

Clinical Briefs in Primary Care

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Evidence-based updates in primary care medicine

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Is the Intestinal Microbiome the Culprit in Obesity?

SOURCE: Komaroff AL. The microbiome and risk for obesity and diabetes. *JAMA* 2017;317:355-356.

Apparently, the gut bacteria — currently called the microbiome — are much more than simple innocent bystanders. There are two primary families of intestinal microbiota: *Bacteroidetes* and *Firmicutes*, which comprise approximately 90% of all gut bacteria. Recently, it has been appreciated that the microbiome actually generates proteins, hormones, neurotransmitters, and inflammatory molecules. These products of the microbiome may enter the circulation and produce far-reaching effects.

For instance, obese persons are populated with greater numbers of *Firmicutes*, which are more efficient in providing energy sources than *Bacteroidetes*. Confirming the causal role of this relationship, transplantation of gut microbiota from obese mice promptly converts lean mice into obese ones. Equally remarkable, and much more hopeful, is the observation that transplantation of microbiota from lean mice into obese ones produces a favorable effect on weight.

The story is complicated even further by the observation that the microbiome is capable of remodeling: When obese persons consume weight-reducing diets, the disproportion of *Firmicutes* declines, and it resumes when excess calories are again introduced. We are only beginning to understand the magnitude of the role the microbiome plays in health and disease. ■

The Dubious Benefits of Urinalysis in Asymptomatic Patients

SOURCE: Bush LM, Vazquez-Pertejo MT. The unintended deleterious consequences of the 'routine' urinalysis. *Am J Med* 2017;130:3-4.

The only population in which treatment of asymptomatic bacteriuria might be beneficial appears to be pregnant women, and even that widely held belief has been challenged recently. Part of the problem of addressing asymptomatic bacteriuria is that often we are dealing with results of a test we may not have thought was really pertinent to the patients well-being (or lack thereof) in the first place. That is, so-called "routine" urinalysis — usually by urine dipstick — may be part of standard protocol for patients presenting with no symptoms even remotely referable to the genitourinary tract.

Were asymptomatic bacteriuria rare, perhaps the problem would not be so vexing. On the contrary, the prevalence in long-term care facility residents may be as high as 25-50% in women and 15-40% in men. When presented with such abnormal results, clinicians often are tempted to treat, hoping to avoid more serious consequences. However, clinical trial data do not demonstrate achieved benefit.

Both the Infectious Diseases Society of America and the American Board of Internal Medicine advise against treatment of asymptomatic bacteriuria in non-pregnant adults. Clinicians would be wise to heed such advice, and perhaps even better, be more selective about seeking urine testing only when clinically pertinent. ■

Comparing Treatments for Peripheral Artery Disease Patients

SOURCE: Hiatt WR, Fowkes FG, Heizer G, et al. Ticagrelor versus clopidogrel in symptomatic peripheral artery disease. *N Engl J Med* 2017;376:32-40.

Clopidogrel has demonstrated superiority to aspirin for reducing cardiovascular events in patients with stable vascular disease (i.e., post-myocardial infarction, post-stroke, prevalent peripheral arterial disease). In the CAPRIE trial, patients on clopidogrel experienced an almost 9% lower relative risk of cardiovascular events than patients on aspirin, although the absolute risk reduction was very small (0.5%). At the time of publication of the CAPRIE trial, this presented a dilemma for clinicians, primarily because of cost issues.

Ticagrelor is in the same class of agents as clopidogrel: Both are P2Y12 inhibitors, which lead to reduced platelet aggregation. The success that ticagrelor has achieved in acute coronary syndromes prompted the question of whether ticagrelor might provide greater reduction in cardiovascular events than clopidogrel, since the presence of peripheral arterial disease (whether symptomatic or not) is indicative of coexisting coronary artery disease.

Hiatt et al conducted a randomized, double-blind, placebo-controlled trial of ticagrelor vs. clopidogrel in patients with peripheral arterial disease (n = 13,885). The primary outcome was incident cardiovascular events over 2.5 years.

There was no statistically significant difference in cardiovascular outcomes between the two agents. The additional expense of ticagrelor, plus the fact that it is administered b.i.d in contrast to the q.d. dosing of clopidogrel, suggest that clopidogrel should remain the preferred agent. ■

Cardiovascular Risk Induced by NSAIDs

SOURCE: Nissen SE, Yeomans ND, Solomon DH, et al. Cardiovascular safety of celecoxib, naproxen, or ibuprofen for arthritis. *N Engl J Med* 2016;375:2519-2529.

Ever since the publication of the VIGOR trial, in which it was noted that cardiovascular (CV) events were four times more frequent in patients receiving rofecoxib (subsequently withdrawn from the market) than naproxen, warnings about the risk of CV events attributable to nonsteroidal anti-inflammatory drugs (NSAIDs) have become progressively more strident. For instance, the most recent American College of Cardiology/American Heart Association guidelines on acute coronary syndromes place NSAIDs at the bottom of the list of choices to treat musculoskeletal pain, preferring instead even

opioid agents such as tramadol. How does the CV safety profile of various NSAIDs stack up? To address that question, the administrators of the PRECISION trial randomized a large group of arthritis patients (n = 24,081) who were high risk for CV events to naproxen, ibuprofen, or celecoxib. The population was followed for approximately three years.

Although celecoxib produced fewer adverse gastrointestinal and renal events, there was no statistically significant difference among the three agents for CV events. No safe harbor among the NSAIDs has yet been confirmed in a large randomized trial, and the previous supposition that naproxen was a safer NSAID (from the CV perspective) appears to be incorrect. ■

The Way to a Man's Heart Is Through His Stomach?

SOURCE: Afsar B, Vaziri ND, Aslan G, et al. Gut hormones and gut microbiota: Implications for kidney function and hypertension. *J Am Soc Hypertens* 2016;10:954-961.

Our primary concerns about hypertension relate to adverse cardiovascular effects. Who would have guessed that the gastrointestinal tract could play an important role?

As an example, glucagon-like peptide-1 (GLP1; agents such as exenatide, liraglutide, etc.) has been shown in animal studies to increase sodium excretion. In type 2 diabetes, GLP1 treatment reduces blood pressure. Indeed, a trial with liraglutide even found a reduction in cardiovascular events.

The microbial population of the gastrointestinal tract also may play a role. Two of the primary bacterial teams of the gastrointestinal microbiome, *Bacteroidetes* and *Firmicutes*, have been demonstrated to be elevated in spontaneously hypertensive rats; rebalancing of the flora by antibiotic treatment improved blood pressure.

Alimentary bacteria generate a variety of short-chain fatty acids, some of which can stimulate the sympathetic nervous system and induce renin release from the afferent arteriole. Pharmacologic treatments that address potential toxicities produced by the gastrointestinal microbiome are under study and show some promise.

Although the aphorism “the way to a

man's heart is through his stomach” may have been intended to reflect another agenda, it may turn out to be far more true than most of us expected. ■

A Melodious Path to Addressing Dementia Issues

SOURCE: Long EM. The effect of a personalized music playlist on a patient with dementia and evening agitation. *Ann Longterm Care* 2016;24:31-33.

A substantial minority of the Medicare (31%) live in long-term facilities, and staff often have to contend with such issues as agitation, aggression, wandering, and other mood changes.

Patients who present behavior problems often are treated with antipsychotic medications, since few other tools are known to be beneficial, despite the observation that antipsychotic medications feature a well-established adverse effect profile, including increased risk of death. Might music therapy be beneficial?

The author presented a case report of a dementia patient who had been treated with antipsychotics. A nursing student visited with the patient and shared headphones with her that played popular music from the time of the patient's youth and young adulthood. Ultimately, the patient began to demonstrate progressively more involvement with the music, including singing along and tapping her fingers. The previously reticent patient became progressively more communicative. Problem behaviors diminished to the point that caregivers discontinued antipsychotics (previous weaning efforts had failed).

I have had a similar experience with one 95-year-old dementia patient. She has been very religious through much of her life, and her personality blossoms forth if I bring in an old hymnal and sing songs with her (somehow, despite her inability to remember her own children or any specifics about her prior life, she remembers *dozens* of lengthy hymns).

Learning music that is meaningful to our patients is a time-intensive endeavor. On the other hand, problematic behavior issues also can be quite taxing. Clinicians might consider informing involved family members or caretakers of the potential positive effects of music therapy. ■

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