incidents jointly with the British Association for Accident and Emergency Medicine.

The association organises courses on major incidents, and the five day course on immediate care includes formal training on the same subject. The diploma in immediate medical care of the Royal College of Surgeons of Edinburgh examines candidates on skills gained in these courses. The courses and the diploma are much more relevant to on site medical services at major incidents than the much promoted advanced trauma life support courses, which relate to the care of a single patient by a single doctor in hospital.[4]

We believe that the key issues are, firstly, that the person serving as medical incident officer must be properly trained in managing major incidents and must participate regularly in exercises with colleagues from other services; and, secondly, that members of site medical teams must regularly work outside hospital on the many cases of trauma seen in day to day practice.

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UK major trauma outcome study

EDITOR,—D W Yates and colleagues provide evidence on deficiencies in the trauma system in the United Kingdom.[1] It cannot be assumed, however, that all the observed excess mortality occurs in patients with severe injury. In the major trauma outcome study in the United States the mortality in the group of less seriously injured patients (injury severity score 1-8) was 0·37% (24/6557 patients altogether; 18/4816 with blunt injury only).[2] In the study in the United Kingdom the death rate was 1·8% (93/5019, excluding patients with fractured neck of femur). If the death rate from the United States was applied to the numbers in the United Kingdom 19 deaths could be expected, signifying 74 excess deaths in patients with minor injury.

The reason for the excess mortality in this group may be poor care, but the more likely explanation is a difference in the type of patients in the dataset. Even if patients with fractured neck of femur and penetrating injuries are excluded the number of patients injured by a fall was much greater in the British study (4990/10 745; 46%) than the American study (2736/11 482; 24%).[2] This group contains many elderly patients injured by simple falls. The TRISS method of determining the probability of survival makes no allowance for the appreciable pre-existing morbidity in this group. Previous work has cast doubt on the validity of using TRISS methods where such patients form a considerable part of the caseload.[3,4]

This hypothesis, however, may explain only part of the difference in mortality between the two countries. There is excess mortality in the seriously injured group, and efforts should continue to improve the trauma systems in Britain.

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1 Yates DW, Woodford M, Hollis S. Preliminary analysis of the care of injured patients in 33 British hospitals: first report of the United Kingdom major trauma outcome study. *BMJ* 1992;**305**:737-40. (26 September.)
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EDITOR,—D W Yates and colleagues' preliminary analysis of the care of injured patients shows that only one hospital in the United Kingdom is fit (by the standard of the United States Trauma Research Center in 1987) to admit patients with trauma.[1] The report confirms the report of a working party of the Royal College of Surgeons in 1988 that at least 2000 to 3000 patients die unnecessarily from trauma each year and it is therefore not unreasonable to expect that many more patients are unsatisfactorily treated. Indeed, this argument may be carried further: surely, the treatment of the most seriously ill patients must be a not unreasonable indicator of health care in a hospital.

To put the figures into perspective, we can now assert on a good statistical basis that for every consultant neurosurgeon in Britain one patient dies unnecessarily of a head injury every five weeks and, similarly, for every consultant in accident and emergency one patient dies unnecessarily from multiple trauma every month.

Clearly, when considering the health of the nation the government must not only try to prevent accidents, which cost all of us a large amount of money, but look at our whole hospital care system.

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1 Yates DW, Woodford M, Hollis S. Preliminary analysis of the care of injured patients in 33 British hospitals: first report of the United Kingdom major trauma outcome study. *BMJ* 1992;**305**:737-40. (26 September.)
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EDITOR,—D W Yates and colleagues chose to compare the performance of accident departments in the United Kingdom with that of similar units in the United States.[1] Perhaps they should also compare the cost per patient.

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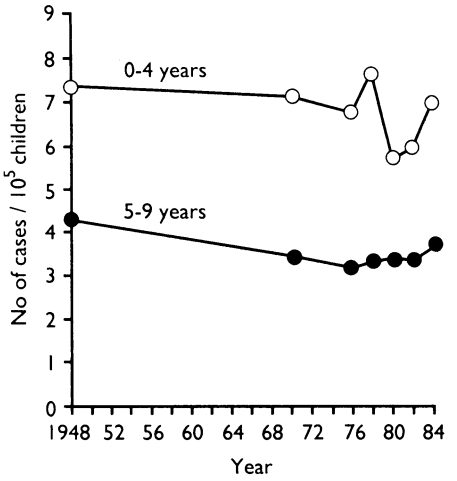
Vitamin K and childhood cancer

EDITOR,—Jean Golding and colleagues report that vitamin K given intramuscularly at birth may double the incidence of leukaemia and perhaps other cancer in children under 10 years old.[1] In raising questions about the study G J Draper and C A Stiller call for large cohort studies to be carried out as rapidly as possible to settle the issue.[2] Before such studies are conducted consideration should be given to data from the United States, where since 1961 almost all children have been given intramuscular vitamin K at birth as recommended by the American Academy of Pediatrics.[3] No increase in the incidence of leukaemia occurred in 1969-84 compared with 1947-50 (figure). The data, collected for the second and third national cancer surveys (1947-50; 1969-71) and the surveillance, epidemiology, and end results programme of the National Cancer Institute (1973-84), are from five areas combined: the cities of Atlanta, Detroit, and San Francisco-Oakland and the states of



Incidence of leukaemia over time among white children in United States

Connecticut and Iowa (6-7% of the American population).[4]

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1 Golding J, Greenwood R, Birmingham K, Mott M. Childhood cancer, intramuscular vitamin K, and pethidine given during labour. *BMJ* 1992;**305**:341-6. (8 August.)
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EDITOR,—The use of vitamin K to prevent haemorrhagic disease of the newborn and its implication as a risk factor in the development of childhood cancer have been widely debated in the medical journals and popular press over the past year. Paediatricians are now often summoned to the delivery unit to discuss the need for vitamin K and the best route of administration. These discussions with parents can last up to an hour.

The recommendations of A W McNinch and colleagues and Jean Golding and colleagues are well known.[1-3] From the recent letters of Beverley A Lawrence Beech and H P Dunn it seems that there could be a shift in treatment.[4,5] At best there will be an increase in oral prophylaxis; at worst only those thought to be at risk will be treated. Both options could have tragic results, and parents must be counselled.

In a two month period two babies with confirmed haemorrhagic disease of the newborn were referred to Addenbrooke's Hospital. Both had been born at another hospital where no vitamin K prophylaxis was given. Neither baby had any risk factors, both had had normal vaginal deliveries at full term, and both were breast fed. They had been well until about 6 weeks of age. The first had warning bleeds for three days before presenting unconscious at the local hospital. The second presented with a two day history of lethargy, poor feeding, and then focal fits. In both cases intracranial haemorrhages were diagnosed and the babies were transferred for paediatric and neurosurgical intensive care. Both babies survived; the first required evacuation of intracranial blood clots on two occasions, and the second required monitoring of the intracranial pressure. Follow up computed tomography showed appreciable cerebral atrophy, and both children may have some handicap.

Our paediatric practice of giving vitamin K intramuscularly remains unchanged. If parents

refuse this we give 2 mg phytomenadione (vitamin K_1) orally at birth and at 12 and 24 hours of age. We await information on the efficacy of this oral regimen. Recent work by Cornelissen *et al* will further fuel the controversy as they suggest that a single dose of vitamin K, whether given orally or intramuscularly, is insufficient to protect against late haemorrhagic disease of the newborn.[6] I wonder whether, in the meantime, the adverse publicity surrounding vitamin K will result in a resurgence of this preventable condition; I hope that it remains a condition that is rarely seen.

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1 McNinch AW, Upton C, Samuels M, Shearer MJ. Plasma concentrations after oral or intramuscular vitamin K1 in neonates. *Arch Dis Child* 1985;**60**:814-8.
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Antenatal screening for Down's syndrome

EDITOR,—In maternal serum screening for Down's syndrome based on several markers the human chorionic gonadotrophin assay can measure either the intact molecule or the free β subunit (a small fraction of the total), or both. Kevin Spencer advocates using an assay of the free β subunit,[1] and, though N J Wald and colleagues are uncertain,[2] we believe that there are two good reasons to prefer the free β subunit.

Firstly, when screening takes place—generally at 15-20 weeks' gestation—the predicted detection rate is higher for the free β subunit. In meta-analysis of 17 studies that used intact or total human chorionic gonadotrophin the average level for 530 Down's syndrome pregnancies was 2·0 multiples of the normal gestation specific median (95% confidence interval 1·9 to 2·1).[3] When this approach is applied to the five reported studies that used free β (the four cited by Spencer[2] and that of Ryall *et al*[4]) the average level for 228 affected pregnancies is 2·3 multiples of the median (2·1 to 2·5).

The table shows the predicted effect of the increase in levels when screening using human chorionic gonadotrophin in combination with α fetoprotein and unconjugated oestriol. For the tabulated cut offs the predicted detection rate is 11-12% higher for free β, with a 0·4-0·7% increase in the false positive rate. For a fixed false positive rate there is an 8-10% higher predicted detection rate for free β. Possibly some of the increase in levels is an artefact of storage of the serum samples. This, however, is likely to be a small effect since the results of prospective screening at Oldchurch Hospital[1] are consistent with the model predictions: the detection rate is 73% (11/15) for a false positive rate of 5·5%.

*Detection rate and false positive rate (percentages) obtained in screening for Down's syndrome pregnancies with maternal serum α fetoprotein, unconjugated oestriol, and human chorionic gonadotrophin (free β, intact or total) concentrations**

	Human chorionic gonadotrophin			
	Free β		Intact or total	
Cut off risk†	Detection rate	False positive rate	Detection rate	False positive rate
1 in 150	61	2·9	49	2·4
1 in 200	66	4·0	54	3·3
1 in 250	69	5·0	58	4·4
1 in 300	72	5·9	60	5·4
1 in 350	74	6·8	63	6·4

*Rates predicted from multivariate gaussian model with medians, standard deviations, and correlation coefficients of Spencer *et al*[1] and maternal age distribution of England and Wales in 1989 and 1990.
†Result of screening is positive if risk of Down's syndrome term pregnancy exceeds cut off.

The second reason for preferring the free β subunit is that, like α fetoprotein and unconjugated oestriol but unlike intact human chorionic gonadotrophin, it can be used for screening before 15 weeks. In the six published studies (three cited by Wald and colleagues[2] and three others[6-8]) of samples obtained in early pregnancy tested using intact or total human chorionic gonadotrophin the average level from 102 Down's syndrome pregnancies was only 1·2 multiples of the normal median. In contrast, in a recent study that used a free β assay at 7-13 weeks to test 13 affected pregnancies the average level was 1·85 multiples of the median, which is consistent with the average level after 15 weeks' gestation.[9]

These reasons have compelled us to change to assaying the free β subunit in our screening programme for Down's syndrome and to offer screening from 13 weeks' gestation. A disadvantage of screening for the syndrome before 15 weeks is that the α fetoprotein concentration cannot be interpreted in relation to neural tube defects. Many centres, however, would be confident enough in their use of routine ultrasound examination in screening for anomalies to abandon biochemical screening for this disorder in order to provide an earlier diagnosis of Down's syndrome.

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EDITOR,—Antenatal screening for Down's syndrome using maternal serum markers during the second trimster together with the woman's age is currently under investigation.[1] Haddow *et al* have reported the result of a large prospective study.[2] They showed the validity of predictions based on retrospective studies, indicating that use of the three markers α fetoprotein, chorionic gonadotrophin, and unconjugated oestriol is more effective than use of maternal serum α fetoprotein alone. Their results also suggested that not using unconjugated oestriol values would lead to a 5% reduction in the rate of detection.

We conducted a prospective study using the two markers human chorionic gonadotrophin and unconjugated oestriol together with the woman's age. Such a protocol has been recommended for prenatal screening centres that do not measure α fetoprotein routinely to detect neural tube defects and are willing to use only two markers instead of three.[3] We studied 26 128 women aged 18 to 37 who underwent prenatal screening for Down's syndrome between January 1990 and April 1992 in a limited area in north west France where the annual number of births is around 20 000. Gestational age was estimated by biparietal diameter ultrasonography before screening. Predictive risk factors were calculated by crossing hormone measurements with maternal age. Eligibility for amniocentesis or chorionic villus sampling was set up at a risk cut off of 1 in 150, leading to a positive screening rate of 4·7%. The risk factor calculation was based on published retrospective studies.[4,5] Recent readjustment of reference values from our own study, however, indicated that risk factors had been overestimated and that our risk cut off was nearer 1 in 200.

Results of prospective study of prenatal screening for Down's syndrome based on human chorionic gonadotrophin and unconjugated oestriol concentrations and woman's age, according to second trimster risk cut off of 1 in 200

Maternal age (years)	No screened	Positive screening (%)	Cases of Down's syndrome: Detected	Cases of Down's syndrome: Not detected	Detection rate (%)
18-29	18 382	3·6	6	6	50
30-37	7 746	7·4	13	5	72
All ages	26 128	4·7	19	11	63

The table shows the effectiveness of our protocol. As expected, the detection rate was higher in the group of older women. We also observed that not using unconjugated oestriol values would lead to a net loss in detection of three cases (four cases missed and one additional case detected) for a similar positive screening rate (4·6%). Taken together with the data from Haddow *et al*, our results confirm the usefulness of measuring unconjugated oestriol concentrations—this had been questioned in a study by Macri *et al*.[6]

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1 Correspondence. Antenatal screening for Down's syndrome. *BMJ* 1992;**305**:768-71. (26 September.)
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EDITOR,—In our recent letter on antenatal screening for Down's syndrome we said that the effect of the age distribution of women on the performance of serum screening for Down's syndrome would be small and that, regardless of the variation in the age distribution, such screening would yield a higher