Integrated Test Technology under license from Intema Ltd, UK

Please be aware that unless the person being tested specifically prohibits such use in writing, the specimen and information obtained during the testing process becomes the property of the State of Iowa and may be used for program evaluation or research by the Department of Public Health or Department-approved scientific researchers to improve the health of mothers and children. An example of such research would be finding a blood test or tests which may predict the birth of a premature or growth retarded baby. Such studies are published without identifying the person or persons from whom these results were obtained. There are no known risks from being in these studies, and the person being tested will not benefit personally from participating in this research. However, others may benefit in the future from what we learn as results of these studies. You can find a link to the study or studies currently being conducted at the screening program website. The address is: *http://www.medicine.uiowa.edu/programs/screening/*. If you have questions about the rights of research subjects, please contact the Human Subjects Office, 300 College of Medicine Administration Building, The University of Iowa, Iowa City, IA 52242, (319) 335-6564, or e-mail: irb@uiowa.edu. To offer input about your experiences as a research subject or to speak to someone other than the research staff, call the Human Subjects Office at the number above.

University of Iowa Hospitals & Clinics
University of Iowa Health Care

Changing Medicine.
Changing Lives.®

Department OB/Gyn
Maternal Screening Consultant
University of Iowa Health Care
200 Hawkins Drive
Iowa City, IA 52242
Telephone: 319/356-3561
Fax: 319/356-7556

Iowa Department of Public Health
Birth Defects Institute
State Coordinator for Genetic Services
Lucas State Office Building
321 East 12th St.
Des Moines, IA 50319
Telephone: 515/281-7584
Fax: 515/242-6384

University Hygienic Laboratory
102 Oakdale Research Campus
#H101 Oakdale Hall
Iowa City, Iowa 52242-5002
Phone: 319/335-4500
Fax: 319/335-4555

www.medicine.uiowa.edu/programs/screening

Revised May 2008

Iowa Maternal Screening Program

The University of Iowa

The Iowa Integrated Screen

Seeing your healthcare provider early to begin prenatal care is an important part of preparing for the birth of your baby. Although most babies are born healthy, about 3 to 4% are born with a birth defect or genetic problem. It is normal to wonder about the health of your developing baby, and there are tests designed to provide you and your healthcare provider with information during your pregnancy.

The Iowa Integrated Screen is a test available to all women during pregnancy. This screening test is designed to identify women with an increased risk to have a baby with Down syndrome, Trisomy 18, or an open neural tube defect. The screen may also identify women with an increased risk to have a baby with other kinds of birth defects or women at risk to develop a problem later in pregnancy.

For most women the results of the Iowa Integrated Screen will be screen-negative (lower risk) and no further tests are offered. This is reassuring, but does not guarantee that the developing baby is healthy. The Iowa Integrated Screen is the first in a series of tests that may be offered. It cannot directly diagnose birth defects and chromosome abnormalities, but can help you and your healthcare provider decide when other tests such as an ultrasound and amniocentesis may be of value.

This brochure answers some of the common questions women ask about the Iowa Integrated Screen. You are encouraged to discuss this information with your healthcare provider.

What is Down syndrome?

Down syndrome, also called Trisomy 21, is caused by an extra chromosome number 21 in every cell of the body. It is the most common chromosome abnormality in liveborn infants; in an unscreened population about 1 in every 800 babies is born with Down syndrome. Children with Down syndrome have characteristic facial features, low muscle tone and mental retardation. About half of children with Down syndrome also have a birth defect, with heart defects being the most common. People with Down syndrome are also more likely to have medical problems, including difficulties with vision and hearing. Each person with Down syndrome is different and there is no way to know before a child is born how serious the medical and mental disabilities will be. There is no cure for Down syndrome, but resources are available to help people with Down syndrome and their families.

What is Trisomy 18?

Trisomy 18 is a chromosome abnormality caused by an extra chromosome number 18 in every cell of the body. Serious problems with growth and development are present before birth and physical problems such as an open spine or heart defect may be present. Many pregnancies with Trisomy 18 will miscarry and only 1 in 10 babies who are born with Trisomy 18 survive to one year of age, with most passing away soon after birth. Trisomy 18 is less common than Down syndrome; in an unscreened population, about 1 in every 6000 babies is born with Trisomy 18.

What are open neural tube defects?

In the first weeks of pregnancy, when the fetus is less than one inch long, a structure known as the neural tube begins to form along the fetal back. The top of this tube develops into the brain and the rest becomes the spinal cord. Open neural tube defects occur when the skull or spine does not close properly around the brain or spinal cord.

The two major types of open neural tube defects are spina bifida and anencephaly. About one in 1,000 pregnancies in Iowa will have an open neural tube defect. About half of these have spina bifida and half have anencephaly.

Babies born with spina bifida (open spine) have an opening in the bones of the spine, which can result in damage to the nerves which control the lower part of the body. The effects from spina bifida may range from mild to severe, from weakness of the leg muscles to actual paralysis. The severity of the problem depends upon where along the spinal cord the defect is located; a higher defect in the spine will result in more paralysis. Because the nerves that direct bowel and bladder functions are at the base of the spinal cord, there may be problems with bowel and bladder control. Over 80% of newborns with spina bifida have hydrocephalus (water on the brain). Corrective surgery and physical therapy can help lessen the disability in these children so that some may lead relatively normal lives. In severe cases of spina bifida a baby may be stillborn or die soon after birth.

Anencephaly (open brain) occurs when the skull and brain do not develop normally. Babies with this severe condition are almost always stillborn or die very soon after birth.

What does the Iowa Integrated Screen involve?

The Iowa Integrated Screen is a prenatal screen that combines or “integrates” information from an early ultrasound and two blood tests to give your chance of having a baby with Down syndrome, Trisomy 18 or an open neural tube defect in the current pregnancy. The Iowa Integrated Screen is performed in two stages. Stage One is performed in the first trimester, ideally at 10-11 weeks. Stage Two is performed in the second trimester between 15 and 20 weeks of pregnancy.

Stage One involves:

- Performing an ultrasound to measure the fetus and accurately determine the gestational age of the pregnancy. The nuchal translucency (NT) may also be measured if the ultrasound is being done by an NT-certified sonographer. The nuchal translucency is a collection of fluid behind the fetal neck that can be seen in any fetus in the first trimester of pregnancy. Having an NT measurement done improves the performance of the Iowa Integrated Screen.
- Taking a blood sample to measure the concentration of pregnancy associated plasma protein-A (PAPP-A). This is usually drawn after the ultrasound and is often drawn on the same day.

Stage Two involves:

- Taking a second blood sample to measure the concentration of alpha-fetoprotein (AFP), human chorionic gonadotrophin (hCG), and unconjugated estriol (uE3).
- Integrating the measurements of the markers in your blood from both stages, together with your age and the NT measurement, if available. If an NT measurement was not done, integrating the results of the two blood tests is still an effective screen for Down syndrome, Trisomy 18 and open neural tube defects.
- Notifying your healthcare provider of this Integrated Screening result after the ultrasound and both blood tests are completed.

All of the blood markers are made by the developing baby and the placenta. The levels of these markers may be altered in a predictable way when a developing baby has a chromosome problem such as Down syndrome or Trisomy 18, or certain birth defects such as an open neural tube defect.

- In pregnancies with Down syndrome, the levels of PAPP-A, AFP, and uE3 *tend* to be lower and the nuchal translucency (NT) measurement, and hCG *tend* to be higher than average.
- In pregnancies with Trisomy 18, the levels of PAPP-A, AFP, uE3, and hCG *tend* to be lower and the NT measurement *tends* to be higher than average.
- In pregnancies with an open neural tube defect, the level of AFP is *usually* increased. If the defect is in the spinal cord itself, but is covered by skin, AFP will not leak into the amniotic fluid and so the AFP level may not be increased. These defects will not be detected by the blood test and the effects tend to be less severe.

Any woman can have a baby with Down syndrome or Trisomy 18, but it is known that these and other chromosome abnormalities are more likely to occur as women get older. This is why the Iowa Integrated Screen includes maternal age in the risk calculation. This means that as a woman gets older she is more likely to have a result that is screen-positive (higher risk) and so be offered a diagnostic test. The chance of having a baby with an open neural tube defect does not increase with a woman's age.

What do "screen-positive" and "screen-negative" results mean?

It is important to remember that a screening test does not give a diagnosis; it only predicts the likelihood for a problem to occur. The Iowa Integrated Screen can indicate whether you have an increased or decreased risk to have a baby with Down syndrome, Trisomy 18 or an open neural tube defect. The Iowa Integrated Screen will detect about 85% of pregnancies with Down syndrome, 80% with Trisomy 18 and 85% with open neural tube defects.

An Iowa Integrated Screening result is considered screen-positive (higher risk) if the risk for Down syndrome or Trisomy 18 is greater than or equal to a predetermined risk as set by the Screening laboratory. It is considered screen-positive for an open neural tube defect if the AFP level is greater than or equal to 2.2 times the average level for your stage of pregnancy. It is important to remember that a screen-positive result does not mean that your baby has a problem, only that the chance that your baby might have Down syndrome, Trisomy 18, or an open neural tube defect is elevated.

If your Iowa Integrated Screening result is screen-positive for Down syndrome or Trisomy 18, you will be offered an amniocentesis for diagnosis. If you have a result that is screen-positive for an open neural tube defect, you will be offered an ultrasound examination and possibly an amniocentesis. Fortunately, most women who undergo further testing will find out that their developing babies do not have these problems.

An Iowa Integrated Screening result is considered screen-negative (lower risk) if the risks for Down syndrome, Trisomy 18 and open neural tube defects are below the predetermined risk as set by the Screening laboratory. A screen-negative result suggests that the baby is unlikely to have one of these problems, and further testing is not offered. It is important to remember that a screen-negative result, while reassuring, does not guarantee that your developing baby is healthy. A small number of babies with Down syndrome, Trisomy 18 or an open neural tube defect will be missed by this screening.

Why wait until Stage Two to have a risk calculated?

By integrating the information from both stages, the Iowa Integrated Screen is more effective than screening which uses information from Stage One or Stage Two alone. Integrated Screening is more effective at distinguishing affected from unaffected pregnancies because it has a lower screen-positive rate for Down syndrome and Trisomy 18 than single-stage screening options while still detecting the same number of affected pregnancies. A lower screen-positive rate reduces the chance that you will be offered a diagnostic test, such as an amniocentesis, which carries a small risk of complications, including miscarriage.

What if I am too late for Stage One?

If you are too far along in your pregnancy for Stage One, the Iowa Integrated Screen cannot be done. However, women who are between 15-20 weeks of pregnancy may choose the Quad Screen, which measures the same markers as Stage Two of the Iowa Integrated Screen (AFP, hCG, uE3) plus a fourth marker, inhibin A. While the Quad Screen/Stage Two alone is not as effective as the Iowa Integrated Screen, it is still a good screen for Down syndrome, Trisomy 18 and open neural tube defects.

What if I miss the Stage Two blood test?

If you do not have the Stage Two blood test drawn between 15-20 weeks of the pregnancy we cannot report a result for the Iowa Integrated Screen. It is possible to determine a risk for Down syndrome and Trisomy 18 based on information from Stage One alone, provided that a nuchal translucency measurement has been performed by an NT-certified sonographer. However, using information from Stage One alone yields higher screen-positive rates, making the screening less effective than the Iowa Integrated Screen. Screening that uses information from Stage One alone also cannot screen for open neural tube defects.

Are there other conditions which may be detected by this screening?

The Iowa Integrated Screen is specifically designed to detect Down syndrome, Trisomy 18 and open neural tube defects. However, sometimes the result of an Iowa Integrated Screen will suggest the possibility of other problems with the pregnancy or the developing baby. It may indicate a risk for delivering the baby early or having a baby with a low birth weight. It also may indicate a problem with the placenta or the need for extra medical help before the baby is born or at the time of delivery.

An increased level of AFP, along with screening for open neural tube defects, may also suggest an increased risk for abdominal wall defects. An abdominal wall defect refers to an opening in the developing baby's belly that causes the intestines to be on the outside of the body. Babies with abdominal wall defects need specialized medical care and surgery soon after birth. Those who receive the necessary medical care usually do well if they do not have other birth defects or genetic problems.

What if I am carrying twins?

If you are carrying twins, the risk for open neural tube defects can be evaluated by determining the level of AFP in the second trimester (Stage Two only). We do not provide Down syndrome or Trisomy 18 screening for twins. We do not provide any screening for pregnancies with more than two fetuses.

Are there any risks involved in this screening process?

One risk of this form of screening is anxiety for those who have a screen-positive result. It is always stressful to discuss the possibility that your developing baby may have a problem, and it is natural to be anxious or afraid. Fortunately, most women with a screen-positive result will have healthy babies.

If you choose to have an amniocentesis because of a screen-positive result, there is a small risk of pregnancy loss associated with this procedure. Ask the doctor who does the amniocentesis to discuss this possibility with you.

What can be done if a birth defect or genetic condition is discovered?

It is a shock to learn that your developing baby has a problem. You will need information about the specific condition and any treatment that may be available. There are two primary options to consider: you may begin to plan for the birth of a baby who may need special care after birth or you may choose to end the pregnancy.

Remember that it is more likely that your baby does not have Down syndrome, Trisomy 18 or an open neural tube defect, even if your Integrated Screening result is screen-positive. However, if your baby is found to have a problem, a physician, nurse, and/or genetic counselor will be able to discuss the specific condition and all of your options with you at the time the diagnosis is made.

SUMMARY

1. The Iowa Integrated Screen is a screening test for Down syndrome, Trisomy 18 and open neural tube defects. This screening test is available to all women during pregnancy.

2. The Iowa Integrated Screen is performed in two stages. Stage One involves an ultrasound and a blood sample in the first trimester. Stage Two involves a second blood sample drawn between 15-20 weeks of pregnancy.

3. A screen-positive result does not necessarily mean that your baby has Down syndrome, Trisomy 18 or an open neural tube defect, only that there is an increased chance for one of these problems.

4. A screen-negative result provides reassurance but does not guarantee that your baby is healthy, only that there is a decreased chance for Down syndrome, Trisomy 18 and open neural tube defects.

5. If the Iowa Integrated Screen is screen-positive, you will be offered an ultrasound and may be offered a diagnostic test such as an amniocentesis to find out if the developing baby has a chromosome abnormality or birth defect.

6. If you are too far along for Stage One of the Iowa Integrated Screen, a result may still be calculated using Stage Two only (the Quad Screen).

7. If you miss Stage Two of the Iowa Integrated Screen, a result may still be calculated using the information from Stage One, provided that the nuchal translucency (NT) measurement was done. Stage One alone cannot screen for open neural tube defects.

8. Integrated Screening is a more effective screen for Down syndrome and Trisomy 18 than either Stage One or Stage Two alone.

9. Even though most babies will be healthy, the period of screening and testing can be a stressful time. If a problem is found you will need support and guidance.

You are encouraged to read this information and discuss any questions with your healthcare provider. If you have further questions you may call 319-356-3561 to speak with an Iowa Integrated Screening nurse or genetic counselor. The maternal serum prenatal screening program is administered by the Iowa Department of Public Health. General questions regarding this program may be directed to the State Genetics Coordinator at 1-800-383-3826.

The choice is yours!