Clinical Briefs in Primary Care

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Evidence-based updates in primary care medicine

Online Supplement to *Clinical Cardiology Alert, Critical Care Alert, Hospital Medicine Alert, Infectious Disease Alert, Integrative Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports*

Volume 22, Number 10 October 2017

Routine Preoperative Lab Tests for Elective Surgery

SOURCE: Martin SK, Cifu AS. *JAMA* 2017;318:567-568.

Many U.S. clinicians may be unfamiliar with the U.K.'s National Institute for Health and Care Excellence (NICE) agency. Since 1999, NICE has been a world-recognized leader in the development of guidelines for management of disorders such as hypertension, dyslipidemia, and other epidemiologically important topics. Recently, NICE provided recommendations about which laboratory tests (if any) might be considered routinely appropriate preoperatively for elective surgery. The rationale for providing this guidance stems from the observation that, historically, there have been an excessive number of pre-op tests performed that not only provide no benefit for patient outcomes, but actually may cause harm because of unnecessary expense as well as need for follow-up of incidental (usually irrelevant) abnormal findings.

For example, recommendations pertinent to "intermediate surgery" (i.e., inguinal hernia repair, tonsillectomy and adenoidectomy, knee arthroscopy) in essentially healthy individuals are to eliminate preoperative testing entirely. Less healthy individuals, such as those with a severe systemic disease (American Society of Anesthesiologists Grade 3 or Grade 4), should undergo pre-op renal function testing only. For patients with symptomatic cardiovascular or renal disease, the guidelines call for a complete blood count. Space limitations preclude a comprehensive review of the full contents of this document, which may be accessed readily online. The authors of the guideline acknowledged a very limited literature from which to draw evidence-based conclusions, and encourage further definitive research on this topic. ■

Managing Diabetes: First Things First, or Vice Versa

SOURCE: Abdul-Ghani M, DeFronzo RA. *Diabetes Care* 2017;40:1121-1127.

In the absence of contraindications or medication intolerance, metformin has been recommended as the initial treatment choice for patients with type 2 diabetes mellitus (T2DM) for more than a decade. This advice arose from a combination of favorable metformin attributes, including cost, tolerability, safety, and (albeit limited) a relatively favorable cardiovascular profile. But the winds of change are suggesting a potential reconsideration.

Although reduction of microvascular adverse events in T2DM is well-established with "older" antidiabetic agents (e.g., sulfonylureas, metformin, insulin), the authors of this publication argue that our scope of focus for choosing optimum medications should include both efficacy in correcting hyperglycemia as well as the ability of pharmacologic intervention to address the currently recognized basic pathophysiologic defects of T2DM.

Accordingly, glucagon-like peptide-1 (GLP-1) receptor agonists (albiglutide, dulaglutide, exenatide, liraglutide, lixisenatide) demonstrate an attractive "better fit." That is, the four cardinal activities of GLP-1 receptor agonists: glucose-dependent insulin secretion, which minimizes the risk of hypoglycemia; glucose-dependent glucagon inhibition, which blocks excess glucagon while maintaining responsiveness of glucagon to hypoglycemia; improved satiety, potentially empowering more effective adherence to healthful dietary restrictions; and delayed gastric emptying, reducing postprandial glucose excursions. These provide complementary activities that address more of the basic pathophysiologic defects of T2DM than most other agents.

Finally, members of the class of GLP-1 receptor agonists recently have been shown to reduce cardiovascular events. Together, these attributes suggest GLP-1 receptor agonists might be an appropriate initial treatment for T2DM, supplanting metformin. ■

Measuring Urine Calcium in Nephrolithiasis Patients

SOURCE: Song L, Maalouf NM. *JAMA* 2017;318:474-475.

Most kidney stones contain calcium, often comprised of calcium oxalate (responsible for up to 80% of cases). Prevention of stone recurrence focuses on dietary interventions, pharmacologic interventions, and hydration. Since stone recurrence is related linearly to the level of calcium in the urine, with no "floor" to this relationship (that is, progressively lower urinary calcium is associated with proportionately lower risk for recurrence), it is valuable to identify the level of urinary calcium excretion in patients with nephrolithiasis and provide interventions to reduce urinary calcium. Currently, the threshold of urinary calcium defined as "hypercalciuria" is > 300 mg/day in men or

> 250 mg/day in women. A more gender-agnostic metric is based on body weight: > 4 mg/kg/day for either gender is considered hypercalciuric. Since studies using so-called "spot urine" measurements have indicated poor correlation with 24-hour specimens, the only accurate way to determine urinary calcium excretion is to perform the 24-hour urine measurement.

High sodium content in the diet increases calcium excretion in the urine, so sodium restriction may be beneficial. Thiazide diuretics reduce urinary calcium excretion and are useful when dietary and hydration steps are insufficient. ■

BCG Vaccinations and the False-positive Effect

SOURCE: Mancuso JD, Mody RM, Olsen CH, et al. *Chest* 2017;152:282-294.

A placebo-controlled trial of bacille Calmette-Guerin (BCG) vaccination was performed among Native Americans from Alaska, Arizona, North Dakota, South Dakota, and Wyoming from 1935-1947. Varying opinions appear in the literature about the length of time during which prior BCG vaccination influences reactions to tuberculin skin testing. For instance, the CDC suggests that tuberculin cross-reactivity is unlikely to persist longer than 10 years post-BCG vaccination.

A publication by Mancuso et al offers us a 55-year follow-up of 3,151 subjects who received the BCG vacccines inclusive of up to 55 years post-BCG vaccination. In this population, within the first five years of follow-up, > 60% of BCG recipients registered positive tuberculin testing results. Although this number waned somewhat over time (only 33% were positive after 50 years of follow-up), more than half of BCG vaccines remained tuberculin-positive throughout the initial 44 years of follow-up.

Based on this data, clinicians should consider that the BCG vaccination effect could influence tuberculin testing responsivity for an essentially indefinite period. ■

Azithromycin Reduces Asthma Exacerbations

SOURCE: Gibson PG, Yang IA, Upham JW, et al. *Lancet* 2017;390:659-668.

In my early years of training, I was tempted occasionally to consider an antibiotic during an asthma exacerbation, but was quickly advised about the basic foolhardiness of such a consideration. After all, asthma exacerbations essentially are induced exclusively by viral infections (as well as thermal and atopic stimuli). Is it time to reconsider that posture?

In the AMAZES clinical trial, symptomatic adult asthmatics (n = 420) on a long-acting bronchodilator and inhaled steroid were randomized to azithromycin 500 mg thrice weekly vs. placebo for 48 weeks. The primary outcome was number of asthma exacerbations. In a previous similarly designed trial of COPD patients receiving azithromycin 250 mg/day for one year, a decrement in hearing function was noted in the azithromycin treatment arm; hence, patients with any hearing impairment were excluded from this trial.

At 48 weeks, subjects on azithromycin experienced a 61% reduction in asthma exacerbations, as well as a statistically significant improvement in quality of life. Tolerability of azithromycin was very good, although diarrhea was twice as common in the azithromycin group as the placebo group (34% vs. 19%, respectively; $P < 0.05$). The authors reminded us that macrolides, in addition to antibacterial effects, also possess anti-inflammatory and antiviral activity. ■

Separating Celiac Disease From Non-celiac Gluten Sensitivity

SOURCE: Leonard MM, Sapone A, Catassi C, Fasano A. *JAMA* 2017;318:647-656.

The consequences of celiac disease include intestinal symptoms as well as diverse extraintestinal disorders such as anemia, osteoporosis, and increased risk of lymphoma. Gluten sensitivity has become sufficiently "popular" that an entire industry of "gluten-free" products has been created to satisfy the needs of a gluten-wary populace that too often views gluten as a toxin.

Patients with celiac disease possess specific human leukocyte antigen genotypes (DQ2 and DQ8) that allow an aberrant immunologic response to gluten-containing proteins, leading to the recognized signs and symptoms of celiac disease. Clinicians confirm the disease through intestinal biopsy. Consistently, this leads to not only symptom remission but also gluten antibody decline (anti-transglutaminase and antigliadin).

Anyone can experience a "food intolerance," unpleasant symptoms ranging from dyspepsia to diarrhea and beyond in response to individual foods. Most patients who experience an adverse symptom in response to a particular food simply choose to avoid that food in the future and do not label it "broccoli sensitivity syndrome" or "lima bean sensitivity syndrome." Because adverse abdominal symptomatology is commonplace in otherwise healthy individuals periodically, and there is high public awareness of gluten as a cause of abdominal pain in celiac disease, some simply remove gluten from their diet after which adverse abdominal symptoms (or sometimes other symptoms) disappear. Many of these individuals believe they suffer from celiac disease and never undergo appropriate diagnostic testing to affirm the diagnosis. As there is no diagnostic test to confirm any patient's "non-gluten celiac sensitivity," whether this clinical constellation should be considered a legitimate disorder remains a matter of controversy. However, there is no uncertainty about the necessity for long-term follow-up of patients with confirmed celiac disease. ■

CLINICAL BRIEFS IN PRIMARY CARE™
is published monthly by AHC Media, a Relias Learning company.

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