

CHOOSING WISELY XII

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This is my twelfth article on “Choosing Wisely” from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing “Five Things Physicians and Patients Should Question.”

The Choosing Wisely topics in this issue are from the Infectious Diseases Society of America (IDSA), the American Association of Clinical Endocrinologists (AACE), and The Endocrine Society (TES), and the Society of Thoracic Surgeons.

RECOMMENDATIONS FROM THE INFECTIOUS DISEASES SOCIETY OF AMERICA (IDSA)

1. Asymptomatic bacteriuria (ASB) should not be treated with antibiotics.

ASB, the asymptomatic presence of a significant number of bacteria in the urine, is a major contributor to antibiotic overuse. Antibiotics are appropriate for ASB, in pregnant patients, patients undergoing prostate or other invasive urologic surgery, and kidney or pancreas transplant patients in the first year after receiving their transplant. Otherwise, antibiotics for ASB are not beneficial and do not improve morbidity or mortality. Catheter-associated asymptomatic bacteriuria does not require screening or antibiotic therapy. Not only is overtreatment of ASB costly but it can lead to C-difficile infection and resistant pathogens.¹

2. Don't give antibiotics for upper respiratory infections.

The majority of these are viral in etiology; antibiotics should be reserved for proven infections with Group A Streptococcal disease or pertussis. URIs should be treated to control symptoms. The important issue here is for providers to explain to patients the consequences of misusing antibiotics in viral infections, including resistance, adverse side effects, and costs.

3. Stasis dermatitis of the lower extremities should not be treated with antibiotics.

Unfortunately, stasis dermatitis is sometimes misdiagnosed and antibiotics are used, but they do not improve healing rates for stasis dermatitis.² Proper treatment consists of leg elevation and compression. (We

have an excellent lymphedema section in the LGH physical therapy department to help with this regimen.)

4. In the absence of diarrhea, do not test for Clostridium difficile.

Only perform this test on unformed diarrheal stool, unless this organism is suspected to be causing ileus. If there is no diarrhea, the presence of C-difficile indicates a carrier state which should not be treated or tested for.

5. Do not give prophylactic antibiotics for mitral valve prolapse.

Prophylaxis is no longer recommended in patients with mitral valve prolapse for the prevention of infective endocarditis. The risk exceeds any potential benefit. Antibiotics increase resistant strains and perhaps the occurrence of C-difficile-associated colitis.³

JOINT RECOMMENDATIONS FROM THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS (AACE) AND THE ENDOCRINE SOCIETY (TES)

1. In adults with stable type II diabetes receiving agents that do not cause hypoglycemia, avoid routine daily self-glucose monitoring.

Self-monitoring is beneficial when one is learning and adjusting therapy, but once control is achieved the results of self-monitoring become predictable. Exceptions arise in acute illness; when new medications are added; when weight fluctuates; and when the A1C becomes abnormal.

2. There is no need to measure 1,25-dihydroxyvitamin D unless the patient has hypercalcemia or abnormal renal function.

Vitamin D tests can be confusing and costly. The active form of vitamin D is 1,25-hydroxyvitamin D, but serum levels have little or no relationship to vitamin D stores but rather are regulated primarily by parathyroid hormone levels, which in turn are regulated by calcium and/or vitamin D. In vitamin D deficiency, 1,25-dihydroxyvitamin D levels go up, not down.

A 25-hydroxyvitamin D is the correct test to order when screening for vitamin D deficiency in *individuals at risk for deficiency*. Unregulated production of 1,25-hydroxyvitamin D (i.e., granulomatous diseases, sarcoidosis) is an

uncommon cause for hyperglycemia; in such cases blood levels of calcium should be high and parathyroid hormone levels low. The enzyme that activates vitamin D is produced by the kidney, so levels of 1,25-dihydroxyvitamin D are sometimes of interest in patients on dialysis or with end-stage kidney disease. Otherwise, a 1,25-hydroxyvitamin D test would not be helpful and doing it or the vitamin D profile to test for Vitamin D deficiency is quite expensive compared with the serum 25-hydroxyvitamin D.⁴

3. A thyroid ultrasound is not needed for abnormal thyroid function tests unless there is a palpable abnormality of the thyroid.

The thyroid ultrasound is used to identify and characterize thyroid nodules. Incidentally discovered thyroid nodules are common, and should not divert the clinical evaluation away from the abnormal thyroid function. If the patient is thyroid toxic, a thyroid scan should be chosen over an ultrasound.

4. When assessing levothyroxine (T4) in hypothyroid patients, do not order a total or a free T3.

A total or free T3 level may be misleading in patients taking levothyroxine. Because T4 is converted into T3 at the cellular level, patients taking T4 may have higher blood T4 and lower blood T3 levels. A normal TSH indicates an adequate dose of T4.⁵

5. Testosterone therapy should only be prescribed when there is biochemical evidence of testosterone deficiency.

Symptoms attributed to male hypogonadism are seen in normal male aging or with other comorbid conditions. Significant side effects can be caused by expensive testosterone therapy. When indicated, biochemical testing should be done with a total testosterone level obtained in the morning. Another low level should be confirmed on a different day, again measuring total testosterone. A free or bioavailable testosterone may be of additional value in some situations.

RECOMMENDATIONS FROM THE SOCIETY OF THORACIC SURGEONS

1. Preoperative stress testing prior is not necessary prior to non-cardiac thoracic surgery if there is no cardiac history and the patient has good functional status.

Management is rarely changed by preoperative stress testing in highly functional asymptomatic patients. Unnecessary stress testing can increase the cost of care and delay treatment. Low-risk patients who undergo testing are more likely to receive additional invasive testing with further risk of complications. Patients should be evaluated with a thorough history,

physical examination, and resting EKG.⁶

2. Routine evaluation of carotid artery disease prior to cardiac surgery should not be done in the absence of symptoms or other high-risk criteria.

Patients with symptoms of carotid stenosis such as stroke or transient ischemic attacks are known to be at risk for a cardiovascular accident and preoperative testing is appropriate. However, the presence of a carotid bruit does not equate to an increased risk of stroke after cardiac surgery. There is no evidence that prophylactic or concomitant carotid surgery decreases the rate of complications in asymptomatic patients.

The ACC/AHA 2011 guidelines for coronary artery bypass graft surgery indicated that carotid artery duplex scanning was reasonable in selected patients with high-risk features, but that recommendations was based on a consensus and a low level of evidence. A more recent consensus report from the UK questioned whether neurologic sequelae in cardiac surgery patients with asymptomatic carotid disease are due to the carotid disease or to atherosclerotic aortic disease, for which carotid disease is a marker of increased stroke risk.

The Northern Manhattan Stroke Study found that carotid auscultation had poor sensitivity and poor positive predictive value for carotid stenosis. The decision to order carotid duplex studies should be based on symptoms or risk factors rather than auscultatory findings.⁷

3. A routine pre-discharge echocardiogram after cardiac valve replacement surgery is not indicated.

Although echocardiography is useful prior to discharge after cardiac valve repair, evidence to support its routine use after valve replacement is lacking. Other reasons for pre-discharge echocardiography include: clinical signs and symptoms that suggest valve malfunction or infection; inability to perform intraoperative transesophageal echocardiography; or a large pericardial effusion.

4. Patients with suspected or proven stage I non-small cell lung carcinoma (NSCLC) and no neurologic symptoms don't require imaging of the brain.

Occult brain metastases occur in less than 3% of patients with stage I lung cancer. Routine brain imaging increases costs, delays therapy, and it rarely changes management. False-positive studies occur in up to 11% of patients, and cause further invasive testing or incorrect over-staging. Prior to surgical resection of early lung cancer, some clinicians perform a routine MRI or CT to rule out occult brain metastasis in asymptomatic patients, but this practice has not been evaluated by a randomized clinical trial and may not be necessary or cost effective.

A joint statement of the European Respiratory

Society and the American Thoracic Society also did not advocate preoperative imaging of the brain in patients with NSCLC who present without neurologic symptoms. Finally, current National Comprehensive Cancer Network (NCCN) guidelines for stage IA NSCLC do not recommend preoperative brain imaging for asymptomatic patients.

5. Prior to cardiac surgery, pulmonary function testing is unnecessary in the absence of respiratory symptoms.

Patients without pulmonary symptoms are unlikely to benefit, but respiratory symptoms that are attributable to cardiac disease should be better characterized with PFTs. Although some data are beginning to emerge about preoperative pulmonary rehabilitation prior to cardiac surgery for patients with even mild to moderate obstructive disease, this trend does not directly extrapolate to asymptomatic patients.⁸

TOP TIPS

FIREARM-RELATED INJURIES AND DEATH

Firearm-related injuries and death are becoming more evident, if not more common. The following are recommendations from eight medical associations and the American Bar Association:^{9,10}

- Improved access to mental health care; caution against broadly prohibiting all persons with any mental or substance-use disorder from purchasing firearms.
- Criminal background checks for all firearm purchases, including sales by gun dealers, at gun shows, and between private individuals.
- Opposition to state and federal mandates that interfere with physician free speech and the patient-physician relationship, including laws that forbid physicians to discuss gun ownership.
- Adequate resources to facilitate coordination among physicians and state, local, and community-based behavioral health systems.
- Restrictions for civilian use or the manufacture and sale of large-capacity magazines and firearms with features designed to increase their rapid and extended killing capacity.
- Robust research about the causes and consequences of firearm violence and unintentional injuries and for strategies to reduce firearm-related injuries. Access to data should not be restricted, so researchers can do studies that enable the development of evidence-based policies to reduce the rate of firearm injuries and deaths in this nation.
- For persons whose right to purchase or possess a

firearm has been suspended on grounds relating to a mental or substance-use disorder, there should be a fair, equitable, and reasonable process established for restoration that balances the individual's rights with public safety.

UPDATE IN VITAMIN D RESEARCH

Vitamin D And Cancer

A new study in *The Journal of Clinical Oncology* found that people with lower vitamin D levels prior to treatment for follicular lymphoma die or relapse earlier than patients with sufficient vitamin D levels. Prior studies of diffuse large B-cell lymphoma and chronic lymphocytic leukemia have shown a survival benefit among patients with higher vitamin D levels. Earlier peer-reviewed research at Wilmot Cancer Institute showed that in women with breast cancer, low vitamin D levels correlated with more aggressive tumors and poorer prognosis. These findings could be related to the fact that Vitamin D deficiency among African Americans leads to higher death rates from colorectal cancer.

Heart Disease and Diabetes

Researchers at The Washington University School of Medicine are examining connections among vitamin D, immune function, atherosclerosis, and insulin resistance in genetically altered mice that lack vitamin D receptors in monocytes and macrophages. Findings showed that vitamin D pathways in immune cells play a key role in chronic inflammation that affects development of insulin resistance and atherosclerosis. The group is now conducting clinic trials in people with type II diabetes to see if vitamin D treatment can prevent some of the complications of diabetes and inflammation.

Vitamin D and The Brain

Vitamin D regulates about 1000 different types of genes in the body, roughly 5% of the human genome. Researchers from Children's Hospital Oakland Research Institute hypothesize that high levels of vitamin D in maternal blood increase tryptophan and produce normal amounts of regulatory cells and serotonin in the placenta, thus allowing normal fetal brain development. With low levels of vitamin D, there will be fewer of these cells and higher serotonin levels; without regulatory cells, autoantibodies attack tissue leading to abnormal brain development. Regulation of serotonin in developing brains could potential affect the development of autism or attention deficit hyperactivity disorder.

Vitamin D deficiency has been linked to brain atrophy, the risk of ischemic stroke, and vascular dysfunction.¹¹ Analysis of data from the Cardiovascular Health Study

showed that the risk of developing both all-cause dementia and Alzheimer's disease was increased 51% in participants who were 25 (OH) D deficient, and 122% in those who were severely deficient. Vitamin D receptors are expressed throughout the brain, including areas involved in memory such as the hippocampus and dentate gyrus. In vitro, vitamin D stimulates macrophages, increasing the clearance of amyloid plaques. Vitamin D also reduces amyloid-induced cytotoxicity and apoptosis in primary cortical neurons.

Low serum levels of vitamin D are associated with clinically significant symptoms of depression in otherwise healthy individuals.¹² After taking into account season, body mass index, race/ethnicity, diet, exercise, and time outside, the researchers found that lower vitamin D3 levels across the study predicted clinically depressive symptoms (P<.05).

The optimum level of vitamin D for general health remains controversial with The Institute of Medicine recommending 50 nmol/L and The Endocrine Society recommending 75 nmol/L. Results from the current study in Neurology clarify that the threshold above which older adults are unlikely to benefit from supplementation with regard to dementia risk is likely in the region of 50 nmol/L.

PREVENTION OF DERMATOLOGY BIOPSY MISTAKES

The Journal of Family Practice gave multiple suggestions on how to properly accomplish skin biopsies.

Do the appropriate type of biopsy for the suspected diagnosis. Each type of biopsy has advantages and disadvantages. The punch biopsy is the best for

most "rashes" (inflammatory skin disorders) because the pathologist can examine the superficial and deep portions of the dermis.

When doing a shave biopsy, make sure that you get a sample that is deep enough. If it is not, it can be very difficult to establish an accurate diagnosis. If properly sewn up, a punch biopsy leaves patients with linear scars rather than round scars from shave biopsies.

Excisional biopsy is used to remove melanocytic neoplasms or larger lesions. It typically includes 1-3 mm of normal skin around the lesion to completely remove it. Lesions that are not definitively benign (atypical melanocytic neoplasms) are removed with this technique.

Curettage biopsy uses a surgical tool with a scoop, loop, or ring at the tip in a scraping motion to retrieve tissue. It destroys the architecture of the tissue of the lesion and can make it difficult to establish a proper diagnosis. Don't use this for a melanocytic lesion.

The biopsy must be submersed in formalin or it is difficult to give an accurate diagnosis. If the tissue is left out of the fixative for greater than a few hours, an appropriate assessment can be impossible. Don't aggressively manipulate the biopsy as it can cause a crush artifact.

To properly record the site of the biopsy for future exams, take pictures of the lesion at the time of the biopsy. When using measurements, be specific and accurate using anatomic terms.

A sufficient history includes the distribution and appearance of the lesion as well as how long the patient has known about it. Medication use or new exposures can also be helpful.

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