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Medibytes

Medibytes offer readers short, informative synopses of important or interesting papers published in specialty and other general medical journals. They are edited by Dr J Ferguson.

ABBREVIATIONS Confidence interval (CI), impaired glucose tolerance (IGT), ischaemic heart disease (IHD), odds ratio (OR)

Malignant melanoma, sunbeds, cheap flights and education

The most recent figures from Cancer Research UK[1] suggest that between 1995 and 2004 the incidence of malignant melanoma rose by 43%, with an incidence in 2004 of 13 per 100,000 and a mortality of 2·5. This increase appears to be occurring mainly in young women between 20 and 39, and no similar trend has been seen over the past 30 years in British young men and older women aged 55 to 74. This has led to speculation that eliminating sunbeds would reduce the number of newly diagnosed cases in young women by about 25%.[2]

A recent survey in two local authority areas in Scotland[3] has found that the number of sunbeds emitting high levels of ultraviolet radiation has increased since the previous survey in 1998 and that the predominant users are young women. In Australia and elsewhere attempts have been made to license and regulate sunbed parlours, and a private members bill to license sunbeds in Scotland is part of the Scottish Government's programme for the present session. It is perhaps worth noting that several studies in Australia have shown the sunbed industry to flout the regulations.

However, the increased regulation of the sunbed industry ignores the fact that the greatest incidence occurs in middle-aged and older men and persons of lower economic status.[4] In the US, a four-fold increase has occurred in men between 55 and 64, and a somewhat greater increase in men over 65, between 1973 and 2002. In Scotland, between 1979 and 2003, the increase in incidence rate was also greater for men than women.[5] Compared with Poland and Italy, the higher incidence in Norway and Sweden would suggest that in the northern hemisphere the intense, intermittent sun exposure that occurs during vacations in the south is a major factor.

The good news is that the five-year survival rates in the US, Australia and Sweden exceed 90% and in Scotland rose from 58% in 1978 to 80% in 1993,[4] a trend that has continued.[5] The improvement is the quick result that can be achieved by early detection. Unfortunately, it will take decades for the promotion of sun protection and sunbed avoidance to produce similar results. A focus by government on the regulation of sunbeds must not avoid the need to implement other measures to make screening for skin lesions available to the high-risk members of the population, as well as the education of health professionals. A recent study from Australia suggested that the estimated average cost of screening and treating of men over 50 for melanoma and non-melanoma skin cancer would be about £11,000 per 1,000 – similar to that spent on breast cancer screening in Australia.[6] However, the incidence of melanoma in Australia may be three times greater[7] and the costs of screening in Scotland may be proportionately smaller. An interesting account on the use of sunscreens,[7] published in the *Journal* in 2005, made the important point that they do not protect against malignant melanoma but do reduce the risk of other skin cancers.

References

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6 Gordon L, Youl PH, Elwood M *et al.* Diagnosis and management costs of suspicious skin lesions from a population-based melanoma screening programme. *J Med Screening* 2007; **14(2):**98–102.
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JS Kelly

An aspirin a day keeps colorectal cancer away?

Although randomised trials have shown that aspirin reduces the short-term risk of recurrent colorectal adenomas in patients with a history of adenomas or cancer, its effectiveness in the primary prevention of colorectal cancer was not known. Given the prolonged nature of the adenoma carcinoma sequence, a longer-term follow-up of aspirin trials was therefore required. A group from the University of Oxford studied the effect of aspirin in two large randomised trials with reliable post-trial follow-up for more than 20 years: the British Doctors Aspirin Trial (n=5139, two-thirds allocated 500 mg aspirin for five years, one-third to open control) and the UK-TIA Aspirin Trial (n=2449, two-thirds allocated 300 mg or 1,200 mg aspirin for one to seven years, one-third placebo control).

Allocation to aspirin reduced the incidence of colorectal cancer (pooled hazard ratio 0·74, 95% CI 0·56–0·97, p=0·02 overall; 0·63, 0·47–0.85, p=0·002 if allocated aspirin for five years or more). However, this effect was only seen after a latency of ten years (years 10–19: 0·60, 0·42–0·87, p=0·007), was dependent on the duration of the scheduled trial treatment and compliance, and was

greatest 10–14 years after randomisation in patients who had had scheduled trial treatment of five years or more (0·37, 0·20–0·70, p=0·002; 0·26, 0·12–0·56, p=0·0002, if compliant). No significant effect on incidence of non-colorectal cancers was recorded (1·01, 0·88–1·16, p=0·87). In a systematic review of observational studies, regular use of aspirin or non-steroidal anti-inflammatory drugs was consistently associated with a reduced risk of colorectal cancer, especially after use for ten years or more, but this was only seen with use of 300 mg or more of aspirin a day, with diminished and inconsistent results for lower or less frequent doses.

In conclusion, the use of 300 mg or more of aspirin a day for about five years is effective in primary prevention of colorectal cancer in randomised controlled trials, with a latency of about ten years, which is consistent with findings from observational studies. As well as its use in cardiovascular disease, aspirin appears have a role in colorectal cancer chemoprevention, although clinicians should still be aware of its potential side effects, especially at the higher doses required.

From Flossmann E, Rothwell PM; British Doctors Aspirin Trial and the UK-TIA Aspirin Trial. Effect of aspirin on long-term risk of colorectal cancer: consistent evidence from randomised and observational studies. *Lancet* 2007; **369(9573)**:1603–13.

N Bhala

Cancer, schizophrenia and bipolar disorder

A nested case-control study examined the risk of six common cancers (breast, respiratory, colon, prostate, rectum and gastroesophageal) among patients with schizophrenia or bipolar disorder. Data were extracted from a primary care database (454 general practices), and 40,441 incident cases were matched demographically with general population controls. Confounding factors such as smoking and obesity were taken into account. After adjustment, bipolar patients did not differ from the general population, but among schizophrenic patients the risks of respiratory cancer was reduced (OR 0·53; 95% CI 0·34–0·85) and colon cancer increased (OR 2·90; 95% CI 1·85–4·57), and more so if taking antipsychotics (OR 4·08).

From Hippisley-Cox J, Vinogradova Y, Coupland C *et al.* Risk of malignancy in patients with schizophrenia or bipolar disorder. *Arch Gen Psychiatry* 2007; **64:**1368–76.

Management of co-morbid depression in primary care

This prospective, primary care-based Dutch study investigated whether patients newly diagnosed with depression (n=991) were managed differently if they had co-existing chronic physical illnesses, broadly categorised under 13 headings. Analyses took into account variation among practices, socio-demographic variables, past history of depression and psychiatric co-morbidity. The presence of ischaemic heart disease (72%) or cardiac arrhythmia (59%) was associated with less likelihood of any care for depression compared with physically healthy individuals (88%). No other significant differences emerged. Depression exerts a negative effect on heart disease so this finding indicates GPs need to be encouraged to manage depression more energetically in this group of patients.

From Nuyen J, Spreeuwenberg PM, Van Dijk L *et al.* The influence of specific chronic somatic conditions on the care for co-morbid depression in general practice. *Psychol Med* 2008; **38:**265–77.

G Masterton

Iron-overload-related disease in hereditary haemochromatosis

HFE alleles related to hereditary haemochromatosis were studied in 29,676 Australian subjects of north European origin aged 40–69 years; 203 were homozygous for C282Y (0·68%), 3,295 were heterozygous for C282Y (11·1%) and 719 (2·4%) were compound heterozygotes (C282Y/H63D). Eighty-two per cent of male homozygotes had serum ferritin >300 ug/l (normal 20–300), 55% of female homozygotes had levels >200 ug/l (15–150) and 28% of male homozygotes, but only 1·2% of female homozygotes, had iron-overload-related disease. Male homozygotes with serum ferritin >1,000 ug/l had significantly more symptoms and more increases of serum transaminase activity. One compound heterozygote had iron-overload-related disease, but all others with iron-overload-related disease were C282Y homozygotes. Male C282Y homozygotes are at significant risk of iron-overload-related disease; female homozygotes are at much less risk and others are not at significant risk. C282Y homozygote mortality was not greater than those without C282Y (hazard ratio 1·04), and iron-overload-related disease was not related to excess alcohol intake.

From Allen KJ, Gurrin LC, Constantine CC *et al.* Iron-overload-related disease in HFE hereditary hemochromatosis. *N Engl J Med* 2008; **358**:221–30.

Back to dietary basics – how far back to go?

Diet, impaired glucose tolerance (IGT), type 2 diabetes mellitus and ischaemic heart disease (IHD) are closely related. A Mediterranean diet (whole-grain cereals, vegetables, fruits, legumes and fats rich in monounsaturated fatty acids) is usually advised in IGT and IHD, but a diet derived from a much earlier period in human evolution, the Palaeolithic diet (lean meat, fish, shellfish, fruit, vegetables, roots, eggs and nuts but not grains, dairy products, salt or refined fats and sugars), may be better. This Swedish study compared the Palaeolithic and Mediterranean diets in 29 men with IHD and IGT or diabetes mellitus over a 12-week period. There was a 28% decrease in the oral glucose tolerance test area under the curve glucose (0–120 mins) with the Palaeolithic diet compared with an 8% decrease with the Mediterranean diet. Weight, waist circumference and insulin tolerance improved in both groups.

From Lindberg S, Jonsson T, Granfeldt Y *et al.* A Palaeolithic diet improves glucose tolerance more than a Mediterranean-like diet in individuals with ischaemic heart disease. *Diabetologia* 2007; **50(9):**1795–807.

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