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The essential monthly primary care update

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A Strategy to Reduce Cardiovascular Disease by More Than 80 Percent

Source: Wald NJ, Law MR. *Prog Cardiovasc Dis*. 2003;46:31-38.

Despite impressive results in cardiovascular risk reduction by applying an individual treatment (eg, statin, antihypertensive), the effect of multiple risk factor reduction has been much more elusive to quantify. Wald and Law suggest that the literature supports consideration of a combination product they call the Polypill which is a multicomponent pill containing treatments which have demonstrated efficacy to reduce CV end points by means of LDL reduction, blood pressure control, attenuation of platelet aggregability, and reduction of homocysteine (although data referable to homocysteine is predominantly observational at this time). They base their suggested composition of the Polypill upon numerous large randomized, controlled trials and metaanalyses.

Their suggested Polypill would contain either atorvastatin 10 mg or simvastatin 40 mg, 3 different antihypertensives at half-standard dose (thiazide + ARB + CCB would be best tolerated, but thiazide + beta blocker + ACE would be less expensive, albeit at almost triple that adverse effect incidence profile), folic acid 800 mg and 75 mg of ASA. Wald and Law are remarkably optimistic in their anticipation of benefits for persons older than 55 without previous CV end points: They claim, "As 96% of deaths from IHD or stroke occur in people aged 55 and over, treating everyone in this group would prevent nearly all such deaths." They go on to opine that risk factor measurement prior to institution of the Polypill would be unnecessary, since risk reduction has been demonstrated regardless of initial risk level. Wald and Law acknowledge the radical nature of their suggestions, but support the rationale with highly attractive potential benefits. ■

Pearly Penile Papules: Still No Reason for Uneasiness

Source: Hogewoning C, et al. *J Am Acad Dermatol*. 2003;49:50-54.

It is not uncommon for adult men to present to clinicians with lesions on their penis, which ultimately turn out to be pearly penile papules (PPP). These lesions appear around the margins of the glans and have been sometimes mistaken for condylomata from human papilloma virus (HPV). Indeed, some early reports misattributed PPP to HPV. Recent polymerase chain reaction specimens have failed to demonstrate HPV in PPP. Pathologic and histologic studies have shown that these small, punctuate lesions are angiofibromata, are covered with normal squamous epithelium, and may occur on the glans or corona of the penis. Because these are normal structures, patients who present with PPP should be reassured that no treatment is required.

In this trial, Hogewoning et al assayed PPP lesions in adult men (n = 71) and were unable to find any association between PPP and HPV. In the occasional case where HPV was detected in other, non-PPP skin lesions, the HPV varieties were those of low risk for carcinogenesis. PPP is an innocent cutaneous lesion, which does not have precancerous potential, nor does it predict involvement with HPV. Clinicians should reassure concerned patients about the benignity of the disorder. ■

The Epidemiology of Major Depressive Disorder

Source: Kessler RC, et al. *JAMA*. 2003;289:3095-3105.

The first major national population survey to establish the demographics of depression using DSM III criteria occurred 1990-1992 and reported a lifetime prevalence of 14.9%, with 12 month prevalence of 8.6%. Since that report, an evolution of diagnostic criteria (ie, DSM IV) coupled with an enhanced public and professional awareness of the seriousness, prevalence, and treatability of depression, have occurred. These changes were pertinent for a new national survey to update prior information. The National Comorbidity Survey (NCS) is data collected from face-to-face interviews with a representative cross-section of the adult American public (n = 9090) in 2001-2002.

According to NCS data, the lifetime prevalence for major depressive disorder was 16.2%, which equates to 32-35 million Americans affected during their lifetime. Disturbingly, the number of days "out of role" because of depression was more than twice that seen for most other chronic conditions. Of all the persons who had suffered depression within the last 12 months, slight-

ly more than half had received treatment for it. Depression remains a prevalent and costly condition in America. ■

Urinary Tetrahydroaldosterone as a Screen for Aldosteronism

Source: Abdelhamid S, et al. *Am J Hypertens*. 2003;16:522-530.

It has recently been suggested that a substantial minority of persons with hypertension—as many as 1 out of 7 or 8—suffer overlooked primary hyperaldosteronism (PHA) as an etiology. Although unprovoked hypokalemia, when present, is a useful stimulus to direct investigation toward PHA as a cause, the inconsistency of this finding, coupled with the frequency of other equally rational explanations for hypokalemia present in hypertensive patients (eg, diuretic therapy), conspire to obscure the diagnosis.

A variety of biochemical diagnostic tests have been used to establish the diagnosis of PHA, including plasma rennin-to-aldosterone ratio, plasma aldosterone concentration, 24-hour urinary aldosterone-18-glucouronide, and free aldosterone. Abdelhamid and colleagues sought to prospectively compare the measurement of 24-hour urinary tetrahydroaldosterone (THA), a primary hepatic metabolite of aldosterone, with other commonly used diagnostic measures in a population (n = 1976) of hypertensives, compared to controls.

The diagnostic test with the best sensitivity (96%) and specificity (95%) for PHA was THA, which compared very favorably with plasma aldosterone (89% and 90%), 24-hour urinary free aldosterone (87% and 91%), plasma aldosterone-to-renin ratio (85% and 85%), and even the combination of the latter 2 tests (82% and 85%). Based upon these data, Abdelhamid et al suggest that THA is the appropriate initial best diagnostic test; in the uncommon scenario of a false-negative THA, measuring urinary free aldosterone and aldosterone-18-glucuronide would discover essentially all of the other PHA cases. ■

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Finasteride and Prostate Cancer

Source: Thompson IM, et al. *N Engl J Med*. 2003;349:215-224.

It is apparent that androgenic hormones, in particular dihydrotestosterone (DHT), are participants in the generation of prostate cancer (PCA). Since 5-alpha-reductase inhibitors (5ARI) like finasteride (Proscar) and dutasteride (Avodart) are well demonstrated to reduce levels of DHT and have a favorable effect on the progression of BPH, the idea that such agents might also favorably affect development of PCA has been conceptually appealing for several years.

In the Prostate Cancer Prevention Trial, men aged 55 years or older (n = 18,882) with normal digital rectal examination (DRE) and serum PSA (< 3.0 ng/mL) were randomly assigned to either 5ARI (finasteride) or placebo and followed for 7 years. Men underwent prostate biopsy if an abnormal DRE or PSA elevation (> 4.0 ng/mL) occurred during follow-up. For men who were receiving 5ARI, the PSA was appropriately adjusted (measured PSA multiplied by 2.3) due to the well-known PSA-reducing effect of 5ARI treatment.

PCA was found in 18.4% of the 5ARI group, as opposed to 24.4% of the placebo group, indicating a statistically significant 25% reduction in prevalence. PCA with high Gleason scores (ie, highly aggressive) were seen significantly more frequently in the 5ARI than placebo group (37% vs 22%), but overall there was a net reduction in all PCA. Erectile dysfunction, reduced ejaculate volume, loss of libido, and gynecomastia were more frequent in the 5ARI group; BPH and related symptoms, urinary retention, need for invasive prostate procedures, and UTI were more frequent in the placebo group. Finasteride has been demonstrated to prevent or delay the onset of PCA; for men who seek clinician's advice on such treatment, it will be important to acknowledge the slight increase of aggressive PCA tumor incidence and other potential adverse effects that need to be weighed in the risk benefit analysis. ■

Impermeable Bed Covers in Patients with Allergic Rhinitis

Source: Terreehorst I, et al. *N Engl J Med*. 2003;349:237-246.

Sufferers of allergic rhinitis (ALR) are often sensitive to a variety of allergens, of which house-dust mites are a commonplace troublemaker. The 2 most common offending house-dust antigens, *Dermatophagoides pteronyssinus* and *D farinae*, are readily measured in samples of dust from floors and fabric. Although numerous environmental control measures have been advocated for patients with dust and mold allergy, their efficacy in producing symptom reduction is only scantily supported.

This trial included patients with ALR (n = 279) who were randomly assigned to impermeable bedding covers (which reduce house-dust mite populations) vs standard coverings (placebo). Outcomes measured included concentrations of house-dust mite antigens, as well as clinical symptoms, over 12 months' observation.

Despite reductions in concentration of house-dust mite antigen, no clinically meaningful improvements in ALR symptom scores were seen. Because substantial amounts of time, energy, and economic resources are spent upon environmental manipulation for persons with allergy, these negative outcomes should stimulate reappraisal of the role of tools like impermeable mattress covers in the management of AR ■