EARLY PRENATAL DIAGNOSIS

Screening

- Ultrasound: 16–18 weeks
- Serum α fetoprotein: 16–18 weeks
- *Mother over 37 years*

(a) Chorionic villus biopsy: 8–12 weeks

or

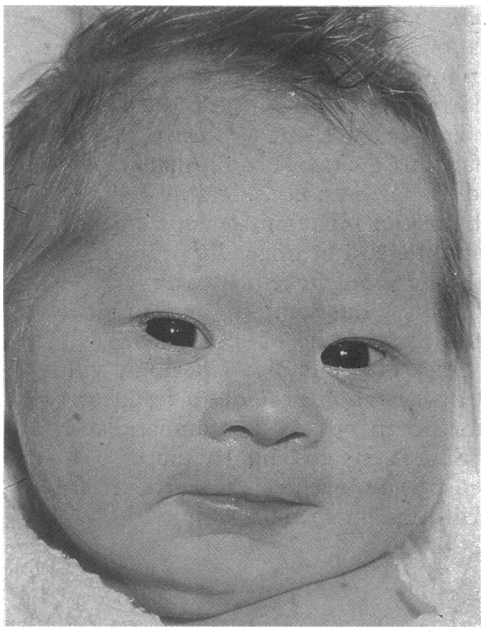
(b) Amniocentesis: 16 weeks

- Full blood count
- Group
- Rh antibody titre
- Rubella antibody titre
- Test for syphilis

Recent advances in ultrasound techniques and molecular biology have increased the range of antenatal diagnoses. Some methods are available only at specialised centres. This chapter will give a background to the successful techniques. An anomaly may be detected during routine examination of the fetus which is carried out by ultrasound in most pregnancies at 16–18 weeks of gestation. In some districts all mothers have a *serum* α fetoprotein estimation as a screening test for neural tube or other defects and in all districts mothers of more than a certain age, usually 37 years, are offered a chorionic villus biopsy or amniocentesis to exclude Down's syndrome. 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 a 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.

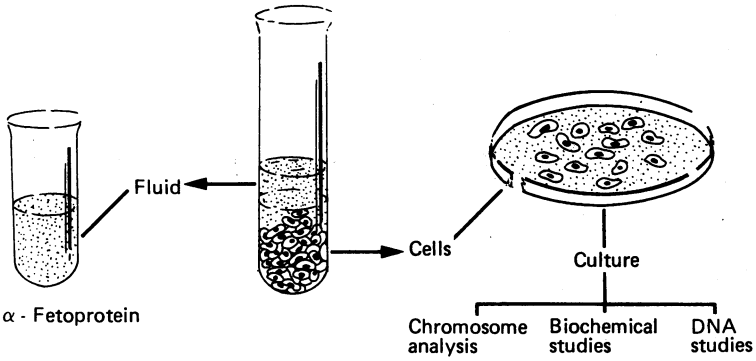
At the first antenatal visit it is still important to carry out a full blood count, blood grouping, rhesus antibody titre, rubella antibody titre, and a test for syphilis. Where indicated haemoglobin electrophoresis may indicate that the mother has a haemoglobinopathy and the father's red cell investigations may suggest that further studies of the fetus are needed.

Chorionic villus biopsy



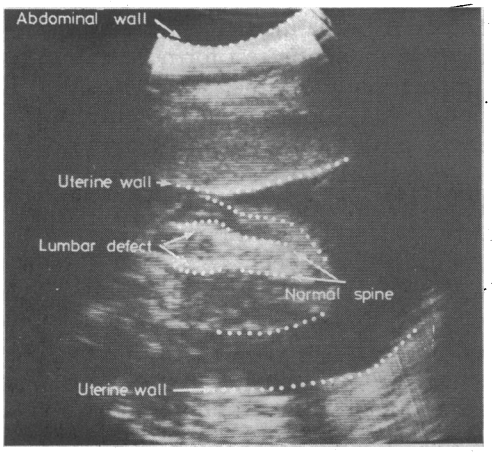
Chorion sampling may be carried out by the transvaginal or, less commonly, by the transabdominal route under ultrasound guidance. The main indications have been maternal age, previous chromosomal anomaly, fetal sexing, enzyme assay, and gene probe assessment. Gene probes have been developed for several diseases including cystic fibrosis, Duchenne muscular dystrophy, and the haemoglobinopathies. Deoxyribonucleic acid (DNA) is extracted from the chorion sample and the probe is used to determine whether a specific part of a particular gene is present or absent.

Amniocentesis



Amniotic fluid is removed by passing a needle into the amniotic cavity through the mother's abdominal wall and uterus. Amniocentesis yields amniotic fluid with cells which have been shed from the skin of the fetus. Amniocentesis is performed when screening has shown a raised maternal plasma α fetoprotein concentration. A raised concentration of α fetoprotein is found in the amniotic fluid when the infant has anencephaly or myelomeningocele. The level of various enzymes can be measured in the fluid and are abnormal if the fetus is affected—for example, in cystic fibrosis. Examination of the cultured cells reveals the chromosome constitution of the fetus, including the sex; specific enzymes can be sought and DNA probes used.

Ultrasound studies



The first routine examination of the fetus by ultrasound is usually performed at the gestational age of 16–18 weeks. The gestational age is confirmed and anomalies of the central nervous system, kidneys, heart, intestinal tract, and skeleton are sought and may be detected. The consultant obstetrician, ideally with the paediatrician, should discuss the diagnosis and prognosis of the anomaly with both parents. Termination of the pregnancy may need to be considered, or serial ultrasound is performed during the pregnancy and in the neonatal period.

Ultrasound guidance has been used in taking samples of the chorion and amniotic fluid, and in selected centres it has been used to take blood samples from the umbilical cord (cordocentesis) and to give blood transfusion by that route. The blood samples can be used in gene probe techniques, enzyme estimations, and chromosome studies. In rhesus incompatibility a low haematocrit in the cord blood indicates the need for fetal transfusion. Cordocentesis has also been used in the assessment of renal function and oxygen transport in the fetus with intrauterine growth retardation.

Risks

Procedure	Gestational age performed (weeks)	Spontaneous abortion	Risk of abortion after procedure (%)
Chorionic villus biopsy	9–12	2–3	3–5
Cordocentesis	18–20	< 1%	1–2%
Amniocentesis	16–18	0·5	1
Ultrasound	16–18		
Serum α fetoprotein	16–18		
Chorionic villus biopsy	9–12		
Amniocentesis	16–18		

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 the table opposite has been compiled from expert advice on the available evidence. The risk of abortion after amniocentesis at 16 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 club foot, is probably slightly increased in fetuses who have undergone early amniocentesis. Chorionic villus sampling has a higher risk of abortion of about 5% against a background of spontaneous abortion of 3%. Cordocentesis has a risk of about 2%. Chorionic villus sampling 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 or cordocentesis. Some investigations can only be performed on specific samples.