CHAPTER 1

Prenatal Assessment

OVERVIEW

- All pregnant women are offered antenatal screening tests after explanation
- Some screening tests provide an assessment of risk (e.g. for Down syndrome) rather than confirmation or exclusion of a diagnosis
- Ultrasound scanning does not exclude all congenital anomalies
- Preterm labour is often associated with maternal infection

Recent advances in ultrasound technique, equipment and training, together with rapid advances in molecular biology have increased the range of antenatal diagnoses (Box 1.1). Some methods are available only at specialized centres. This chapter will give a background to successful techniques.

An anomaly may be detected during routine examination of the fetus which is carried out by ultrasound between 18 and 20 weeks of gestation. The risk of the most common chromosomal anomaly, Down syndrome, can be evaluated by several methods.

After the birth of an abnormal baby or the detection of genetic disease in an older child, a paediatrician or geneticist may recommend a specific test at a particular week in the subsequent pregnancy. Some tests are at an early stage in development and the false positive and negative rates have not been assessed. Some genetic tests are not yet sufficiently precise to enable an accurate prognosis to be given to every family with that disease.

At the first antenatal visit it is still important to carry out a full blood count and haemoglobin electrophoresis, blood grouping, rhesus antibody titre, and tests for rubella, hepatitis B, human immunodeficiency virus (HIV) and syphilis (Box 1.2). The haemoglobin electrophoresis may show that the mother has β-thalassaemia trait or sickle cell trait and the father's red cell investigations may suggest that further studies of the fetus are needed.

Box 1.1 **Routine screening**

- Ultrasound scan for gestational age assessment at 11–14 weeks
- Detailed anomaly ultrasound scan at 18–20 weeks
- Combined screening test for Down syndrome
- Routine blood screening

Box 1.2 **First antenatal visit – routine blood screening**

- Full blood count and haemoglobin electrophoresis
- Blood group
- Rhesus antibody titre
- Rubella antibody status
- Hepatitis B antibodies
- HIV antibodies
- Syphilis serology

Ultrasound studies

The first routine examination of the fetus by ultrasound is usually performed at the gestational age of 11–14 weeks. The gestational age is confirmed and anomalies of the central nervous system or cystic hygromas may be detected. A further scan at 18–20 weeks may detect anomalies of the central nervous system, heart, kidneys, intestinal tract and skeleton (Figure 1.1). Signs that suggest the possibility of a chromosome abnormality include choroid plexus cysts, echogenic cardiac foci, renal pelvic dilatation and echogenic bowel. They occur in approximately 1 in 250 pregnancies and are associated with a 1 in 300 risk of a chromosome abnormality. These isolated 'soft' signs do not merit the fetal risks of amniocentesis, but full discussion is necessary and the mother may still opt for karyotyping to be performed. Mothers with a family history of congenital heart disease should be offered a detailed fetal echocardiogram at 18–24 weeks as the risk of the fetus having a heart problem is 3–5%. The consultant obstetrician or fetal medicine specialist, ideally with the neonatal paediatrician, should discuss the diagnosis and prognosis of an anomaly with both parents. Termination of the pregnancy may need to be considered, or serial ultrasound examination performed during the pregnancy and in the neonatal period.

Ultrasound guidance is used in taking samples of the amniotic fluid (amniocentesis) and in selected centres it has been used to take blood samples from the umbilical cord (cordocentesis) and very occasionally to give blood transfusion by that route.

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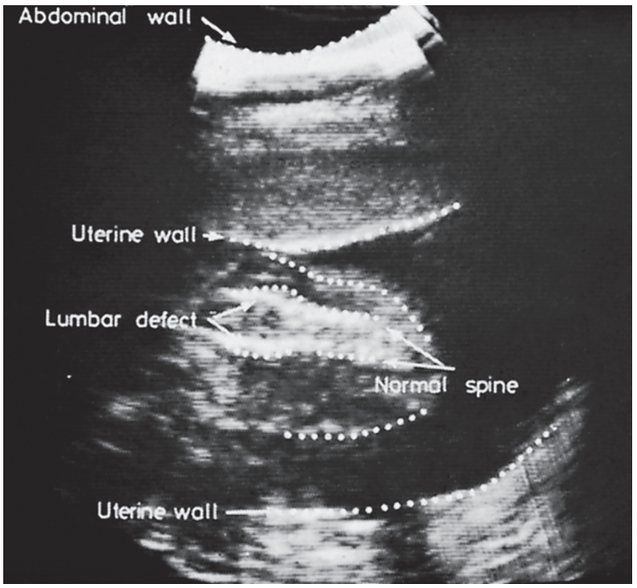

Figure 1.1 Ultrasound showing lumbar spine defect.

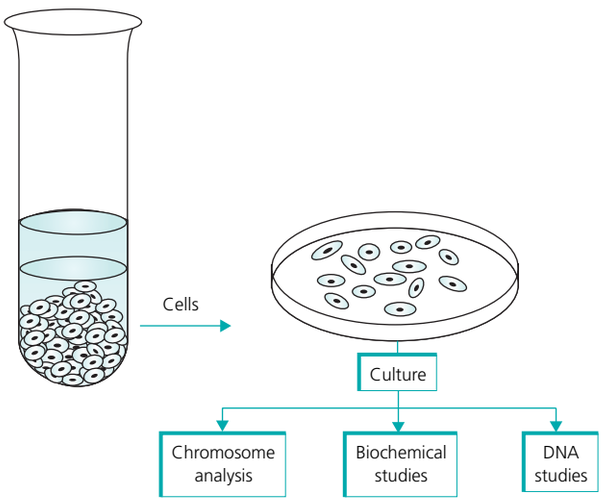

Figure 1.2 Examination of amniotic fluid.

The samples can be used in gene probe techniques, enzyme estimation and chromosome studies. In rhesus incompatibility, a low haematocrit in the cord blood in association with rhesus-negative status of the mother indicates the need for fetal transfusion.

Amniocentesis

Amniotic fluid is removed by passing a needle into the amniotic cavity through the mother's abdominal wall and uterus under ultrasound guidance. Amniocentesis yields amniotic fluid containing cells that have been shed from the skin of the fetus. Examination of the cultured cells reveals the chromosome constitution of the fetus, including sex (Figure 1.2). Specific enzymes can be sought and deoxyribonucleic acid (DNA) probes used (Figure 1.3). Women

Autosomal dominant
- Huntington's chorea
- Myotonic dystrophy
- Adult polycystic kidneys
- Tuberous sclerosis
- Von Recklinghausen's disease

X linked
- Duchenne muscular dystrophy
- Haemophilia A and B
- Fragile X

Autosomal recessive
- α and β-thalassaemia
- Sickle cell disease
- Cystic fibrosis
- Phenylketonuria
- α1-Antitrypsin deficiency
- Congenital adrenal hyperplasia

Figure 1.3 Examples of conditions for which DNA gene probes are available.

who are found to be at higher risk for Down syndrome on a screening test are offered amniocentesis. In high-risk women a fluorescent in situ hybridization (FISH) test may be offered which uses the polymerase chain reaction (PCR) to detect chromosome abnormalities such as the common trisomies 21, 18 and 13 – Down, Edward and Patau syndrome respectively. The results are available within a few working days.

Chorionic villus biopsy

Chorionic villus biopsy is carried out mainly by the transabdominal route under ultrasound guidance after 10 weeks gestation. The main indications are maternal age, previous chromosome anomaly, fetal sexing, enzyme assay and gene probe assessment. Gene probes have been developed for several diseases including cystic fibrosis, Duchenne muscular dystrophy and the haemoglobinopathies. DNA is extracted from the chorionic villus sample and the probe is used to determine whether a specific part of a particular gene is present or absent.

There is a higher miscarriage rate with chorionic villus biopsy compared to amniocentesis. As there is a risk of limb reduction deformities and facial anomalies when it is performed early, it should be carried out after the 10th week of gestation.

Maternal serum screening for Down syndrome

The majority of babies with Down syndrome are born to mothers under the age of 37 years because they form the largest proportion of mothers. Screening for Down syndrome should be offered to all mothers irrespective of maternal age. It provides an assessment of the risk but not a definite diagnosis of Down syndrome. In the UK, pregnant women are offered a screening test which provides a detection rate above 75% and a false positive rate of less than 3%. There are several tests which meet this standard. The combined test in the first trimester (between 11 and 14 weeks gestation) is offered using nuchal translucency measurement, free β-hCG, pregnancy-associated plasma protein A (PAPP-A) and maternal age.

Box 1.3 **Antenatal screening for Down syndrome (1)**

Combined test in first trimester using maternal age plus

1 Ultrasound scan (at 11–14 weeks):
- gestational age
- nuchal translucency measurement

2 Maternal blood levels of:
- free β-human chorionic gonadotrophin (β-hCG)
- pregnancy-associated plasma protein A (PAPP-A)

Box 1.4 **Antenatal screening for Down syndrome (2)**

Two-stage integrated test using maternal age plus measurements from the first and second trimesters integrated into a single test result.

Stage one at 11–14 weeks

1 Ultrasound scan to assess:
- gestational age
- nuchal translucency measurement

2 Maternal blood level of:
- pregnancy-associated plasma protein A (PAPP-A)

Stage two at 14–20 weeks

Maternal blood levels of:
- α-fetoprotein (AFP)
- free or total β-human chorionic gonadotrophin (β-hCG)
- unconjugated oestriol (uE_3)
- inhibin-A (inhibin)

Accurate gestational assessment as well as measurement of nuchal translucency is undertaken by ultrasound scanning and a maternal blood sample taken at the same antenatal visit (see Box 1.3). The most effective and safe method of screening for Down syndrome is by integration of measurements from the first and second trimesters into a single test result (see Box 1.4). The combined test has the advantage of a risk assessment result being available at an earlier stage in gestation than the integrated test and is therefore more likely to be acceptable to parents. Women who do not attend until the second trimester can be offered a quadruple biochemical test with age standardization. It is hoped that in future, with improved techniques of DNA gene replication, it might be possible to karyotype a fetus using fetal cells in the maternal circulation.

Risks

The risk to a particular fetus depends on the gestational age of the fetus, the indication for the procedure and the experience of the operator. The incidence of complications has fallen as skill in the newer techniques has increased. The abortion rates are difficult to assess but Table 1.1 has been compiled from expert advice on the available evidence. The risk of abortion after amniocentesis at 15 weeks is about 1%, which is about twice the spontaneous incidence in normal pregnancies. Fetal or maternal bleeding has been considerably reduced by the use of ultrasound, but a slight risk of infection remains and the incidence of respiratory distress syndrome and orthopaedic problems, such as talipes, is probably slightly increased in fetuses who have undergone early amniocentesis. Chorionic villus biopsy has a higher risk of abortion of about 5% against a background of spontaneous abortion of 3%. Chorionic villus biopsy carried out at about 10 weeks gestation provides a result early in pregnancy, when termination of the pregnancy is less traumatic and more acceptable for many mothers. Some tests are slightly more accurate when the sample is obtained by amniocentesis. Some investigations can be performed only on a specific sample.

Table 1.1 Risk of abortion.

Procedure	Gestational age performed (weeks)	Spontaneous abortion (%)	Risk of abortion after procedure (%)
Amniocentesis	14–18	0.5	1
Chorionic villus biopsy	>10	2–3	3–5
Cordocentesis	18–20	<1	1–2

Preterm labour

Preterm birth is the major cause of death and disability in babies. The aetiology of preterm labour is multifactorial, but there is increasing evidence to implicate infection as a possible cause in up to 40% of cases. This information may not help once a woman is admitted in preterm labour, since by that time there may be irreversible changes in the cervix. Where the information may be useful is in the prediction and prevention of preterm labour. A few recent studies have reported that abnormal colonization of the vagina in the form of bacterial vaginosis carries an up to fivefold increased risk of the subsequent development of preterm labour and late miscarriage. Whether by reversing this condition it is possible to reduce the incidence of preterm labour and delivery is currently being tested (Figure 1.4).

The fetal fibronectin test in women with suspected preterm labour and intact membranes between 24 and 34 weeks gestation is a useful adjunct to clinical assessment in deciding whether tocolysis or *in utero* transfer to a perinatal centre should be planned. A negative test indicates that the risk of delivery in the next 7 days is less than 1%.

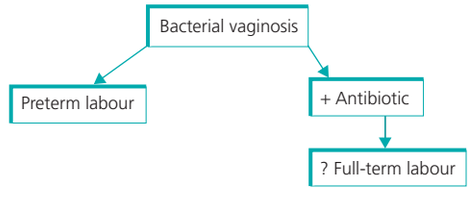

Figure 1.4 Bacterial vaginosis.

Follow-up of fetal renal tract anomalies

Mild dilatation (<10 mm) of the fetal renal pelvis is often found on the routine antenatal ultrasound scan done at 18–20 weeks

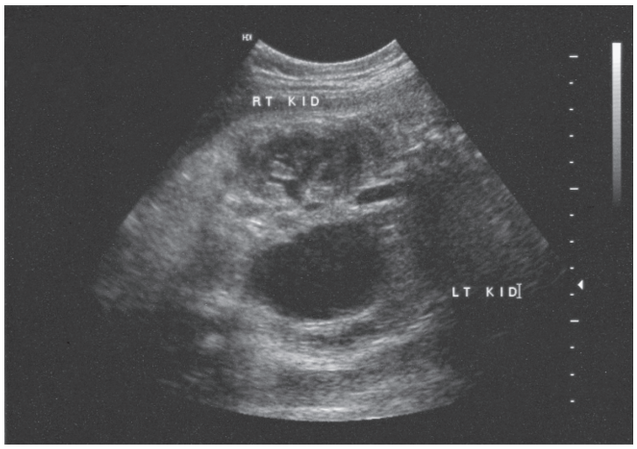

Figure 1.5 Ultrasound scan showing dilatation of left fetal renal pelvis.

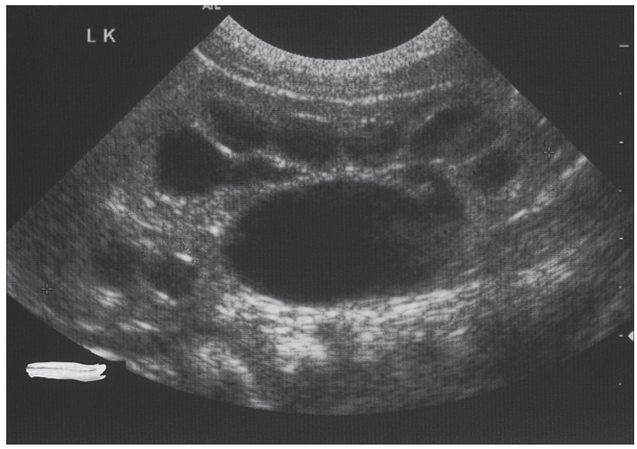

Figure 1.6 Postnatal scan showing dilatation of renal pelvis.

gestation (Figure 1.5). Serial scans at 2–4-weekly intervals will establish whether there is any progressive change before birth. The finding of reduced liquor, a distended thick-walled bladder or progressive dilatation >20 mm may be suggestive of an obstructive uropathy. Preterm delivery or antenatal surgical intervention is rarely indicated, except very occasionally in a male fetus where posterior urethral valves are causing renal compromise at <34 weeks gestation.

For most infants, postnatal investigation with several ultrasound scans over the first few months of life and sometimes a micturating cystourethrogram (MCUG) or renal isotope scan will be necessary. Until the results of these investigations are known, most infants will be given a small daily dose of prophylactic oral antibiotics (usually trimethoprim 1–2 mg/kg). This is to prevent urinary tract infections in those infants who may be at risk because they have vesicoureteric reflux. The radiological investigations are rarely urgent and some are more meaningful when the infant is a little older (for example, isotope scans).

All infants should be followed up postnatally, as it is not easy to predict which infants will have significant ongoing dilatation, but most antenatally diagnosed fetal renal tract dilatation is found to be benign or transient on serial postnatal follow-up (Figure 1.6). A small number of infants will be diagnosed as having pelviureteric junction obstruction, multicystic dysplastic kidney or bladder outlet obstruction, but only the latter requires urgent diagnosis and surgery in the neonatal period.

Further reading

NHS. *Antenatal and newborn screening programmes*. www.nscfa.web.its.manchester.ac.uk/screeninginfo

Royal College of Obstetricians. *Antenatal screening for Down syndrome*. www.rcog.org.uk/resources

Lamont RF (2003) Recent evidence associated with the condition of preterm prelabour rupture of the membranes. *Current Opinion in Obstetrics and Gynaecology* 15: 91–99.