

# Clinical Briefs in Primary Care<sup>™</sup>

The essential monthly primary care update

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## Functional Decline in Peripheral Arterial Disease

Source: McDermott MM, et al. *JAMA*. 2004;292:453-461.

PERIPHERAL ARTERIAL DISEASE (PAD) may be stratified in severity by the ankle-brachial index (ABI), measured by dividing the ankle systolic BP by the brachial systolic BP. Normally, this number is 1 or greater. Progressive atherosclerotic disease reduces the index, with a number < 0.9 considered indicative of PAD.

Observational studies from prior decades may have given the impression that PAD is a relatively static disorder, with as few as 15-30% of subjects experiencing symptom progression over intervals as long as 10 years. However, the lack of discernible symptomatic worsening might actually reflect a reduction in activities which induce symptoms, rather than lack of disease progression.

McDermott and colleagues studied subjects older than age 55 (n = 676) with PAD as demonstrated by ABI < 0.9. Functional status over time was measured by means of the 6-minute walk performance, usual-pace walking velocity, and fastest-pace walking velocity.

The presence of PAD, whether symptomatic or not, was associated with decrements in the 6-minute walk performance over time. For symptomatic PAD patients, performance declines were proportional to the degree of baseline ABI. Even amongst asymptomatic persons with PAD, the likelihood of ultimately being unable to walk was almost 4-fold greater than persons without PAD. Previous guidance that minimized the importance of disease progres-

sion may have overlooked and seriously underestimated the functional consequences of even asymptomatic PAD. ■

## Topical Capsaicin for Chronic Pain

Source: Mason L, et al. *BMJ USA*. 2004;4:349-358.

TOPICAL ANALGESICS, SUCH AS CAPSAICIN (CAP), methylsalicylate, and transdermal lidocaine, are agents which are applied topically for a local effect, as opposed to agents applied topically for a systemic effect (eg, transdermal fentanyl). Topical analgesics have recently enjoyed greater application in primary care, perhaps to some degree due to the endorsement of agencies such as the American College of Rheumatology, whose guidelines include CAP as foundation therapy for osteoarthritis of the knee.

Mason and colleagues performed a metaanalysis of double-blind placebo controlled trials of CAP used for neuropathic pain (6 trials; n = 656) or musculoskeletal pain (3 trials, n = 368). Clinical success was defined as approximately a 50% reduction in pain. Adverse effects monitored included local adverse events and withdrawal due to adverse events.

CAP was superior to placebo for both pain syndromes. For example, the mean number of persons achieving at least 50% reduction in neuropathic pain at 4 weeks was 57% vs 42% with placebo, and similar results were seen in musculoskeletal syndromes.

The rate of adverse events leading to withdrawal was 13% in CAP subjects (3% in placebo). Overall, 54% of patients experienced some adverse local event in 4-8 week trials. Although the positive effects of

CAP are modest, some patients achieve substantial benefit, and CAP treatment may reduce the need for concomitant systemic pharmacotherapy. ■

## Topical Tacrolimus Therapy for Vitiligo

Source: Grimes PE, et al. *J Am Acad Dermatol*. 2004;51:52-61.

VITILIGO (VIT) IS A DISORDER characterized clinically by one or more skin sites of depigmentation caused by loss of melanocyte activity. Demonstrated etiologies include genetic factors, autoimmune disorders, and viral infections, although in most cases the underlying pathology remains elusive. Recently, the role of blood and cutaneous cytokine expression in VIT has received increasing attention, resulting in recognition of alterations in interleukin and tumor necrosis factor alfa in these patients.

Tacrolimus (TAC) is a topical immunomodulator currently used to treat atopic dermatitis. Its putative primary mechanism is immune modulation by inhibition of T-cell activation, resulting in decreased proinflammatory cytokine production and release. Based upon favorable results from a small pilot study in VIT, Grimes et al performed this trial of TAC in subjects with VIT.

All subjects (n = 19) applied TAC as 0.1% ointment twice daily for 24 weeks. In addition, they used sunscreen (SPF 30 with Parsol 1789) each morning. VIT disease severity was assessed on a 6-point scale.

The degree of repigmentation varied with tissue site, with greatest success on the face and neck (68% experiencing greater than 75% repigmentation). Cytokine

expression (which was elevated at baseline) showed a significant decrease over time with use of TAC. Tacrolimus shows promise as a therapeutic tool for VIT. ■

## US Prevalence and Impact on Axillary Hyperhidrosis

**Source:** Strutton DR, et al. *J Am Acad Dermatol.* 2004;51:241-248.

**T**HE DIAGNOSIS OF HYPERHIDROSIS, OR excessive sweating, is achieved by clinical inquiry rather than laboratory testing, though quantitative metrics are available for clinical research. Primary hyperhidrosis (HHD) can be manifest on the palms and soles, face, axillae, and other areas, and is felt to be secondary to sympathetic overactivity. Of course, persons who are anxious about, or embarrassed by, their HHD, tend to magnify their sweating because of further increases in sympathetic tone, heightening the intensity of their problematic symptoms.

The demographics of HHD are only weakly established, with most literature resources citing a single unpublished pilot study from the 1970s. Using data from a consumer survey, screening information

from 150,000 US households was obtained. HHD was sought whether formally defined by a clinician, or simply fitting clinical criteria as described by the screening instrument.

The HHD prevalence was determined to be 2.9%, which would equate to almost 8 million individuals in the United States adult population. No gender predilection was found, and average age of onset was 25. Half of HHD sufferers had axillary HHD. Only one-third had discussed the condition with their physician. Approximately one-third said that HHD was barely tolerable-intolerable; this same proportion reported frequent, relentless life interference with daily activities caused by HHD.

Numerous effective treatments for HHD are available, hence there is ample room for enhanced clinician communication with HHD sufferers.

## Mortality and Incidence of Cancer During 10-Year Follow-Up of the Scandinavian Simvastatin Survival Study (4S)

**Source:** Strandberg TE, et al. *Lancet.* 2004;364:771-777.

**A**LTHOUGH THE VALUE OF STATINS for both primary and secondary prevention of cardiovascular events is widely accepted, inconsistent background signals of disproportionate cancer risk have sporadically surfaced. For instance, prospective epidemiologic surveys have sometimes noted an increased cancer mortality risk in persons with the lowest cholesterol levels. Similarly, animal studies (rodents) sometimes show increases in cancer risk subsequent to cholesterol lowering. In 2 separate pravastatin trials (CARE and PROSPER), breast cancer and total cancer, respectively, were increased in statin recipients.

Reassuringly, meta-analyses from larger trials, including the Heart Protection Study (n = 20,000), do not demonstrate any increased cancer risk, but skeptics maintain a degree of circumspection due to the relatively short duration of lipid trials, generally 3-5 years in length.

The 4S trial was originally concluded in

1994, and Strandberg and colleagues now report on data at the conclusion of an extended follow-up. At a mean of 10.4 years, there was no suggestion of increased cancer risk. In fact, a trend towards lower cancer deaths in simvastatin recipients narrowly missed being statistically significant. Long-term follow-up confirms both the continued cardiovascular benefits, as well as neutral (trending towards favorable) effects on cancer mortality. ■

## Effects of Extended Outpatient Rehabilitation After Hip Fracture

**Source:** Binder EF, et al *JAMA.* 2004;292:837-846.

**F**OR SENIOR CITIZENS WHO DO NOT succumb to the sequelae of hip fracture (HFX), the long-term consequences remain daunting for most. Insurers may provide coverage sufficient only to sustain a patient to the point of being independently ambulatory, despite continued partial disabilities which may incur risk of future falls. Whether a high-intensity, long-term (6 months) rehabilitation program, including resistance training, provides better outcomes for HFX sufferers than a low-intensity, short-term program was studied in this report. All subjects (n=90) had undergone surgical treatment of a proximal femur fracture within the prior 16 weeks, and had completed a course of standard physical therapy.

The high intensity regimen included progressive resistance exercises for the upper and lower body; exercise sessions were scheduled 3 times weekly.

Persons in the control group were provided a home exercise protocol, guided by a single session in which they received instruction on how to perform the exercises at home (also recommended 3 times weekly).

The primary end point, physical performance and degree of disability, was significantly better for participants in the high intensity regimen. Although traditional exercise programs at home help HFX victims maintain functional status, long-term, high intensity regimens provide more favorable outcomes. ■

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