SHORT REPORTS

Deaths from Rh haemolytic disease in England and Wales in 1984 and 1985

Since 1977 deaths registered as being due to haemolytic disease of the newborn in England and Wales have been analysed in an attempt to discover the circumstances in which each mother became immunised and also to assess the accuracy of certification of deaths. Results from 1977 to 1983 have been published previously[1]; we describe here results up to 1985.

Methods and results

Cases were categorised as described previously.[1]

During 1977-84 there was a substantial reduction in the death rate from Rh(D) haemolytic disease, but deaths in 1985 were as numerous as in 1983[1] (see table), suggesting that from now onwards the rate of fall may be less.

The table shows the circumstances in which each mother was immunised to Rh. Twenty eight of the 58 women in 1984-5 had not been given anti-Rh after a previous pregnancy (category 1); of these, six had been immunised before 1970, when anti-Rh immunoglobulin was not widely available. Among the 22 immunised from 1970 onwards the reasons for the omission of immunoprophylaxis appear to have been as follows: anti-Rh not available locally (four), Rh grouping errors (three), pregnancy terminated before the 30th week and treatment with anti-Rh believed to be unnecessary (10 (eight before 15th week)), full term delivery (reasons for "not given anti-Rh" unknown) (five).

Whereas there was a substantial fall in the numbers of cases in category 1, the number of deaths in the offspring of women immunised during their first pregnancy (category 2) or who became immunised despite having been given anti-Rh after their first delivery (category 3) showed very little fall in 1977-85, perhaps surprisingly in view of advances in the treatment of haemolytic disease.

Deaths from haemolytic disease due to antibodies other than anti-D (category 5) also remained roughly constant. In 1977-85 there were about four such cases a year; the antibodies concerned were anti-c±−E (23), −K (eight), −c+−K (two), −C (one).

The numbers of deaths registered as being due to haemolytic disease but judged on inspection of death certificates and hospital notes not to have been so (category 6) fell strikingly. One of the remaining relatively common causes of false certification is failure to realise that hydrops fetalis may be non-immunological, often associated with congenital abnormalities.[2]

Comment

Our analysis is based on registered deaths and, since stillbirths before the 28th week are not registrable in England and Wales, must underestimate the true mortality from haemolytic disease. Experience in the Oxford area—seven registered and 19 unregistered "pregnancy losses"[3]—suggests that the underestimate may be large. Figures from Yorkshire are apparently similar: in 1983-5 there were five registered deaths and 16 cases in which a pregnancy in an Rh immunised woman ended in fetal death before the 28th week of pregnancy (L A D Tovey, personal communication). Figures from two other centres, however, give a different impression. In Northumberland and Durham records are available for almost all women whose pregnancy continued for more than 16 weeks. Registered deaths (87) represented about two thirds of the total loss from haemolytic disease (E Hey, personal communication). In Finland, where all stillbirths are registrable, regardless of gestational age, virtually all Rh immunised pregnant women are tested by the Finnish Red Cross Blood Transfusion Service. Of 42 deaths from Rh haemolytic disease occurring in 1975-85, 10 were stillbirths occurring before the 28th week of pregnancy (J Eklund and H R Nevanlinna, personal communication). The variation in these estimates emphasises the difficulty of discovering the true mortality from Rh haemolytic disease.

Our data suggest that many women become immunised because they are not given anti-Rh immunoglobulin after an abortion. Even more important is the finding that in about half the mothers whose infants died in 1984 and 1985 Rh immunisation could have been prevented only by antenatal treatment. The introduction of antenatal immunoprophylaxis combined with recent advances in treating the affected infant[4] should eventually reduce mortality from this disease to a very low level.

We thank the many obstetricians who made this study possible, Dr M R Alderson, who supplied the death certificates, and Mr M McDowall and Mrs J I Jordan for discussions. We should also like to thank Drs Jarl Eklund, H R Nevanlinna, E Hey, and L A D Tovey for kindly supplying us with unpublished data.

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Deaths from Rh haemolytic disease (stillbirths and livebirths) 1977 to 1985

Category	Description	1977	1978	1979	1980	1981	1982	1983	1984	1985
1	No postnatal anti-Rh immunoglobulin after one or more previous deliveries:									
	At least one of which occurred before 1970 (before anti-Rh Ig widely available)	53	40	40	31	14	17	4	1	5
	Occurring from 1970 onwards (anti-Rh Ig widely, but not universally, available)	32	28	24	23	12	16	12	11	11
2	Anti-D detected during or within seven days after first delivery (immunised during first pregnancy)	12	11	10	6	6	5	8	3	9
3	Immunised despite postnatal anti-Rh after previous pregnancies (failures of prophylaxis)	9	7	12	11	9	6	9	9	8
4	Immunised by blood transfusion	—	2	1	1	—	—	1	1	—
Total deaths from Rh(D) haemolytic disease*		106	90†	87	72	41	44	34	25	33
Deaths per 100 000 births		18·3	15·0	13·6	9·2	6·4	7·0	5·2	3·9	5·0
5	Haemolytic disease not due to anti-D	4	3	3	4	3	4	4	5	4
6	Not haemolytic disease*	45	49	21	28	14	19	17	9	7
Total number of death and stillbirth certificates provided by the OPCS for cases in which haemolytic disease was thought to be implicated		155	142	111	103	57	67	55	39	44

*Authors' assessment after scrutiny of notes.
†Includes two cases which could not be categorised.

Acute psychosis as idiosyncratic reaction to quinidine: report of two cases

Confusion, delirium, and psychosis are known neuropsychiatric manifestations of quinidine toxicity (cinchonism).[1] When used in the usual therapeutic doses quinidine rarely has effects on the central nervous system. Nevertheless, in people with an idiosyncrasy cinchonism may occur with small doses.[2] We describe two patients presenting with acute psychotic manifestations as an idiosyncratic reaction to quinidine.

Case reports

Case 1—A 73 year old man, admitted because of palpitations, was started on quinidine sulphate 250 mg four times daily after a 24 hour Holter electrocardiogram recording had shown supraventricular tachyarrhythmia. He gave no history of physical or mental illness and was taking no medication. The results of physical examination and routine laboratory tests were normal, apart from a creatinine clearance of 54 ml/min. Some 90 minutes after the first dose of quinidine he developed visual hallucinations, delusions, and psychomotor agitation. A plasma quinidine concentration at that time was 0·8 mg/l (therapeutic values 3-6 mg/l). Twenty four hours later he had recovered completely.

Case 2—In a 67 year old man with palpitations an electrocardiogram showed recurrent supraventricular arrhythmia; treatment with quinidine sulphate 250 mg thrice daily was started. He had a history of mild hypertension but was receiving no treatment. Physical examination before the administration of quinidine was said to have shown no signs of cardiac failure and his blood pressure was 175/95 mm Hg. Routine laboratory investigations gave normal results, apart from a creatinine clearance of 64 ml/min. Two hours after receiving his first dose of quinidine he developed psychotic features consisting of psychomotor hyperactivity with paranoia and vocal hallucinations and was admitted to hospital. These features gradually subsided over 20 hours; his plasma quinidine concentration on admission was 1 mg/l.

In both patients the results of physical and neurological examination as well as of the laboratory investigations (liver function values, serum electrolyte concentration, and blood gases) were normal during the psychotic state. Additional neurological investigations (computed tomography of the brain and electroencephalography) showed no organic brain disease.

Comment

Though both our patients had impaired renal function, quinidine elimination has been said to be unimpaired in patients with poor renal function.[3,4] Furthermore, plasma quinidine concentrations were subtherapeutic in both patients, which makes quinidine toxicity unlikely. Hence we assume that idiosyncrasy was the responsible mechanism.

So far we have found no report of psychosis presenting as the only manifestation of idiosyncrasy to quinidine. Given that the drug is widely used, we believe that this possibility should be borne in mind.

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Is smoking a risk factor for pneumonia in adults with chickenpox?

Pneumonia is a serious complication of chickenpox in adults, with a mortality of up to 20%.[1] Risk factors have not previously been shown; identification of patients with such risk factors offers the possibility of antiviral chemoprophylaxis. We report on 29 patients admitted with varicella infection.

Patients, methods, and results

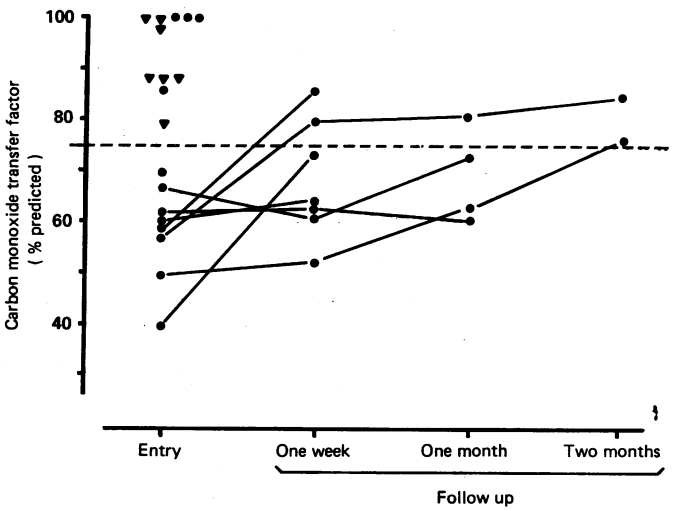
We studied 29 adults admitted from March 1985 to February 1986 with cutaneous varicella infection. Smoking histories were taken, and chest radiography and tests of lung function (forced expiratory volume in one second, forced vital capacity, the forced expiratory flow between 25% and 75% of the forced vital capacity (FEF_{25-75}), and carbon monoxide transfer factor) were performed in 20 of the patients on admission. Fisher's exact test was used for statistical analysis.

Of the 29 patients, 19 were regular or recent smokers and 10 had never smoked. Seven of the 19 smokers but none of the non-smokers had pneumonia ($p=0·032$).

The 20 patients who underwent lung function tests comprised 13 men (mean age 31 (SD 12)) and seven women (mean age 27 (6)); 12 were regular or recent smokers and eight had never smoked. Of the 12 smokers, five developed clinical pneumonia (confirmed radiologically), another three had an abnormal carbon monoxide transfer factor (<75% predicted) but no evidence of pneumonia, and four had no evidence of pneumonia or a reduced carbon monoxide transfer factor. One smoker with pneumonia was pregnant. None of the eight non-smokers tested developed pneumonia; only one had an abnormally low carbon monoxide transfer factor, but she had a history of extensive pulmonary tuberculosis. The association between smoking and low carbon monoxide transfer factor was significant ($p=0·0066$). All patients with radiologically confirmed pneumonia received intravenous acyclovir 10 mg/kg eight hourly for five days; all had improved considerably at one week. None required ventilation.

Seven of the eight smokers with a low transfer factor had serial lung function tests at one week, one month, and two months after treatment or until results were normal. The figure shows the findings in these smokers, although several were lost to follow up. One of the patients with a low carbon monoxide transfer factor at one month was retested at six months, when the value was low normal.

Ventilatory function was normal (>75% predicted) in all patients except for the FEF_{25-75} value, which was reduced (<75% predicted) in patients with pneumonia but improved as the carbon monoxide transfer factor improved, except in one patient. In the three smokers with a reduced carbon monoxide transfer factor without pneumonia the FEF_{25-75} was normal. Chest radiography in all patients at follow up did not show any evidence of obstructive airways disease or emphysema; there was no history of respiratory disease in any patient.



Carbon monoxide transfer factor in the patients admitted with chickenpox. (The patient with tuberculosis was excluded.) Broken line indicates lower limit of normal. ●=Smoker. ▼=Non-smoker.

Comment

Chickenpox pneumonia occurred only in smokers, an association not previously reported. The carbon monoxide transfer factor was reduced in some smokers without pneumonia; their normal ventilatory function suggests that this was due to subclinical chickenpox pneumonitis rather than smoking itself. The reduction of carbon monoxide transfer factor in our patients with chickenpox pneumonia confirms previous findings,[2] but such a reduction has not been described in adults without pneumonia. We also showed a reduction in FEF_{25-75}, indicating small airways obstruction.

Pneumonia occurs more commonly in adults than children with chickenpox. In severe cases assisted ventilation is necessary, but since acyclovir became available in 1981 none of the patients admitted to this unit with chickenpox (some with pneumonia) has required it (B K Mandal, personal communication). It may, therefore, be worth while giving acyclovir to adults with chickenpox who smoke.

We thank our colleagues, Dr B K Mandal and Dr E M Dunbar, consultant physicians, for permission to study patients under their care. We also thank Mr Alan Gibbs, lecturer in community medicine, Medical School, University of Manchester, for the statistical analyses.

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