Recommendations from Pediatric Hospital Medicine and the American Academy of Pediatrics

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This is my 40th article on Choosing Wisely from the American Board of Internal Medicine (ABIM) Foundation. As noted in previous issues of *JLGH*, each specialty group is developing "Five or More Things That Physicians and Patients Should Question."

All items are developed to encourage discussion between physicians and their patients about which tests and procedures are best in each case. Additional resources are available online at choosingwisely.org.

RECOMMENDATIONS FROM PEDIATRIC HOSPITAL MEDICINE

1. IV antibiotics for predetermined durations for patients hospitalized with infections such as pyelonephritis, osteomyelitis, and complicated pneumonia should not be prescribed. Consider early transition to oral antibiotics. Recent publications have demonstrated that strategies for early transition to oral antibiotics achieve equal or better outcomes for common inpatient infections and are safer than prolonged intravenous antibiotics in children. Antibiotic courses with predetermined durations are often not based on high-quality evidence and ignore individual response to treatments, which can vary significantly from patient to patient.[1]

2. Hospitalization in well-appearing febrile infants once bacterial cultures (i.e., blood, cerebral spinal, and/or urine) have been confirmed negative for 24-36 hours should not be continued if adequate outpatient follow-up can be assured. Routinely continuing hospitalization beyond 24-36 hours of confirmed negative bacterial cultures for well-appearing infants admitted for concern of serious bacterial infections does not improve clinical outcomes.

3. Phototherapy should not be initiated in term or late preterm well-appearing infants with neonatal hyperbilirubinemia if their bilirubin is below levels at which the clinician AAP guidelines recommend treatment. The risk of poor neurologic outcomes, such as cerebral palsy due to kernicterus, is extremely low for term and late preterm newborns with modestly elevated bilirubin levels. Confirmed cases of kernicterus have average bilirubin levels near 40 mg/dL and are typically associated with hemolysis. While phototherapy for bilirubin with values above published thresholds may be useful to prevent severe hyperbilirubinemia and exchange transfusions, its use for bilirubin values below published thresholds is unnecessary and is associated with additional costs and unnecessary hospitalization.[2]

4. Broad-spectrum antibiotics such as ceftriaxone for children hospitalized with uncomplicated community-acquired pneumonia (CAP) should not be used. Use narrow-spectrum antibiotics such as penicillin, ampicillin, or amoxicillin. The use of narrow-spectrum antibiotics for children hospitalized with CAP can limit the development of multi-drug-resistant organisms while achieving similar or better outcomes.

5. IV antibiotic therapy should not be started on well-appearing newborn infants with isolated risk factors for sepsis such as maternal chorioamnionitis, prolonged rupture of membranes, or untreated group-B streptococcal colonization. Use clinical tools such as an evidence-based sepsis risk calculator to guide management. Unnecessary exposure of infants to antibiotics is associated with increased parental anxiety, length of stay, increased cost, gut microbiome dysbiosis, necrotizing enterocolitis, and possibly allergic and autoimmune diseases. The use of evidence-based sepsis calculators has demonstrated reductions in antibiotic use of 50% or more without a concomitant increase in the incidence of early onset sepsis.

RECOMMENDATIONS FROM THE AMERICAN ACADEMY OF PEDIATRICS — SECTION ON EMERGENCY MEDICINE AND THE CANADIAN ASSOCIATION OF EMERGENCY PHYSICIANS

1. Radiographs should not be obtained in children with bronchiolitis, croup, asthma, or first-time wheezing. Radiographs rarely yield important positive findings and expose patients to radiation, increased cost of care, and prolonged emergency department

length of stay. Radiography performed in the absence of significant findings has been shown to be associated with overuse of antibiotics. Findings of significant hypoxia, focal abnormalities, prolonged course of illness, or severe distress are situations prompting radiographs. If wheezing is occurring without a clear atopic etiology or with upper respiratory tract infection symptoms (e.g., rhinorrhea, nasal congestion, and/or fever), appropriate diagnostic imaging should be considered on a case-by-case basis.[3]

2. Screening laboratory tests should not be obtained in the medical clearance process of pediatric patients who require inpatient psychiatric admission unless clinically indicated. A large body of evidence, in both adults and children, has shown that routine laboratory testing without clinical indication is unnecessary and adds to health care costs.

3. Laboratory testing or a CT scan of the head should not be ordered for a patient with an unprovoked, generalized seizure or a simple febrile seizure who has returned to baseline mental status. CT scans are associated with radiation-related risk of cancer, increased cost of care, and added risk if sedation is required to complete the scan. A head CT scan may be indicated in patients with a new focal seizure, new focal neurologic findings, or high-risk medical history (such as neoplasm, stroke, coagulopathy, sickle cell disease, age <6 months).[4]

4. Abdominal radiograph should not be obtained for suspected constipation. Constipation is a clinical diagnosis and does not require testing, yet many of these children receive an abdominal radiograph. Use of abdominal radiographs to diagnose constipation has been associated with increased diagnostic error.

5. Comprehensive viral panel testing should not be obtained for patients who have suspected respiratory viral illnesses. This Choosing Wisely item was released on December 1, 2022, with a note that there is a lack of consistent evidence to demonstrate the impact of comprehensive viral panel (i.e., panels simultaneously testing for 8-20+ viruses) results on clinical outcomes or management, especially in emergency department settings.

Testing for specific viruses might be indicated if the results of the testing may alter treatment plans (e.g., antivirals for influenza) or public health recommendations (e.g., isolation for SARS-CoV-2). For more specific recommendations related to diagnosis and management for SARS-CoV-2, please see aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/).[5]

Top Tips

DO MOUTHWASHES AND/OR SALINE NASAL IRRIGATION SUPPRESS SARS-COV-2?

Covid spreads from the oral and nasal cavities transmitted by aerosols. In addition to the well-known division and spread of the virus in the cells of the respiratory tract, SARS-CoV-2 is also known to infect the cells of the lining of the mouth and the salivary glands.

Commercially available mouthwashes contain antibiotic and antiviral components that act against microorganisms in the mouth. As shown by a team of researchers at Hokkaido University, one of these — cetylpyridinium chloride (CPC) — reduces the viral load of SARS-CoV-2 in the mouth, primarily by disrupting the lipid membrane surrounding the virus. While other chemicals have similar effects, CPC has the advantage of being tasteless and odorless.

Mouthwashes in Japan typically contain a fraction of the CPC compared to previously tested mouthwashes, thus researchers were interested in studying Japanese mouthwashes. They tested the effects of CPC on cell cultures that express trans-membrane protease serine 2 (TMPRSS2), which is required for SARS-CoV-2 entry into the cell.

They found that, within 10 minutes of application, 30-50 µg/mL of CPC inhibited the infectivity and capability for cell entry of SARS-CoV-2. Interestingly, commercially available mouthwashes that contain CPC perform better than CPC alone. Researchers also showed that saliva did not alter the effects of CPC. Most significantly, they tested four variants of SARS-CoV-2 and showed that the effects of CPC were similar across all strains.

This study shows that low concentrations of CPC in commercial mouthwash suppress the infectivity of four variants of SARS-CoV-2. The authors are now assessing the effect of CPC-containing mouthwashes on viral loads in saliva of COVID-19 patients. Future work will also focus on fully understanding the mechanism of the effect, as lower concentrations of CPC do not disrupt lipid membranes.[6]

As reported in the Winter 2022 issue of *JLGH*, the Medical College of Georgia at Augusta University has found that irrigating your nose twice a day with a saline solution after testing positive for COVID-19 can decrease your chances of hospitalization and death in higher-risk patients. In that study, those who per-

formed nasal irrigation were more than eight times less likely to be hospitalized than the national rate.

DOES COVID-19 CONFER RISK FOR VENOUS THROMBOEMBOLISM IN AMBULATORY PATIENTS?

Evidence has been mixed about risk for venous thromboembolism (VTE) among patients with ambulatory SARS-CoV-2 infections, but in this U.K. population-based cohort study, researchers determined the 30-day risk for VTE (i.e., deep venous thrombosis or pulmonary embolism) among 19,000 outpatients (mean age: 64) with ambulatory COVID-19.

SARS-CoV-2 positive patients had significantly higher risk for VTE within 30 days than did matched controls (incident rate: 51 vs. 2 per 1,000 person-years; hazard ratio: 21). Excess risk was higher for unvaccinated people (hazard ratio: 28) than for vaccinated people (hazard ratio: 6). Among patients with SARS-CoV-2 infections, older age, male sex, obesity, inherited thrombophilia, and no or partial vaccination were independent risk factors for VTE.

These results reinforce the value of vaccination. Whether thromboprophylaxis also would be beneficial in ambulatory patients, as it is in hospitalized COVID-19 patients, remains unclear.[7]

HEART FAILURE CLINICAL PRACTICE GUIDELINES UPDATED

Updated and revised guidelines on the management of heart failure (HF) were published in 2022 by the American College of Cardiology (ACC), American Heart Association (AHA), and Heart Failure Society of America (HFSA) in the journal *Circulation.* The top 10 key points are:

1. Four core foundational medication classes are now included in the guideline-directed medical therapy recommendations for heart failure with reduced ejection fraction (HFrEF). These are sodium-glucose cotransporter-2 inhibitors (SGLT2Is), beta blockers, mineralocorticoid receptor antagonists (MRAs), and renin-angiotensin system (RAS) inhibitors.
2. SGLT2Is are a class 2a (moderate) recommendation for heart failure with moderately reduced ejection fraction (HFmrEF), whereas angiotensin receptor-neprilysin inhibitors (ARNIs), angiotensin-

Elizabethtown University Student Art on Exhibit at Lancaster Medical Heritage Museum

"We are proud to be a community space as well as a museum," says Kim Jovinelli, executive director of the Lancaster Medical Heritage Museum. "Education, exhibition, and research have been a major tenet of our mission since our founding in 1982, and we will continue that tradition," she adds. In this vein, the museum has been working with Elizabethtown College and Millersville University to connect with the academic community.

At Elizabethtown College, Dr. Anya Goldina, professor of biology, each year encourages her students to complete an art project as part of an extra-credit initiative. Dr. Goldina and her students graciously lent the art pieces pictured above to the museum as part of a joint exhibition, currently on display at the museum's new location at 410 North Lime Street, Lancaster. At Millersville University, history and anthropology students can complete museum-related work for extra credit, plus the museum benefits from summer research internships graciously sponsored by Penn Medicine Lancaster General Health and WellSpan Ephrata Community Hospital. Internship applications are open to students from all over the country to learn what it's like to work in a museum, while also completing a research topic of their choice. Turn to page 19 for an article from this year's LG Health intern, who researched the Lancaster County Vaccine Farm.

The museum is open Monday/Wednesday/Friday, 10:00 a.m. to 3:00 p.m. Summer hours (Tuesday-Saturday, 10:00 a.m. to 3:00 p.m.) begin April 28. Admission is free to LG Health employees with a badge and children under 3; $8.00 for all others. Follow the museum on social media (Facebook: LancasterMedicalMuseum; Instagram & TikTok: lmh_museum) or visit lancastermedicalheritagemuseum.org for the most current information.

converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), MRAs, and beta blockers are class 2b (weak) recommendations for this patient population.
3. There are new recommendations for heart failure with preserved ejection fraction (HFpEF) for SGLT2Is (class 2a), MRAs (class 2b), and ARNIs (class 2b).
4. Patients with previous HFrEF who now have a left ventricular (LV) EF above 40% should be referred to as having improved LVEF; they should continue their HFrEF treatment.
5. The ACC/AHA/HFSA created value statements for select recommendations in which there are high-quality cost-effectiveness studies of the intervention published.
6. New amyloid heart disease recommendations include screening for serum and urine monoclonal light chains, bone scintigraphy, genetic sequencing, tetramer stabilizer therapy, and anticoagulation.
7. Of importance is evidence to support increased filling pressures for the diagnosis of HF if the LVEF is over 40%. Such evidence can be obtained from noninvasive or invasive testing.
8. Refer those with advanced HF who desire prolonged survival to a team that specializes in HF.
9. Primary prevention is crucial for those at high risk of HF (stage A) or pre-HF (stage B). The revised stages of HF emphasize the new terminologies of "at risk" for HF for stage A and pre-HF for stage B.
10. Updated and new recommendations cover select patients with HF and iron deficiency anemia, coronary artery disease, AF, valvular heart disease, cardiomyopathy, hypertension, type 2 diabetes, sleep disorders, and malignancy.[8]

MEDICARE SPENT BILLIONS ON DRUGS WITHOUT CONFIRMED BENEFITS

The Centers for Medicare and Medicaid Services (CMS) spent $18 billion on drugs without confirmed benefits, according to findings of an Office of Inspector General (OIG) for the Department of Health and Human Services report. The money was spent over three years on medications for which there was no proof of significant clinical benefit. The goal of this process is to speed the approval of promising medications for serious and fatal diseases even though evidence of efficacy is limited.

The Federal Drug Administration's expectation is that drug companies will continue research to definitively prove the efficacy of medications approved via this process. However, sponsors don't always complete trials promptly for a variety of reasons, which can result in drugs staying on the market — and being administered to patients — for years without their predicted clinical benefit being verified and insurers (including Medicare and Medicaid) paying billions for treatments that are not verified to have clinical benefit.

In a statement, the drug makers' trade group, the Pharmaceutical Research and Manufacturers of America, said its members tried to hold up their end of the agreements for further studies of drugs granted accelerated approvals. Confirmatory trials sometimes take longer than expected owing to several factors, including the inability to enroll patients as quickly as anticipated because of patients enrolling in other studies aimed at the same population, patients being less willing to volunteer for studies of FDA-approved medicines, or small patient populations.

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