S U M M A R Y

SUMMARY

Antenatal diagnosis of hereditary disease and congenital defects, coupled with the available option of elective abortion, provides an acceptable, albeit imperfect, alternative for the prevention of certain conditions for many families. Further investigations are needed to provide effective therapies or even cures for many of these conditions.

The techniques for antenatal diagnosis include ultrasound, amniocentesis, fetoscopy (for visualization, blood sampling, skin biopsy and liver biopsy), needling and chorion biopsy.

Recombinant DNA technology permits analysis of gene dysfunction at the DNA level.

It is important to make early diagnosis possible for the majority of abnormalities so that first trimester termination can be carried out if the fetus is abnormal.

Screening tests for NTDs include amniotic fluid AFP and acetylcholinesterase (AChE) determination and ultrasonic examination of the fetus. Screening for open spina bifida and anencephaly is performed by maternal serum AFP (MSAFP) measurement. The elevated MSAFP may also indicate the presence of other fetal anomalies such as gastroschisis, omphalocoele, congenital nephrosis, sacrococcygeal teratoma, and duodenal or oesophageal atresia. At present the main method for antenatal diangosis of open spina bifida is amniotic fluid AFP. Ultrasonography and amniotic fluid gel AChE determination are valuable additional tests.

The antenatal diagnosis of hydrocephaly is made by measurig the cerebral ventricles. Serial scans throughout the second trimester diagnose most cases of microcephaly.

The reliable antenatal diagnosis of metabolic disorders has been based almost entirely on the use of cultured amniotic fluid cells for biochemical analysis. Apporximately 150 recessively inherited diseases can now be detected by assay of cultured fibroblasts. For certain disorders where the affected enzyme is not normally expressed in cultured fibroblasts, a definitive diagnosis can be made by enzymic assays of a tissue biopsy e.g. liver biopsy in case of glucose-6-phosphatase deficiency.

A proportion of chromosome anomalies can be diagnosed antenatally by amniocentesis and chromosome analysis of cultured amniotic fluid cells. First trimester chorion biopsy is an alternative approach to antenatal diagnosis of chromosome anomalies.

Many of the congenital anomalies are now amenable to antenatal diagnosis. Malformations involving the fetal head, spine, chest, abdomen, heart, kidneys, gastrointestinal tract and extremities have been diagnosied antenatally.

The relative rates of globin chain synthesis in the fetal blood have been estimated in 1975. Since then, antenatal diagnosis of haemoglobinopathies has been carried out.

Sickle cell trait can be screened for by sickledex test, and is diagnosed by haemoglobin electrophoresis.

Recently, DNA analysis permits the antenatal diagnosis of haemoglobinopathies. Sickle cell haemoglobin, the mild and severe forms of alpha-thalassaemia and few of beta-thalassaemia have been diagnosed directly by restriction enzyme analysis. The majority of beta-thalassaemia can be detected by establishing linkage to a restriction fragment length polymorphism (RFLP).

Antenatal diagnosis of haemophilias is feasible. Pure fetal blood can be obtained from virtually all fetuses, enabling factor VIIIC and IXC bioassays to be performed in addition to platelet and other measurements. The prospect of identifying heterozygous carriers of haemophilia, as well as affected fetuses, by DNA analysis is increasingly real.

Antenatal sex determination may be of help in severe X-linked diseases. Sex determination depends on amniocentesis and nuclear sex chromatin analysis with confirmation by karyotype. Fetal sex can also be determined by the use of chorionic villi as a source of fetal DNA in the first trimester of pregnancy.

Elevated serum creatine phosphokinase (CK) is considered to be the most helpful test for carrier detection of Duchenne muscular dystrophy (DMD). The antenatal diagnosis of DMD has become both feasible and reliable in a large poprortion of instances by using linked restriction fragment length polymorphisms.

For antenatal detection of Rh incompatibility, repeated Rh-antibody titrations are carried out on maternal serum. Spectrophotometric estimation of bilirubin in amniotic fluid is an important supplementary test.

The only sure way of diagnosing multiple pregnancy, especially if more than twins is ultrasonography.

Lecithin sphingomyelin (L/S) ratio is an excellent indicator of maturity. Intrauterine growth retardation can be diagnosed by low levels of urinary oestriol excretion. Ultrasonography is also essential in diagnosing the condition. The ratio of head circumference to abdominal circumference is a good indicator of intrauterine growth.

A gross evaluation of fetal well-being may be given by the electronic fetal stress and nonstress tests.

Methods for detection of fetal distress are available and the most commonly employed is electronic monitoring of the fetal heart rate. The more traditional alternatives to the assessment of fetal distress are the detection of meconium staining in the amniotic fluid, and auscultation of the fetal heart. Fetal scalp blood pH test is the most frequently advocated supplementary test for following up on a positive EFM tracing.