Prenatal Screening Tests

The use of prenatal serum alpha-fetoprotein (AFP) determinations to monitor fetal abnormalities has become accepted practice since 1986 when the American College of Obstetrics and Gynecology recommended its use to detect the presence of open neural tube defects (NTD) in developing fetuses [1]. Since then, the use of AFP measurements has been extended to the detection of chromosomal anomalies, principally trisomy 21 (Down syndrome) [2] and trisomy 18 [3]. Although the original investigations into the prenatal detection of Down syndrome relied solely on AFP results, more recent studies have shown an improvement in detection when measurements of unconjugated estriol (uE3) and human chorionic gonadotropin (hCG) are combined with AFP [4,5]. More recently, further improvement in the detection rate for down syndrome was realized with the development of the quadruple screen in which dimeric inhibin-A (DIA) is combined with testing results of the previous three tests (i.e., AFP, hCG, and uE3) [7]. In order to permit comparison of test results between testing centers, all values are expressed as multiples of the median (MoM) for the gestational age of the fetus.

CORRECTION OF MoM RESULTS

MoM values for AFP, hCG, uE3, and DIA are affected by the weight of the mother and twin gestations. Each of these MoMs is corrected for maternal weight. Correction is not made for twins. The AFP MoM is also affected by insulin dependent diabetes mellitus and race. Corrections for these factors are made when the information is available.

NEURAL TUBE DEFECTS

The incidence of NTD in the white race is 6 in 10,000, while in the black race it is only 3 in 10,000. Insulin dependent diabetics have an *a priori* risk of 35 in 10,000. Patient-specific risks are calculated from the corrected AFP MoM and the *a priori* risk. When the AFP MoM is greater than 2.5, 75% of open spina bifida and 79% of ventral wall defects will be detected [6].

CHROMOSOMAL ANOMALIES

Trisomy 21 has been associated with low AFP MoM values, less than 0.5. Using a combination of age (≥35 years) and AFP MoM, approximately 35% of Down syndrome affected fetuses can be detected *in utero* [4]. When uE3 and hCG MoMs are added to the risk assessment, the detection is increased to 67% [4,5,7]. The quadruple marker improves the detection rate to 77% when ultrasound dating is used and the false positive rate is held at 5% [7]. Additionally, the rarer trisomy 18 anomaly may also be identified. Approximately 85% of trisomy 18 will be identified by triple marker screening when all of the following are present: the combination of AFP MoM is less than 0.75, the uE3 MoM is less than 0.60, and the hCG MoM is less than 0.55 [3].

RISK CALCULATIONS

When the gestational age of the fetus is 15 weeks or less, only the corrected MoM is reported. For gestational age less than 15 weeks or greater than 20 weeks, maternal serum AFP monitoring is not recommended. Maternal serum AFP testing should be done between 15-20 weeks of gestation. Genetic counseling is recommended for all patients whose age at EDC is 35 years or older.

NOTE

Because of the complexity of the risk calculations involved in both the triple and quadruple marker tests, the tests are not even marginally interchangeable. Make certain that the appropriate test has been ordered to avoid delay of testing results and added

expense.

References:

1. Prenatal Detection of Neural Tube Defects. American College of Obstetrics and Gynecology Technical Bulletin 1986;99:1-6
2. Palomaki GE, Haddow JE. Maternal serum "-fetoprotein, age, and Down syndrome risk. Am J Obstet Gynecol 1987;156:460-3
3. Palomaki GE, Knight GJ, Haddow JE, Canick JA, Saller DN, Panizza DS. Prospective intervention trial of a screening protocol to identify fetal trisomy 18 using maternal serum alpha-fetoprotein,unconjugated estriol, and human chorionic gonadotropin. Prenatal Diag1992;12:925-30.
4. Haddow JE, Palomaki GE, Knight GJ, Williams J, Pulkkinen A, Canick JA, Saller DN, Bowers GB.Prenatal screening for Down's(sic) syndrome with use of maternal serum markers. N Engl J Med 1992;327:588-93.
5. Phillips OP, Elias S, Shulman LP, Andersen RN, Morgan CD, Simpson JL. Maternal serum screening for fetal Down syndrome in women less than 35 years of age using alpha-fetoprotein, hCG, and unconjugated estriol: A prospective 2-year study. Obstet Gynecol 1992;80:353-8.
6. Adams MJ, Windham GC, James LM, Greenberg F, Clayton-Hopkins JA, Reimer CB, Oakley GP. Clinical interpretation of maternal serum "-fetoprotein concentrations. Am J Obstet Gynecol 1984;148:241-54
7. Benn, PA, Fang, M, Egan, JFX, Horne, D, and Collins, R. Incorporation of Inhibin-A Second Trimester Screening for down Syndrome. Obstetrics and Gynecology: 2003:101:3:451-454.