

tamoxifen in younger women (aged 35) in some preventive trials. Information from epidemiological and laboratory studies suggests that the breast tissue is most receptive to carcinogens early in puberty<sup>15,16</sup> and antihormonal prevention is most effective nearer the time of the insult.<sup>17</sup> This is why young women are being recruited. Only young women at the highest risk of developing breast cancer, however, are being included in the prevention studies.

Carefully monitored adjuvant clinical trials can guide the use of tamoxifen in normal women. The physiological impact of tamoxifen in premenopausal women warrants closer attention; the drug's effects on bone density and lipid concentrations might tip the balance of risks and benefits in its favour.

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## Long term management of patients after splenectomy

### *Pneumococcal vaccine, lifelong penicillin, and avoidance of protozoal infections*

For centuries it has been known that the spleen is not essential to life. But it represents about a quarter of the body's lymphoid tissue and, among other things, filters encapsulated organisms from the blood. Overwhelming infection may occur after removal of the spleen: the clinical syndrome comprises fulminant bacteraemia, disseminated intravascular coagulation, multiple organ failure, severe hypoglycaemia, and often rapid death.<sup>1</sup> Its reported incidence after splenectomy varies from 0.9% to 69%<sup>2,3</sup>; mortality may exceed 50%.<sup>4</sup>

While the syndrome is most likely to occur within the first few years of surgery, especially in children and immunosuppressed patients, cases have occurred many years after splenectomy for trauma and other non-malignant conditions.<sup>5,6</sup> Carrying out a proper randomised trial to decide how long prophylaxis should be given is impossible, but an analysis of published data suggests that it should be given to patients for the rest of their lives. We cannot agree with Holdsworth *et al*, who recently concluded that in people with no underlying pathology removal of the spleen was not associated with an increased risk of infection.<sup>2</sup> Previously published studies,<sup>3</sup> literature reviews,<sup>5,6</sup> and a paper by Deodhar *et al* in this week's journal (p 1408)<sup>7</sup> support our contention that removing the spleen leads to an increased lifelong risk of infection. Deodhar *et al* report that post-mortem review of patients who had had a splenectomy showed that 37% had died of infection, which in 11% of cases was pneumococcal. Nearly 60% of their patients who had had a splenectomy were not protected against infection.<sup>7</sup>

The commonest infecting organisms are *Streptococcus pneumoniae* (accounting for more than half the cases<sup>8</sup>), *Haemophilus influenzae*, *Neisseria meningitidis*, and *Escherichia coli*. Although polyvalent pneumococcal vaccine prevents pneumococcal infection in immunocompetent patients who have not had a splenectomy,<sup>9</sup> the antibody response to vaccination after splenectomy is impaired.<sup>10</sup> The disease

necessitating the splenectomy may also affect the antibody response to vaccination. Although currently available pneumococcal vaccine is effective against 23 strains of pneumococci, it does not protect against all pneumococcal infections. Despite this, vaccination is worth while. Current guidelines from the Department of Health recommend that pneumococcal vaccine should be given, if possible, two weeks before splenectomy and repeated every five to 10 years.<sup>11</sup> Should vaccination prove impossible before surgery it should be carried out as soon as possible after. Kinnersley *et al* in this issue show that a large group of patients who have had a splenectomy remain unvaccinated (p 1398).<sup>12</sup>

Prophylaxis with penicillin also protects against pneumococcal infection, although failures occur; some may be due to non-compliance.<sup>13-15</sup> We recommend that patients should take phenoxymethylpenicillin 250 mg twice a day for life; patients allergic to penicillin should take erythromycin. Because episodes of overwhelming infection many years after splenectomy are rare, many patients may be unwilling to comply with long term prophylaxis. Most patients who develop overwhelming infection have a prodromal illness of at least a few hours: patients unwilling to take regular penicillin should be made aware of the risks and should have a readily available supply of penicillin so that they can start treatment immediately on developing suggestive symptoms. Wearing a Medic-Alert bracelet increases the awareness of patients and doctors alike.

Problems with penicillin resistant pneumococci may require us to review the recommendation. As *H influenzae* is responsible for some cases of overwhelming infection<sup>16</sup> vaccine against *H influenzae* type b may be useful in patients after splenectomy and needs to be studied further.

In cases of trauma, salvage of the damaged spleen should be attempted when possible, especially in children. Conservative management of splenic injuries, with surveillance with ultrasonography and computed tomography, may avert

surgery. When operation is imperative, splenorrhaphy, partial splenectomy, or heterotopic autotransplantation should be considered.<sup>17</sup> Autotransplantation may lead to the return of functioning splenic tissue and provide some protection against subsequent overwhelming infection.<sup>18</sup> Animal studies have shown, however, that the immune function of autotransplanted tissue is inferior to that of normal splenic tissue.<sup>19</sup> Vaccination and prophylaxis with antibiotics are still required after autotransplantation.

The absence of a spleen leads to impaired resistance to bloodborne protozoal infection. Malaria and babesiosis (infections transmitted by ticks) have a high mortality in people without spleens.<sup>20</sup> Such people should therefore avoid areas where malaria is endemic and those who work with animals should be aware of the dangers of tick bites.

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## 45 Alcohol and heart disease: the implications of the U-shaped curve

*The recommended weekly limits of 21 units (men) and 14 units (women) should be adhered to*

Numerous studies have shown that people who drink small amounts of alcohol experience lower rates of ischaemic heart disease than those who do not drink alcohol.<sup>1</sup> These studies show consistency, specificity, and a dose-response effect, thereby fulfilling the criteria for believing an association to be causal.<sup>2</sup> Furthermore, a protective effect of alcohol against heart disease is biologically plausible. A few authorities still argue that the epidemiological evidence can be explained without causality being invoked,<sup>3</sup> but most concede that small amounts of alcohol may be cardioprotective.<sup>4</sup> Ischaemic heart disease is common, and in most studies the relative risks for moderate drinkers compared with abstainers are of the order of 0.5-0.7, so the effect could be more than trivial.

In Britain it has been accepted that there is no harm in consuming small amounts of alcohol. Drinking that results in intoxication, a high intake long term, or dependence, however, causes considerable harm. The harm includes various physical and psychological illnesses and a broad range of social problems. Heavy drinkers are heavy users of hospital inpatient services, accident and emergency departments, and general practice.<sup>5</sup>

Advice to individual members of the public has been fairly consistent over the past decade. Men should keep their alcohol consumption below 21 units a week and women below 14 units a week (a half pint of beer, a glass of wine, and a single measure of spirits each contains about a unit of alcohol). Everyone accepts that these limits are arbitrary, that people differ in their susceptibility to harm from alcohol, and that there is a continuum of risk with increasing intake. None the less, patients advised to cut down on their drinking may reasonably ask, "Well, how much can I drink, doctor?" and a rough and ready guide is much better than no answer.

Although unreliable estimates of alcohol intake and varying groupings of levels of consumption make comparison between studies difficult,<sup>6</sup> some broad conclusions are possible. In most studies men who drink about 7 units a week have rates of heart disease that are close to the lowest. The

curve is flat bottomed, and men who drink considerably more do not have higher rates of heart disease until they drink over 40 units a week. For other causes of death, such as accidents, stroke, and liver disease, the rates start to rise at lower intakes. In studies recording all cause mortality the lowest rates coincided with an alcohol consumption of about 7 units a week, with higher rates in those drinking more than 21 units a week. The longstanding recommended limit for men of 21 units a week fits surprisingly well with these data. For women we need more data, but the 14 unit a week limit will probably prove reasonable.

Public health doctors have advised that the whole population should reduce its mean consumption.<sup>7</sup> Public policy on alcohol must consider not only mortality and rates of medically defined non-fatal disease but also alcohol's harmful effects on family and social life, public order and criminality, and productivity at work. These probably have more impact on people's health than any "medical" effects of alcohol. The data are insufficient to allow a quantitative discussion of the relation between different levels of individual consumption and this non-medical harm, but harm certainly occurs at fairly low levels of consumption.<sup>8</sup> Ignoring the likely effect of any change in advice on drinking on these types of harm would be rash.

Any effect of alcohol on rates of ischaemic heart disease in England and Wales has been swamped by other factors. Between 1940 and 1980, when deaths from ischaemic heart disease were rising most rapidly, alcohol consumption also rose sharply; the fall in heart disease in the past decade has coincided with a period of fairly stable alcohol consumption.

Any general encouragement to drink alcohol will predictably increase the number of heavy drinkers: the mean consumption of alcohol correlates closely with the prevalence of heavy drinking in population groups.<sup>9</sup> The balance of evidence still suggests that Britain would be healthier if we could shift the curve of alcohol consumption to the left. For men to limit their alcohol consumption to below 21 units a