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Tuberculosis Screening in Internationally Adopted Children: Test Twice

ABSTRACT & COMMENTARY

By Hal B. Jenson, MD, FAAP

Professor of Pediatrics, Tufts University School of Medicine; Chief Academic Officer, Baystate Medical Center, Springfield, MA

Dr. Jenson is on the speaker's bureau for Merck.

This article originally appeared in the August 2008 issue of Infectious Disease Alert.

Synopsis: *A high proportion of internationally adopted children arriving in the United States have an initial false-positive tuberculin skin test. All internationally adopted children with an initially negative tuberculin skin test should have a repeat tuberculin skin test after three months in the United States. This should be the standard of care for identifying latent tuberculosis infection and preventing tuberculosis disease in these children.*

Source: Trehan I, et al. Tuberculosis screening in internationally adopted children: The need for initial and repeat testing. *Pediatrics*. 2008;122:e7-e14.

A cohort of 549 internationally adopted children ≥ 3 months of age (mean age, 22.9 months; range, 1.2-200 months) was evaluated at Cincinnati Children's Hospital between 1999 and 2004, with a post-adoption health visit within two months (mean, 12 days) after arrival in the United States. Children arrived from 29 different countries, with 81% coming from Russia, China, Guatemala, Kazakhstan, and South Korea; none of the children tested positive for HIV infection.

The initial tuberculin skin test (TST) was read at 48-72 hours in 527 children (96%) and was positive (≥ 10 mm induration) in 111 children (21%). Of the 416 children with a negative initial TST, 92% had no induration and 8% had 1-9 mm of induration. In these 416 children, a second post-adoption TST was performed at least three months later in 203 children and read at 48-72 hours in 191 (94%). The repeat TST was positive in 38 children (20%). All of the children had normal physical examinations and chest radiographs and were diagnosed with latent tuberculosis infection (LTBI). They began the recommended nine-month course of isoniazid; there was no apparent association of positive repeat TST and country of birth.

The majority (81%) of children had evidence of BCG vaccination, except for children from South Korea, with only 15% having evidence of BCG vaccination. Only eight children had documentation of multiple BCG vaccinations. Children with evidence of BCG vaccination were more likely to have a positive

TST result than children without evidence of BCG vaccination (OR: 15.3; 95% CI 3.3-70.1; $p = 0.0004$).

The median age (14.8 vs 13.1 months) and institutionalization history of children with a positive TST was not significantly different from children with a negative TST. The TST was positive 19.7% of the time for children who had lived in an orphanage or hospital at any time, 19.5% for children who had lived in an orphanage at least six months, and 24.1% for children who had resided in a foster home. Malnutrition (defined as a weight-for-age *z* score less than 2.0) was present in 158 (30%) children. The median (range) *z* score for children with a positive TST result, 1.13 (5.40-1.31), was slightly higher than for children with a negative TST result, 1.38 (7.00-3.94), $p = 0.06$. Children with an initially negative TST result were more likely to be malnourished compared to children with an initially positive TST result (31% vs 22%, $p = 0.06$).

■ COMMENTARY

More than 20,000 children are adopted into the United States each year, many from areas of high tuberculosis endemicity. The initial health screening guidelines include testing for tuberculosis using the TST for all immigrants from high-prevalence countries. Consensus guidelines recommend that TST results be interpreted without consideration of the BCG vaccination history, and that the TST be repeated once the child is better nourished, if malnutrition is initially suspected.

Because of the long incubation period of tuberculosis infection, the TST has poor sensitivity following recent exposure and during early developing infection. Other factors that may contribute to anergy and false-negative TST results include undernourishment, recent live virus vaccine administration, concomitant infections, and immunosuppression.

Tuberculosis remains a major global public health threat. This study demonstrates that many additional cases of LTBI can be identified among internationally adopted children by repeat TST after a few months in the United States. It is unlikely that these children represent acquisition of tuberculosis infection in the United States, but rather that the ability to mount an appropriate delayed hypersensitivity response to TST occurs after nutritional status has improved. Although not statistically significant, the results of this study showed that malnourished children were less likely to have a positive TST result at the initial visit. A history of BCG vaccination is not a contraindication to placement of a TST, and the interpretation of the TST result should not be influenced by a history of BCG vaccination. ■

Fatigue—Can It Be Due To Cardiac Malfunction?

ABSTRACT & COMMENTARY

By Harold L. Karpman, MD, FACC, FACP

Dr. Karpman is Clinical Professor of Medicine, UCLA School of Medicine

Dr. Karpman reports no financial relationships related to this field of study.

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Synopsis: *Complaints of fatigue were not associated with changes in blood pressure or heart rate but were significantly associated with decreased cardiac index and stroke index even after controlling for demographic variables and depressive symptoms.*

Source: Neleson R, et al. *Arch Inter Med.* 2008;168(9): 943-948.

Fatigue is one of the most commonly encountered complaints in medical practice, especially in the elderly. It is frequently accompanied by a decreased capacity or motivation for work activities and by feelings of weariness and sleepiness. It is a non-specific symptom commonly associated with medical conditions such as obstructive sleep apnea, hypothyroidism, anemia, infections, renal or hepatic disease, heart failure, severe stress, chronic fatigue syndrome and/or a variety of other medical or surgical conditions. Patients with severe chronic fatigue syndrome have been shown to have significantly lower stroke volumes (SV) and cardiac output (CO) than the control patients.[3,4] Individuals who reported more sleepiness were found to have lower CO and significantly lower SVs and, furthermore, increased sleepiness has even been found to be related to decreased CO in a sample of patients with obstructive sleep apnea but without known cardiac disease.[5]

Because fatigue occurs with and without other symptoms which have been demonstrated to be associated with hemodynamic cardiovascular malfunction, Neleson and his colleagues mounted a study to examine the relationship between self-reported fatigue and hemodynamic functioning at rest and in response to a stressor (ie, public speaking) in healthy individuals.[10] Heart rate, SV, and CO were measured using impedance plethysmography in a total of 142 individuals at rest and during a speaking stressor. SV and CO were converted to stroke index (SI) and cardiac index (CI) by adjusting for body surface area. Those study participants complaining of excessive fatigue demonstrated lower SI and CI levels than did individuals with moderate and minimal fatigue both at rest and in response to the speaking stressor, suggesting that the fatigue may have been, at least in part, secondary to hemodynamic cardiovascular abnormalities even in ostensibly healthy individuals.

■ COMMENTARY

Subtle hemodynamic changes in SI and CI had been noted to occur in veterans with Gulf War Syndrome and even in reasonably healthy individuals who complain of chronic fatigue.[3,4,6-9] These findings suggest that fatigue is often associated with a weak but measurable relationship with cardiac malfunction as determined objectively by altered measurements of CI and SI. However, simple office measurements such as heart rate or blood pressure are rarely significantly altered only by fatigue and, therefore, these simple measurements on the usual office patient are rarely abnormal enough to explain significant fatigue in that patient. The results of the Neleson study[10] should be interpreted with caution because of the small number of patients in the trial and because impedance cardiography tends to underestimate the true SI and CI; in fact, other techniques such as echocardiography should be considered for any future studies which may be mounted to evaluate hemodynamic abnormalities associated with complaints of fatigue.

In summary, the results of the Neleson study[10] suggest that decreased hemodynamic functioning (ie, decreased CI and SI) may be related to complaints of fatigue at rest and during acute stress even in apparently healthy subjects. It should be recognized that the effects of fatigue and/or stress on cardiovascular functioning as observed in this study may even be more significant in patients with known cardiovascular disease (ie, for example, some studies suggest that excessive fatigue may be an early manifestation of heart failure[1, 2]) and therefore, the abnormal hemodynamic effects observed in patients with fatigue may also explain the beneficial response observed to occur on both cardiovascular conditioning and on symptoms of fatigue with exercise.[11,12] Because so many studies have demonstrated the solid benefits of regular exercise in cardiac patients, it would seem that there would be little to lose by extending the benefits of exercise to healthy individuals as well as to cardiovascular patients complaining of fatigue since hemodynamic abnormalities secondary to fatigue may be at least partially responsible for the fatigue in both groups of patients. ■

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HIV Screening of Elderly Can Be Cost-effective

By Melinda Young

This article originally appeared in the July 2008 issue of AIDS Alert. Editor Melinda Young, Managing Editor Gary Evans, and Associate Publisher Coles Mckagen report no relationships with companies related to this field of study. Physician Reviewer Morris Harper, MD, reports consulting work with Agouron Pharmaceuticals, Gilead Sciences, Abbott Pharmaceuticals, GlaxoSmithKline, and Bristol-Myers Squibb. Nurse Planner Kay Ball is a consultant and stockholder with Steris Corp. and is on the speaker's bureau for the Association of periOperative Registered Nurses

Source: Sanders GD, Bayoumi AM, Holodniy M, et al. Cost-effectiveness of HIV screening in patients older than 55 years of age. *Ann Intern Med.* 2008; 148:889-903.

Although many HIV infections occur in older adults, national guidelines recommend screening only for persons age 13 to 64 years. However, researchers have found that expanding screening in people age 55 to 75 can be reasonably cost effective under the following circumstances:

- HIV prevalence is 0.1% or greater;
- a streamlined counseling process is implemented;
- and the person has a partner at risk for HIV infection.

To examine the costs and benefits of HIV screening in elderly patients the researchers used a Markov modeling technique targeting patients age 55 to 75 years with unknown HIV status. Outcome measures included life-years, quality-adjusted life-years (QALYs), costs, and incremental cost-effectiveness. For a 65-year-old patient, HIV screening using traditional counseling costs $55,440 per QALY compared with current practice when the prevalence of HIV was 0.5% and the patient did not have a sexual partner at risk. In sexually active patients, the incremental cost-effectiveness ratio was $30,020 per QALY. At a prevalence of 0.1%, HIV screening cost less than $60,000 per QALY for patients younger than age 75 years with a partner at risk if less costly streamlined counseling is used, the authors reported. Cost-effectiveness of HIV screening depended on HIV prevalence, age of the patient, counseling costs, and whether the patient was sexually active. Sensitivity analyses with other variables did not change the results substantially. Study limitations included the effects of age on the toxicity and efficacy of highly active antiretroviral therapy, but sensitivity analyses exploring these variables did not qualitatively affect the results.

"If the tested population has an HIV prevalence of 0.1% or greater, HIV screening in persons from age 55 to 75 years reaches conventional levels of cost-effectiveness when counseling is streamlined and if the screened patient has a partner at risk," the authors conclude. "Screening patients with advanced age for HIV is economically attractive in many circumstances." ■

CME Objectives

- To present the latest data regarding the diagnosis and treatment of various travel-related diseases;
- To present new data concerning recommended precautions and prophylaxis for patients traveling to specific areas of the world; and
- To alert the readers to recent disease outbreaks and epidemics. ■

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Defining Diagnosis and Management of Prediabetes

In This Issue: Guidelines for prediabetes from The American College of Endocrinology; statins for the prevention of dementia? Possible help for women suffering from sexual side effects while on antidepressants; government incentives for electronic prescribing; FDA Actions.

The American College of Endocrinology has issued its Consensus Statement on the diagnosis and management of prediabetes. The guideline was prompted by evidence that complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes. They define impaired fasting glucose (IFG) as a fasting glucose 100-125 mg/dL, and impaired glucose tolerance (IGT) as 2 hour post glucose load 140-199 mg/dL. (Diagnostic for diabetes are fasting levels ≥126 mg/dl and post challenge ≥ 200 mg/dL). The guideline recommends intensive lifestyle management for pre-diabetes patients, including weight reduction by 5-10%, regular moderate-intensity physical activity for 30-60 minutes daily at least 5 days a week, a diet low in total saturated fat and transfatty acids, adequate dietary fiber along with low sodium intake, and avoidance of excess alcohol. Although they acknowledge that there are no approved pharmacologic therapies for prevention of diabetes there is evidence that both metformin and acarbose may reduce the rate of development of diabetes from prediabetes. There are safety concerns with thiazolidinediones and they must be used with caution. Persons with prediabetes should have the same lipid goals of those with established diabetes, including statin therapy to achieve LDL cholesterol, non-HDL-cholesterol, or apoB treatment goals of 100 mg/dl, 130 mg/dL, and 90 mg/dL respectively. Other lipid-lowering drugs may be used as considered appropriate. Niacin should be used with caution because of its potential to raise blood sugar. Blood pressure control should also be at the same targets as recommended for diabetics including systolic blood pressure <130 and diastolic less than 80 mmHg. ACEI/ARB should be first-line agents, with CCBs as appropriate second line treatment approaches. Thiazides, beta-blockers, or their combinations should be used with caution due to adverse effects on blood sugar. Antiplatelet therapy with aspirin is recommended for all persons with prediabetes who have no contraindications for aspirin. The full guideline can be found online at www.aace.com/meetings/consensus/hyperglycemia/hyperglycemia.pdf.

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Questions and comments, call: (404) 262-5431. E-mail: iris.young@ahcmedia.com.

Statins and Dementia

Do statins help prevent dementia and cognitive impairment? The medical literature has been conflicting on this issue, but now a new study from the University of Michigan raises hope that there is benefit. In a population-based cohort study, 1674 older Mexican Americans who were free of dementia or cognitive impairment at baseline were studied over 5 years. Overall, 27% of the participants took statins during the study. After adjusting for education, smoking status, genetic testing, and history of stroke or diabetes at baseline, persons who had used statins were about half as likely as those who did not to develop dementia or cognitive impairment (HR = 0.52; 95% CI 0.34-0.80). The authors conclude that statin users were less likely to have incident dementia or cognitive impairment without dementia during a 5-year follow-up. They also suggest that these results add to the emerging evidence suggesting a protective effect of statin use on cognitive outcomes (*Neurology.* 2008; 71: 344-350).

Help for Women on Antidepressants Who Suffer from Sexual Side Effects

Women with antidepressant related sexual side effects improved with sildenafil (Viagra) according to a new study. In the 8-week randomized double-blind placebo-controlled trial, 98 women who were stabilized on a serotonin reuptake inhibitor were randomized to sildenafil or placebo at a flexible dose starting at 50 mg adjustable to 100 mg. before sexual activity. The primary outcome was change in baseline to study end in the Clinical Global Impression sexual function scale. Women treated with sildenafil had significantly improved sexual function scores even factoring in women who discontinued the medication prematurely. Baseline endocrine levels were the same in both groups as were depression scale scores. Headache, flushing, and dyspepsia were the most commonly reported side effects of sildenafil. The authors conclude that sildenafil treatment of sexual dysfunction in women taking serotonin reuptake inhibitors was associated with a reduction in adverse sexual side effects (*JAMA.* 2008; 300: 395-404). The study was sponsored by Pfizer, the manufacture of sildenafil.

Electronic Prescribing Worth Your While

If you are not already utilizing electronic prescribing, the government may soon make it worth your while by providing incentive payments to physicians and qualified health care professionals who utilize the technology. Beginning in 2009 Medicare will provide incentive payments for electronic prescribers which will include 2% incentive payments in 2009 and 2010; 1% incentive payment in 2011 and 2012, and a 0.5% incentive payment in 2013. On their website, Health and Human Services states that E-prescribing is more efficient, convenient for consumers, improves the quality of care, and lowers administrative costs. They also suggest that widespread E-prescribing would eliminate thousands of medication errors every year. More information can be found at www.HHS.gov/news/facts/eprescribing.html.

FDA Actions

The FDA has ordered safety-related changes to the labeling of erythropoietin products (Procrit, Ecogen, Aranesp) to reflect safety concerns based on recent data. The new labeling states that the drugs are "not indicated for those receiving myelosuppressive therapy when anticipated outcome is cure." Additionally the agency recommended therapy should not be initiated at hemoglobin levels of 10 g/dL and above, and dosage should be withheld if hemoglobin levels exceed a level needed to avoid transfusion. The FDA also encourages health-care professionals to discuss with their patients the risk of erythropoietin therapy including increased risk of vascular events, shortened time to tumor progression recurrence, and shortened survival.

The FDA has approved the first generic divalproex (Depakote delayed-release tablets) for the treatment of seizures and bipolar disorder, and the management of migraine headaches. Both the brand and generic versions of divalproex carry a Boxed Warning regarding the risk of liver damage and pancreatitis. Eight generic companies have received approval to market divalproex including Upsher-Smith laboratories and TEVA Pharmaceuticals.

The FDA has added a Boxed Warning to fluoroquinolone antibiotics regarding the risk of tendinitis and tendon rupture. The risk is higher in patients older than 60, those taking corticosteroids, and patients with kidney, heart, and lung transplants. Patients experiencing pain, swelling, or inflammation of the tendon or tendon rupture should stop taking their fluoroquinolone immediately and contact their health-care professionals. Fluoroquinolones requiring new labeling include ciprofloxacin (Cipro, Proquin), gemifloxacin (Factive), levofloxacin (Levaquin), moxifloxacin (Avelox), norfloxacin (Noroxin) and ofloxacin (Floxin). ■