Clinical Briefs in
Primary Care

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Evidence-based updates in primary care medicine

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Systemic Markers of Hidradenitis Suppurativa

SOURCE: Hessam S, et al. *J Am Acad Dermatol* 2015;73:998-1005.

Hidradenitis suppurativa sometimes has been called a "heart sink" diagnosis. Patients often suffer chronic bacterial infections in multiple body sites (axillae, chest wall, perineum, glutei) that are unsightly, often painful, and require multiple, often not fully satisfactory treatments. Recently, insights into some of the underlying immunologic pathologies in hidradenitis have prompted utilization of systemic pharmacotherapies usually reserved for patients with rheumatoid arthritis or advanced psoriasis. Though such rheumatologic immunomodulatory agents are expensive, and not without risk, the serious disease burden of hidradenitis, coupled with the generally poor results seen with "traditional" therapies, justifies their consideration. Probably the two most commonly used scales in the dermatological literature to stratify disease severity in hidradenitis are the Hurley stage scale (stages I, II, and III, with III being most severe) and the modified Hidradenitis Suppurativa Score. Both scores use characteristics noted on physical exam, such as number of lesions, presence of fistulas, presence of sinus tracts, etc. to assess severity. Hessam et al studied whether systemic markers of inflammation, such as C-reactive protein (CRP) and white blood cell (WBC) count, might correlate with disease severity as assessed through the two severity scales. By evaluating 275 cases of hidradenitis in which CRP and/or WBC had been reported, the investigators determined that there was significant correlation between CRP levels and both clinical scoring systems; WBC correlated only with Hurley stage scores. The authors suggested that measurement of CRP, an inexpensive and readily available test, in hidradenitis patients may enhance assessment of disease severity. ■

Can Antibiotic Exposure Cause Some Mood Disorders?

SOURCE: Lurie I, et al. *J Clin Psychiatry* 2015;7:1522-1528.

There might be a more important gut-brain connection than we have previously recognized. Animal data indicate that germ-free mice, whose intestinal tract is absent bacteriae, have magnified hypothalamic-pituitary-adrenal responses to stress, which may be normalized by restoration of the intestinal microbiome with probiotics (*Bifidobacterium infantis*). Similarly, germ-free mice differ in turnover of neurotransmitters associated with mood disorders (e.g., norepinephrine, dopamine, serotonin) from mice with established intestinal bacterial flora. Since gut flora alteration through antibiotic administration is a commonplace experience for most adults, might such exposures, by altering the intestinal microbiome, also be associated with mood disorders in humans? Lurie et al performed a case-control study using medical records from a very large database in the United Kingdom inclusive of the interval from 1995-2013. Patients with depression (n = 202,974 with 803,961 age- and sex-matched controls), anxiety (n = 14,570 with 57,862 matched controls), and psychosis (n = 2690 with 10,644 matched controls) were compared for likelihood of having received an antibiotic prescription at least 1 year prior to the recorded mental health diagnosis. Patients who had received a prescription for penicillin, cephalosporin, or quinolone were more than 20% more likely to incur depression, which increased to 40% more likely if multiple penicillin prescriptions had been issued. Similar odds ratios for anxiety occurred in relation to penicillin and sulfa drugs. Psychosis was not associated with antibiotic administration. Indeed, all antibiotic classes studied demonstrated increased risk for subsequent incident depression. Of course, it could be that persons with anxiety and depression, even in the pre-morbid state, might be more likely to become ill and receive an antibiotic prescription, nullifying a cause-and-effect relationship. Until the causal relationship between antibiotic administration and mental health is better understood, clinicians could consider adding still another rationale for why we might need to be ever more judicious about the appropriate use of antibiotics. ■

Benefits of On-demand Antiretroviral Pre-exposure Prophylaxis Among MSM

SOURCE: Molina JM, et al. *N Engl J Med* 2015;373:2237-2246.

There is no doubt that continuous pre-exposure prophylaxis (PrEP) with antiretroviral therapy in HIV-discordant men who have sex with men (MSM) substantially reduces the risk of seroconversion (> 40%). Curiously, similar trials among heterosexual women have not demonstrated the same risk reduction. Experts opine that failed efficacy in this population might be attributed to poor compliance. Might PrEP administration timed immediately before

and after sexual activity, rather than daily, be effective? Molina et al randomized MSM (n = 400) to antiretroviral treatment (tenofovir + emtricitabine) or placebo administered before and after sexual activity. The method of administration was two pills 2-24 hours before sex, a third pill 24 hours after the first dose, and a fourth pill 24 hours later. At a median of 9.3 months follow-up, there was a relative risk reduction in incident HIV infection of 86% (two cases in the antiretroviral group vs 16 in the placebo group). These results stack up very favorably with continuous prophylaxis trials, and may be less cumbersome for some patients to administer. The authors cautioned that early enthusiasm for treatment might support better adherence, which could wane over time and potentially reduce efficacy. ■

Can Vitamin D Deficiency Cause Hypertension?

SOURCE: Chen S, et al. *J Am Soc Hypertens* 2015;9:885-901.

Should we just cut to the chase and accept that vitamin D deficiency causes everything? That's the way it seems these days. Chen et al made a convincing case for at least a potential etiologic role of vitamin D in development of hypertension. Premises for consideration of vitamin D in relationship to hypertension include the observation that persons with less opportunity for vitamin D metabolism as a result of living in higher latitudes, having skin of color, or living in a colder climate with less outdoor sun exposure manifest a higher prevalence of essential hypertension. As part of "proof of concept," one clinical trial enhanced vitamin D through ultraviolet B radiation in vitamin D-deficient patients, resulting in lower blood pressure. While it should seem simple to test the vitamin D-hypertension relationship hypothesis, the results of 40 randomized trials addressing the issue have been mixed. The authors provided some explanation for this by noting that younger hypertensives (< 45 years of age) have more effective counterregulatory mechanisms for maintaining vascular tone than older patients, and, hence, vitamin D repletion in younger patients has less effect on blood pressure. Since most trials have incorporated populations of diverse age, younger patients may have diluted potential blood pressure effects of vitamin D repletion. The authors noted that vitamin D deficiency tends to lead toward vasoconstriction, a common component of essential hypertension. Perhaps identification of particular populations that are strong responders (and elimination of non-responder groups from clinical trials) will define better a therapeutic role for the prevention or treatment of hypertension with vitamin D. ■

Why We Can't Allow Physical Exam Skills to Languish

SOURCE: Verghese A, et al. *Am J Med* 2015;128:1322-1324.

With more highly evolved and readily available technology at our fingertips, it is sometimes tempting to let the echocardiogram sort out the abnormal heart sounds we detected, or allow the pelvic ultrasound to inform whether the uterus is enlarged, or short-cut parts of the physical exam we anticipate to be unlikely sources of pertinent information. At the same time, there may not be large-scale clinician awareness that a textbook of *Evidence-based Physical Diagnosis* even exists. (McGee, S. *Evidence-based Physical Diagnosis*, 3rd Edition. Philadelphia: Elsevier Saunders Publishers; 2012.) Could over-reliance on technology lead to meaningful errors? Verghese et al reported on 208 vignettes that were volitionally reported to them in response to a survey soliciting instances of oversights related to the physical exam. The most common consequence of an inadequate physical exam was missed/delayed diagnosis. However, unnecessary treatment, delay in treatment, unnecessary exposure to radiation or contrast, and complications related to treatment were also reported. Commonly missed items included abdominal masses, pregnancy, neurologic findings, murmurs, adenopathy, breast masses, heart failure, and herpes zoster. The authors reported that most of the cases in which inadequate physical examination led to consequences were the result of simply not performing the appropriate physical exam (rather than, for example, misinterpretation of an appropriately performed exam). The authors made a case for reminding clinicians that appropriate physical examination skills need to be taught and maintained. Inadequate performance of the physical exam, as documented here, can lead to important consequences. ■

Teasing Relationships Between Uric Acid, Fructose, and Hypertension

SOURCE: Madero M, et al. *J Am Soc Hypertens* 2015;9:837-844.

Uric acid has been under scrutiny for decades since its identification as a cardiovascular risk factor in the Framingham Heart Study. Whether elevations in uric acid are causally related to cardiovascular disease continues to be hotly debated. Elevations of plasma and intracellular uric acid are associated with higher blood pressure. Similarly, fructose, especially high-fructose corn syrup, has been suspect for its contribution to metabolic syndrome. Since fructose leads to increased intracellular and serum uric acid, a plausible pathologic pathway is evident. Madero et all performed a two-step, controlled trial among 72 obese prehypertensive patients to examine the sequential effect of restricted dietary fructose for 4 weeks, followed by the addition of allopurinol 300 mg/day for another 4 weeks, compared to a control group. All subjects were advised to restrict sodium. There was a trend for greater blood pressure reduction in the low-fructose diet group that did not achieve statistical significance. A post-hoc analysis of the second step of the trial (adding allopurinol to the diet) produced a reduction in office systolic blood pressure compared to the control group, but not in systolic blood pressure as measured by ambulatory blood pressure monitoring, which is considered more accurate and a better predictor of adverse effects of blood pressure. The roles of fructose restriction and allopurinol need more clarification. ■

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