DLS Laboratory Medicine Bulletin

PRENATAL TESTING: QUADRUPLE SCREEN

by Wesley J. Kim, M.D.

The majority of babies born do not have any significant birth defects. However, there are a small number of women whose babies are at greater risk for certain birth defects.

Down syndrome (trisomy 21) occurs in approximately 1 out of 700 babies born. These babies have a distinctive physical appearance, varying degrees of mental retardation, poor muscle tone, and a high frequency of heart defects. The risk of having a child with Down syndrome increases in women age 35 or older.

Edwards syndrome (trisomy 18) only occurs in approximately 1 out of 8,000 births. The majority of pregnancies with an affected fetus end in miscarriage. Of those infants that are born, 90% will die within the first year of life. Babies with trisomy 18 also have certain distinct physical features, congenital heart disease, and severe mental retardation. Like Down syndrome, the risk increases in women age 35 or older.

Neural tube defect (NTD) occurs in approximately 1 out of 1700 babies born. The two main types of NTD are spina bifida and anencephaly. In spina bifida, there is failure of the neural tube to close properly, resulting in nerve damage ranging from mild to very severe. It can result in difficulty walking, paralysis, and absence of bowel and bladder control. Spina bifida is also associated with hydrocephalus. Anencephaly occurs when the neural tube in the area of the brain fails to close properly. It is a very severe birth defect and most babies usually die at birth or shortly thereafter.

There are a number of "screening tests" that can be performed during pregnancy to help determine the risk for these birth defects. Maternal serum AFP and the Triple Screen are well known tests that are utilized to help identify those pregnancies at increased risk and thus require additional testing and genetic counseling. However data published in the literature has identified a number of other possible screening panels with improved performance.

The Quadruple Screen (Quad Screen) is similar to the triple screen in that it involves the measurement of certain analytes in maternal serum during the second trimester (15 to 20 weeks). These include alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), and unconjugated Estriol (UE3). The difference however is the addition of a fourth analyte known as dimeric inhibin A, a molecule normally synthesized by the placenta and ovaries. On average, maternal serum inhibin A levels are about two times higher in Down syndrome than in unaffected pregnancies. Although not yet clear, the increase is thought to be secondary to abnormal syncytiotrophoblast formation and placental secretion in affected pregnancies. As with the Triple Screen, the results of these four analytes, in combination with additional required medical history, results in an overall risk assessment for certain birth defects.

How does the Quad Screen perform? The percent detection rate varies slightly in the literature depending on the false positive rate that is accepted, however in general, the Quad Screen increases the detection rate of Down syndrome to 80% while still maintaining an approximate 5% false positive rate. By comparison, the Triple screen has a detection rate of about 70% for Down syndrome with the same 5% false positive rate. The detection of unborn babies with NTDs (80 to 90%) and trisomy 18 (60 to 75%) essentially remain the same between the Triple and the Quad Screen.

DLS is pleased to announce that beginning December 1 2005, the Quad Screen will be performed in-house at DLS Central Laboratory. This change to on-island testing allows for risk-related results based on median values derived from the local population, improved turn around time for results, and the ability to directly control and monitor the performance of the test in association with local geneticists and genetic counselors.

The patient medical information required for the Quad Screen is the same as for the Triple Screen (e.g. race, body weight, gestational age, multiple gestations, DM, etc.). DLS has developed a new Quad Screen requisition form that will be distributed to all clients. Appropriate changes in the reporting of Quad Screen results have also been made following discussions with Genetics and Obstetrical departments. Any recalculation requests will be managed the same as current protocol. Since the Quad Screen offers better performance, all orders for a Triple screen will be converted to a Quad Screen, with prior authorization from the ordering physician.

Further development and improvement in prenatal testing does not end at the Quad Screen. First trimester screening, which involves the measurement of maternal serum Pregnancy Associated Plasma Protein A (PAPPA) and free Beta-hCG, in combination with radiographic assessment of Nuchal Translucency (NT), and integrated screening which combines the data from the first trimester and second trimester screens, can offer even better detection rates and lower false positive rates. DLS plans to offer first trimester screening and integrated screening in the near future.

For general information or questions about this test, please call DLS Client Services at 589-5101 or your Marketing Representative. You may also call Dr. Wesley Kim at 589-5131 for any specific questions or information.

Ordering Information

Test Name: Quadruple Screen

Test Code: 5087

CPT Codes: 82105, 82677, 84702, 86336

Specimen Requirement
Serum only.

Specimen Storage and Stability
Serum stable at ambient up to 8 hours.
Serum stable refrigerated up to 48 hours.
Serum stable frozen up to a month.

Testing Schedule
Monday through Friday