Active surveillance of hepatitis C infection in the UK and Ireland

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Abstract

***Aim*—To investigate the prevalence, distribution, and clinical details of paediatric hepatitis C virus (HCV) infection in the UK and Ireland.**

***Methods*—Active monthly surveillance questionnaire study coordinated through the British Paediatric Surveillance Unit, to all consultant paediatricians in 1997 and 1998.**

***Results*—A total of 182 HCV infected children were reported from 54 centres and by paediatricians from eight different specialties. In 40 children HCV was acquired through mother to child transmission (MTC children); 142 were infected by contaminated blood products (n = 134), organ transplantation (n = 2), needles (n = 4), or unknown risk factor (n = 2). Intravenous drug use was the risk factor for 35 mothers of MTC children. Twelve children were coinfected with HIV and four with HBV. Recent serum aspartate aminotransferase or alanine aminotransferase values were at least twofold greater than the upper limit of normal in 24 of 152 children; this occurred in five of 11 HIV coinfected children. Liver histology, available in 53 children, showed normal (7%), mild (74%), moderate (17%), or severe (2%) hepatitis. Twenty eight children had received therapy with interferon alfa.**

***Conclusion*—Most current paediatric HCV infection in UK and Ireland has been acquired from contaminated blood products, and most children are asymptomatic. There is a need for multicentre trials to inform clinical practice and development of good practice guidelines in this area. Long term follow up of this cohort of HCV infected children is planned to help determine the natural history over the long term of HCV acquired during infancy and childhood.**

(*Arch Dis Child* 2000;**82**:286–291)

Keywords: hepatitis C infection; surveillance; natural history; UK and Ireland

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Accepted 6 October 1999

Hepatitis C virus (HCV) is a leading cause of chronic liver disease, and because of the magnitude of the infection worldwide, has important implications for public health.[1–3] Once infection has occurred, the virus persists in the host in a high proportion of cases and can lead to chronic liver disease or hepatocellular carcinoma.[1 4] Because of the long latency of the disease, many individuals acquiring HCV infection during adulthood may die with, rather than of the infection.[5] However, children infected in their early years may be more likely to develop hepatic sequelae in early adulthood.

The major routes for HCV transmission to children include perinatal transmission from an infected woman (mother to child (MTC) transmission), transfusion of infected blood or blood products, and transplant of an infected organ. Intrafamilial transmission has also been reported but appears to be relatively uncommon if possibilities of blood–blood contact are excluded.[6] In the UK, routine screening of blood, blood products, and organ donors for HCV started in September 1991. However, although some children were identified through the blood transfusion service "look-back exercise" which commenced in 1995 with the aim of tracing, counselling, and testing recipients of HCV infected blood, children who received blood or blood products prior to 1991 have not been systematically screened. The main future burden of paediatric HCV infection will be from MTC transmission, where the risk is approximately 5%,[7–10] and higher if the mother is coinfected with HIV.[7 11] Although it is currently recommended that children of known HCV positive mothers in the UK are tested for HCV, it is unclear how frequently this is carried out or what proportion of HCV infections in pregnancy are recognised.

Between 1992 and 1996, there were over 5000 laboratory reports of anti-HCV antibody positive individuals in England and Wales. The most commonly reported risk factor (in about 80% of those with risk factors reported) was intravenous drug use (IDU).[12] Approximately 20% of HCV infected adult reports were in women of childbearing age.[12] There were also 54 positive HCV antibody reports in children aged 1–15 years, but only three of these were reported to be acquired from MTC transmission, although a further 22 reports were in infants whose infection status could not be ascertained.[12] In 1997 and 1998, 99 of 7523 laboratory reports were in children; 66 of these were in babies under 12 months with indeterminate infection status (M Ramsay, personal communication).

Paediatricians from a range of specialties including haematology, oncology, hepatology, infectious diseases, and neonatology may be involved in the diagnosis, management, and follow up of HCV infected children. The aims of this study were to collate and describe information on the prevalence, distribution, clinical, and management details of known paediatric HCV infection in the UK and the Republic of Ireland.

Methods

The study was carried out through the British Paediatric Surveillance Unit (BPSU) of the Royal College of Paediatrics and Child Health (RCPCH), an active monthly reporting scheme involving all consultant paediatricians in the UK and Ireland, with a response rate in 1997 of 93%.[13] Paediatricians were asked to report all children under 16 years with symptomatic or asymptomatic HCV infection and children under 18 months born to women with known HCV infection in pregnancy. HCV infection was defined by the presence of confirmed positive HCV antibody in a child over 18 months, or two consecutive positive HCV RNA tests at any age.

In the first month of surveillance, paediatricians were requested to report all eligible children under their care. Case ascertainment was checked against laboratory reports to the Communicable Disease Surveillance Centre (CDSC) and the Scottish Centre for Infection and Environmental Health (SCIEH), reports of children traced during the National Blood Authority's HCV lookback exercise, and reports of children coinfected with HIV that were reported through the BPSU to the National Paediatric HIV Programme at the Institute of Child Health (ICH), London.[14]

Demographic and birth/perinatal details, risk factors for HCV infection, clinical presentation, serology and virology data on HCV diagnosis, liver function tests (aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT)), liver histology results, and details of treatment were collected by questionnaire from reporting paediatricians. For children at risk of acquiring HCV through MTC transmission, maternal demographic and risk information were also collected. Paediatricians were requested to classify liver histology results as normal, mild, moderate, or severe hepatitis, or cirrhosis. Where possible they were also requested to provide copies of histology reports, which were scored blind by two independent hepatologists for both inflammation and fibrosis as normal, mild, moderate, or severe. In a subset of children, where sera or plasma were available and genotypic testing had not been done, HCV genotyping was undertaken in a single laboratory using an amplification nested polymerase chain reaction (PCR) method described previously.[15] Date of acquisition of HCV was estimated by date of birth in MTC acquired cases and from date of risk exposure in other cases, classified as known, likely, or inferred.

Analyses were undertaken using Statistical Analysis System (SAS, Cary, New Carolina, USA), using descriptive statistics and χ^2 tests where appropriate. If both AST and ALT liver enzyme results were reported, the higher result in relation to the upper limit of normal was used. Where date of HCV acquisition was unknown, a minimum follow up time was calculated from the date of the first positive HCV test.

Table 1 Demographic details of 182 children with HCV infection reported through the BPSU between April 1997 and December 1998

	Blood product recipient (n = 134)	*Organ transplant recipient (n = 2)*	*Other* (n = 6)*	*Infection from presumed MTC transmission (n = 40)*	*Total (%) (n = 182)*
Current residence					
Thames regions	29	1	2	11	43 (23.7)
Rest of England and Wales	72	1	2	17	92 (50.5)
Scotland	19	0	1	3	23 (12.6)
Republic of Ireland	14	0	1	9	24 (13.2)
Ethnicity					
White	102	2	4	38	146 (80.2)
Indian subcontinent	17	0	2	0	19 (10.4)
Black	3	0	0	0	3 (1.7)
Oriental	3	0	0	0	3 (1.7)
Other†	9	0	0	2	11 (6.0)
Sex					
Male	103	2	4	20	129 (70.9)
Female	31	0	2	20	53 (29.1)
Age at report (y)					
<2	0	0	0	12	12 (6.6)
2 to <5	1	0	1	7	9 (4.9)
5 to <10	35	1	2	14	52 (28.6)
>10	98	1	3	7	109 (59.9)

*Needlestick injury (4), not known (2).
†Includes children from Middle East (4), Latino (1), mixed (3), unknown (1).
MTC, mother to child.

Results

Between April 1997 and December 1998, 660 notifications were received through the BPSU and a further 113 from other sources. A total of 51% of BPSU notifications were in the first month, 41% over the subsequent six months, and the remainder (average 10 per month) over the next 17 months. Excluding 157 duplicates and 70 outstanding reports, there were reports on 546 children. Of these 182 had definitive HCV infection. A further 364 children of indeterminate infection status and born to HCV infected women will be reported elsewhere.

The 182 infected children were reported from 54 paediatric centres in all parts of the UK and the Republic of Ireland (table 1). Six centres, each reporting 10 or more children, were caring for a total of 84 children (46%) whereas 34 centres each reported only one child. Reports were received from 32 general paediatricians, and from 12 haematology/oncology, seven gastroenterology/hepatology, two nephrology, one endocrinology, two infectious diseases, one neonatology, and two community paediatric specialists.

RISK FACTORS FOR HCV INFECTION

HCV acquired through MTC transmission

Among the 40 children with HCV infection acquired from presumed MTC transmission, 17 were born to mothers whose infection status was known before or during pregnancy. In the other 23 children, MTC transmission was assumed but infection could have been acquired postnatally. In 19, the mother was confirmed to be HCV infected after detection of infection in the child. The remaining four had no other risk factors and their mothers were intravenous drug users, but untested for HCV (table 2). Median age at report was 1.9 years (range 0.3–6.5) in the children followed from birth, compared with 8.3 years (range 0.2–14.4) in children diagnosed later.

Children acquiring HCV through other routes

A total of 134 children (74%) were reported to have acquired HCV infection from contami-

Table 2 Underlying disorder or maternal risk factor in 182 children with HCV infection

Risk factor	*Underlying disorder or maternal risk factor*	*Total (%) (n = 182)*
Blood product recipient (n = 134)	Haemophilia	41 (23.0)
	Leukaemia	27 (14.0)
	Thalassemia	9 (5.1)
	Aplastic anaemia	3 (1.7)
	Cardiac surgery	7 (3.9)
	Renal disease	3 (1.7)
	Neonatal problems*	12 (6.7)
	Miscellaneous†	6 (2.9)
	Unknown	26 (14.0)
Organ recipient (n = 2)	Renal	2 (1.1)
Other (n = 6)	Needlestick injury	2 (1.1)
	Child IDU	2 (1.1)
	Not known	2 (1.1)
Presumed MTC transmission (n = 40)	Mother IDU	35 (19.6)
	Mother blood product	4 (2.3)
	Not known	1 (0.6)

*Received blood/blood products after birth for: anaemia of prematurity (2), neonatal sepsis (3), biliary atresia (2), ABO incompatability (1), surgery (1), birth asphyxia (2), unknown (1).
†Gaucher's disease (1), congenital abnormality (1), von Willebrand's disease (3), Goodpasture's syndrome (1).
MTC, mother to child; IDU, intravenous drug use.

Table 3 Results of up to three HCV RNA test results by risk factor and treatment with alfa interferon

	Blood or organ recipient and "other" group		*Presumed MTC transmission*		
	Treated (n = 28)	*Untreated (n = 114)*	*Treated (n = 3)*	*Untreated (n = 37)*	*Total (n = 182)*
Consistently PCR positive					
P	4	36	0	2	42
PP	3	15	0	13	31
PPP	6	13	1	14	34
Consistently PCR negative					
N	0	7	0	1	8
NN	0	19	0	0	19
NNN	0	8	0	2	10
Mixed PCR results					
PN or PPN or PNN	11	6	2	1	20
PNP or NPP	4	0	0	3	7
No PCR result	0	10	0	1	11

P, positive PCR; N, negative PCR; MTC, mother to child.

nated blood or blood products, two from organ transplantation, four from contaminated needles, and in two children the risk factor was unknown (table 1). Ten children who received contaminated blood products also had organ transplants: four bone marrow, three kidney, and three liver. Treatment for haemophilia and leukaemia were the most common reasons for receiving blood products but the underlying reason was not known in 26 children, most of whom received transfusions early in life and had transferred to the care of a different paediatrician. Only one child, who received contaminated blood in Russia, was born after September 1991. Boys were over-represented among children infected by contaminated blood products; this group included 41 boys with haemophilia and 21 with leukaemia (tables 1 and 2).

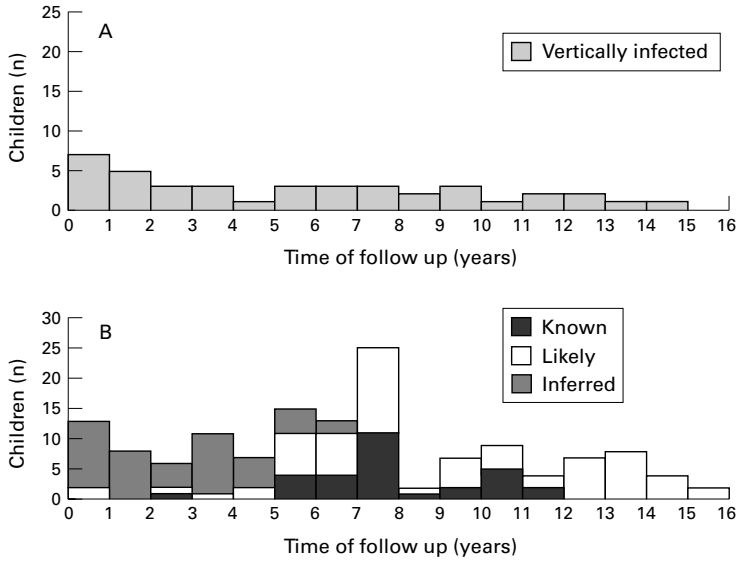

Figure 1 Duration of follow up. (A) children infected through presumed MTC transmission (n = 40). (B) Children infected by other means (n = 142).

DIAGNOSIS OF INFECTION, HCV RNA POSITIVITY, AND DURATION OF FOLLOW UP

A total of 171 children over 18 months of age were HCV antibody positive by either two second or third generation enzyme linked immunosorbent assay (ELISA) tests or by an ELISA test supplemented by recombinant immunoblot asay. One child coinfected with HIV and HCV from MTC transmission was repeatedly HCV antibody negative but HCV RNA positive on two consecutive occasions at the age of 9 years. The mother was also dually infected with HCV and HIV, and anti-HCV negative but HCV RNA positive. Ten children aged 18 months or less at the time of report were considered to have acquired infection through MTC transmission on the basis of two consecutive positive HCV RNA tests.

A total of 171 children (94%) had one (n = 50), two (n = 53), or three (n = 68) consecutive HCV RNA test results reported. Of these, 107 (62%) were positive on one or more tests, 37 (22%) were consistently negative, and 27 (16%) had mixed results (table 3). None of the children with only PCR negative results had received any specific anti-HCV therapy. Of the two children with infection acquired from MTC with three consecutive negative PCR results, both mothers had tested HCV antibody positive (one before and one after the birth of the child) and the children remained HCV antibody positive after 18 months of age.

Figure 1 shows the distributions of duration of follow up for presumed MTC infected children and those acquiring HCV through other routes. Among children infected through other routes, follow up duration was similar among children with known and those with likely date of HCV acquisition. The minimum median duration of follow up for all children was estimated to be 6.7 years (range 0.04–15.6).

CLINICAL DETAILS

Coinfections with HBV and HIV

Six children (5%) infected through contaminated blood products (four with haemophilia) had HIV infection. One of the children with haemophilia and HIV was also reported to have hepatitis B infection; a further three children (two with leukaemia) had hepatitis B infection without HIV. Ten (25%) of the children infected through MTC transmission were born to mothers coinfected with HIV, and six of these children were themselves dually infected with HIV and HCV (table 4). A further 14 mothers (35%) were known to be HIV negative; in the

remaining 16 (40%), HIV status was unknown. The HIV and HCV coinfected mothers all had IDU as a risk factor for both infections and were reported from Dublin (n = 5), Scotland (n = 3), and London (n = 2).

Signs/symptoms, liver function, and HCV genotypes

Only one child was reported to have symptoms of clinical significance. This child had received an HCV infected blood transfusion at 16 months of age, subsequently developed cryptogenic cirrhosis, and required a liver transplant at age 3 years and 4 months. Although it was reported that cirrhosis was probably not caused by HCV infection, HCV was isolated from the diseased liver at the time of transplantation and therefore the possibility of rapid progression to cirrhosis in this child cannot be excluded.

AST or ALT results taken closest to the time of reporting were normal or less than twice the upper limit of normal in 128 of the 152 children (84%) in whom they were reported (table 4). Five of the 11 children (45%) with HIV coinfection had AST results over twice the upper limit of normal compared with 11 of 141 (8%) HIV negative children (χ^2 18.0, p = 0.001). Liver enzyme results were not reported for the children with HBV infection. Only one of the 37 children with consistently negative HCV RNA results had abnormal liver enzyme values.

In 53 children from 25 centres, results of liver histology were available (table 4). Most were children with previous malignant disease and only one child with haemophilia had undergone a biopsy. One child with mild hepatitis had coinfection with HIV and one with moderate hepatitis had HBV infection. All children who had biopsies had one or more positive HCV RNA results reported. Ten children (19%) were reported on the questionnaire to have moderate (n = 9) or severe hepatitis (n = 1) at the time of biopsy, and none to have cirrhosis. Full histology reports were received for 33 children (62%) and scored by two independent reviewers. Exact concordance of scoring between the two reviewers for the degree of both inflammation and fibrosis occurred for 21 reports (64%). In general, fibrosis and inflammation scores concurred but where there was discrepancy, the fibrosis scores given by the reviewers were generally higher than their inflammation scores or the hepatitis gradings reported on the questionnaires. Taking fibrosis scores, reviewers scored one of the biopsy specimens (3%) as severe and seven (21%) as moderate, compared with one report (3%) of severe and three (9%) of moderate hepatitis on the questionnaire. Length of time since HCV acquisition, and underlying disease (excluding children with haemophilia) did not differ between children with normal or mild biopsy findings, compared to those with moderate or severe findings. Data on genotype and viral load were too incomplete to be analysed.

HCV genotypes were established for 73 of the 114 children (64%) with most recent positive HCV RNA results. Countries of birth were known for 17 MTC infected children with genotypes. All were born in the UK (n = 11) or Ireland (n = 6) and all but one mother were born in the UK or Ireland. The majority (60%) were type 1a or 1b but all types were represented in both MTC acquired HCV and infection acquired through other routes (table 4). Owing to the incomplete nature of these data, it was not possible to relate genotype to other disease characteristics. Similarly, although data on HCV viral load were requested, they were reported for only 37 children, and in this principally cross sectional study, could not be reliably related to other factors.

Table 4 Clinical details of 182 HCV infected children

	*Blood** (n = 134)	*Other†* (n = 8)	*MTC‡* (n = 40)	*Total (%)* (n = 182)
Other associated infections				
Hepatitis B	3	0	0	3 (1.7)
HIV infected	5	0	6	11 (6.0)
HIV+ and hepatitis B	1	0	0	1 (0.5)
HIV− but mother HIV+	n/a	n/a	4	4 (2.2)
No associated infection	125	8	30	163 (89.6)
Reported signs and symptoms				
Liver failure§	1	0	0	1 (0.6)
Fatigue and bruising	1	0	0	1 (0.6)
Hepatomegaly	0	0	5	5 (2.8)
None	132	8	35	175 (96.0)
Transaminases (AST or ALT¶) (n = 152)				
Normal	70	4	13	87 (57.2)
<2 × ULN	30	2	9	41 (27.0)
2 to <5 × ULN	8	0	11	19 (12.5)
5 to <10 × ULN	3	1	1	5 (3.3)
>10 × ULN	0	0	0	0
Liver histology (n = 53)				
Normal	3	0	1	4 (7.5)
Mild hepatitis	30	3	6	39 (73.6)
Moderate hepatitis	6	0	3	9 (17.0)
Severe hepatitis	1	0	0	1 (1.9)
Cirrhosis	0	0	0	0
Genotypes (n = 73)				
1	1	0	1	2 (2.7)
1a	18	0	6	24 (32.9)
1b	15	0	3	18 (24.7)
2	1	0	0	1 (1.4)
2a	2	0	0	2 (2.7)
2b	2	0	0	2 (2.7)
3	4	0	2	6 (8.2)
3a	9	1	6	16 (21.9)
4	0	0	1	1 (1.4)
5	1	0	0	1 (1.4)

*Acquired from HCV infected blood/blood products; †organ transplant and other; ‡presumed mother to child transmission.
§Probably not HCV related.
¶AST was used for 77 and ALT for 75 children.
ULN, upper limit of normal.

Therapy

A total of 28 children (21%) who had received infected blood products or an organ transplant had received treatment with interferon alfa compared with three (8%) of the children acquiring HCV through MTC transmission. No child was reported to have received any other therapy. Nineteen of the treated children (61%) were reported from four centres caring for 64 children (35%), whereas the remaining 12 children were from 10 different centres. Thirteen children with haemophilia received interferon alfa without having a pretreatment biopsy. Among the 15 with biopsy results reported pretreatment, 10 were classified as mild and five as moderate hepatitis, both by the independent reviewers and on the questionnaires.

In 22 children, more detailed information on the duration and response to interferon alfa therapy was available, although dose, which varied from 1 to 6 million units given three

times weekly, was reported for only eight children. In 11 children, HCV PCR remained negative at or near the end (n = 7) or after completion (n = 3) of therapy, and one child still on therapy at the time of report, was PCR negative one month after starting therapy. In 11 children, PCR either remained positive throughout therapy (n = 6) or rebounded after completion of therapy (n = 5), with one of these children responding to a further longer course of interferon alfa. Duration of therapy was 12 months or longer in 10 of the 11 courses where response occurred, compared with a duration of six months or less in nine of the 11 courses resulting in non-response or relapse. Toxicity was cited as the reason for stopping interferon alfa therapy at two months in one non-responding child.

Discussion

In this paper, we have described the epidemiology, natural history, and management details of paediatric HCV infection reported through active surveillance in the UK and Republic of Ireland up until the end of 1998. The majority of reported children acquired HCV through blood or blood products. Among children with presumed MTC transmission of HCV, nearly 90% of mothers had current or past IDU as the risk factor for HCV acquisition. The possibility of postnatal intrafamilial acquisition rather than peripartum transmission was present in about half these children, and has been reported elsewhere.[6] It should be noted that children under 18 months of age all had definitive HCV infection, based on at least two consecutive positive HCV RNA PCR results. Children recently born to infected women and reported to the study with indeterminate HCV infection status are currently being followed up and will be the subject of a future report.

We are aware that not all known paediatric HCV infection will have been reported to our study during the 20 month period of active surveillance. Apart from failure to report among some paediatricians, some children may be under the care of adult physicians, or not receiving specialist care. Infected children are distributed throughout the UK and despite the relatively small numbers, are cared for in a large number of centres with only six centres looking after 10 or more children. Supplementary sources of case ascertainment including laboratory reports to the Public Health Laboratory Service and SCIEH (where demographic data allowed matching to take place) and HCV infected children traced during the National Blood Authority's (NBA) lookback exercise suggest that as many as 30% of infected children may not have been reported to us. It is of interest that the 20 children (36%) identified by the NBA and not reported in this study tended to be older (p = 0.06) and were more likely to have negative HCV RNA results (p = 0.02) compared with those in our study (Helen Harris, personal communication, 1999). All HIV and HCV coinfected children reported to the National Study of HIV in Pregnancy and Childhood at the Institute of Child Health, London were reported to our study. There appears to be little overlap between HCV and HIV infection acquired through MTC transmission, except in Ireland and Scotland where IDU is the maternal risk factor for both. Whereas over 80% of vertically acquired HIV in the UK is among children of African origin residing in the Thames regions,[14] only 28% of HCV acquired through MTC transmission was from London and there were no reported cases among black African children. HCV testing policies for children, whether prospectively or retrospectively known to be born to HCV infected women, are likely to differ by unit and among different groups of paediatricians. It is also likely that more children will be diagnosed in the future, particularly if more effective therapies for HCV become available.

As previously reported, among definitively HCV antibody positive children, there is evidence of spontaneous clearance of HCV. A total of 29 children (16%), including both those with HCV through MTC transmission and those infected through other routes had two or more consecutive samples negative for HCV RNA by PCR. Wide intraindividual variation in PCR positivity has been previously reported among vertically infected children[16] and longer follow up is required to confirm whether these children have really cleared infection. Intermittent viraemia is well recognised in adult HCV infection, and viraemia in pregnant women has been shown to be positively related to the risk of MTC HCV transmission.[8] In our study, all children with two or three consecutive negative HCV RNA results also had normal aminotransferase results; none had had a liver biopsy, and none had received any therapy. Because of the nature of this cross sectional survey, these figures must be interpreted with caution. However, they are in keeping with other studies in adults and children.[17 18] The converse situation of HCV RNA positivity with negative HCV antibody results was only reported in one child in this study and could be explained by immune suppression as a result of coinfection with HIV. This case emphasises the need to undertake HCV RNA as well as HCV antibody tests, if HCV is suspected in an immunosuppressed child.

The median duration of infection for children with known or likely dates of HCV acquisition at the time of reporting was almost eight years, and the minimum follow up since infection for the whole cohort was nearly seven years. Very few children had any signs or symptoms over this period. However, among those where liver biopsies were performed (and in whom follow up was similar to that in non-biopsied children—data not shown), about a quarter had progressed to moderate or severe hepatitis, but none to cirrhosis. The exception was a child who required a liver transplant for cryptogenic cirrhosis and in whom it was not possible to exclude cirrhosis caused by HCV acquired less than two years previously. As these children have acquired infection in childhood, even assuming long incubation periods, those who have not cleared infection are likely to require therapy for

chronic liver disease, including transplantation in early to mid adulthood at considerable cost to the community.[1]

We did not attempt to relate AST or ALT values to liver histology results, because the time relation between the two parameters could not easily be determined in this cross sectional study. In an observational study by García-Monzón *et al*, the authors suggested that histological changes in children with HCV may be slower to develop than in adults, although duration of infection and prevalence of 1b genotypes were similar in the adults and children in their study.[19] It was unclear how subjects were selected for this study which could have been biased by differences in referral patterns between HCV infected adults compared with children.

We did not collect data on reasons for treating with interferon alfa. It is of interest that the proportion of children treated did not seem to be related to severity of hepatitis as classified by reporting paediatricians or reviewers. Duration and dose of alfa interferon varied considerably although full reasons for this cannot be analysed from this study. These factors may reflect the large number of centres treating relatively few children, but may also reflect changes in clinical practice over time, as regimens of interferon alfa have changed with emergent data from adult trials. The data presented in this paper on response to therapy must be interpreted with caution, as we had little information on durability of response after stopping therapy. Furthermore, the short duration of therapy in non-responders may have been the result of clinicians choosing to stop therapy early in children who did not become PCR negative on therapy. No child had received ribavirin therapy at the time of reporting to this study.

Only a few small randomised controlled trials of alfa interferon have been undertaken in paediatric HCV infection.[20 21] With recent increased evidence of the efficacy of ribavirin in combination with alfa interferon in adults,[2 22 23] this situation may change and it is important that studies of its efficacy and toxicity in children are undertaken.

In conclusion, this paper reports on some aspects of known HCV infection in children in the UK and the Republic of Ireland. The magnitude of the problem is likely to be greater than reported here because of under reporting, loss to follow up of asymptomatic infected children, and variation in testing policies for children who received blood or blood products prior to 1991, and among children born to known HCV infected women. Long term follow up of this cohort of HCV infected children through the National HCV Registers in England and Wales[24] and in Scotland is planned to help determine the natural history of HCV acquired during infancy and childhood. In view of differing management and treatment and the large number of centres caring for small numbers of children in the UK and in other European countries, it is important that clinical trials of management strategies and therapies are undertaken to inform paediatricians on the most appropriate way to manage children with HCV infection.

We thank the BPSU, all reporting paediatricians, and other health professionals who have completed questionnaires, in particular those with larger numbers of children at their centres including Alistair Baker, Karina Butler, Mary Healy, Anna Lloyd, Jacqueline Mok, Jean Petrie, Cath Sinay, Jaswant Sira, Sharon Sneddon, and Cecilia Ward. We thank Trinh Duong and Janet Masters from the National Study of HIV in Pregnancy and Childhood for their support and collaboration; Kathryn Harris at PHLS who undertook centralised HCV genotyping; AE Ades and Trinh Duong for help with the statistical analysis; and Catherine Peckham for comments on the paper. This research was funded by the UK Department of Health. All views, and any errors are the responsibility of the authors alone.

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