Welcome to the Fall 2009 edition of the NT Examiner. In this edition we will be exploring some of the additional benefits of first trimester scanning. There is increasing evidence that a significant number of fetal anomalies can be detected at the time of the NT measurement. In fact in the morbidly obese patient, an endo-vaginal scan at this gestational age may be the best opportunity to evaluate fetal anatomy. We will also begin a series on genetic syndromes associated with increased NT measurements. In addition, we will discuss the management of NT measurements greater than 3 millimeters. We hope that the NT Examiner will continue to be a resource of consensus information for our almost 5,000 participants.

Steven L. Warsof, MD

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Top Tip: AVAILABLE NOV 1, 2009
Submit Your Own NT / CRL Data

Now at NTQR.org
Patient Education Presentation: First Trimester Risk Assessment

The NTQR is pleased to present a ten minute education video for your patients. The presentation may be viewed at http://www.ntqr.org. The audio and slides provide information about screening and diagnostic tests for aneuploidy in the first trimester of pregnancy. Patient options are outlined in a reassuring manner and patients are encouraged to ask their physician or health provider for additional information.

The Education committee of the NTQR wishes to thank Dr. Greggory DeVore, MD for his technical assistance and Renee Chard, certified genetic counselor for her assistance with the script. NTQR is interested in your feedback on this presentation and your ideas for additional patient education offerings. Please send comments to NTQR through e-mail (ntqrsupport@ntqr.org) or by phone (405.753.6534). If you are interested in mounting this presentation on your own practice website please contact NTQR.

The Management of NT of 3mm or Greater: The NTQR Position

By Pe’er Dar, MD, FACOG, FACMG
Albert Einstein College of Medicine

Prior to the inclusion of the maternal serum markers into a combined screening, NT of 3 millimeters or more was used as the cut-off for offering diagnostic testing. It is now clear based on extensive research and backed by ACOG’s statement, that the combination of NT and maternal serum markers adjusted for maternal age, is more effective than NT measurements alone. An NT measurement greater than 3 millimeters is not common, and in a low risk population it is identified in less than 1% of screens. Nonetheless, the direct correlation between the size of the NT and the risk of aneuploidy is noteworthy. When the NT measurement is over 3 millimeters, the aneuploidy risk begins to rise. Overall in these fetuses the aneuploidy risk averages 30% and the prognosis remains poor even for many of those with a normal karyotype.

As a result, some providers, when encountering an NT of 3 millimeters or greater, might feel more comfortable to offer an immediate diagnostic test without obtaining the serum markers. But will they be providing their patients with the optimal care?

The question: “Is there a NT millimeter measurement above which there is no added benefit from first trimester serum screening” was examined by the FASTER Research Consortium. The researchers looked at 36,341 screens with complete first trimester NT and serum marker data. 0.09% of screens had NT measurements of 4 millimeters or greater. In this group, when serum markers were added to the NT measurement the lowest risk assessment for trisomy 21 was 1:8. In light of the rarity of such increased measurements and insignificant additive value of the serum markers in these cases, the authors concluded that it would be reasonable to offer immediate
"Data Submission." The screen will allow you to insert individual data sets and also allow you to upload data directly to NTQR in MS Excel spreadsheets. Most laboratories will provide complete data sets to clinicians upon request and these may be forwarded to NTQR as well. NTQR "cleans" the data that we receive to eliminate duplicates. For more information e-mail ntqrsupport@ntqr.org.

When NT measured between 3 and 4mm, the lowest risk assessment for trisomy 21 was 1:1479 and 8% of patients had a risk assessment lower than 1:200. It is reasonable to assume that some of the patients with similar results may elect not to proceed with invasive testing after receiving their complete risk assessment. Therefore, it is the NTQR committee position that in an era in which access to diagnostic testing is offered to all women regardless of their age, patients who initially elect a screening approach should benefit from the comprehensive test at all levels of NT. While it is reasonable to assume that over certain maternal age the addition of serum markers to NT's that measure between 3 and 4 mm might have a limited value, the data to support this assumption is lacking. Hopefully future reports will clarify the impact of maternal age in counseling these patients. Patients with NT of 4mm or greater should be advised of the limited additive value of the serum markers and may be offered the option of an immediate diagnostic test without obtaining the serum markers.

REFERENCES


The Fetal Anatomy Scan: Could it be Performed at the time of the First Trimester Screen?

By Karin M. Fuchs, MD, Ilan E. Timor-Tritsch, MD, RDMS Mary E. D'Alton, MD

Over the last decade, risk assessment for Down syndrome has shifted from the second trimester to the first trimester. Although the first trimester nuchal translucency scan may detect a small proportion of fetal structural malformations, fetal anatomy is not routinely assessed until the fetal anatomical survey is performed in the second trimester between 18 and 22 weeks. The development of high frequency transvaginal ultrasound transducers, however, has led to vastly improved ultrasound resolution and improved visualization of fetal anatomy earlier in gestation. In the morbidly obese patient a transvaginal late first trimester scan may be the best opportunity to visualize fetal anatomy.

In a prospective cross-sectional study of over two hundred women between 11 and 14 weeks’ gestation, Timor-Tritsch et al demonstrated that trained sonographers could successfully visualize 37 anatomic structures in 64-99% of cases. 5Souka et al also found that non-cardiac anatomy was seen in 84% of patients with a crown rump length (CRL) of 45-54 mm and in 96% with CRL more than 65 mm. 2 With an improved understanding of fetal development, there is a growing body of literature reporting the detection of a number of structural anomalies between 11 and 14 weeks. For example, there have been several reports of early detection of anomalies of the urinary tract 3 and within the developing skeletal system. 4 The anterior abdominal wall of the fetus can also be well visualized early in gestation, and there have been reports of omphalocele and gastrochisis detected in the first trimester as well as body stalk anomaly, Pentalogy of Cantrel, and ectopia cordis. 5,6 While certain anomalies of the central nervous system and heart cannot be diagnosed between 11 and 14 postmenstrual weeks, there have been numerous case reports demonstrating the detection of congenital and major anomalies of the central nervous system (CNS) using
transvaginal ultrasound in the first trimester.  

With the growing success in visualizing fetal anatomic structures and identifying structural anomalies in the first-trimester, several studies have assessed the ability of a formal first-trimester anatomic survey to detect fetal structural malformations. These pilot studies have reported detection rates that are comparable to those achieved by the routine second-trimester anatomic survey (Table 1). 11 In the majority of studies evaluating the role of a first trimester anatomic survey, fetal anatomy was assessed in the first trimester and again in the second trimester as part of a two-stage protocol. Among 20 studies, seven reported relatively low detection rates ranging between 16-41%, whereas the majority of the remaining 13 studies reported detection rates well over 50% (range 48-84%). After the second trimester ultrasound, the majority of these two-stage protocols reported detection of more than 75% of major fetal malformations (range 48-100%). Despite the promising detection rates, these published studies varied significantly with regard to the populations screened, the gestational age at which the scan was performed, the use of transvaginal ultrasound, the training and experience of the practitioner performing the scan, and the time allowed for the anatomic survey.

Given improving technology and the shift of prenatal diagnosis into the first trimester, a routine first trimester anatomic survey may be both feasible and convenient. Before a first trimester survey of fetal anatomy can be introduced into widespread clinical practice, however, formal research studies will have to be conducted to determine its diagnostic capability as a screening tool for the general population and to determine if it should be added to the current screening paradigm. In addition, concerns regarding the relative cost and potential burden of the first-trimester anatomic survey on the healthcare system will have to be addressed. If the clinical utility of a first trimester ultrasound is ultimately proven, efforts must also be focused on developing of a standardized training program and on developing a quality assurance program similar to that currently in place for nuchal translucency measurements.

### Table 1: Detection rates of 1st and 2nd trimester ultrasound screening for fetal structural malformations

Adapted from Timor, et al, 2009

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REFERENCES
Genetic Syndromes Associated with Increased NT Measurements

By Renee Chard, MS, CGC
Genetic Counselor and Member
Nuchal Translucency Oversight Committee

Nuchal translucency (NT) measurements greater than the 95th centile have been associated, not only with an increased chance for aneuploidy, but also with a significantly increased risk for structural defects, especially congenital heart defects and diaphragmatic hernia, and with genetic syndromes. The NT Examiner will be publishing a series of articles reviewing the genetic syndromes most frequently reported in association with increased NT measurements beginning with Noonan syndrome. Future articles will review skeletal dysplasias and disorders of fetal movement.

Noonan syndrome has an estimated prevalence of 1 in 2000. Features include short stature, congenital heart disease especially pulmonary valve stenosis, lymphedema due to dysplasia of lymphatic system, short webbed neck, low posterior hairline, broad chest with widely spaced nipples, cryptorchidism, and characteristic facies with low-set ears, bright green or blue irises, hypertelorism, ptosis, down-slanting palpebral fissures and epicanthal folds. Approximately 33% of patients with Noonan syndrome have mental retardation, which is often mild. The phenotype is variable and tends to become less apparent with age, therefore, mild cases may be unrecognized.

Noonan syndrome is a genetically heterogeneous autosomal dominant condition with a high new mutation rate. Approximately 50% are de novo cases. 70-85% have a detectable mutation in one of four genes: PTPN11 (50%), SOS1 (13%), RAF1 (3-17%), and KRAS (<5%). Mutation analysis is available; however, since the etiology is unknown in 15-30%, a negative result does not rule-out the diagnosis. It is rare for Noonan syndrome to be caused by a chromosomal duplication or deletion, therefore prenatal chromosomal microarray analysis is of limited value for testing of this condition. In a family with a known mutation, molecular testing of at risk relatives is highly accurate both pre- and postnatally.
Lymphatic dysfunction can result in ultrasound examination findings of increased nuchal translucency, cystic hygroma, pleural effusions, pericardial effusions, scalp edema, hydrops fetalis and associated polyhydramnios. Cardiac defects associated with Noonan syndrome can sometimes be detected prenatally. These findings are nonspecific and they can overlap with other conditions and might not warrant mutation analysis for Noonan syndrome. Ultimately, it is important to obtain a careful family history with attention to signs of Noonan syndrome in family members to determine whether genetic testing is indicated and to follow the pregnancy with ultrasound examination including fetal echocardiography.

REFERENCES


2 GeneReviews -- NCBI Bookshelf.


NTQR Benefits

The Benefits committee of the NTQR focuses on participant needs and satisfaction. The committee has developed a survey that participants will soon have the opportunity to complete. Recently the committee developed a list of existing benefits for participants with NTQR. The benefits listed for those who are already credentialed are as follows:

1. Monitoring for quality is done by statistical review of measurements, with image submission required only if remediation is necessary.
2. Statistical reports are provided 3-4 times per year, with data sorted by physician-sonographer pairs.
3. Interactive website provides ongoing education for providers and patients, information about providers by location or name, practice guidelines, and administrator functionality.
4. E-mail and phone support is available.
5. Recommendations are based on consensus of NTQR committees with representation from:
   - American College of OB / GYN (ACOG)
   - American College of Osteopathic OB / GYN (ACOOG)
   - American Institute of Ultrasound in Medicine (AIUM)
   - American College of Radiology (ACR)
   - National Society of Genetic Counselors (NSGC)
   - Society of Diagnostic Medical Sonographers (SDMS)
   - Society of Maternal Fetal Medicine (SMFM)
6. NTQR advocacy and influence is directed towards healthcare organizations and third-party payers to assure accessible, quality care is provided to patients by credentialed individuals.

NIH-Sponsored Study of Women Carrying a Baby with Spina Bifida

The Management of Myelomeningocele Study (MOMS), a randomized, controlled clinical trial, continues to enroll pregnant women. Health care professionals can play an important role by helping to identify and refer candidates for this study funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD). The trial is designed to compare the safety and efficacy of prenatal versus postnatal closure of myelomeningocele. Approximately 160 women have been enrolled with another 40 needed. For the duration of the study, prenatal surgery for spina bifida is not available outside of the trial. Participating MOMS Centers are: The Children's Hospital of Philadelphia, Vanderbilt University Medical Center in Nashville, and the University of California at San Francisco. The George Washington University Biostatistics Center serves as the Coordinating Center and performs the centralized screening.

Patients can begin the evaluation process as soon as the diagnosis is made. For the initial screening process, women or their health care
providers should contact Ms. Jessica Ratay (see below). Ms. Ratay, a genetic counselor, can explain the trial at length and/or provide information on spina bifida. If a patient remains interested in participating and consents to be screened, her medical records will be reviewed for inclusion and exclusion criteria. Healthcare providers are also encouraged to contact Ms. Ratay for information about this fetal condition and the trial.

Qualifying participants are referred to a MOMS Center for further screening where they are evaluated for eligibility and decide if they wish to enroll. If so, they are randomly assigned to either the prenatal or postnatal surgery group of the trial.

Participants in the prenatal group undergo surgery to repair the myelomeningocele between the 19th and 25th week of pregnancy and remain at the MOMS Center until cesarean delivery at 37 weeks. Those assigned to postnatal surgery go home after randomization and return to the MOMS Center at 37 weeks for cesarean delivery and myelomeningocele repair. Follow-up evaluations are performed at the center on all infants at 12 and 30 months of age. All travel, food and lodging costs are covered by the research study.

To refer a patient or for information

Contact the Study Coordinator, Jessica Ratay, MS, CGC at:

1-866-ASK MOMS ( 1-866-275-6667 )
E-mail: MOMS@bsc.gwu.edu
http://www.spinabifidamoms.com

I Am NTQR Credentialed, Now What?

To maintain your credentials you only need to...

- Submit your NQTR ID (and the NTQR ID of the Physician if credentialed) on each and every lab requisition form
- Pay the yearly participation fee assessed on the anniversary of your NTQR Credentials. Once your anniversary date has arrived you may log on to your NTQR account and the payment screen will appear.
- Submit images ONLY if you fall into remediation. Our remediation policy is currently under review and will be implemented in the coming months.

The NTQR is committed to education, credentialing, and ongoing quality monitoring to insure appropriate risk assessment services for patients. One major difference between NTQR and other credentialing organizations that participants notice is the quality monitoring system. NTQR based on literature that demonstrates that ongoing image review may be subjective has based their quality monitoring on an automated (for most users) system of epidemiologic analysis. In the NTQR system once you are credentialed you do not have to submit images again unless you fall into a remediation protocol.

There is no expiration of your NT credentials and there is no need to send us any images for renewal. Currently, once a Provider has acquired their NT credentials we monitor their data through the laboratories. The data monitoring and reporting is completely automated. Periodically, each participating lab sends us data. It is this data that we compile and on a quarterly basis we issue epidemiologic reports to all of our credential members. Depending on the results of those reports will determine if the Provider falls into remediation. Additional images may be required in the remediation phase. We last issued our reports to all credentialed Providers in July 2009. The next round of reports is scheduled to be sent in the next several days.

In order to adequately provide an analysis for our Providers we require 30 data points every 12 months to be submitted to the laboratories. With respect to our remediation policy we are currently deciding what to do with Providers that would not collect 30 data points every 12 months.

NTQR credentials do not expire. However, a Provider can fall into remediation. Our quality monitoring works by analyzing the data we receive from all the laboratories. On a quarterly basis we issue reports. If on subsequent reports a Provider’s Median NT MoM is outside the expected range then that Provider would fall into remediation. Only then would further education and images be required to be removed from remediation. So, as long as a Providers’ reports continuously show median NT MoM within the expected range that Provider will always be in good standing. We are expected to fully implement our remediation policy in the few months.

It is extremely important for you to write on each lab req form the NTQR ID of the Sonographer and the NTQR ID of the Reading MD (if credentialed).

The Sonographer and Physician should be putting their NTQR ID on the lab requisition form. There should be two slots on the forms, depending on the laboratory you work with. While some laboratories have modified their forms to display the Sonographer and Reading MD fields, other laboratories only display the Sonographer field. Still other laboratories do not have any slots listed. And in some cases the laboratory sales representative has produced pre-printed sheets with the IDs on them. In all cases, it is important for the Provider to put their
NTQR ID on the form. The Sonographer who scans the patient should put the NTQR ID in the Sonographer field. The Physician who reads the scan should put their ID in the Reading MD field. If the Physician scans and reads the image then his/her ID would go in both fields. But, only if there is no Sonographer involved. If the form does not explicitly display these fields we are asking the Providers to write their ID somewhere prominently on the form.

Once we receive the data we then produce two types of reports. The first report is for the Sonographer grouped out by the Reading MD. The second report is the reverse. It is a report for the Physician grouped out by the Sonographer. Depending on whether we receive data from you based on the Sonographer and/or Sonologist field will depend if you receive one or both reports. That is, if we receive data with a Provider’s NTQR ID in the Sonographer field then they would receive the Sonographer report. If we receive data with a Provider's NTQR ID in the Sonologist field then they would receive the Sonologist report.

A listing of participating laboratories can be found at https://www.ntqr.org/SM/Lab/wfParticipatingLab.aspx.

If you do not send your bloodwork to a participating laboratory you still have three alternatives in order to continue participating in our data monitoring program and to continue receiving our reports. They are:

- Send your data to the NTQR in Microsoft Excel or ASCII format. For the NTQR to perform yearly ongoing data monitoring of its Providers and issue quarterly epidemiologic reports we require the following information in a text or Microsoft Excel file sent to us via E-mail.
  1. Sonographer NTQR ID
  2. Reading MD NTQR ID (if physician is credentialed)
  3. NT Measurement
  4. CRL Measurement
  5. UltraSound Date
  6. Total Fetuses
  7. If Total Fetuses > 1 then I would need the NT and CRL Measurement for each additional fetus
- Have your laboratory send your data directly to the NTQR.
- Upload records yourself using our new upload functionality that is set to be released November 1, 2009.

If you can send the above data periodically (perhaps monthly) to the NTQR that would be great! If your lab is listed at https://www.ntqr.org/SM/Lab/wfParticipatingLab.aspx you do not need to send the NTQR anything. You just need to make sure the Sonographers and Physicians (if credentialed) place their NTQR ID on the lab requisition forms.

**ISUOG Sonographer Survey**

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) has created a survey through which the group hopes to gain insight into sonographers and their needs. The survey is available at the link below:

http://www.surveymonkey.com/s.aspx?sm=_2fAtjqA_2fmxA31v7YXXhi_2flA_3d_3d

**Join NTQR and Get Credentialed**

The Nuchal Translucency Quality Review Program (NTQR) is a United States based effort seeking to establish a NT quality control system and help formalize set standards. NTQR offers a unique opportunity to learn about the proper techniques and theories involved in obtaining accurate and reproducible NT measurements from the 11-14 week ultrasound scan and first trimester risk assessment for Down Syndrome, while also offering a method to evaluate and track provider proficiency though ongoing NT quality monitoring reports.

**Two ways to join NTQR and get credentialed!**

1. **On Line**
   1. Go to www.ntqr.org
   2. Register
   3. On your computer, watch the same lectures given at NTQR's land-based courses. (This doesn't have to be done in one sitting)
   4. Take the same on-line test as land-based course participants
   5. Submit 5 NT images for quality review
   6. Get credentialed
2. Plan to attend one of these upcoming NTQR land-based courses:
   1. Register and attend a 2009 - 2010 planned Land-Based Courses (see below)
   2. Take the on line exam
   3. Submit 5 NT images for quality review
   4. Get credentialed

A Practical Approach to the High Risk Pregnancy: Management and Ultrasound
Minneapolis Airport Marriott
Minneapolis, MN
October 24-25, 2009
Registration Information

18th Annual OB / GYN Ultrasound Update for Clinical Practice
Lago Mar Resort & Club
Ft. Lauderdale, Florida
December 3-6, 2009
Registration Information

18th Annual Advanced Ultrasound Techniques in Obstetrics and Gynecology
FireSky Resort and Spa
Scottsdale, Arizona
November 5-7, 2009
Registration Information

National Conference on OB / GYN Ultrasound
The Westin Chicago River North
Chicago, Illinois
December 4-6, 2009
Registration Information

Society of Maternal Fetal Medicine
30th Annual Meeting
The Pregnancy Meeting
Hilton Chicago
Chicago, Illinois
February 1-6, 2010
Registration Information

NTQR Program Fast Facts
Program Statistics

- 4,968 providers of NT measurements have registered with the Nuchal Translucency Quality Review Program
- 3,518 providers have been credentialed through NTQR
- Over 24,000 NT images have been reviewed by NTQR’s Expert Reviewers
- Over 575,000 data sets have been provided by participants or by our partner laboratories. These data sets were analyzed to produce individual epidemiologic reports. 3,384 personalized reports were sent to participants in July 2009.
- To see a list of our partner laboratories, go to www.NTQR.org
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You may also send e-mail to NTQR Support.

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