Although the present results indicate a possible occupational cause of prostatic cancer, this had little effect on the overall health of the atomic energy authority's workforce. Exposure to the radionuclides associated with prostatic cancer was uncommon: only 3% of the controls in this study had known contamination and 11% had worked in places where contamination might have occurred. Fourteen men with known contamination and 28 who had worked in places where contamination might have occurred developed prostatic cancer in the 41 years from 1946 to 1986. During the same period 5509 deaths were reported in the authority's cohort study, and the total death rate was 22% below the national average.⁵

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Antibiotic induced fatigue

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Antibiotics are prescribed for various reasons.¹ Some patients demand antibiotic treatment for fatigue and others refuse such treatment because they believe it to be responsible for the onset of fatigue. It is reasonable to assume that fatigue is secondary to the initial illness rather than to the treatment itself. To check this hypothesis we compared placebo with amoxycillin in a double blind, randomised crossover trial in healthy volunteers. Our particular aim was to find out whether certain psychological characteristics are linked to side effects during clinical trials.

Subjects, methods, and results

Informed, healthy medical students or nurses volunteered for the study. A personality questionnaire including Bortner's rating scale² and Levenson's locus of control scale³ was completed at the start of the trial. Bortner's scale ranges from 0 (extreme type A behaviour: competitive, impatient) to 24 (extreme type B behaviour: relaxed, easy going). Levenson's scale measures whether subjects consider themselves to be in control of life events (internal locus of control) or more dependent on outside factors (external locus of control). Subjects received in a randomised order amoxycillin 500 mg thrice daily or placebo for one week, with a two week wash out period.

At the end of each treatment period the subjects were compared for the presence or absence of fatigue

by using the χ^2 test. Psychological profiles were compared with the sum of the fatigue scores recorded at the end of the two treatment periods (verbal score with six points from 0 to 5) by using the non-parametric Kruskal-Wallis test. We estimated that 80 subjects would be needed in a crossover design to obtain a sample with a 20% difference in incidence of fatigue (10% with placebo *v* 30% with amoxycillin) at a risk of $\alpha = 5\%$, $\beta = 10\%$.

The study included 79 subjects (50 women); their mean (SD) age was 28.4 (6.9) years. The only side effect noted was a mild generalised erythematous rash after the first day of the initial treatment (placebo); the subject withdrew from the study. On Bortner's scale four subjects were type A, 38 type AB, and 37 type B; on Levenson's scale 21 subjects had an internal locus of control, 27 a median locus, and 24 an external locus.

Six subjects recorded fatigue after amoxycillin and five after placebo ($p = 0.76$) with no period effect. Only one subject recorded fatigue during both treatment periods. The fatigue score at the end of the treatments was associated with type B behaviour ($p < 0.05$) and the external locus of control ($p < 0.03$). Medians and interquartile ranges for Bortner's scale were respectively 0 and 0 to 1 in type A subjects, 1 and 0 to 2.25 in type AB subjects, and 2 and 0 to 4 in type B subjects (Kruskal-Wallis test, $p < 0.05$, $A < B$). For Levenson's scale medians and interquartile ranges were respectively 1 and 0 to 3 in those with an internal locus, 2 and 0 to 4 in those with a median locus, and 2 and 0 to 4 in those with an external locus (Kruskal-Wallis test, $p < 0.03$, internal < median, internal < external).

Comment

Patients often believe antibiotics to be responsible for generalised fatigue. This widely held view has clearly been invalidated by this trial, which shows that

one week of treatment with amoxycillin is no more tiring than treatment with placebo. Such a study would have no discriminatory value had it been conducted in patients with an illness inducing fatigue or requiring antibiotic treatment.

Type B subjects and those with an external locus of control more often reported fatigue as a result of treatment. These subjects are more sensitive to the effects of outside factors, such as the intake of drugs, on their lives. Results in psychological tests are good predictors of adherence to and efficacy of treatment.^{4,5} We have shown that the psychological profile of subjects can either increase or decrease the incidence of side effects. This idea has to be confirmed on a larger

scale, but it may be important in the conception of all clinical trials.

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Pneumococcal vaccination after splenectomy: survey of hospital and primary care records

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Vaccination against pneumococcal infection has been recommended since 1977 to prevent overwhelming infection in patients having splenectomies; it is safe with proved efficacy, and there is consensus on its use.¹⁻⁴ There is international evidence of deficiencies in vaccination policy but no reports from the United Kingdom.⁵ Our study was prompted by the deaths of two young unvaccinated patients from pneumococcal septicaemia in South Glamorgan. We aimed to determine the vaccination rate among patients having splenectomies in Cardiff over 15 years and to facilitate vaccination of those at risk.

Patients, methods, and results

Patients having splenectomies between 1975 and 1990 were identified from the histology register in three Cardiff hospitals. Of the 737 entries, 557 (76%)

patients' hospital notes were found and searched. The general practitioners of the living, apparently unvaccinated patients were asked to search their primary care records for evidence of subsequent vaccination and to comment on each patient's present health status. All general practitioners were sent an information package about pneumococcal vaccine and were contacted four months later to establish whether this information had led to vaccination.

The hospital records showed that 60 (11%) patients had received pneumococcal vaccination and the primary care records that 27 (5%) patients had received it—a total of 87 (16%) patients (figure). Cause of death was available from the hospital records for 166 of the 263 patients who had died. Thirty seven (22%) of them had died of septicaemia or other infections.

Vaccination rates were higher in children (32%, 25/79) than in adults (7%, 35/477) and had improved between 1975-80 (0.7%, 2/295), 1981-85 (14.2%, 24/169), and 1986-90 (35.5%, 33/93). Analysis of vaccination rate according to reason for splenectomy showed higher rates in those with benign diseases.

Recording of splenectomy was incomplete in the hospital records, being absent from the operation notes in 19 (3%) cases and from the discharge letter to the general practitioner in 130 (23%). The records of 170 living unvaccinated patients were examined by their general practitioners. Of these, 150 (88%) patients had the splenectomy recorded, with this information being considered "easy" or "very easy" to find in 110 cases. A further 27 patients were found to have been vaccinated by this search. Ninety six (69%) of the 140 unvaccinated patients were considered to be in good health. Of those general practitioners responding at follow up, 65 (46%) had vaccinated their patients and 34 (24%) had not.

Comment

We identified a large group of patients who had had a splenectomy but not been vaccinated. Although vaccination rates have improved over time, it is of concern that such groups probably exist throughout the United Kingdom. Furthermore, the primary care records showed that most of the unvaccinated patients were currently in good health. Clear guidelines for the vaccine were not included in the Department of Health publication *Immunisation Against Infectious Diseases* until 1992.³ Such omissions, coupled with the sporadic nature of cases, may have led to the slow uptake of vaccination.

It is gratifying that 65 previously unprotected patients were vaccinated as part of this study by their general practitioners since they are responsible for the long term care of such patients. Because of the difficulty in diagnosing early sepsis primary care records must mention both the splenectomy and the vaccination status. General practitioners are well

Follow up of vaccination status of patients who had had a splenectomy between 1975 and 1990 in three Cardiff hospitals