PAPERS AND ORIGINALS

Deaths from rhesus haemolytic disease in England and Wales in 1977: accuracy of records and assessment of anti-D prophylaxis

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Summary and conclusions

All the death certificates for deaths in 1977 where haemolytic disease of the newborn (HDN) was the principal, an antecedent, or a contributory cause were obtained from the Office of Population Censuses and Surveys (OPCS). The hospital notes of all 54 of the live-born cases and all of the 101 stillbirths were also obtained. The cause of death indicated by the notes was compared with the cause and coding on the death certificate.

In about a quarter of the cases death was not due to haemolytic disease of any type. The commonest errors arose because the International Classification of Diseases (8th edition) stipulates that hydrops without mention of cause should be coded as HDN and because stillbirths to rhesus-negative mothers tend to be attributed to rhesus HDN automatically. Though deaths from HDN may be overestimated in this way, they are also underestimated because rhesus disease, although mentioned on the certificate, is not selected as the underlying cause, which it may be. These cases were found through multiple coding of all the contributory causes of death, which OPCS performs on a 25% sample of all death certificates for research purposes. These two sources of inaccuracy tend to cancel each other out, but statistics from death certificates give a misleading picture of the efficacy of anti-D prophylaxis because anti-D can never prevent cases which are not in fact due to rhesus HDN.

Most of the mothers studied had become immunised before anti-D became available, but in those who could have been treated 75% had not received prophylaxis. As

this was a sample of deaths, however, it would not be accurate to extrapolate this high figure to the population at risk. Nevertheless, the organisation of prophylaxis is clearly deficient and should be remedied before providing antenatal anti-D to supplement postnatal treatment.

Introduction

It is about eight years since prophylactic anti-D gamma-globulin became generally available to prevent immunisation of rhesus-negative women. Since babies still die from the disease we decided to look at the circumstances in which those women who had dead babies in 1977 had become immunised. We have suggested¹ that inaccuracies in death certification and in classifying causes of death might lead to wrong conclusions in epidemiological research. The present survey provides a useful series in which to look at this problem.

Methods

In response to our request for information on all deaths from rhesus (and other) haemolytic disease of the newborn (HDN) in England and Wales during 1977 copies of the death certificates of 54 liveborn babies and of 101 stillbirths were provided by the Office of Population Censuses and Surveys (OPCS). The usual coding on the certificate was 774 and 775 with their subunits (see key), these rubrics relating to cases where HDN was given as the primary ("underlying") cause of death.²

Part I of a death certificate deals with the causes leading directly to death, where section (a) the direct cause is due to (b) the intervening antecedent cause, which is due to (c) the underlying antecedent cause. The general rule is that the certified cause of death is the entry on the lowest line used in part I. Part II of the death certificate deals with other conditions contributing to the death but not related to the disease causing it.

As well as recording certified causes of death the OPCS undertakes an additional procedure—multiple coding. To use all the medical information on death certificates, experiments during the last 10 years have been carried out in coding all causes mentioned. Since 1974 a 25% sample of death certificates has been so analysed. Whenever HDN occurs as an "antecedent" or "subsidiary" cause on a certificate it is coded 774 or 775, and these additional cases are stored in the

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computer. They do not appear in the official returns since each individual is recorded as dying from only one event—the “underlying” cause—but the multiple coded cases are available for those interested in a particular disorder.

For the certificates sent to us as HDN in 1977 multiple coding contributed nine of the 54 liveborn deaths and 18 of the 101 stillbirths. Scrutiny of the case notes in the cases identified through multiple coding often showed that what had been certified as an antecedent or subsidiary cause was in fact the primary cause. The increase in technical procedures tends to magnify the problem. For example, if necrotising enterocolitis follows an exchange or intrauterine transfusion the bowel condition is sometimes given as the primary cause of death with HDN an antecedent. Clearly the certifiers are wrong and such cases should not have to be detected only by multiple coding. Under the present coding rules for selecting the cause of death, therefore, deaths from rhesus disease are greatly, and probably increasingly, underestimated, and a factor of up to $\times 4$ (since the sample coded was only 25%) may have to be applied to those cases which are detected only as a result of multiple coding, as some of them are misdiagnosed in the same way as some of the 774 and 775 cases (rhesus incompatibility is much the commonest cause of HDN).

To obtain the information about the mothers and their babies we approached the obstetrician in charge of each case. Usually he or she sent us the actual case notes, which gave the reproductive history of the mother. To find out when immunisation occurred, however, we often had to obtain a patient's case notes from several hospitals. Occasionally hospitals had ruled that notes must not leave the hospital, and in these cases one of us (CAC) usually went to look at them. In a few cases the consultant preferred to send us a complete summary rather than the notes.

In each case we assessed the evidence for the time when immunisation occurred and assigned the mother to one of the categories in table III. This was sometimes difficult. For example, even though there was no record of anti-D having been given in some cases (category 6) it may have been given but not entered in the notes. This seems unlikely, however, because when anti-D was given there was contributory evidence in the form of a sticker from the pathology laboratory, indicating the batch number. In no case did we find a sticker without a record of prophylaxis having been given.

Key to coding used in tables I and II

009.2	Diarrhoeal disease, gastroenteritis
038.9	Septicaemia, unspecified
560.9	Intestinal obstruction without mention of hernia, intestinal stenosis
741.9	Spina bifida, meningocele
743.2	Other congenital anomalies of nervous system: multiple anomalies of brain
746.3	Congenital anomalies of heart, interventricular septal defect
748.6	Congenital anomalies of respiratory system, hypoplasia lung
758.9	Other and unspecified congenital anomalies: congenital anomaly of unspecified site
762.1	Toxaemia or pre-eclampsia of pregnancy
766.4	Difficult labour with malposition of fetus, with anoxia
769.1	Other complications of pregnancy and childbirth: premature rupture of membranes
769.4	Other complications of pregnancy and childbirth: multiple pregnancy
769.9	Other complications of pregnancy and childbirth: anaemia of pregnancy
770.0	Conditions of placenta: placenta praevia
770.1	Conditions of placenta: antepartum haemorrhage
770.8	Conditions of placenta: abnormality of membranes
770.9	Conditions of placenta: placental insufficiency
772.0	Birth injury without mention of cause: brain injury
774.0	HDN with kernicterus, with Rh incompatibility
774.9	HDN with kernicterus, without mention of cause
775.0	HDN without mention of kernicterus, with Rh incompatibility
775.9	HDN without mention of kernicterus, without mention of cause
776.2	Anoxic and hypoxic conditions not elsewhere classified: congenital pneumothorax
776.3	Anoxic and hypoxic conditions not elsewhere classified: fetal distress
776.9	Anoxic and hypoxic conditions not elsewhere classified: asphyxia of newborn, unspecified
778.2	Other conditions of fetus or newborn: haemorrhage of newborn
778.9	Other conditions of fetus or newborn: hydrops or kernicterus of newborn not due to haemolytic disease

Results and comment

ACCURACY OF RECORDS

Liveborn deaths

The results are shown in table I; 40 of the 54 deaths were due to rhesus HDN. Among the 45 cases where the coding on the death

TABLE I—Real cause of death in liveborn infants certified as dying from HDN and sources of error on certificates

Case No	Code No on death certificate	As judged by case notes, Does coding on death certificates give accurate cause of death?	Rhesus death?	Comments
1-3	775.0	Yes	Yes	
4	774.0	Yes	Yes	
5-6	775.0	Yes	Yes	
7	775.9	No	Yes	Correctly coded from DC. Rh data only in notes. Coding should have been 775.0
8	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
9	748.6	Yes, multiple coding	Yes	
10	009.2	Yes, multiple coding	Yes	
11	775.0	Yes	Yes	
12	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
13	775.0	Yes	Yes	
14	778.2	Yes, multiple coding	Yes	
15-18	775.0	Yes	Yes	
19	038.9	Yes, multiple coding	Yes	
20	776.2	Yes, multiple coding	Yes	
21	560.9	Yes, multiple coding	No	HDN was due to ABO incompatibility. Correctly coded. Obstruction primary cause of death
22	775.0	Yes	Yes	
23	775.9	No	No	<i>Not due to HDN</i> . Notes showed mother Rh positive and death due to cytomegalovirus. DC gave (a) bleeding diathesis <i>plus hydrops</i> , (b) heart failure, (c) anaemia, jaundice. Extraction error
24	775.0	Yes	Yes	
25	770.8	Yes, multiple coding	No	<i>Not due to HDN</i> . Death due to fetomaternal haemorrhage. Extraction error (hydrops mentioned on DC)
26	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
27	775.0	Yes	Yes	
28	775.9	Yes	Yes	Notes show that death was due to anti- $\bar{c}$ and E antibodies. Mother D positive
29	775.0	Yes	Yes	
30	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
31-32	775.0	Yes	Yes	
33	775.9	No	No	Congenital ascites, <i>not due to HDN</i> . Should have been 778.9
34	772.0	Yes, multiple coding	Yes	
35	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
36	775.0	Yes	Yes	
37	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
38	774.9	Yes	No	Kernicterus, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
39-40	775.0	Yes	Yes	
41	776.9	Yes, multiple coding	Yes	
42-48	775.0	Yes	Yes	
49	775.9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778.9
50	775.0	Yes	Yes	
51	775.9	No	No	DC gave (a) septicaemia, (b) relative immunoincompetence. Inaccurate coding
52	775.9	Yes	Yes	DC gave cause of death as hydrops fetalis and coding was correct
53	774.9	Yes	Yes	
54	775.9	No	No	DC gave massive ascites as cause of death. Coding inaccurate. Mother Rh positive and had pre-eclamptic toxemia

DC = Death certificate.

TABLE II—*Real cause of death in stillborn infants certified as dying from HDN and sources of error on certificates*

Case No	Code No on death certificate	As judged by case notes, Does coding on death certificates give accurate cause of death?	Rhesus death?	Comments
1-6	775-0	Yes	Yes	Case 1—Notes show that death was due to anti-c. Mother D positive
7-8	775-9	Yes	Yes	Correctly coded on information on DC. Rh data found only in notes. Coding then would become 775-0
9	775-0	Yes	Yes	
10	775-9	No	No	Hydrops, unknown cause, and not due to HDN. Should have been coded 778-9
11-13	775-0	Yes	Yes	
14	770-1	Yes, multiple coding	Yes	Death due to antepartum haemorrhage and HDN. Mother D positive with c antibodies
15	769-9	Yes, multiple coding	No	<i>Not HDN death</i> but "mother Rh negative" on DC. No antibodies. Earlier threatened abortion gives coding
16	741-9	Yes, multiple coding	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Spina bifida gives coding
17-18	775-0	Yes	Yes	
19	775-0	No	No	Cause unknown but <i>not HDN</i> . "Mother Rh negative" on DC. No antibodies. Coding mistake due to DC error
20	775-0	Yes	Yes	Same mother as case 32 (2 stillbirths in one year)
21	775-0	No	No	Cause of death placental insufficiency. <i>Not HDN</i> . Mother Rh negative but no antibodies. "Rh antibody" on DC
22-26	775-0	Yes	Yes	
27	775-0	No	No	DC inaccurate. Cause of death neonatal asphyxia, <i>not HDN</i> (though D positive mother had anti-c)
28	770-9	Yes, multiple coding	No	Cause of death placental insufficiency, <i>not HDN</i> . Mother Rh negative but no antibodies. DC inaccurately states "Rh incompatibility"
29-31	775-0	Yes	Yes	
32	775-9	Yes	Yes	Same mother as case 20 (2 stillbirths in one year). Coding should have been 775-0
33-34	775-0	Yes	Yes	
35	775-9	Yes	No	HDN due to spherocytosis. Correctly coded
36	770-0	Yes, multiple coding	Yes	Placenta praevia—rhesus HDN
37	775-0	No	No	Cause unknown but <i>not HDN</i> . Mother Rh negative but never had antibodies. DC inaccurately states Rh incompatibility
38	775-9	Yes	Yes	Should have been 775-0. Minor inadequacy of DC
39-43	775-0	Yes	Yes	
44	769-1	Yes, multiple coding	No	Cause of death on DC: I (a) fetal asphyxia, (b) haemolytic streptococcus, (c) premature rupture of membranes. II Prematurity. Twins. Extraction error, probably due to word "haemolytic." <i>Not HDN deaths</i>
44 (twins)	769-1	" " "	No	
45-47	775-0	Yes	Yes	
48	776-3	Yes, multiple coding	Yes	Fetal distress and rhesus HDN
49	775-0	No	No	Cause of death placental insufficiency, not rhesus HDN, though mother immunised (in spite of anti-D prophylaxis). DC wrongly stated Rh incompatibility. Not recorded as failure in this paper as mother had no deaths from HDN
50-52	775-0	Yes	Yes	
53	762-1	Yes, multiple coding	No	Cause on DC I pre-eclamptic toxemia in mother, II thalassaemia. II is error—"carrier" only. <i>Not HDN death</i>
54-56	775-0	Yes	Yes	
57	775-9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778-9
58	775-0	Yes	Yes	
59	770-1	Yes, multiple coding	Yes	Antepartum haemorrhage plus rhesus HDN
60	775-0	Yes	Yes	
61	775-9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778-9 (mother Rh positive)
62-65	775-0	Yes	Yes	Case 63 D positive mother immunised to c antigen
66	775-9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778-9
67	775-0	Yes	Yes	
68	743-2	Yes, multiple coding	No	Multiple abnormalities including hydrops led to incorrect extraction. Mother Rh positive. <i>Not HDN death</i>
69-72	775-0	Yes	Yes	
73	775-9	Yes	Yes	Minor inadequacy of DC (Rh not mentioned)
74	775-0	No	No	DC: "Fresh fetus, cause unknown; mother Rh negative." Incorrectly certified—mother never had antibodies. <i>Not HDN death</i>
75	775-0	Yes	Yes	
76	766-4	No, multiple coding	No	Mother immunised to Rh but <i>no evidence of HDN</i> in 1977 stillbirth. Error of certification. Death due to asphyxia
77	775-0	Yes	Yes	
78	775-9	No	No	DC states "Hydrops fetalis of unknown aetiology." Should have been 778-9. <i>Not HDN death</i>
79	746-3	Yes, multiple coding	No	Hydrops mentioned among congenital malformations, incorrect extraction. <i>Not HDN death</i>
80	775-9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778-9. Mother Rh positive
81-82	775-0	Yes	Yes	
83	769-4	Yes, multiple coding	No	DC gave (a) gross intrauterine anoxia and anaemia, (b) transplacental transfusion, (c) twin 1 of twin pregnancy. Extraction error, probably because of confusion over "transplacental transfusion." <i>Not HDN death</i> . Mother Rh positive and no antibodies on 8 Feb 1979
84	741-9	Yes, multiple coding	No	Error of extraction. Hydrops mentioned with spina bifida. <i>Not HDN death</i>
85	775-0	No	No	DC erroneously states "Rhesus incompatibility." Mother Rh negative but no antibodies on at any time. Hydrops possibly due to ABO incompatibility
86-88	775-0	Yes	Yes	
89	775-9	No	No	Hydrops, unknown cause, and <i>not due to HDN</i> . Should have been 778-9
90	758-9	Yes, multiple coding	No	DC gave "I (a) fetal asphyxia, (b) fetal abnormality, (c) hydrops fetalis. II Hydramnios. "Hydrops" error of extraction in multiple coding. Mother Rh negative, no antibodies. Baby Rh negative (Rh not mentioned on DC). <i>Not HDN death</i>
91	775-0	Yes	Yes	DC: I (a) intrauterine death. ? Hydrops fetalis, Rh incompatibility
92	775-0	Yes	Yes	
93	770-1	Yes, multiple coding	No	DC stated I (a) fetal anoxia, (b) fetal anaemia, (c) retroplacental haemorrhage. Evidently picked up because of (b)
94	775-0	No	No	DC stated I (a) intrauterine death, (b) ? isoimmunisation Rh factor; no antibodies. Wrong certification by doctor—coder also wrong
95	775-9	Yes	No	DC states hydrops fetalis, cause unknown; coding erroneous
96	762-1	Yes, multiple coding	No	Death due to pre-eclamptic toxemia. "Mother Rh negative" given as contributory cause; irrelevant
97	775-0	Yes	Yes	
98	775-0	Yes	Yes	
99	775-0	Yes	Yes	
101*	775-0	Yes	Yes	

DC = Death certificate.

*No case given No 100 as two cases 44 (twins).

certificate was 774.0, 774.9, 775.0, or 775.9 the case notes showed that in 12 cases the cause of death was not related to HDN. When hydrops or ascites (10 cases) or kernicterus (one case) had been mentioned as the primary cause of death the coding number had been automatically recorded as HDN—that is, category 775.9 or 774.9 (as required by the International Classification of Diseases 1965).² These cases should have been recorded as 778.9—that is, hydrops or kernicterus not due to haemolytic disease. The 12th wrongly coded case (case 51) was coded 775.9 presumably because “immunoincompetence” was thought to mean HDN.

In one further case (case 25), obtained by multiple coding, death was due to fetomaternal haemorrhage, but because hydrops was mentioned it had been (wrongly) allotted to 775 and extracted and sent to us as a case of HDN. Those who formulate the international rules should point out that there is more than one cause of oedema or kernicterus,³ as is allowed for by category 778.9 in the 8th edition of the International Classification of Diseases.²

Walker (personal communication) states that hydrops, both in liveborn and stillborn infants, is extremely rare if not due to haemolytic disease or some gross condition such as the rubella syndrome. On the other hand, oedema of the newborn infant is not unusual and we think that where death needs to be accounted for hydrops may well be certified.

In this series there was one death due to HDN that was not rhesus HDN but due to ABO incompatibility (case 21). Thus 14 of the 54 deaths were not cases of rhesus HDN.

Stillbirths

The results are shown in table II; 69 of the 101 deaths were due to rhesus HDN. In the 83 cases where the coding on the death certificate was 775.0 or 775.9 the notes showed that in 16 cases the cause of death was not related to HDN (in case 35 it was, being due to spherocytosis). In eight of the 16 the same miscoding of hydrops had occurred, but in others there was a further difficulty that is particularly likely to occur with stillbirths. Mothers immunised to Rh may have stillbirths from other, often unknown, causes, but the death certificate often includes “Rh incompatibility” even when this is not relevant. This is the certifying doctor’s mistake, and it occurred in two of the 16 cases. A worse error (also the doctor’s fault) is to record “rhesus” on the death certificate when the mother is rhesus-negative but no antibodies are present and the cause of the stillbirth is again either unknown or at any rate not due to the Rh factor. Six of the 16 cases fell into this group.

In the stillbirths there were 18 multiple coded cases, and examination of the notes showed that in four of these (cases 14, 36, 48, and 59) rhesus HDN was the primary cause of death. In the other 14 (cases 15, 16, 28, 44, 44 (twins), 53, 68, 76, 79, 83, 84, 90, 93, and 96) rhesus incompatibility played no part, even in case 76, where the mother had antibodies. Among these 14 cases, hydrops contributed five cases (cases 16, 68, 79, 84, and 90). Altogether, therefore, there were 13 “hydrops” errors among the stillbirths (multiple coded cases 5, non-multiple coded cases 8).

When the stillbirth was not due to rhesus HDN even though maternal antibodies were present multiple coding contributed one case (case 76) and non-multiple coding two. In the category where no rhesus antibodies were present yet Rh was cited multiple coding gave three cases (15, 28, and 96) and non-multiple coding six. The remaining five multiple coding cases where death was due to miscellaneous causes but not to rhesus HDN were cases 44 and 44 (twins), 53, 83, and 93 (table II).

Therefore, among the 101 stillbirths we studied there were 31 cases where the cause of death was not due to rhesus HDN, and in 30 of these it was not connected with HDN of any type.

Two major errors

Our findings in the death certificates of both the live births and the stillbirths show two major errors. Firstly, since some of the antecedent or subsidiary causes were in fact primary (“the underlying cause”), particularly in the liveborn infants (7 out of 40 cases compared with 4 out of 69 stillbirths), the number of rhesus deaths will have been greatly underestimated because multiple coding, which revealed these cases, was performed for only 25% of deaths. Secondly, over a quarter of the cases sent to us were not rhesus deaths at all (45 out of 155). In terms of numbers these mistakes tend to cancel each other out.⁴ For example, we estimate that the number of deaths from HDN

among live births in 1977 was about 60 and among stillbirths about 75 (total 135) whereas the OPCS (J A C Weatherall, personal communication) gave 48 and 92 (total 140). Nevertheless, the official statistics are misleading for assessing the effectiveness of prophylaxis since about a quarter of the deaths among liveborn infants (14 out of 54) and rather more (31 out of 101) among the stillbirths recorded as rhesus deaths were incorrect. These deaths could not have been prevented by any form of prophylaxis.

ASSESSMENT OF ANTI-D PROPHYLAXIS

Table III shows how the mothers of the liveborn and stillborn infants had become immunised and whether anti-D had been given.

TABLE III—Immunisation of mothers in relation to anti-D prophylaxis: numbers of cases in each category

Category No	Category	Liveborn infants	Stillbirths
1	Immunised after term deliveries before anti-D available	12	36
2	Immunised by abortion before anti-D available after abortions	3	1
3	Immunised during pregnancy*: (a) Before 28th week (b) After 28th week	1 6	0 9
4	Immunised by Rh antigens $\bar{c}$ and/or E (mother D-positive and therefore no prophylactic anti-D given)	1	3
5	Immunised despite anti-D prophylaxis (failures)	2	7
6	Immunised and no record of anti-D having been given when indicated	15	14
Total		40	70

*All after anti-D became available.

In 1969 routine prophylaxis became available for unsensitised Rh-negative women delivered of their first Rh-positive ABO-compatible baby. The dose of anti-D gammaglobulin was then 200 μ g. In 1971 the treatment was extended to all unsensitised Rh-negative women delivered of Rh-positive babies after the 30th week of pregnancy, and the dose was then reduced to 100 μ g. In addition, a dose of 50 μ g was advised for all women known to be Rh-negative who had abortions before the 21st week of pregnancy, and after 20 weeks the standard dose of 100 μ g was advised.^{5, 6}

Many of our cases, particularly the stillbirths, fell into the category (1) where the mother had been immunised before anti-D was available. This is not surprising, bearing in mind the dates when prophylaxis was introduced, since rhesus disease usually occurs in multiparas, the second affected baby tends to be more severely affected than the first, and we studied only deaths. Category 1 also included five foreign women with very bad obstetric histories who came to Britain for expert treatment. If many such high-risk mothers (for any disorder) are included in UK statistics they will contribute to the UK’s relatively high perinatal mortality.

The DHSS is considering the question of antenatal as well as post-natal anti-D, combined treatment being the practice in parts of Canada, Australia, and Sweden.⁷ Theoretically, 15 deaths in our series (category 3b) might have been prevented, since they were all recorded after anti-D became available. There will also have been others in earlier years, scored here as category 1, and the total number of women immunised in this way is considerable.

Category 5 suggests a substantial failure rate of anti-D but the matter is complicated because we are considering only deaths and not the prevention of immunisation, where it is known that the failure rate is 1% to 2%.⁸

Another disturbing finding at first sight is the non-administration of anti-D (category 6). In categories 1 to 4 anti-D would never have been given for the reasons noted in table III, and therefore categories 5 and 6 need more careful consideration. Only nine mothers out of 38 received anti-D. It would be wrong, however, to argue from this that about 75% of rhesus-negative mothers at risk in the general population are not being treated. If we assume, for example, that 80% of women are being treated, then about 57 of the treated and 14 of the untreated mothers will have rhesus-positive babies in their next pregnancy. About two of the infants of untreated mothers will have rhesus HDN, and, with a mortality of about 15%, there will be 0.3 deaths in the offspring of the untreated mothers. On the other hand, we know from the MRC trials⁸ that, in the offspring of the 80% treated, the incidence

of rhesus HDN will amount to only about 1.5%, and deaths to 0.1 to 0.15. Therefore 65% to 75% of deaths from rhesus HDN will be among infants born to the 20% of women who have not been treated.

It is interesting to compare our results with those from an area where virtually the whole population is known to be protected. In Connecticut (population 3.5 million) almost all women have their confinement in hospital, and over 99% of those eligible for anti-D prophylaxis receive it. In 1977 there were three deaths there from rhesus HDN⁹: in two immunisation occurred before anti-D was available and in one (a stillbirth) during the pregnancy in which the fetus died. Since the birth rate in Connecticut is about the same as in Britain and the population about 1/16th of that in England and Wales we should have had only about 50 deaths, all in categories 1-3 (assuming roughly the same management of pregnancy) if we had had full coverage by anti-D.

Discussion

The first practical question is how to improve the coverage by anti-D. Among all the other necessary activities associated with a birth a relatively new and very simple procedure can easily be forgotten, but if, as in some hospitals, it was the responsibility of one particular person—for example, a midwife or one of the pathology laboratory staff—this should help.

Until the loopholes in the postnatal anti-D programme have been closed it is unjustifiable to start an antenatal anti-D programme, which is much more complicated. Anti-D production would have to be increased by a factor of 4.4, putting more donors to inconvenience and possible future risks, to say nothing of added expense. When the postnatal programme has been fully implemented there would then be a strong case for combining postnatal with antenatal anti-D.

The second problem is how to improve the accuracy of death certification and coding, so that epidemiological studies become more reliable. Walker and Mollison,¹⁰ when investigating the circumstances of every death certified as due to HDN (particularly in relation to exchange transfusion), found that 97 of their 409 traced cases (ascertained through death certificates) were not due to HDN, the main error concerning kernicterus of prematurity and (as in our series) non-haemolytic hydrops. But Knox,¹¹ for example, took no account of the type of error we have described when he was forecasting trends in HDN. The fact that there is a "levelling out" of the curve showing a fall in the incidence of death from rhesus HDN might have been caused by the group of cases incorrectly certified because these will form an irreducible residuum. The paper by Tovey *et al*¹² is not subject to the same criticism because it deals with immunisation rates.

Compared with many other procedures that junior staff have to learn, the accurate filling in of a death certificate and the appreciation of its importance are simple. All that doctors need is some basic information (with examples), and they should know that the coders are only rarely permitted to override the sequence written by a doctor. It would also help if those responsible for the International Classification of Diseases could give more specific instructions about conditions such as hydrops for which there are many causes. The 9th revision of the International Classification of Diseases,¹³ which came into effect on 1 January 1979, gave an opportunity for this, and there are now more details about the classification of hydrops. Nevertheless, in the 8th edition² category 778.9 was reserved for "Hydrops of newborn, not due to haemolytic disease."

We have already pointed out that errors in death certification are found in many conditions,¹ but we have been taken to task on several grounds: we exaggerated the discrepancies; death certificates are not intended for research purposes; mistakes cancel each other out; and what we wrote has been stated more clearly by others.¹⁴⁻¹⁸ We accept some of these criticisms but by studying a special problem in detail, as we have done here, we think that many of them have been answered.

We have also refuted the idea that doctors are not willing to discuss problem cases. Before we began our study Sir John

Dewhurst, then president of the Royal College of Obstetricians and Gynaecologists, kindly put a notice in the *Newsletter* of the Royal College of Obstetricians and Gynaecologists, asking obstetricians to give us their co-operation, and this undoubtedly contributed to the 100% ascertainment—all 54 of the liveborn infants and all of the 101 stillbirths. The obstetricians sent us not only the notes of their cases but often their detailed views on the cause of death, which were most helpful, particularly in deciding that death was not due to haemolytic disease.

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ONE HUNDRED YEARS AGO The following are the conclusions at which Dr Martin has arrived in his recent thesis for the doctor's degree, regarding disorders of the eyes produced by tobacco. 1. It is easy to distinguish between amblyopia caused by alcoholic poisoning and by abuse of nicotine, as in both cases the affection presents characteristic symptoms. 2. The most important of these symptoms is the condition of the pupil, which is dilated in alcoholic amblyopia and contracted in the other case. In the first case, the affection progresses irregularly and with occasional changes for the better, which are followed by relapses; while, in the second case, its progress is slow but uninterrupted. In the one, both eyes are always affected to the same extent; in the other, they are not both affected, or at least not simultaneously. The patients do not see as well at night as during the daytime, and do not suffer from hallucinations, illusions of sight, or diplopia. In alcoholic amblyopia, on the contrary, the patients cannot bear a strong light, see better during the night, and complain of hallucinations, polyopia, and diplopia. 3. Visual disturbances, when connected with poisoning by tobacco, are manifested under the following forms: *a*. binocular amblyopia; *b*. muscular amblyopia with central scotoma; *c*. amblyopia caused by both tobacco and alcohol. (*British Medical Journal*, 1879.)