This statement is for the pediatrician who may be called upon to care for the child with a birth defect or genetic disorder. The involved family may wish to know and may benefit from methods that convert probability statements about recurrence risks into facts about the fetus. Many families will find knowledge and choice better than chance.

Rapid advances in technology have prompted the Committee on Genetics to retire the June 1980 statement and to prepare a new one. The purpose of this revised statement is to inform the pediatrician about the current status of antenatal diagnosis as it relates to genetic and family counseling in clinical practice.

The pediatrician may be called upon to help address questions about the natural history of the disorder under consideration and the possibility of intrauterine treatment. Prenatal diagnosis can give information that may improve the outcome of pregnancy and can be helpful to the obstetrician in the management of labor and delivery. The availability of prenatal diagnosis gives couples options they might not otherwise have, including termination of an affected pregnancy or preparation for the birth of an abnormal child. This enables many couples to have children, when without this information they would have chosen to be childless.

The techniques currently in use or under investigation for prenatal diagnosis include (1) fetal tissue sampling: amniocentesis, chorionic villus sampling, percutaneous umbilical blood sampling, percutaneous skin biopsy, and other organ biopsies; (2) fetal visualization: ultrasound, fetoscopy, magnetic resonance imaging, and radiography; and (3) maternal serum α-fetoprotein screening.

INDICATIONS FOR FETAL TISSUE SAMPLING

Chromosome Analysis

Fetal chromosome analysis should be offered when any of the following apply: (1) advanced maternal age; (2) a previous offspring has had one of the trisomic syndromes and perhaps other chromosome aberrations; (3) a chromosome abnormality is present in either parent, eg, aneuploidy, balanced translocation, or clinically significant inversion; (4) the fetus is at risk for a serious X-linked condition and specific intrauterine diagnosis is not available. Determination of fetal sex may also be appropriate as an initial screen before molecular genetic studies or fetal blood sampling; (5) a parent is a fragile X carrier. The mothers are usually identified by virtue of having a mentally retarded child, brother, or uncle who has the fragile X syndrome. Fragile X studies on amniocytes and/or chorionic villi are still considered investigational; (6) a combination of low maternal serum α-fetoprotein and maternal age in a woman who is younger than those in whom prenatal diagnosis is considered on the basis of maternal age alone. This is still considered investigational; (7) ultrasound has identified an anatomic abnormality, eg, omphalocele, hydrocephalus, or dysplastic kidney, that might indicate an increased risk for karyotypic abnormalities. Even when these abnormalities are found in the third-trimester of pregnancy, chromosome analysis of amniotic fluid cells may be indicated. The use of percutaneous umbilical blood sampling or transabdominal chorionic villus sampling for chromosome analysis in the third trimester is now also under investigation. Information obtained from these studies can influence decisions regarding the advisability of intrauterine therapy. The findings may also be important to the obstetrician in the management of labor and delivery and to the pediatrician, neonatologist, and geneticist in patient management in the newborn period.

Biochemical Studies

Biochemical studies are indicated when (1) there has been a previous child affected with a biochem-
Prenatal Diagnosis

A medical condition that can be diagnosed prenatally\textsuperscript{15}; (2) couples are at risk because of their carrier status, often related to ethnic origin, eg, Tay-Sachs disease in Ashkenazi Jews, sickle cell disease in American blacks, and thalassemia in those of Italian, Greek, or Oriental descent\textsuperscript{15}; (3) neural tube defects are present in a parent or sibling of the fetus\textsuperscript{10,16}; (4) couples have been identified as being at increased risk for an offspring with a neural tube defect, eg, as the result of maternal serum \alpha-fetoprotein screening.\textsuperscript{10,16}

Routine and Electron Microscopy

Routine and electron microscopy have been used to diagnose rare genetic diseases, eg, epidermolysis bullosa letalis.\textsuperscript{5-7}

Molecular Genetic Studies

The use of molecular biologic techniques is rapidly increasing.\textsuperscript{17} These methods of diagnosis are based upon the fact that the DNA complement is identical in every cell of the body, and therefore any hereditary defect detectable at the DNA level should be found in any nucleated cell from that organism. Enzymes (restriction endonucleases) that cleave DNA within a specific base sequence recognition site are used to identify mutant genes. This is currently a clinical tool in the prenatal diagnosis of hemoglobinopathies, hemophilia A, Duchenne and Becker muscular dystrophy, and cystic fibrosis. It is being applied experimentally to the prenatal diagnosis of hemophilia B, adult polycystic kidney disease, Huntington chorea, and other disorders. New applications are rapidly being made available. It is often necessary to contact a genetic center to determine whether or not this technique is available and accurate for a given genetic disorder.

Techniques for Tissue Sampling

Amniocentesis

Transabdominal amniocentesis at 16 weeks of pregnancy is the most commonly used technique for obtaining fetal tissue.\textsuperscript{2} The results are accurate (more than 99\% for most biochemical and cytogenetic studies). Processing of the cultures can take 2 to 4 weeks, but results of cytogenetic analysis are routinely available in less than 2 weeks in an increasing number of laboratories. Significant maternal injury is rare. Although injury to the fetus is also rare, there remains a small, procedurally related risk of fetal loss. Early amniocentesis between 11 and 14 weeks of gestation is currently being investigated.

Chorionic Villus Sampling

This is still technically considered an investigational procedure for obtaining fetal tissue.\textsuperscript{4,18-22} The major advantage of this procedure is that earlier diagnosis is possible. At 9 to 11 weeks of gestation, a plastic catheter with a solid flexible stylet is inserted transcervically, under ultrasonic guidance, to an area of placental development. A sample of villus tissue is removed by aspiration. The villi are then dissected from the decidual tissue and can be cultured or assayed directly. The disadvantages of this technique are the complications of the procedure including fetal loss and the possibility of contamination of the villus sample with maternal decidua. The safety and accuracy of this procedure are still being investigated.

A promising new investigation procedure is transabdominal chorionic villus sampling.\textsuperscript{23,24} This is also performed at 9 to 11 weeks of gestation. Transabdominal chorionic villus sampling may also be performed later in gestation, including the third trimester.

Fetal Blood Sampling

Fetoscopy for fetal visualization and fetal blood sampling has been largely replaced by percutaneous umbilical blood sampling and better ultrasonic visualization but still may be useful in selected situations.\textsuperscript{5-7,25}

A technique for percutaneous sampling of fetal blood from the umbilical cord or hepatic vein is available. Preliminary data suggest, that when this is done under ultrasonic guidance, there is a lower risk of spontaneous abortion than with fetoscopy.\textsuperscript{25} This technique is still considered investigational. For some conditions, fetal biopsy has been replaced by molecular genetic studies of amniocytes or chorionic villi.

Fetal Skin Sampling

A number of serious skin disorders, eg, epidermolysis bullosa letalis and harlequin ichthyosis, may be diagnosed histologically by skin biopsies obtained percutaneously under ultrasonic guidance, with or without fetoscopy.\textsuperscript{5-7}

Organ Biopsies

Techniques for biopsy of other fetal organs are still considered investigational.

Techniques for Fetal Visualization

Ultrasound

This technique is used to monitor fetal growth and to establish gestational age and placental lo-
cation. Many referral centers have ultrasound imaging equipment that provides sharp resolution and detail. Many anatomic lesions can be visualized, including some genitourinary, gastrointestinal, skeletal, and central nervous system abnormalities.\textsuperscript{8,16} Fetal echocardiography may identify some cardiac lesions.\textsuperscript{8,27}

**Fetoscopy**

Because of the risk of spontaneous abortion associated with fetoscopy, it is only used in selected situations.\textsuperscript{9}

**Magnetic Resonance Imaging**

As a fetal imaging technique, magnetic resonance imaging is being actively investigated.\textsuperscript{8}

**Radiography**

Although radiography has been largely replaced by ultrasonography for the detection of anatomic lesions, it may still be indicated for specific disorders and selected cases, particularly after the first trimester.

**SERUM \(\alpha\)-FETOPROTEIN**

Detection of Neural Tube Defects

Please refer to the statement on maternal serum \(\alpha\)-fetoprotein screening by the Committee on Genetics.\textsuperscript{10}

Identification of Trisomy 21

Results of recent studies have suggested that low maternal serum \(\alpha\)-fetoprotein concentrations may be associated with an increased risk for trisomy 21 and perhaps other chromosomal aneuploidies in the fetus.\textsuperscript{9}

**RECOMMENDATIONS**

Pediatricians should be familiar with the principles of antenatal diagnosis and know how to apply them to specific problems in genetic counseling, diagnosis, and management in clinical practice. At the same time, pediatricians should be familiar with resources available in their region. The technology of prenatal diagnosis is changing particularly rapidly, and pediatricians may find that their genetic consultants can assist them in keeping their information and practice current in this field.

**REFERENCES**

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Prenatal Diagnosis for Pediatricians

*Pediatrics* 1989;84;741

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