Choosing Wisely XXX

Recommendations from the American Academy of Pediatrics Section on Rheumatology, American Society for Clinical Pathology, and American College of Preventive Medicine

Alan S. Peterson, M.D.
Emeritus Director, Environmental and Community Medicine
Walter L. Aument Family Health Center

This is my 30th article on Choosing Wisely from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing "Five or more Things that Physicians and Patients Should Know."

I. Recommendations from the American Academy of Pediatrics Section on Rheumatology

1. Patients who need chronic pain management and have autoimmune disease should not receive opioids. Research has shown that morphine and similar medications are not superior to ibuprofen, and have significantly more adverse effects. Use of opioids for medical purposes in adolescents also increases the risk of long-term use and misuse in adulthood. Opioids do not reduce inflammation from active arthritis.

2. Unless there is a strong suspicion or specific signs of autoimmune disease, antinuclear antibody (ANA) and other autoantibody testing should not be ordered in a child. The ANA has a high sensitivity for only one disease, systemic lupus erythematosus (SLE), but has very poor specificity for SLE and every other rheumatic disease. A positive ANA may occur secondary to polyclonal activation of the immune system following an infection, or it may be positive without any identifiable reason/disease in up to 32% of the population.

3. Children with musculoskeletal symptoms without an exposure history or appropriate exam findings should not be tested for Lyme disease. The musculoskeletal manifestations of Lyme disease include brief attacks of arthralgia with early disseminated Lyme, and/or intermittent or persistent episodes of arthritis in one or a few large joints, with predilection for the knee in late disease. Diffuse arthralgias, myalgias, or fibromyalgias alone are not criteria for musculoskeletal Lyme disease. False positive results may lead to unnecessary followup testing and therapy.[1]

4. Periodic fever syndrome should be evaluated with genetic panels only after an infectious and oncologic workup, and only in patients with clear evidence of recurrent fever. Fever is a common complaint in the pediatric age group; an infectious etiology is the most common cause, followed by malignancy. Most children with a periodic fever syndrome do not have a genetic mutation, and the most common fever syndrome — PFAPA (periodic fever, adenitis, pharyngitis, aphthous ulcer) — is not associated with a monogenetic mutation.

5. In children with musculoskeletal complaints, do not order a rheumatoid factor (RF), whether alone or as part of a "panel" or "cascade," to look for rheumatologic diseases such as juvenile idiopathic arthritis (JIA). Laboratory results should not guide referral. JIA is a clinical diagnosis and laboratory studies are used to prognosticate severity. Only 10%-30% of children with JIA have a positive RF compared to the majority of adults with rheumatoid arthritis. The relevance of other antibodies such as anti-cyclic citrullinated peptide (anti-CCP) has not been established in a pediatric population. These laboratory tests are typically expensive, and RF is non-specific; it can be positive in other diseases, infections, or in healthy individuals.

II. Recommendations from the American Society for Clinical Pathology (ASCP)

The first 20 Choosing Wisely items by this group have been printed previously in the Journal of Lancaster General Hospital. Here I will present items 21 through 30.

21. A Kidney Profile (serum creatinine with eGFR and urinary albumin-creatinine ratio) should be requested to test adults with diabetes and/or hypertension for CKD. A serum creatinine to test adult patients is not sufficient. Use the National Kidney Foundation updated evidence-based Kidney Profile test for CKD with the following common tests to more effectively assess kidney function:

- "Spot" urine for albumin-creatinine ratio

(ACR) to detect albuminuria.

- Serum creatinine to estimate glomerular filtration rate (GFR) using the CKD EPI equation.[2]

22. Don't transfuse plasma to correct a laboratory value: treat the clinical status of the patient. Plasma transfusion in a patient with an INR of <1.6 has minimal effect, and transfusion for INR values between 1.6 and 2 should be carefully considered. A mildly elevated INR is not usually associated with spontaneous hemorrhage and does not increase the risk of bleeding during routine invasive procedures. One also does not want to increase the risk of transfusion-associated circulatory overload (TACO) which is a leading cause of transfusion associated morbidity and mortality. To avoid unnecessary transfusion, consider judicious use of vitamin K and/or prothrombin complex concentrate according to evidence-based clinical practice guidelines.

23. IgM antibody serologic studies should not be ordered to look for acute infections that are no longer endemic in the US. In general, avoid using IgM antibody serologies to test for acute infection in the absence of sufficient pre-test probability. For example, according to the CDC, rubella is no longer endemic in the US. As such, nearly all positive rubella IgM antibody tests are false positives, resulting in unnecessary follow-up testing and unnecessary anxiety. Even for diseases not yet eradicated and for which low level outbreaks still occur (such as measles), if overall prevalence remains low, the predictive value of positive IgM serology will still be low. False positive measles IgM serology for example, has been documented due to cross-reactivity to parvovirus and human herpes virus 6, among others. Practitioners should report to, and engage the help of, their state Public Health Department and/or the CDC in further evaluating possible acute infection.[3]

24. Peripheral flow cytometry should not be performed to screen for hematological malignancy in the settings of mature neutrophilia, basophilia, erythrocytosis, thrombocytosis, isolated anemia, or isolated thrombocytopenia. Its use should be limited to settings in which there are morphologically abnormal cells on a peripheral blood smear (blasts, lymphoma cells), or there are clinical and/or laboratory findings that suggest a high probability of disorders amenable to the immunophenotypic detection of neoplastic cells in the blood. The latter include patients with neutropenia, absolute lymphocytosis, lymphadenopathy, or splenomegaly.

25. Procalcitonin testing should not be performed without an established, evidence-based protocol. Procalcitonin is a biomarker that has been used successfully to identify patients with certain bacterial infections (e.g., sepsis). Appropriate use includes serial (usually daily) measurements of procalcitonin in select patient populations (e.g. patients with fever and presumed serious infection for which antibiotics were initiated). Unfortunately, procalcitonin is often either used in an inappropriate setting or without following established algorithms.[4]

26. Hospitalized patients who develop diarrhea after day three of hospitalization should not routinely be tested for community gastrointestinal stool pathogens. A number of studies have indicated that stool culture and parasitological examination is usually not indicated when diarrhea develops more than three days after admission to the hospital, because these tests are designed to detect agents of community-acquired gastrointestinal infection. In contrast, testing for C *difficile* should be considered in such patients if they are over 2 years of age. Some older adults and immunocompromised patients may have community-type pathogens detected after three days of hospitalization.

27. Hepatitis C virus antibody testing in patients with a previous positive hepatitis C virus (HCV) test should not be repeated. Instead, order hepatitis C viral load testing for assessment of active versus resolved infection. A positive HCV antibody test remains positive for life, so patients who had a remote and resolved HCV infection, and are suspected of being re-infected, should be tested using the HCV viral load test, which distinguishes active from resolved infections. Patients with active infections (i.e. a positive serology and HCV viral load) may often need an HCV genotyping assay to guide therapy.

28. In patients taking direct factor Xa or direct thrombin inhibitors, don't perform a hypercoagulable workup. Direct oral anticoagulants (DOACs) such as dabigatran etexilate, rivaroxaban, apixaban, edoxaban, and betrixaban often interfere with clot-based or chromogenic coagulation assays and may lead to inaccurate results or render the test uninterpretable. Affected tests that should not be done in patients taking DOACs include many common tests on hypercoagulable panels: Lupus anticoagulant (LA) panels, activated protein C resistance, protein C and protein S activity, antithrombin activity, and

specific factor activity levels. Genetic testing, such as PCR for factor V leiden, is unaffected. For those with antiphospholipid antibody syndrome, the Lupus anticoagulant panel may be uninterpretable, but ELISA-based anticardiolipin and anti-beta2 GP1 antibody testing is unaffected.

29. In the evaluation of a patient for pheochromocytoma or paraganglioma, don't order plasma catecholamines; instead use plasma free metanephrines or urinary fractionated metanephrines. When measuring plasma metanephrines, patients should have their blood drawn while in a supine position, and the value should be compared to reference values determined from the same collection position.

30. Broad respiratory pathogen panels should not be routinely ordered unless the result will affect patient management. Consider first using tests of commonly suspected pathogens, which may change according to the location/season. Examples include rapid molecular or point of care tests for RSV, influenza A/B or Group A pharyngitis. Broader testing for other respiratory pathogens may be done when the result will affect patient management.

III. RECOMMENDATIONS FROM THE AMERICAN COLLEGE OF PREVENTIVE MEDICINE (ACPM)

1. Multi-vitamins, vitamin E, or beta carotene should not be taken to prevent cardiovascular disease or cancer. There is insufficient evidence to demonstrate benefit from multi-vitamin supplementation. Beta carotene is also associated with an increased risk of lung cancer in smokers and people who have been exposed to asbestos.[5]

2. PSA-based screening should not be routinely performed for prostate cancer. More than 1,000 symptom-free men need to be screened for prostate cancer in order to save one additional life. As a result, increased harms and medical costs due to wide-spread screening of asymptomatic men are believed to outweigh the benefits of routine screening. There is a high likelihood of having a false positive result leading to worry, decreased quality of life, and unnecessary biopsies, since many of these elevated PSAs are caused by enlarged prostates and infections instead of cancer. In rare circumstances, such as a strong family history of prostate and related cancers, screening may be appropriate.

3. Whole-body scans should not be used for early tumor detection in asymptomatic patients. Whole-body scanning with a variety of techniques (MRI, SPECT, PET and CT) is marketed to screen for a wide range of undiagnosed cancers, but there are no data to suggest these imaging studies improve survival or improve the likelihood of finding a tumor (estimated tumor detection is less than 2% in asymptomatic patients screened). Whole-body scanning has a risk of false positive findings that can result in unnecessary testing and procedures that are costly and pose additional risks. There is considerable exposure to radiation with PET and CT, and a very small increase in the possibility of developing cancer later in life.

4. Expensive medication should not be used when an equally effective and lower-cost medication is available. On average, the cost of a generic drug is 80%-85% lower than the name-brand product, although generic drugs are required to have the same active ingredients, strength and similar effectiveness as brand-name drugs.

5. Don't screen for cervical cancer in low-risk women age 65 and older, or in women who have had a total hysterectomy for benign disease. Screening provides no benefit to patients who have had a hysterectomy and may subject them to potential risks from false-positive results, including physical risks (e.g., vaginal bleeding from biopsies, or psychological ones (e.g. anxiety). Those over age 65 who have a low risk for cervical cancer and have had negative prior screenings should not have further screening for cervical cancer.

REFERENCES

1. Lipsetts, Nigrovic, L. Diagnosis of Lyme disease in the pediatric acute care setting. *Curr Opin Pediatr.* 2016;28(3):287-293.
2. Berns JS. Routine screening for CKD should be done in asymptomatic patients....selectively *Clin J Am Soc Nephrol.* 2014;9:1988-1992.
3. Woods CR: False-positive results for immunoglobulin M serologic results: Explanations and examples. *J Ped Infect Dis Soc* 2013:2(1):87-90.
4. Rhee C. Using procalcitonin to guide antibiotic therapy. *Open Forum Infect Dis.* 2016 Dec 7;4(1):ofw249. doi: 10.1093/ofid/ofw249. eCollection 2017 Winter.
5. Moyer VA. US Preventive Services Task Force. Vitamin, mineral and multi-vitamin supplements for the primary prevention of cardiovascular disease and cancer: US preventive services task force recommendation statement. *Ann Int Med.* 2014;160(8):558-64.