Clinical Briefs in Primary Care™

Evidence-based updates in primary care medicine

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I Wish I Knew the Best BP for Hypertensive Senior Citizens

Source: Mohebi R, et al. *J Am Soc Hypertens* 2014;8:491-497.

The joint national committee (for purists, AKA "the group originally assigned to create JNC8") suggests that for persons aged ≥ 60 years, systolic blood pressure (SBP) should be lowered to < 150 mmHg. Is this the right number? After all, the relationship between SBP and cardiovascular disease (CVD) demonstrated in epidemiologic observational studies appears to be linear, so might CVD risk be better reduced by achieving lower SBP than simply "< 150 mmHg"?

To address this question, Mohebi et al followed a population of senior citizens (n = 1845) for approximately 10 years, looking at the hazard ratio for suffering a CVD event or mortality when comparing various levels of BP to a BP of 120/80 (which they designate as ideal BP). All study participants were aged ≥ 60 years at baseline (mean age = 66 years), and ostensibly free of CVD.

In this population, persons with prehypertension were not at demonstrably greater risk than persons with ideal BP. However, when SBP was 140-150 mmHg, risk for CV events was more than 1.5 times as great as SBP 120 (even though there was no increased mortality signal).

Based on these observations, the authors suggest that the risk of CV events even at a SBP of 140-150 is substantially greater than "ideal BP." At the same time, they acknowledge that clinical trials in senior citizens attempting to clarify whether lower BP levels will improve outcomes more than simply attaining < 150 mmHg have been inconsistent. ■

Be Careful Before Placing Confidence in a Urine Drug Screen that is PCP Positive

Source: Fischer M, et al. *J Clin Psychiatry* 2014;75:7:728-730.

The approach to management of a patient who incurs a positive urine drug test (UDT) screen for an illicit substance is complex. It is even more complex, however, if false positives could be the explanation.

Fischer et al report on their experience with 40 psychiatric patients found to be phencyclidine (PCP, also called "angel dust") positive on UDT. Out of this population, only one patient confirmed taking PCP. The others were receiving psychiatric medications known to potentially produce a false-positive result for PCP. The authors report that the list of medications potentially causing a false-positive PCP UDT — most of which are used for psychiatric disorders — is substantial, and includes lamotrigine, tramadol, ibuprofen, imipramine, diphenhydramine, venlafaxine, and others.

This particular report, however, draws attention to another psychiatric medication, chlorprothixene, which they found to be the most common cause of a false-positive UDT for PCP, being associated with 16 of the 40 cases (venlafaxine was associated with 14 cases). Chlorprothixene has not previously been reported as a cause of false-positive PCP UDT.

These results must be considered preliminary because the investigators did not confirm the absence/presence of actual PCP by a highly sensitive method such as liquid chromatography. Nonetheless, these findings support consideration of chlorprothixene and other commonly used psychiatric drugs as the cause of false-positive PCP UDT results. Positive PCP results on UDT in a patient who denies using PCP may require confirmation with more sensitive assays than are typically used in routine UDT. ■

The Ongoing Salt Saga

Source: Mente A, et al. *N Engl J Med* 2014;371:601-611.

If you thought that another very large clinical trial would finally settle uncertainties about salt — well, I hate to disappoint you. Opinions about the role of salt in cardiovascular disease range from "there is little relationship" to "the relationship is strong and consistent," with all sorts of conjecture in between.

Mente et al report on data obtained from 18 different countries in which a single morning urine specimen measurement of sodium and potassium was used as a metric for dietary ingestion of those same electrolytes. They found a positive linear relationship between salt ingestion and blood pressure (BP), such that every 1 g/d increase in sodium was associated with a 2.11 mmHg increase in SBP.

Their data did not, however, demonstrate a "one size fits all" linearity. Persons with the highest sodium ingestion (> 5 g/d) demonstrated an almost 4-fold greater increment in BP per gram of sodium consumption than persons at the lowest levels (< 3 g/d sodium). Also, old-

er persons and persons with pre-existing hypertension were more sensitive to BP-raising effects of sodium.

Potassium ingestion was inversely associated with BP. So are we *finally* finished with this roller coaster-like journey about sodium? Yes — well, that is until you turn the page on that article in the *New England Journal of Medicine* to find that the very next article also examined sodium in more than 100,000 persons, and did *not* come up with the same answer — oh well, we'll keep searching. ■

Is Type 2 Diabetes Induced by Psychological Stressors?

Source: Virtanen M, et al. *Diabetes Care* 2014;37:2091-2097.

Although the commonly recognized primary predictors of type 2 diabetes (T2DM) include obesity and insulin resistance, it is less clear why some folks with obesity and/or insulin resistance progress to T2DM and others do not. Could psychological stress be a predictor? Results from the Whitehall II Cohort Study suggest that this is indeed the case.

The Whitehall II Cohort Study is comprised of adults employed by the London, England, department of civil service (n = 6895 men and 3413 women) followed prospectively. Data were obtained from a subpopulation of this cohort during various cycles (average observation cycle = 5.46 years) from 1991-2009 to ascertain incidence of T2DM in previously non-diabetic subjects. Psychological stress was measured with the General Health Questionnaire (GHQ-30); a GHQ-30 score > 4 was categorized as "stressed." Proclivity to develop diabetes was further stratified into quartiles by the Framingham Offspring T2DM Risk Score (FOTRS).

Among prediabetic adults in the highest quartile of FOTRS, the adjusted odds ratio for developing T2DM was more than 2-fold greater in stressed individuals than in persons with low stress scores. The mechanism(s) by which stress increases progression to T2DM is not understood. The authors posit that interventions designed to prevent progression from prediabetes to diabetes might well show greater consideration for the potential impact of emotional stressors like depression and anxiety. ■

Distinguishing Malignant Melanoma from Benign Lesions with a Skin Patch Test

Source: Gerami P, et al. *J Am Acad Dermatol* 2014;71:237-244.

All of us in primary care who have been faced with the dilemma of ascertaining whether a particular lesion on the skin of a patient is benign or malignant know that, in the absence of a biopsy, we can rarely respond with certainty. Of course, we would rather *not* biopsy a benign lesion unnecessarily because of time, expense, discomfort, and cosmetic concern for the patient. On the other hand, we don't *ever* want to mistakenly allow a cutaneous malignancy, particularly malignant melanoma, to stay on the skin without being identified.

Gerami et al report on the use of a skin patch to diagnose melanoma on the basis of mRNA profiles. Having obtained mRNA "signatures" from multiple prior cases of malignant melanoma in their study sample, subjects had an adhesive patch placed above the lesion in question, which was vigorously rubbed to create adhesion of skin cells to the patch, which were then analyzed for mRNA. After removing the patch, lesions were biopsied to confirm their pathology.

The sensitivity of skin patch-retrieved mRNA diagnosis for melanoma was 97.6%. Hence, having a negative skin patch mRNA test essentially excluded melanoma. The authors point out that such technology could meaningfully reduce unnecessary skin biopsies for questionable lesions. ■

High-dose Influenza Vaccine vs Standard-dose for Seniors

Source: DiazGranados CA, et al. *N Engl J Med* 2014;371:635-645.

The highest morbidity and mortality consequences of influenza occur in senior citizens. The efficacy of "standard" flu vaccine varies depending on the outcome that is examined. For instance, as has been best demonstrated in nursing home trials, even when standard-dose flu vaccine fails to prevent clinical disease, it mitigates disease severity enough to reduce mortality. Evolving vaccines, such as the high-dose influenza vaccine, are trying to improve on the already impressive results of earlier versions.

High-dose influenza vaccine (HDVax) contains four times the amount of hemagglutinin as standard-dose vaccine (SDVax). It has already been established that higher antibody titers are achieved with HDVax than SDVax, but whether that translates into improved protection from influenza has not been fully clarified.

This very large randomized, double-blind, active-controlled trial (n = 31,989) compared HDVax vs SDVax through two influenza seasons in North America. Both vaccines were highly effective, since < 2% of recipients of either vaccine contracted clinical influenza. HDVax was found to be superior to SDVax for the primary trial endpoint (acquisition of documented clinical influenza), showing a 24% lower frequency than SDVax. As previously demonstrated, higher antibody levels were also achieved with HDVax.

Before we celebrate the 24% risk reduction with HDVax, recall that this is a *relative* risk reduction. The *absolute* risk reduction was *very small* (0.5%), translating into a number needed to treat of 200. Whether using HDVax instead of SDVax is a worthwhile investment — since this trial indicates that 200 persons must be treated with HDVax instead of SDVax to prevent one case of clinical influenza — will require further consideration, especially since there was no difference in mortality between the groups. ■

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