Numbers of children with haemophilia or von Willebrand's disease given hepatitis B vaccine by severity of disease and by age

Condition	Age ≤10 years	Age >10 years	Total
Haemophilia A:			
Severe*	15	9	24
Moderate or mild†	7	3	10
Haemophilia B:			
Severe*	2	1	3
Moderate or mild†	3‡	1	4
Von Willebrand's disease:			
Girls	3	3	6
Boys	2	2	4

*Clotting factor concentration ≤10 U/l.
†Clotting factor concentration >10 U/l.
‡Includes one girl with symptoms.

eight were immunised in the upper arm, 10 in the buttock, and three in the thigh. The injection was given with a 23 gauge needle. Whenever possible pressure was applied to the vaccination site for one to two minutes after the injection.

Six of the 153 injections (4%) resulted in bruising, none severe enough to warrant an injection of concentrate. Three children had repeated attacks of vomiting, which began a few hours after the first dose in two and two days after the third dose in the third. One child had a febrile illness with myalgia two days after the third dose of vaccine. There were no other reactions. We did not routinely measure titres of hepatitis B antibody.

Comment

The manufacturer's data sheet for hepatitis B vaccine has always stated that the vaccine is for intramuscular use only and should not be given intravenously, subcutaneously, or intradermally. We therefore decided to give it by intramuscular injection. Others have given the vaccine subcutaneously[1-3] or intravenously[4] because of the theoretical risk of bleeding. No differences were reported between haemophiliacs given subcutaneous[1-3] or intravenous[4] injections and normal controls. Of the 11 haemophiliacs who responded to a questionnaire in a study by Janco,[2] two (18%) complained of soreness or swelling at the site of injection. In a series of 1083 homosexual men injected intramuscularly the incidence of sore arms was 15·8%.[5] The incidence of bruising in our series was lower (4%). The difference may be due to the fact that in the other series the incidence of side effects was estimated by means of a questionnaire whereas in our series it was established by routine questions at follow up visits. Furthermore, we studied only children, who would perhaps be unlikely to complain to their parents about sore arms for fear of a further injection. None was needed—an important fact at a time of anxiety about the safety of clotting factor concentrates. The point we wish to make, however, is that there were no serious bruises and no treatment was needed for haematoma induced by intramuscular injection.

The low incidence of side effects is probably due to several factors, including the type of material injected, its volume, and the size of the needle. Other products may not prove to be as free from the risk of causing bruising. Our experience shows that intramuscular injections are no longer completely contraindicated in haemophiliacs.

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Increasing suicide rates among young men in England and Wales

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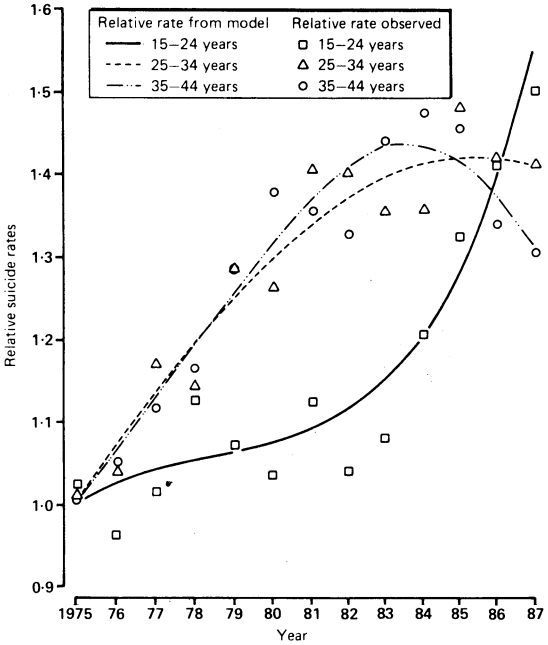
We recently reported an analysis of routinely collected suicide statistics that showed a sharp increase in the suicide rate among young people in Leicestershire.[1] In view of the interest this finding generated,[2] we extended our analysis to cover England and Wales and to investigate age specific and sex specific trends in greater depth.

Methods and results

Numbers of suicides by age and sex and by age and sex specific base populations were obtained from routine data from the Office of Population Censuses and Surveys for 1975-87.[3] Stratum specific suicide rates were treated as having a Poisson distribution. A multiplicative regression model was created with the generalised interactive modelling (GLIM) 3·77 program[4] to investigate temporal changes in the underlying rate of suicide within each age and sex stratum. Age was coded as a seven level categorical factor (15-24 years=1, 25-34=2, ... 65-74=6, 75-84=7) and time was represented by YEAR, a continuous covariate taking values between 0 and 12 (0=1975, 1=1976, ... 12=1987). The model was given parameters such that the age-sex interaction terms estimated stratum specific suicide rates in 1975 and the age-sex-time interactions estimated the manner in which these rates had changed over time. The time changes were found



Relative suicide rates by age and year in young males, England and Wales, 1975-87 (fitted age specific rates in 1975 are defined as 1·0)

to be non-linear; terms in YEAR squared ($p<0.0001$) and YEAR cubed ($p=0.04$) significantly improved the fit of the model. The final model fitted well: residuals were appropriately distributed, no additional regression terms were needed, and a leverage analysis indicated that the results had not been distorted by unrepresentative data points.

In both sexes the fitted suicide rate for 1975 increased consistently with increasing age. Males exhibited a significantly higher rate of suicide than females within all age strata. In males the fitted rate ranged from 61·9 deaths per million per annum (95% confidence interval 55·3 to 69·3) in the youngest age group to 189·2 (163·0 to 219·5) deaths per million per annum in the oldest. In females the equivalent range was from 28·4 (23·9 to 33·7) to 107·2 (93·1 to 123·4) deaths per million per annum.

Among males in each of the age groups 15-24, 25-34, and 35-44 the suicide rate increased significantly ($p<0.0001$) between 1975 and 1987 (figure). No significant changes were observed in the older age groups. In sharp contrast, all females in all age groups showed a decline in suicide rate, ranging from a 33% fall ($p=0.002$) in the age group 35-44 to a 17% fall ($p=0.055$) in the group 25-34.

Comment

This analysis reinforces the findings of our local study and extends the scope of reports of the Office of Population Censuses and Surveys[5]; it suggests that important changes have occurred in the pattern of suicide among young men throughout England and Wales. Among men aged 15-24, in whom the rate of suicide had been fairly stable up to 1982,[5] the rate increased dramatically (40%, 95% confidence interval 25% to 56%) during 1982-7. In contrast, the rate among men aged 25-34 and 35-44, which increased steeply during the late 1970s and early 'eighties,[5] seems to have stabilised and may even have started to fall. The suicide rate among women seems to have been falling throughout the period of the study, a finding that represents a continuation of earlier trends.[5]

As in our previous study[4] our analysis permits no inference about the causes of changing suicide rates among young men. Changing patterns of drug and alcohol use, psychiatric ill health, and a vast array of possible social factors may all play an important part. It seems improbable that coroners throughout England and Wales have become more likely to return a verdict of suicide specifically in young men without any similar changes in relation to other age and sex groups; it therefore seems unlikely that our results are a consequence of recording artefact. The changes we have shown appear to be real, their magnitude is of considerable concern, and further study of the aetiology of these suicides is clearly needed.

ADDENDUM—The trend in suicides has since been emphasised by the mortality statistics for 1988, which show a further 18% increase (to 110·0 deaths per million per annum) in the suicide rate among men aged 15-24.

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Raised concentrations of antibodies to cardiolipin in patients receiving dialysis

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Clinical events such as recurrent arterial or venous thrombosis, spontaneous abortions, and thrombocytopenia have been associated with antibodies to cardiolipin. Many patients have simultaneously been positive for lupus anticoagulant and had clinically verified lupus erythematosus, but symptoms have also developed in patients without this underlying disease. Antibodies to cardiolipin may also be detected after bacterial or viral infections.[1] Patients with uraemia have a high incidence of cardiovascular and thrombotic events. Infections form the second largest group of complications in these patients.[2] Against this background we analysed the prevalence of raised concentrations of antibody to cardiolipin in a cross sectional study of patients receiving dialysis.

Subjects, methods, and results

We studied 146 patients receiving dialysis (34 receiving continuous ambulatory peritoneal dialysis and 112 receiving haemodialysis). Their mean age was 48 (range 13-76), and they had been receiving dialysis for a mean of 37 (0-252) months. Forty three patients had chronic glomerulonephritis (verified by biopsy), of whom six had systemic lupus erythematosus. Twenty seven had diabetic nephropathy, and 16 had amyloidosis secondary to rheumatoid arthritis. Other diseases were polycystic kidney disease, chronic pyelonephritis, and interstitial nephritis. Fifty three healthy subjects and 32 consecutive patients with systemic lupus erythematosus served as controls.

IgG antibodies to cardiolipin in serum were analysed with a quantitative enzyme linked immunosorbent assay (ELISA) (Cheshire Diagnostics, Chester, England); international standards were used. In the 53 normal subjects the mean (SD) concentration of antibody was 3(3) U/l and 95% of the values were below 10 U/l. Thus we regarded only values above 10 U/l as being positive and recorded only these numerically. Student's t test for unpaired values and the χ^2 test were used for statistical calculations.

The proportion of patients with a positive concentration of antibodies to cardiolipin among the patients receiving dialysis was significantly higher than that among the normal controls but about the same as that among the patients with systemic lupus erythematosus (table). Positive concentrations were, however, generally lower in the patients receiving dialysis than in those with systemic lupus erythematosus (mean 20 U/l (95% confidence interval 16 to 24 U/l) *v* 97 (34 to 160) U/l; $p=0.001$); the highest concentration in a patient receiving dialysis was 57 U/l compared with 200 U/l in a patient with systemic lupus erythematosus.

Among the patients receiving dialysis, having a positive antibody concentration was not associated with age or having received a transplant but was more common among the patients with chronic glomerulonephritis than among those with other diagnoses (table). Three of six patients with lupus nephritis had positive antibody concentrations. A higher proportion of patients with chronic glomerulonephritis than with other renal disease had received a transplant, and they had also been receiving dialysis for longer. Neither