



# Therapeutics Today

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**Chronic Stable Angina** is a common clinical problem. A recent paper (*NEJM 2005;352:2524-33*) reviewed its diagnosis and management. Angina occurs when there is local myocardial ischaemia caused by inadequate coronary perfusion. It is usually, but not always, induced by increases in myocardial oxygen ( $O_2$ ) requirements. **Typical symptoms** of chronic stable angina include predictable and reproducible left anterior

chest discomfort (lasting 3-15 minutes) after physical activity, emotional stress or both; symptoms are worse in cold weather or after meals and are relieved by rest or sublingual glyceryl trinitrate. Chronic stable angina shows complete reversibility of symptoms and repetitiveness of anginal attacks typically for months to years. **Diagnosis** is based on the clinical history, a positive stress test and coronary atherosclerosis documented by angiography; however in early stages, angiography may appear normal. Atypical presentation of chronic stable angina (including night time pain, exertional dyspnoea, weakness or sweating) may occur in women, older patients and diabetics.

**Management of chronic stable angina** includes **lifestyle changes** such as a regular exercise programme (shown to produce better disease outcome than angioplasty in single-vessel coronary artery disease), dietary changes and smoking cessation. Active control of other risk factors (e.g. hypertension) is also warranted. **Pharmacotherapy** may be divided into two main groups. **Anti-anginal agents** are known to prolong the duration of exercise before the onset of angina and to decrease the frequency of anginal episodes. They include nitrates,  $\beta$  blockers and calcium channel blockers (CCBs).  $\beta$  blockers work primarily by decreasing myocardial  $O_2$  consumption, through reducing blood pressure, heart rate and myocardial contractility. CCBs and nitrates dilate coronary and systemic arteries and decrease cardiac work and  $O_2$  requirements. None of these agents has been shown to actually reduce myocardial infarction (MI) or cardiac death when used to treat chronic stable angina without prior MI. Underdosing with anti-anginal agents is common, therefore dose titration is important and combination therapy should be considered. However  $\beta$  blockers should not be combined with certain CCBs such as verapamil, because of the risk of bradycardia. **Vasculoprotective agents:** Aspirin (75-150mg) has been shown to reduce cardiac mortality and morbidity by 20-25%; statins have shown improved survival in patients with coronary artery disease - the target LDL cholesterol level in persons with chronic stable angina is  $<2.6\text{mmol/L}$  and  $1.6\text{-}1.8\text{mmol/L}$  for high-risk persons. ACE inhibitors may be used in angina patients with prior MI, in diabetics or in patients with impaired renal function who have no contraindications to their use. **Revascularisation** either via angioplasty or bypass surgery may relieve the symptoms of chronic stable angina but to date has not shown improved survival compared with lifestyle changes and vasculoprotective therapy.



**Vitamin E does not prevent cancer or cardiovascular disease.** The Women's Health Study recently evaluated the benefit of vitamin (vit) E in the primary prevention of cardiovascular (CVS) disease and cancer (*JAMA 2005; 294: 56-65*). Healthy women ( $n=39,876$ )  $\geq 45$  years were randomised to receive either vit E (600 IU) every second day or placebo, and followed up for an average of 10 years. Primary endpoints were total invasive cancer and a composite CVS disease endpoint (CVS death, non-fatal MI, non-fatal stroke). Results showed no overall difference in CVS outcomes between the groups (482 events for vit E vs. 517 for placebo) or in the incidence of cancer (1,437 cases for vit E vs. 1,428 for placebo). There was no difference in overall deaths between the groups. The authors state that these **results do not support use of vit E for primary prevention of either CVS disease or cancer in healthy women.** [Editor's note: these findings are in keeping with CVS studies such as the Heart Protection Study where vit E showed no cardiovascular benefit over placebo].



### ***Vaccine effective against Shingles - hope for the future?***

Herpes Zoster or shingles (HZ) is caused by reactivation of latent varicella-zoster virus within the sensory ganglia (after primary varicella infection). The incidence and severity of HZ and postherpetic neuralgia (PHN) increase with age, due to a progressive decline in cell-mediated immunity to the virus. A randomised placebo-controlled study (*NEJM 2005; 352: 2271-84*) evaluated the efficacy of an investigational zoster vaccine in prevention of HZ in adults (n=38,546) >60 years old. After a follow-up of 3 years, vaccinated persons showed a significant reduction, compared with controls, in the incidence of confirmed cases of HZ (n=315 vs. 642) and postherpetic neuralgia (n=27 vs. 80). There were more adverse reactions (ADRs) in the vaccinated group (mostly local reactions) but no difference in the rate of serious ADRs. **The potency of the investigational vaccine was 14 times that of the currently authorised varicella vaccine;** the authors believe that such a high potency vaccine will be needed to boost cell-mediated immunity in older persons and thereby reduce morbidity and longterm sequelae associated with HZ. [Editor's note: While we wait for this new vaccine, in addition to the use of antiviral agents, it has been proposed that the risk of PHN may be reduced by the early use of drugs such as TCAs during the acute HZ infection. (BNF 49<sup>th</sup> edn., *J Pain Symptom Manage 2004; 28:396-411, Drugs 2000;59;1113-26*)]



### ***Herbal remedies may interact with anti-rheumatic drugs.***

There is a risk of interactions between complementary remedies and conventional anti-rheumatic drugs because of high rates of polypharmacy and co-morbidity in rheumatology patients. A recent study (*Ann Rheumatol Dis 2005; 64: 790*) in 238 rheumatology patients showed that 105 patients (44%) had used herbal or OTC remedies in the previous 6 months including cod liver oil (n=83; 35%), glucosamine +/- chondroitin (n=50; 21%) and evening primrose oil (n=26; 11%). Twenty six (11%) were taking remedies that might interact with conventional drugs. These included **use of ginkgo biloba, garlic or devil's claw (all of which have anticoagulant effects) with NSAIDs or corticosteroids in 24 patients (increased risk of bleeding) and use of echinacea in 5 patients who were receiving disease modifying anti-rheumatic drugs (increased risk of hepatotoxicity).** Of interest 24/26 patients were unaware of the risk of harmful interactions and 10 had sought advice from a healthcare professional before starting the remedy. The authors state that more education is needed for healthcare professionals on potential interactions between rheumatology drugs and complementary therapies. [Editor's note: the NMIC has access to a number of data resources on alternative therapies and is happy to answer your queries].



### ***Talking to your doctor helps when you stop HRT!***

Since the publication of the Women's Health Initiative (WHI) and Million Women Studies, hormone replacement therapy (HRT) is now recommended for short-term treatment of menopausal symptoms only. A follow-up from the WHI combination HRT (cHRT) vs. placebo study was published recently (*NEJM 2005; 294: 183-93*). Women (n >8,000) who had received either cHRT or placebo for an average of 5.7 years provided data on current symptoms at 8-12 months post discontinuation of HRT. They reported a wide range of symptoms; prevalence was higher in the HRT group compared with placebo. Symptoms included pain and stiffness (37% vs. 22%), tiredness (21% vs. 12%), vasomotor symptoms (21% vs. 5%), depression (11% vs. 7%) and vaginal dryness (10% vs. 5%). Patients who had experienced moderate-severe symptoms at the start of the WHI study were more likely to report symptoms in this study. **Symptom management strategies included increased fluid intake, increased exercise, lifestyle and dietary changes (all >80% effective).** Medical interventions included a clinician visit, use of vaginal lubricants, complementary or prescription medicines. Of interest, complementary remedies such as vitamin E and herbal remedies were less effective (70%) than a clinician visit (>80%). Few women restarted HRT (4% vs. 1%). The authors recommend that alternative strategies to manage menopausal symptoms should be discussed with the patient.