is helpful where thoracic lesions are atypical or complicated by multiple abnormalities.[53]

Congenital cystic adenomatoid malformation is a developmental abnormality arising from overgrowth of terminal respiratory bronchioles. Ultrasonographic features for congenital cystic adenomatoid malformations are hyperechogenicity of the affected lung, multiple cysts and variable mediastinal shift. In about 70%, the size of the tumour remains stable; 20% of cases shrink antenatally and 10% grow.[54] Prognosis is usually good unless associated with hydrops, polyhydramnios and if extreme mediastinal compression/shift occurs.

In broncho-pulmonary sequestration there is no connection between a part of lung and the airway. Broncho-pulmonary sequestration appears as a discrete rounded hyperechogenic mass; colour Doppler demonstrates vascular supply from the abdominal aorta. It can be intralobar or extralobar and may be below or above the diaphragm. The prognosis is usually very good unless (rarely) high-output cardiac failure occurs.

Congenital diaphragmatic hernia represents the herniation of abdominal viscera into the thorax through an incompletely formed diaphragm. Most are left-sided. It is seen on ultrasound as the fetal stomach, bowel and sometimes liver within the

Table 7 Ultrasound characteristics of common renal tract abnormalities

	Main features	Gestation at which diagnosis can be made	Detection rate (%)
Renal agenesis	Empty fetal bladder, anhydramnios	14 weeks	79.6[45] Unilateral renal agenesis
	Failure to visualise the renal arteries with colour Doppler	17 weeks	83.7 Bilateral renal agenesis
Multicystic dysplastic kidney	Multiple cysts of variable size, scattered throughout the kidney	19–23	97–100[47 51]
Autosomal recessive polycystic kidney disease	Enlarged, echogenic fetal kidneys	16	91.4[45]
Hydronephrosis	AP diameter of renal pelvis >5 mm	<24 weeks	93.4[44]
	>10 mm	>24 weeks	
Ureteropelvic junction obstruction (commonest cause of neonatal hydronephrosis)	Obstruction at the ureteropelvic junction. Marked isolated hydronephrosis ending abruptly at pelvis-ureteric junction with no dilatation of ureter or bladder	19–23	82.8[47]
Ureterovesical junction obstruction	Hydronephrosis Mega ureter Normal bladder	19–23	25[47]
Posterior urethral valve	Only in males Keyhole sign Enlarged thick wall bladder; oligohydramnios Bilateral hydronephrosis	12–14	60–70[52]

thorax with heart deviation. Associated structural abnormalities are reported in 50% fetuses, cardiac malformations in 20% and karyotype abnormalities in up to 34%.[55] Mothers diagnosed with congenital diaphragmatic hernia should be offered detailed fetal cardiac examination and karyotype.

Gastrointestinal tract

Ultrasound characteristics of gastrointestinal tract abnormalities are shown in table 8.

The commonest defects of herniation are gastroschisis and exomphalos; these may be diagnosed in the late first/early second trimesters. Gastroschisis is rarely linked to other structural or chromosomal abnormalities, while exomphalos has a higher association with aneuploidy (10–40%)[56 57] and other structural malformations (10–91%).[58–61] The postnatal prognosis after surgical repair is very good in isolated lesions.

Upper gastrointestinal atresias are usually only diagnosed in the third trimester; large bowel and ano-rectal malformations are rarely diagnosed positively antenatally.

Neck/face

Cystic hygroma is a congenital abnormality of lymphatic vessels resulting into cysts in subcutaneous tissue, most commonly located in the fetal neck and may be diagnosed as early as 11 weeks. Compared with simple increased NT, cystic hygroma has 5-fold, 12 fold and 6-fold increased risk of aneuploidy (most commonly trisomy 21 or Turner's syndrome), cardiac malformation and perinatal death, respectively.[63]

Cleft lip/palate can be diagnosed on coronal (lip) and transverse view (lips and alveolus) on ultrasound at 18–22 weeks' gestation. The detection rate of cleft lip is higher than that of cleft palate and in a low-risk population and ranges between 17.5%[64] and 75%.[65] Midline cleft palate, in the absence of cleft lip, still remains extremely difficult to diagnose antenatally.

With 3D imaging, facial images have greater clarity than with 2D ultrasound and bony structures can be assessed more easily with the "reverse face" view.[66] The sensitivity for the cleft diagnosis increased in a referred population from 91 to 100% and 46 to 90%, respectively, when 2D and 3D ultrasound were combined.[67]

Table 8 Ultrasound characteristics of gastrointestinal tract abnormalities

	Main ultrasound features	Gestation at which diagnosis can be made	Detection rate (%)
Gastroschisis	Anterior abdominal wall defect, usually to the right of cord insertion Herniation of free-floating abdominal contents without a surrounding membrane	13	83[9]
Exomphalos	Midline anterior abdominal wall defect Herniation of abdominal viscera, covered by a membranous sac Umbilical cord insertion at the apex of the sac	15	75[9]
Oesophageal atresia	Small or absent fetal stomach bubble Polyhydramnios	25[54]	0–50[1]
Duodenal atresia	"Double bubble" appearance of dilated stomach and proximal duodenum Polyhydramnios	25[54]	52[62]

Table 9 Ultrasound features of the commoner skeletal dysplasias

	Incidence	Gestation at which diagnosis can be made	Key features	Lethal
Achondrogenesis	1:40 000[10]	>13 weeks	Micromelia, very short but straight long bones, hypomineralisation of skull and vertebral bodies, short trunk and protuberant abdomen	Yes
Osteogenesis imperfecta	1–2:10 000[10]	Type 1, usually postnatally, occasionally 3rd trimester Type 2A/2C >12 weeks Type 2B > 16 weeks Type 3 = 20 weeks Type 4>20 weeks	Varying degree of hypomineralisation, small chest with beaded ribs indicating multiple fractures, short and broad long bones	Yes (types 2 and 4)
Thanatophoric dysplasia	1:20 000[10]	>18 weeks	Short long bones, with/without bowing, very short ribs, short fingers-classical trident hand, platyspondyly, cloverleaf skull, severe polyhydramnios	Yes
Campomelic dysplasia	1:20 000[10]	>Second trimester	Bowing of tibia and femur, unaffected arms, micrognathia, cleft palate, narrow chest, ambiguous genitalia in genetic males	Yes
Achondroplasia	5–15/100 000 births[10]	>22 weeks	Normal length of limbs <22 weeks, frontal bossing, trident hand, polyhydramnios	No
Hypophosphatasia	1:100 000 births[70]	>16 weeks	Demineralised skull, multiple long bone factures	No

Musculoskeletal

Skeletal dysplasias are rare, with a prevalence of 2–7/10 000[68] births. Prenatal diagnosis challenging requires a multi-disciplinary and multi-modality approach, including genetics, neonatology and MRI for diagnosis and prognosis to be ascertained. Even then, a precise antenatal diagnosis may not be possible. Long-bone shortening is invariable; the finding of a hypoplastic thorax allows most accurate prediction of the lethality of the disease.[69]

The key features of the most common dysplasias, together with the gestation at which they can be identified, are shown in table 9.

CONCLUSION

A 20-week detailed scan is offered in most UK units; the timing of this ranges from 16–23 weeks. The UK NSC needs to standardise the minimum requirements of this scan and to define the level of training required for the scan. There is a strong impetus for first trimester anomaly screening and diagnosis together with the NT scan, although this will not be possible for all structural anomalies (particularly CNS and renal tract) due to their natural history. Techniques such as MRI and 3D ultrasound are useful adjunctive modalities in specific situations where an abnormality is detected or suspected but have no proven value in the context of low risk screening.

Competing interests: None.

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Notes