TOP TIPS FROM FAMILY PRACTICE

Choosing Wisely XXVII

Recommendations on Pediatric Infectious Diseases, Blood Management, and Dermatopathology

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This is my 27th article on Choosing Wisely from the Board of Internal Medicine Foundation. As previously noted, each specialty group is developing recommendations of "Five, Ten, or Fifteen Things that Physicians and Patients Should Know."

I. RECOMMENDATIONS FROM THE ACADEMY OF PEDIATRICS - COMMITTEE ON INFECTIOUS DISEASES AND THE PEDIATRIC INFECTIOUS DISEASES SOCIETY

1. **In children with suspected invasive bacterial infection, don't use empiric antibiotic therapy without first confirming that blood, urine, or other appropriate cultures have been obtained, excluding exceptional cases.** Diagnostic testing should include blood cultures and appropriate culture of specimens from the suspected infected site. Optimally, a blood culture can be obtained at the time of intravenous access. If antibiotics are started due to clinical instability before cultures can be obtained, they should still be obtained at the earliest possible time.

In neonates with bacterial or viral sepsis that cannot be differentiated based on the clinical presentation, and both antibiotics and antivirals are initiated, blood cultures should be prioritized and cultures from additional sites (e.g. CSF) and PCR testing (e.g. HSV) should be obtained as soon as clinically feasible.

2. **After an incision is closed for uncomplicated clean and clean-contaminated procedures, a broad-spectrum antimicrobial agent for perioperative prophylaxis should not be used.** Timely administration of perioperative antibiotics can reduce post-operative infections when narrow spectrum antibiotics (e.g., cefazolin) are given *before* surgery. This prophylaxis should not be continued after the incision is closed for uncomplicated clean and clean-contaminated procedures, i.e. respiratory, gastrointestinal, or genitourinary sites are breached but without infection or inflammation. Clean-contaminated procedure is when you cross the respiratory, GI, or urogenital tract without gross contamination. Quality improvement approaches are helpful, especially when it is shown there is poor adherence to published guidelines on the use of perioperative antibiotics.

3. **In otherwise healthy, immunized, hospitalized children, do not treat uncomplicated community-acquired pneumonia (CAP) with antibiotics broader than ampicillin.** Unnecessary use of broad-spectrum antibiotics, including cephalosporins such as ceftriaxone, have been shown to contribute to antibiotic resistance and C. difficile infection. The most common cause of CAP in healthy, immunized children is Streptococcus pneumoniae, of which most strains are highly susceptible to penicillin/ampicillin.[1]

4. **For neonatal intensive care patients, vancomycin or carbapenems should not be used empirically unless an infant is known to have a specific risk for pathogens resistant to narrower-spectrum agents.** Overuse of these antibiotics can exert selection pressure and promote colonization and infection with increasingly resistant organisms, raising the specter of morbidity and mortality due to untreatable infection. Vancomycin in particular, is commonly used as a first-line choice when infections are suspected in a newborn intensive care unit, despite evidence that there is no survival benefit attributed to empiric therapy for most infected infants.

5. **In otherwise healthy children with infections that can be transitioned to an appropriate oral agent, don't place a peripherally inserted central catheter (PICC) and/or use prolonged IV antibiotics.** Most common infections for which PICCs are placed in children respond well to oral antibiotics after a brief course of intravenous therapy. Following hospital discharge, up to 40% of children with PICCs will return to the emergency department with a PICC complication. Studies of children with complicated pneumonia, ruptured appendicitis, and osteomyelitis, have shown that extended intravenous therapy with a PICC does not improve the clinical cure rate, but is often associated with PICC line complications.[2]

II. RECOMMENDATIONS FROM THE SOCIETY FOR ADVANCEMENT OF BLOOD MANAGEMENT

1. **Elective surgery in patients with properly**

diagnosed and correctible anemia should not proceed until the anemia has been appropriately treated. Approximately one-third of patients undergoing elective surgery present with anemia. It is independently associated with significant morbidity and mortality that can be as high as 30%-40% in certain patient populations. Treatment modalities may include nutritional supplements such as iron, B12, and folate, changes in medication, management of chronic inflammatory conditions or previously undiagnosed malignancy, or other interventions based on the etiology.

2. Laboratory blood testing should not be performed unless clinically indicated or necessary for diagnosis or management in order to avoid iatrogenic anemia. Up to 90% of patients become anemic by day three in the intensive care unit. Anemia secondary to iatrogenic blood loss causes an increased length of stay and mortality. Increased phlebotomy for laboratory testing also increases the odds of transfusion, and its associated risks.

3. Do not transfuse plasma in the absence of active bleeding or significant laboratory evidence of coagulopathy. Plasma increases the risk of transfusion-associated adverse events such as acute lung injury, circulatory overload, and allergic reactions. These complications increase the cost of care and the risk of poor outcomes.[3]

4. Use antifibrinolytic drugs when available to minimize surgical bleeding and avoid transfusion. In trauma and obstetric hemorrhage, early (within three hours) administration of tranexamic acid, significantly reduces mortality and bleeding. Antifibrinolytic therapy has been shown to reduce blood loss and transfusion requirements in orthopedic and cardiovascular operations.

5. In non-emergent situations, when alternative strategies are available, avoid transfusion and make discussion of alternatives part of the informed consent process. Informed choice/consent regarding transfusion and other effective methods should be standardized and consistently delivered. Alternative strategies to transfusion include, but are not limited to, pharmacologic agents, cell salvage, normo-volemic hemodilution, and minimally-invasive surgical technics.[4]

III. RECOMMENDATIONS FROM THE AMERICAN SOCIETY OF DERMATOPATHOLOGY

1. When there is clinical and histologic concordance for a diagnosis of pityriasis lichenoides or lymphomatoid papulosis, do not perform studies of T-cell receptor (beta and gamma) gene rearrangement on inflammatory/reactive lesions or papular/papulonecrotic eruptions. There are limitations in the sensitivity and specificity of the test, which has a high false positive rate and is unreliable in differentiating between benign inflammatory dermatoses and T-cell lymphoproliferative disorders.

2. When the histopathology is definitive for a melanoma, diagnostic cytogenetic analysis should not be performed on a lesion from an adult patient. Histologic examination is currently the gold standard in the diagnosis of melanocytic lesions. Cytogenetic analysis can serve as an adjunct test when a definitive diagnosis cannot be rendered on histologic grounds.

3. When histopathology is definitive for a melanocytic nevus in an adult patient, diagnostic cytogenetic analysis should not be performed. Again, histologic examination is currently the gold standard for the diagnosis of melanocytic lesions.

4. In cases of dermatofibrosarcoma protuberans, if the t(17;22) translocation has already been detected by another testing modality, don't perform the FISH assay (fluorescence in situ hybridization). Various testing modalities can be used to detect the translocation, and each can provide confirmation of the presence of the translocation.

5. In cases of clear cell sarcoma in situations where the translocation has already been detected by another testing modality, the EWSR1 fluorescence in situ hybridization (FISH) assay should not be performed. Again, various testing modalities can be used to detect the translocation involving EWSR1 gene in clear cell sarcoma, with each being able to confirm the presence or absence of the translocation.[5]

Top Tips

MAKING MEDICINE AFFORDABLE

As a follow-up to Dr. Bonchek's editorials in the last issue of JLGH[6] and this one, it's notable that in November 2017 an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine issued a 235-page report on Making Medicines Affordable: A National Imperative.[7] The report includes 14 findings about the complexity of the biopharmaceutical marketplace and 18 findings about factors influencing the affordability of prescription drugs. Eight recommendations beginning on page 126 are reproduced below. (In the report, each is accompanied by several suggested actions not reproduced here due to space constraints.)

1. Accelerate the market entry and use of safe and effective generics as well as biosimilars, and foster competition to insure the continued affordability and availability of these products.

2. Consolidate and apply government purchasing power, strengthen formulary design, and improve drug valuation methods. One of the actions suggested to implement this recommendation is modifying existing legislation to allow the Department of Health and Human Services to negotiate drug prices for Medicare, and to include any state agencies that wish to participate in the program.

3. Assure greater transparency of financial flows and profit margins in the bio-pharmaceutical supply chain.

4. Promote the adoption of industry codes of conduct, and discourage direct-to-consumer advertising of prescription drugs, as well as direct financial incentives for patients.

5. Modify the designs of insurance benefits to mitigate the burden of prescription drug costs for patients.

6. Eliminate misapplication of funds and inefficiencies in federal discount programs that are intended to aid vulnerable populations.

7. Ensure that financial incentives for the prevention and treatment of rare diseases are not extended to widely sold drugs.

8. Increase available information and implement reimbursement incentives to more closely align prescribing practices of clinicians with treatment value.

(Pages 52 and 53 of the report cover Medicare drug price negotiation in detail. Pages 96-98 discuss drug reimportation. The full report can be read online[7] or downloaded free of charge by registered users of the National Academies' website.)

HPV TESTING IS BETTER THAN CYTOLOGY FOR WOMEN VACCINATED AGAINST HPV

As more women who have been immunized against HPV age, the question becomes: what is the best means of screening for cervical cancer?

In an Australian study, 1,078 women younger than 33 years who had been offered the HPV vaccine at age 12 or 13 years, or later as a catch-up, were randomized, using concealed allocation, to one of the three strategies for cervical cancer screening that were recommended at that time.[8] (An estimated 50% to 77% of women received all three doses.)

1. Liquid-based cytology (ThinPrep) every 2.5 years with follow-up HPV co-testing if the results were abnormal;

2. HPV testing every five years with follow-up cytology or colposcopy if the results were abnormal; or

3. HPV testing every five years with follow-up cell staining for oncogenic markers in women with identified oncogenic HPV (HPV 16 or 18) on initial screening.

Rates of identification of high-grade precancerous disease (CIN2+) were higher in women in each HPV testing arm (2.6% and 2.9%) than with cytology (0.5%; P = .05). Researchers do not know the percentage of eligible women who received the vaccine, and most of the women had been screened at some point before the study was started, which biased the sample toward lower rates of disease and lowered the study's power.

In women who had received the HPV vaccine, screening for HPV every five years, with cytology and colposcopy follow-up as needed, resulted in higher rates of identification of high-grade precancerous disease (cervical intraepithelial neoplasia grade 2 or higher [CIN2+]) than standard liquid-based cytology every 2.5 years with HPV follow-up cotesting as needed. (Level of Evidence = 1b).

SOME ARE NOT "CHOOSING WISELY" FOR BREAST CANCER IMAGING

Two papers presented at the American Society of Clinical Oncology (ASCO) Quality Care Symposium (QCS) revealed that the "Choosing Wisely" guidelines for breast cancer imaging are not being fully implemented. (The guidelines recommend against routine imaging in patients with early-stage breast cancer (ESBC) who are low risk for metastasis.)

a. The first study reports that 30% of patients with ESBC underwent initial imaging, despite guidelines recommending against it.[9] The prevalence of inappropriate imaging varied from 26% to 68% among oncologists. While the study did not examine the reasons for inappropriate testing, the lead author, Brett Barlow, M.D., offered some thoughts. The time measured was immediately after a three-year period from the publishing of the guidelines, and there may have been some lag time in their dissemination and adoption. There might also have been a perception that patients who were younger, had higher-stage cancers, or had triple-negative receptor status, have worse long-term outcomes, even though they weren't included in the scope of the guideline. Finally, Barlow added, "some physicians just may not believe these guidelines."

b. The second study found that up to 19% of patients with Stage I to II breast cancer had unnecessary scanning, adding almost $5,000 in cost.[10] This paper from Mount Sinai Hospital in New York City looked at adherence rate, and factors associated with

nonadherence to imaging guidelines, in 733 patients with early-stage breast cancer who were treated in a large health care system. The most frequent scanning modality was positron emission tomography/CT, followed by CT. Routine scanning did not identify any cases of metastatic disease. False positive findings were identified in 43% of the patients, and incidental findings in 8%.

Dr. Michael Sabel of the University of Michigan, Ann Arbor, stated "It's not just the cost of these scans that's detrimental, but they lead to additional tests and biopsies. Maybe they show a tiny little nodule that turns out to be nothing." He added that some inappropriate scanning might be driven by patients, so we as physicians need to better communicate that these tests can lead to unnecessary invasive procedures and anxiety, and do not improve outcomes.

ACUTE PANCREATITIS GUIDELINES

The American Gastroenterological Association (AGA) has updated its guidelines concerning acute pancreatitis (AP).[11]

The diagnosis of AP requires at least two of the following features: characteristic abdominal pain; biochemical evidence of pancreatitis (i.e., amylase or lipase elevated to >3x the upper limit of normal); and/or radiographic evidence of pancreatitis on cross-sectional imaging. Patients present along a clinical spectrum, and can be categorized as having mild, moderately severe, or severe pancreatitis.

a. Around 80% of cases are mild, with only interstitial changes of the pancreas, and without local or systemic complications.

b. Moderately severe pancreatitis is characterized by transient local or systemic complications, or transient organ failure (<48 hours).

c. Severe AP is associated with persistent organ failure.

Necrotizing pancreatitis is characterized by the presence of pancreatic and/or peripancreatic necrosis, and is typically seen in patients with moderately severe or severe AP.

There are two overlapping phases of AP – early and late. The early phase takes place in the first two weeks after onset, and the late phase can last weeks to months thereafter.

Treatment Recommendations

In patients with AP, the AGA advises against the use of hydroxymethyl starch (HES) fluids, and further advises against prophylactic antibiotics for severe AP and necrotizing AP. They also recommend against the routine use of urgent ERCP in patients with acute biliary pancreatitis and no cholangitis. Finally, early (within 24 hours) oral feeding as tolerated is recommended, rather than keeping the patient NPO. In those unable to feed orally, enteral feeding is recommended rather than parenteral nutrition. In those with predicted severe or necrotizing pancreatitis requiring enteral tube feeding, recommendations are either for the naso-gastric or naso-jejunal route.

In patients with acute biliary pancreatitis, cholecystectomy is recommended during the initial admission rather than at a subsequent readmission. In patients with acute alcoholic pancreatitis, the AGA recommends brief alcohol intervention during admission.

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