"Welcome to the Winter 2011 edition of the NT Examiner. In this edition important information on NT trends, epidemiologic reports, and the impact that NT risk assessment may have on live births with Down Syndrome are reviewed. In addition, genetic syndromes associated with increased NT are discussed, as well as emphasizing the importance of CRL measurements as part of NT risk assessment. We look forward to being a continuing source of consensus based information on NT population screening.

Steven L. Warsof, MD

INSIDE THIS ISSUE

» Nuchal Translucency Quality Monitoring: Identification and Importance of Trends
» Epidemiologic Report Survey
» Genetic Syndromes Associated with Increased NT Measurements: Disorders of Fetal Movement
» Impact of First Trimester Risk Assessment on Live Births with Down Syndrome
» You Asked, NTQR Answers
» Improve Your CRLs
» Upcoming Courses
» NTQR Program Fast Facts

Top Tip:
Know Your Numbers!

NTQR participants will receive an e-mail the quarterly epidemiologic reports are complete. To access your individual report log into your account at http://www.ntqr.org. Reports are posted under "Performance Improvement" on the top menu. Administrators may request monitoring reports by sending the names of the participants in their practice to ntqrsupport@ntqr.org. A zipped file with the reports requested will be generated and sent by return e-mail. Participants may be assigned to required credentialing. Participants may be assigned to required quality maintenance (RQM) based on their NT median MoM or standard deviation log10 MoM. The NT Multiples of the Median (MoM) is a parametric method used to standardize observed NT values by taking the ratio of the observed NT to the expected NT at a given CRL derived by regression analysis. The expected NT median MoM is 1.0 and the acceptable range is 0.9-1.1. Another way to think of this is that if your NT measurements fall symmetrically on either side of the NT/CRL regression curve or exactly on the curve, your NT median MoM value will be 1.0. The standard deviation log10 MoM reflects consistency in NT measurements. The expected SD value is 0.09 and the acceptable range is between 0.07-0.11.

In a recent article entitled "Under-Measurement of Nuchal Translucencies: Implications for Screening", Evans and colleagues published data on over 180,000 NT measurements reported to Perkin Elmer/NTD Labs from over 320 clinical centers each with an annual volume of at least 100 cases. Their data indicate that a large proportion of centers reported a maximum NT measurement that was less than 2.5 mm, a low median NT, and an excessive number of "low" NTs which they defined as more than 10% of NT measurements falling below the 5th percentile. Although the authors acknowledge that one reason that more than 20% of centers had never reported an NT above 3 mm may be that these practices refer such cases for diagnostic testing without the performance of serum screening, they concluded that there is a widespread tendency to under-measure the NT in clinical care. In order to ensure optimal performance of this screening test, Evans et al called for "analysis of real patient data…[obtained]...under field conditions" and "re-training" for those sonographers whose measurements unacceptably deviate from the expected median.

The call for ongoing quality monitoring of nuchal translucency measurements obtained in clinical practice is not new. In describing NT measurement in 1998, Herman wrote "the examiner is required to produce a result that resembles laboratory results" and "as in any laboratory study, those implementing the program should take upon themselves the task of an ongoing audit to adhere to the required standards…". Similarly, when the American College of Obstetricians and Gynecologists (ACOG) recommended that first trimester aneuploidy screening be offered to all pregnant women, they stated that performance of NT measurements should be limited to "individuals and centers" with "specific training, standardization, …and ongoing quality assessment".

Given the importance of precision and quality in NT measurements, both the Fetal Medicine Foundation (FMF) and the Maternal Fetal Medicine Foundation’s (MFMF) Nuchal Translucency Quality Review (NTQR) program not only conduct stringent credentialing procedures for providers seeking to perform NT measurements, but also provide ongoing quality monitoring for their respective participants. Since its inception in 2005, NTQR has credentialed over 4,000 physician and sonographer participants to perform NT measurements in clinical practice. Ongoing quality monitoring is performed by periodically comparing the distribution and standard deviation of each participant’s NT measurements against those obtained from a standard referent curve. NTQR currently performs these epidemiologic studies of NT data quarterly, and results of these analyses are used to generate a detailed individualized epidemiologic report for each participant submitting more than 30 NT measurements in a 12-month period. This ongoing quality monitoring process has been in place for 4 years and has led to the distribution of over 25,000 epidemiologic reports.

In performing quantitative quality monitoring, NTQR converts a provider’s NT measurements to multiples of the gestational age specific median (MoMs) with the expectation that an individual’s ideal median should be 1.0 MoM and that the 90th percentile range would extend from 0.9 to 1.1 MoMs. The tendency to under-measure reported in the recent article by Evans is also evident in the over 900,000 NT measurements reported to NTQR. In the eleven batches of epidemiologic reports issued by NTQR to date, the majority of providers’ median MoM has been between 0.9 and 1.1. However, of those who are outside this expected range, the number of providers whose median MoM falls below 0.9 is more than 10 times the number whose median MoM is above 1.1. This “left shift” reflects the same tendency to under-measure noted by Evans, and has led to a change in the image review criteria NTQR uses in initial NT credentialing. Specifically, although submitted images are evaluated on each of nine specific criteria, NTQR’s Image Review Committee has recently ranked these criteria, demoting some – such as separation from amnion – while prioritizing criteria that assess caliper placement.
According to this new image scoring system that has been in place since April 2009, correct placement of calipers must be demonstrated on all submitted images and incorrect caliper placement on a single image results in automatic failure of the entire batch.

The tendency to under-measure has not only been recognized in clinical practice, but has also been shown to be “correctable” through sonographer education. In analysis of 23,462 nuchal translucency measurements reported to six North American prenatal screening laboratories over a 6-month period, Palomaki and colleagues noted that - of those providers whose median NT MoMs were outside the expected range of 0.9-1.1 - more sonographers had median MoMs that were below 0.9 than above 1.0.5 Furthermore, when these authors compared sonographer-specific median NT MoMs obtained at two intervals 18 months apart, they found that NT median MoMs improved in response to routine quality assessment and feedback with quantitative data. Specifically, prior to implementation of routine quality monitoring procedures, only 40% of certified sonographers were noted to have NT MoMs within the target range. Following the initiation of routine quality monitoring and notification of the sonographers with outlying MoMs, more than twice as many sonographers - 88% - were within range.

The importance of ongoing provider education and remediation is recognized by NTQR and is an integral part of the quality monitoring process. When an NTQR participant is first identified as having NT values that are minimally outside the expected range, voluntary targeted performance improvement is recommended. For these participants, targeted performance improvement activities - including review of didactic materials and voluntary image submission - are available free of charge on the NTQR website http://www.ntqr.org. In contrast, providers whose NT median MoM and standard deviations are the farthest from the expected range are referred for mandatory remediation.

NTQR participants should know that although the phenomenon of under-measuring is real, this trend has been recognized by NTQR and methods are in place to correct and prevent it. What remains unknown, however, is the impact this under-measurement may have on the detection rates. Published studies demonstrating this phenomenon lack sufficient follow up data to be able to evaluate whether detection rates in clinical practice deviate from those achieved in large-scale research studies.6-8 While an observational study involving many of the larger clinical centers participating in NTQR may be able to determine detection rates in clinical practice, an answer to this definitive question remains several years away. In the interim, recognition of the tendency to under-measure the nuchal translucency demonstrate why it is imperative that continued vigilance is necessary in order to be able to achieve the detection rates demonstrated in clinical trials.

REFERENCES


iPad Apps

iPad Announcement

The NTQR patient education presentation is now available for IPAD. It is a free application available at the link below:


This is an excellent introduction to first trimester risk assessment and the options available to patients. It is the same presentation that is available on our website and on CD. Our thanks to Dr. Gregory DeVore, Renee Chard, CGC, and members of the NTQR Education Committee who worked on the original presentation and to Dr. DeVore who created the IPAD application. We hope that you will find the IPAD application useful for counseling patients.
Epidemiologic Report Survey
Thank you for your Input!

On September 29, 2010 the NTQR sent out a survey regarding the individual epidemiologic reports to 4,015 credentialed providers. Within three weeks we had survey responses from 469 participants including comments from 82. This is approximately a 12% return.

As shown in the chart above, eighty percent (80%) of the respondents find the reports useful or very useful. Eighty-two percent (82%) would not recommend eliminating any of the components although forty-two percent (42%) find the target "box graph" confusing (see tables below). Seventy-one percent (71%) find the NT numbers reflected in the report consistent with the numbers of NT examinations performed or supervised while twenty-eight percent (28%) find the data to be less (18%) or substantially less (10%) than actual.

Most participants, seventy-seven percent (77%) rely on the laboratories to submit data to NTQR and only thirty-one percent (31%) have used the website data self-submission option. Only six percent (6%) consider their reports to be inaccurate though another seventeen percent (17%) are not certain of accuracy. Seventy-nine percent (79%) review their NTQR epidemiologic report each quarter when a new one is available but only twenty-seven (27%) have their reports reviewed by a supervisor.

In the comment section there were 3 comments that were strongly negative and 6 comments that were strongly positive. There were multiple suggestions focused primarily on ways to improve data collection. There were 5 questions on the population referent curve and multiple questions regarding the impact of high risk patients on individual participants' statistics. All of the comments and questions were reviewed by the NTQR quality assessment committee, the Nuchal Translucency Oversight Committee (NTOC) and the MFMF Board of Directors. NTQR will be answering each of these participant questions in this and upcoming issues of the newsletter. NTQR will also be developing a tutorial on the epidemiologic reports to aid participants in using the results for ongoing quality improvement. Thank you for responding so quickly to the survey. Additional input and questions are welcome at any time.

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<thead>
<tr>
<th>The portions of the report that ...</th>
<th>I would recommend eliminating (%)</th>
<th>I find most confusing (%)</th>
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<tr>
<td>Front page with overall results</td>
<td>4.1%</td>
<td>13.2%</td>
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<tr>
<td>The population curve with my data superimposed</td>
<td>6.6%</td>
<td>25.7%</td>
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<tr>
<td>The target &quot;box graph&quot; plotting the standard deviation and NT median MOM</td>
<td>7.3%</td>
<td>41.5%</td>
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<tr>
<td>the table with data from myself and my colleagues</td>
<td>8.0%</td>
<td>24.2%</td>
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<tr>
<td>the history section showing interval changes</td>
<td>7.1%</td>
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<td>none of the above</td>
<td>82.2%</td>
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Impact of First Trimester Risk Assessment on Live Births with Down Syndrome

By Steven L. Warsof, MD
Professor OB/GYN
Eastern Virginia Medical School
EDITOR, The NT Examiner

Two obstetrical trends have had an important impact on the incidence of live births with Down Syndrome (DS). The first of these trends is the aging of the Obstetrical population. As is commonly known, the incidence of live births with Down Syndrome increases with maternal age, from 1:356 at age 35 to 1:94 at age 40, and 1:24 at age 45. As population trends have indicated there has been an increasing percentage of older women having babies. Due to this trend, some studies have anticipated an increase over 20 years in the number of live births with DS, an increase by 30% or greater.

On the other hand with the introduction of population risk assessment for Down Syndrome using either MSAFP4 or the genetic sonogram in the second trimester, or various nuchal translucency based risk assessment strategies in the first trimester with 85-95% sensitivities, it would be anticipated that the incidence of live births with DS would decrease dramatically. Monitoring the incidence of live births with DS and other

REFERENCE

1 ACOG Committee Opinion Number 432, May 2009 Spinal Muscular Atrophy

Genetic Syndromes Associated with Increased NT Measurements: Disorders of Fetal Movement

By Renee Chard, MS, CGC
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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 hemia, and with genetic syndromes. In this issue of the NT Examiner we will review disorders of fetal movement as we continue a series of articles reviewing genetic syndromes reported in association with increased NT measurements.

There are a variety of conditions, neurological, muscular or connective tissue, which can result in reduced fetal movement. Secondary features include joint contractures, lung hypoplasia and fetal hydrops. Spinal muscular atrophy (SMA) is a clinically variable autosomal recessive condition affecting an estimated 1 in 10,000 infants in the United States of America suggesting 1 in 50 carrier frequency. Type 1, sometimes referred to as Werdnig-Hoffman disease, accounts for at least 60% of cases and is the most common and most severe type of SMA with onset before six months of age and sometimes in utero. Features include lack of fetal movement, progressive muscle weakness, joint contractures and respiratory failure due to degeneration of anterior horn cells in the spinal cord and brain stem nuclei.

Deletion of exons 7 and 8 in SMN1 (survival motor neuron) gene accounts for 95-98% of cases of SMA and genetic testing is available. Carrier testing for SMA is also available and some medical organizations and patient advocate groups recommend carrier testing in the general population. However, carrier testing for SMA is complex. There can be false negative results and at this time there is limited genotype-phenotype correlation, based on the number of SMN2 gene copies present. In other words, if a couple is identified as a carrier couple, it is difficult to accurately predict how severe the condition would be in an affected child, when there are no other affected family members. Therefore, at this time ACOG recommends that SMA carrier testing be offered only if there is a positive family history or at the request of a patient and that testing be done in the setting of formal genetic counseling.

Pena Shokir (fetal akinesia deformation sequence) is a heterogeneous group of conditions resulting in intrauterine growth restriction, contractures, pulmonary hypoplasia, rockerbottom feet, clubfoot, short neck, hypertelorism, short umbilical cord, and small placenta. Most cases appear to be inherited in an autosomal recessive manner and some have been associated with mutations in RAPSN and DOR7.

Multiple pterygium syndrome is another category of conditions, most autosomal recessively inherited, that result in significant limitation of fetal movement. Other features include intrauterine growth restriction, joint contractures with pterygia and facial dysmorphism. Mutations have been identified in CHRNQ, CHRNA1, and CHRNA. Like Pena Shokir, these are rare conditions and genetic testing is only indicated in the event of a phenotype consistent with one of these conditions or a known family history.

Genetic counselor, medical geneticist, maternal-fetal medicine specialist and when indicated radiologist and pathologist become the team to provide optimal care to both fetus and patient. Careful pathological evaluation is indicated in instances of increased NT in association with multiple congenital anomalies. A genetic counselor can review medical and family histories for diagnostic clues and provide patient support, education and anticipatory guidance. When each member of the team does his part, the patient is well supported; the likelihood of a diagnosis being made increases and the patient will be empowered to make the choices that are right for them in their current and future pregnancies.

REFERENCE

1 ACOG Committee Opinion Number 432, May 2009 Spinal Muscular Atrophy
chromosomal abnormalities is paramount in determining the efficacy of DS risk assessment as it is being implemented across the globe.

Additional concerns have been raised with reports \(^1\) that as women are increasingly relying on non-invasive risk assessment rather than invasive diagnostic testing, that the incidence of live births with DS have been increasing due to the “residual risk” in women who opt not to have a diagnostic test when they were found to be “screen negative” or low risk from their risk assessment.

Recent reports from around the world show that population screening has had varying impact on the incidence of live births with DS live births with DS. This is highly dependent on the incidence of pregnancy termination when the prenatal diagnosis of DS is made. In populations that have high incidence of pregnancy termination for DS, the impact is greater than in populations that continue pregnancies with this diagnosis. It is critical that these trends be monitored. When children with DS are born, it is important to determine the contributing factors. In some cases it may be from late or insufficient prenatal care. In other cases, it is a result of parental choice either to decline screening, decline diagnostic testing when screen positive, or patients choosing to continue a pregnancy even when it is affected by a diagnosed chromosomal abnormality. In some case, however, it may be due to a false negative risk assessment.

Obviously, NTQR is very interested in monitoring these trends. We encourage NTQR participants to voluntarily submit deidentified cases for review that were screen negative women who delivered infants with chromosomal problems. Please send any cases that you may be aware of to the NTQR at 12316A North May Avenue, Oklahoma City, OK 73120.

REFERENCES

\(^1\)Henry, GP, Britt, DW, Evans ML. Fetal Diagnosis & Therapy 2008:23: 308-15

YOU ASKED, NTQR ANSWERS

Does the NTQR statistical report take into account that we are a high risk OB department and that we receive referrals for patients that already have abnormal findings. If we do not do blood work on high NTs will that skew our reports?

If your practice is high-risk based on maternal age alone or a combination of high-risk and normal risk women your statistical results are not likely to be affected by sending large NTs directly to diagnostic testing. NT size is not directly impacted by maternal age, though the risk level is higher due to age. Low risk and high risk women will have similar NT measurements. In a normal population less than 1% of patients will have an NT measurement greater than 3mm. If these women do not have blood work and the NT/CRL data is not transmitted by the laboratory to the NTQR then there should be little impact. You do however have the option of self-submitting this data through the website in your account under PERFORMANCE IMPROVEMENT.

If you receive large numbers of referrals for patients that have had a large NT measured elsewhere and you measure and send these values to the laboratory your NT median MOM may be increased and your standard deviation increased as well.

How do you self report data to the NTQR?

When you log into your NTQR account you will find a menu at the top. Under PERFORMANCE IMPROVEMENT, click on "data submission." From here you may upload data in a digital database or you may submit data after each examination by completing the self-submission form. NTQR also accepts data submitted by e-mail preferably in a database format.

Why does the NTQR require sonographers to identify an NT credentialed physician supervisor when the sonographer is assigned to required quality maintenance?

The NTQR has recommended since its inception both physician and sonographer credentialing; an "NT credentialed team" available for every patient seeking first trimester risk assessment. The NTQR GUIDELINES FOR PHYSICIAN CREDENTIALING, our newsletter, and our courses have stressed sonographer and physician credentialing. Our governing board consisting of representatives from AIUM, ACOG, ACR, ACOOG, NSGC, SMFM, and SDMS, and SDMS considers this best practice for the following reasons:

- The physician is legally responsible for the accuracy of the measurement.
- The standard criteria for the NT measurement must be learned and reviewed on every image.
- When an accurate NT cannot be obtained the patient needs to be rescheduled or the risk assessment done without an NT.
- Sonographers may not be comfortable making these decisions and may feel pressured to report a suboptimal measurement.
- A measurement variation of only 0.2 mm is known to make a difference in risk reported to the patient.
- NT measurements are known to drift if not monitored.
- Inaccurate measurements may not provide the detection rates quoted to patients.
- It is best practice to have educated reviews of every image and a credentialed sonographer/physician team can provide this.

The NTQR requires sonographers who are placed in quality maintenance because of statistics that are outside the expected range for two consecutive reporting periods to identify an NT credentialed physician supervisor. The physician identified must confirm that he/she will supervise the sonographers' measurements. The "team" working together on quality monitoring and measurement improvement is in the best interests of all.
My reports indicate that my measurements are out of the expected range and low. How can I improve my statistics. Will I be assigned to required quality maintenance.

The NTQR is presently assigning participants to required re-education and image submission only if their reports are outside the expected range for two consecutive quarters. If your NTQR statistical report indicates that you are outside the expected range it is important to make a renewed effort to document all of the standard NT criteria on every measurement. The image reviewers indicate that if the NT median MOM is low you may improve your measurements by focusing on the following during every NT exam:

- Make sure that the NT is measured in the widest location --- not specifically under the neck, in the widest location wherever that may be.
- The caliper crossbars must be IN the nuchal boundary -- not sitting on top or in the nuchal space.
- The NT boundary line needs to be thin so as not to take up space that would be included in the NT measurement.
- In a normal population less than 5% of patients will have an NT less than 1mm. It is worthwhile to spend extra time when the measurement is less than 1 mm to make sure that it is correct.

I was told that my standard deviation was too high. How do I improve?

Your standard deviation should be around 0.09. If it is higher than 0.11 on your statistical report you will want to improve. A high standard deviation indicates that there is inconsistency in your measurements. A common reason for high standard deviation is accepting suboptimal NT measurements. A risk assessment done without an NT is more accurate than a risk assessment done with a poor NT measurement. Make sure that every measurement that you report is an optimal measurement that meets the NT standard criteria.

Improve Your Crown Rump Length Measures

The image on the left is an acceptable CRL; the image on the right is not.

The NTQR does not review crown rump length images. When a participant's NT and CRL measures result in an aberrant distribution there is a question as to whether the CRL measurements rather than the NT measures are the cause. For that reason, the NTQR would like to remind participants of characteristics of an appropriate CRL measure.

An acceptable CRL measurement has the following characteristics.

- The fetus is seen in a mid-sagittal plane.
- The fetal neck is in a neutral position, neither hyperextended or hypoeextended with the chin on the chest.
- The image magnification is such that the fetus occupies more than 50% of the image.
- The measurement is made from crown to rump, not to the posterior thigh, distal spine, or other location.

To provide patients with an accurate risk assessment it is important for clinicians to measure the CRL as well as the NT carefully.
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 through ongoing NT quality monitoring reports.

Two ways to join NTQR and get credentialed!

1. On Line
   1. Go to [www.ntqr.org](http://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 2011 planned Land-Based Courses (see below)
   2. Take the on line exam
   3. Submit 5 NT images for quality review
   4. Get credentialed

Society of Maternal Fetal Medicine
31st Annual Meeting: The Pregnancy Meeting
Hilton San Francisco
San Francisco, California
February 7-12, 2011 [Registration Information](#)

34th Advanced Ultrasound Seminar OB-GYN
Lake Buena Vista, Florida
February 16, 2011 [Registration Information](#)

Advances in Obstetrical Management 2011
Lago Mar Resort & Club
Ft. Lauderdale, Florida
March 4-6, 2011 [Registration Information](#)

American College of OB/GYN
ACOOG Annual Clinical Meeting
Washington, D.C.
April 30-May 4, 2011 [Registration Information](#)

American College of Osteopathic OB-GYN
ACOOG 78th Annual Conference
Orlando, Florida
March 27-31, 2011 [Registration Information](#)

19th Annual Advanced Ultrasound Techniques In OB-GYN
FireSky Resort and Spa
Scottsdale, Arizona
November 3-5, 2011 [Registration Information](#)

National Conference on OB-GYN Ultrasound
The Westin Chicago River North
Chicago, Illinois
November 4-6, 2011 [Registration Information](#)

20th Annual OB-GYN Ultrasound Update for Clinical Practice
Lago Mar Resort & Club
Ft. Lauderdale, Florida
December 1-4, 2011 [Registration Information](#)

Obstetric Ultrasound in the High Risk Patient
Las Vegas, Nevada
October 14-16, 2011 [Registration Information](#)
Growth of the NTQR Database

Program Statistics 12/31/2010

- 5,914 providers of NT measurements have registered with the Nuchal Translucency Quality Review Program
- 4,276 providers have been credentialed through NTQR
- Over 30,000 NT images have been reviewed by NTQR's Expert Reviewers
- Over 1 million data sets have been provided by participants or by our partner laboratories. Valid data sets were analyzed to produce individual epidemiologic reports. Over 3550 personalized reports were sent to participants in November.
- To see a list of our partner laboratories, go to www.NTQR.org
2011
What’s New in Your NTQR Account:

• ‘NT-only’ Risk Calculator
• Voluntary Image Review
• Image Review Self Test
• NT/CRL Data Self-Submission
• Epidemiologic Monitoring Reports

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You may also send e-mail to The NT Examiner.