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Iqbal Malik, Editor,

Ischaemic heart disease

Antioxidants may attenuate the benefits of lipid lowering

► In a three year, double blind trial, 160 patients with coronary disease, low high density lipoprotein (HDL) cholesterol concentrations, and normal low density lipoprotein (LDL) cholesterol concentrations were randomly assigned to receive one of four regimens: simvastatin+niacin (SN), antioxidant vitamins C and E plus carotene and selenium (A), simvastatin+niacin plus antioxidants (SNA), or placebos. The end points were arteriographic evidence of a change in coronary stenosis and the occurrence of major adverse cardiac events (MACE): death, myocardial infarction, stroke, or revascularisation. LDL and HDL cholesterol concentrations were unchanged in the A and placebo groups, but changed substantially (by -42% and +26%, respectively) in the SN group. The protective increase in HDL with SN was attenuated in the SNA group. This was reflected in greater progression of coronary artery disease and higher MACE rates with SNA: 24% with placebos, 3% with SN alone, 21% with A, and 14% with SNA.

▲ **Brown G**, Zhao X-Q, Chait A, Fisher LD, Cheung MC, Morse JS, Dowdy AA, Marino EK, Bolson EL, Alaupovic P, Frohlich J, Serafini L, Huss-Frechette E, Wang S, DeAngelis D, Dodek A, Albers JJ. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. *N Engl J Med* 2001;345:1583-92.

Vitamins may, however, lower restenosis rates ► Restenosis after PTCA is a major clinical problem, and apart from stents, no treatment has shown convincing benefits. Treatment with a combination of folic acid, vitamin B12, and pyridoxine significantly reduced homocysteine concentrations and decreased the rate of restenosis (9.6% v 37.6%, $p=0.01$) and the need for revascularisation of the target lesion (10.8% v 22.3%, $p=0.047$) after coronary angioplasty.

▲ **Schnyder G**, Roffi M, Pin R, Flammer Y, Lange H, Eberli FR, Meier B, Turi ZG, Hess OM. Decreased rate of coronary restenosis after lowering of plasma homocysteine levels. *N Engl J Med* 2001;345:1593-600.

Eat more often to lower cholesterol! ► Smaller, more frequent meals are healthier than one or two big meals. The LDL cholesterol was 0.15 mmol lower in those eating six times per day versus once or twice, once confounding factors had been adjusted for. This is of the same magnitude as achieved by putting people on a low fat diet, and would have the effect of reducing coronary heart disease (CHD) event rates by between 10-20%.

▲ **Titan SMO**, Bingham S, Welch A, Luben R, Oakes S, Day N, Khaw K-T. Frequency of eating and concentrations of serum cholesterol in the Norfolk population of the European prospective investigation into cancer (EPIC-Norfolk): cross sectional study. *BMJ* 2001;323:1286.

Broadening the use of ICDs and amiodarone ► This paper used published data to model the lifetime cost effectiveness of automatic implantable cardioverter-defibrillator (ICD) therapy and amiodarone treatment in reducing arrhythmic death post-myocardial infarction (MI). Using data from more than 3000 patients in the MITI registry, it suggests that they may be cost effective compared with no treatment in patients with left ventricular ejection fraction < 30% as long as ICDs reduce sudden cardiac death by at least 50% and amiodarone reduces total mortality by at least 7%. Both of these efficacies are supported by the literature. Neither amiodarone nor the ICD seemed cost effective in patients with well preserved ventricular function. Real data from trials are awaited.

▲ **Sanders GD**, Hlatky MA, Every NR, McDonald KM, Heidenreich PA, Parsons LS, Owens DK. Potential cost-effectiveness of prophylactic use of the implantable cardioverter defibrillator or amiodarone after myocardial infarction. *Ann Int Med* 2001;135:870-83.

Depression carries as much risk after CABG as a poor ejection fraction

► In a prospective study, 207 men and 102 women who had coronary artery bypass graft (CABG) surgery were followed for one year. Cardiac events included angina or heart failure that needed admission MI, cardiac arrest, CABG or coronary angioplasty (PTCA). A total of 63 patients (20%) met criteria for major depressive disorder. At one year, 17 (27%) of these patients had a cardiac event compared with 25 of 246 (10%) who were not depressed ($p < 0.0008$). In a Cox proportional hazard model major depressive disorder (risk ratio 2.3, 95% confidence interval (CI) 1.17 to 4.56), low ejection fraction (2.3, 95% CI 1.07 to 5.03), and female sex (2.4, 95% CI 1.24 to 4.44) were associated with adverse outcomes.

▲ **Connemey I**, Shapiro PA, McLaughlin JS, Bagiella E, Sloan RP. Relation between depression after coronary artery bypass surgery and 12 month outcome: a prospective study. *Lancet* 2001;358:1766-71.

Hypertension

How often should the BP be checked in non-hypertensive patients?

► Patients with optimum (< 120/80 mm Hg), normal (120-129/80-84 mm Hg), and high normal (130-139/85-89 mm Hg) blood pressure (BP) may progress to hypertension (140/90 mm Hg) over time. A stepwise increase in hypertension incidence occurred across the three non-hypertensive BP categories; 5.3% of participants with optimum BP, 17.6% with normal, and 37.3% with high normal BP aged below age 65 years progressed to hypertension over four years. Corresponding four year rates of progression for patients 65 years and older were 16.0%, 25.5%, and 49.5%, respectively. Obesity and weight gain also contributed to progression: a 5% weight gain on follow up was associated with 20-30% increased odds of hypertension. So, recheck yearly in the over 65s or if the BP is not below 120/80 mm Hg?

▲ **Vasan RS**, Larson MG, Leip EP, Kannel WB, Levy D. Assessment of frequency of progression to hypertension in non-hypertensive participants in the Framingham Heart Study: a cohort study. *Lancet* 2001;358:1682-6.

General cardiology

Left ventricular assist devices for end stage heart failure improve survival

► One hundred and twenty nine patients with end stage heart failure who were ineligible for cardiac transplantation were randomly assigned to receive a left ventricular assist device (68 patients) or optimal medical management (61). All patients had symptoms of New York Heart Association functional class IV heart failure. Kaplan-Meier survival analysis showed a reduction of 48% in the risk of death from any cause in the group that received left ventricular assist devices as compared with the medical treatment group (relative risk 0.52, 95% CI 0.34 to 0.78; $p=0.001$). The rates of survival at one year were 52% in the device group and 25% in the medical treatment group ($p=0.002$); however, these had fallen to 23% and 8%, respectively, by two years.

▲ **Rose EA**, Gelijs AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, Long JW, Ascheim DD, Tierney AR, Levitan RG, Watson JT, Ronan NS, Shapiro PA, Lazar RM, Miller LW, Gupta I, Frazier OH, Desvigne-Nickens P, Oz MC, Poirier VL, Meier P for the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) Study Group. Long-term use of a left ventricular assist device for end-stage heart failure. *N Engl J Med* 2001;345:1435-43.

Torsemide may be better absorbed than furosemide and so prevent admissions with heart failure ▶ The bioavailability of furosemide (furosemide) varies from 11–90%, while torsemide is usually above 80% after oral intake. In an open label study of 234 patients, readmission for heart failure was reduced (17% v 32%, $p < 0.01$), as was the total stay in hospital over the year of follow up (106 days v 296 days, $p = 0.02$).

▲ **Murray MD**, Deer MM, Ferguson JA, Dexter PR, Bennett SJ, Perkins SM, Smith FE, Lane KA, Adams LD, Tierney WM, Brater DC. Open-label randomised trial of torsemide compared with furosemide therapy for patients with heart failure. *Am J Med* 2001;111:513–20.

What patients feel about anticoagulation for AF ▶ Patients and doctors have a different perspective on what risk is acceptable. A survey of 63 physicians and 61 patients at high risk of stroke with atrial fibrillation (AF) showed that the minimum number of strokes that needed to be prevented in 100 patients over two years for warfarin to be justified was significantly lower for patients than for physicians (1.8 v 2.5, $p = 0.009$), whereas for aspirin there was no difference between patients and physicians (1.3 v 1.6, $p = 0.29$). The maximum number of excess bleeds acceptable in 100 patients over two years for use of warfarin and aspirin was significantly higher for patients than for physicians (warfarin 17.4 v 10.3; aspirin 14.7 v 6.7; $p < 0.001$ for both comparisons). Thus patients at high risk for AF placed more value on the avoidance of stroke and less value on the avoidance of bleeding than did physicians.

▲ **Devereaux PJ**, Anderson DR, Gardner MJ, Putnam W, Flowerdew GJ, Brownell BF, Nagpal S, Cox JL, Fahey T. Differences between perspectives of physicians and patients on anticoagulation in patients with atrial fibrillation: observational study. *BMJ* 2001;323:1218.

Basic research

New compounds that may reduce lipid levels further ▶ Despite the success of the statins at reducing LDL, there is still a need for new treatments to lower cholesterol. In this paper the authors identify a new compound that upregulates the transcription of the LDL receptor in human hepatocyte cell lines. When administered to hyperlipidaemic hamsters the compound reduced both LDL cholesterol and triglyceride concentrations by up to 80%, with a three fold increase in LDL receptor mRNA in the livers.

▲ **Grand-Perret T**, Bouillot A, Perrot A, Commans S, Walker M, Issandou M. SCAP ligands are potent new lipid-lowering drugs. *Nature Med* 2001;7:1332–8.

Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

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C Baker, E Barnes, V Bhatia, R Desilva, M Earley, K Fox, D Gorog, G Jenkins, R Kaprilian, A Kapur, M Khan, P Lambiase, V Markides, M Poullis, P Ramrakha, J Strange, B Wasan, H Walker

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November 2001;86:579–85. (Education in Heart)

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MF Dorsch, RA Lawrance, RJ Sapsford, N Durham, J Oldham, DC Greenwood, BM Jackson, C Morrell, MB Robinson, AS Hall

November 2001;86:494–8. (Cardiovascular medicine)

3 Joint British recommendations on prevention of coronary heart disease in clinical practice

December 1998;80(suppl 2):S1–29.

4 The diagnosis of hypertrophic cardiomyopathy

ED Wigle

December 2001;86:709–14. (Education in Heart)

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D Oakley

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9 Endocarditis: basics

SJ Eykyn

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S H Wong, N T Mulvihill, M Norton

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