Prenatal Diagnosis for Pediatricians

This statement is for the pediatrician who may be called on to care for the child with a birth defect of Mendelian or multifactorial origin—namely all pediatricians! The involved family may wish to know and may benefit from methods that convert probability statements about recurrent risks into facts about the fetus. Many families will find knowledge and choice better than chance.

Antenatal (prenatal) detection of certain forms of disease, largely those of genetic origin, has become an accepted part of medical care for mother and child, where resources permit it. Excellent reviews on the subject are available, and a National Institute of Child Health and Human Development Consensus Development Conference report reflects a prevailing familiarity with the new technology in the United States. Accordingly, the modern pediatrician has a new responsibility to recognize families at risk and advise the parents about the indications for and availability of antenatal diagnosis. The purpose of this statement is to inform pediatricians about the present status of antenatal diagnosis as it relates to genetic and family counseling in clinical practice.

INDICATIONS

Amniocentesis, when performed under the proper conditions and guidelines, is a safe method for antenatal diagnosis. The accepted indications for intrauterine monitoring by amniocentesis are as follows:

1. Cytogenetic problems: (a) advanced maternal age (35 years or above); (b) previous offspring with chromosomal aberration; (c) chromosomal anomaly in either parent; and (d) determination of fetal sex where there is a probability that a serious X-linked condition may be manifest and for which specific intrauterine diagnosis is not feasible.
2. Inborn errors of metabolism detectable in amniotic fluid or cultured amniotic fluid cells.
3. Neural tube defects.
4. Certain hemoglobinopathies. (The antenatal diagnosis of hemoglobinopathies, in general, remains in the developmental stage, although large numbers of patients have already been monitored. The pediatrician should consult the local center for available tests.)

Antenatal diagnosis of other clinical conditions by fetal blood sampling, fetoscopy, and echosonography (ultrasound) is under investigation, but these procedures are not yet in wide use.

TECHNICAL CONSIDERATIONS: RISKS OF AMNIOCENTESIS

Transabdominal amniocentesis for fetal conditions detectable in the midtrimester should be performed prior to 20 weeks of pregnancy, and preferably in the 16th week. Echosonography preceding amniocentesis, to define fetal maturity and the position of the placenta, is strongly recommended. The initial attempt at amniocentesis, when done at centers with the requisite technical experience, yields the required amount and quality of fluid and cells 95% of the time; cytogentic and biochemical analyses will be successful on 99% of this material at competent centers.

Amniocentesis is not without some risk for mother and fetus. Although significant maternal injury is virtually nonexistent, abortion sometimes occurs after the procedure, but the risk is apparently modest. There are unexplained differences in the abortion rates quoted for various collaborative studies in the United States, Canada and Great Britain where amniocenteses are performed in large numbers by a relatively few, skilled teams. At regional centers, the additional risk for abortion after transabdominal amniocentesis apparently is not greater than 0.5%.

Cosmetic or more severe injury to the surviving fetus is extremely rare. However, the degree of risk for isoimmunization in the appropriate circumstance is still uncertain; accordingly, there is no consensus regarding routine use of Rh immune globulin (Rhogam) with amniocentesis.

NEW TECHNOLOGY

Fetal blood sampling under direct visualization by fetoscopy has been feasible for several years. However, the application of this technology in the antenatal diagnosis of such conditions as thalassemia and sickle cell disease is still under evaluation. The risk for abortion after midtrimester fetoscopy and fetal blood sampling is at least about 5% higher than the natural risk. The risk for premature deliv-
ery of a surviving infant or the occurrence of other complications is unknown.

The analysis of fetal blood samples to detect hemoglobinopathies has risen to become a fine and established art at selected centers; however, the detection of other disorders such as hemophilia, chronic granulomatous disease, and Duchenne muscular dystrophy is still either in the experimental stage or not recommended on the basis of current experience.

Visualization of the fetus by echosonography, various roentgenographic methods, and fetoscopy is under evaluation. Diagnosis of certain birth defects may be feasible and of significance at some future time with each of these methods. However, at present—and particularly for echosonography—the use of these methods is largely as an adjunct to other forms of prenatal screening and diagnosis. For example, echosonography must play an essential role in the dating of pregnancy and in detection of twins in any mass program of α-fetoprotein (AFP) screening for neural tube defects in populations (vs AFP screening on amniotic fluid from specific pregnancies at risk).

SUMMARY

Pediatricians should be familiar with the principles of antenatal diagnosis and how they should be applied to specific problems in genetic counseling, diagnosis, and management in clinical practice. At the same time, pediatricians should be familiar with the resources for the new technology available to them in their region, and they should assure themselves that the performance of antenatal diagnosis meets current standards.

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