Clinical implications

- Detecting urinary tract infection in early childhood is important for preventing renal damage
- Suprapubic aspiration of urine is considered in Britain to be a difficult technique
- This study showed that use of ultrasound guidance makes suprapubic aspiration in children and babies easy and safe
- Low bacterial counts were present in the urine of two fifths of the children with abnormalities of the urinary tract
- Clinicians should regard low bacterial counts as important

had vesicoureteric reflux. Secondly, few of the non-bacteriuric specimens showed pyuria. All the children from whom these specimens came were being investigated for febrile illnesses. Thus the view that pyuria often occurs as a non-specific response to fever seems untenable. Two thirds of the children with sterile pyuria were neonates, of whom many were premature and many were taking antibiotics; the possibility of bloodborne urinary tract infection, known to occur in neonates,[13] is strong. Radiological abnormalities were found in about a third of the children who were investigated.

We suggest that clinicians should always seek an explanation for sterile pyuria and should consider the possibility of urinary tract infection if sterile pyuria persists.

We thank Drs G M Lewis, M J Hardman, and E R Wozniak for permission to include their patients and Veronica Symes for typing the manuscript.

1 Smellie JM. Reflections on 30 years of treating children with urinary tract infections. *J Urol* 1991;**146**:665-8.
2 Chiu N-C, Huang F-Y, Tsai T-S. Urinary tract infections in children. *Acta Paediatr Sin* 1989;**30**:225-31.
3 Airede AI. Urinary tract infections in African neonates. *J Infect* 1992;**25**: 55-62.
4 O'Callaghan C, McDougall PN. Successful suprapubic aspiration of urine. *Arch Dis Child* 1987;**62**:1072-3.
5 Austin N, Maskell R, Hallett RJ. Diagnosis of urinary tract infection in children. *Lancet* 1992;**339**:65.
6 Maskell R. *Urinary tract infection*. London: Edward Arnold, 1982:24.
7 Smellie JM. Medical aspects of urinary infection in children. *J R Coll Physicians Lond* 1967;**1**:189-96.
8 Ahmad T, Vickers D, Campbell S, Coulthard MG, Pedler S. Urine collection from disposable nappies. *Lancet* 1991;**338**:674-6.
9 Lee P, Verrier Jones K. Urinary tract infections in febrile convulsions. *Arch Dis Child* 1991;**66**:1287-90.
10 Kellogg JA, Manzella JP, Shaffer SN, Schwartz BB. Clinical relevance of culture versus screens for detection of microbial pathogens in urine specimens. *Am J Med* 1987;**83**:739-44.
11 Powell HR, McCredie DA, Ritchie MA. Urinary nitrite in symptomatic and asymptomatic urinary infection. *Arch Dis Child* 1987;**62**:138-40.
12 Woodward MN, Griffiths DM. Use of dipsticks for routine analysis of urine from children with acute abdominal pain. *BMJ* 1993;**306**:1512.
13 Bergström T, Larson H, Lincoln K, Winberg J. Studies of urinary tract infection in infancy and childhood. XII. Eighty consecutive patients with neonatal infections. *J Pediatr* 1972;**80**:858-66.

(Accepted 12 November 1993)

Skin test reactivity and number of siblings

Erika von Mutius, Fernando D Martinez, Christian Fritzsch, Thomas Nicolai, Peter Reitmeir, Hans-Heinrich Thiemann

University Children's Hospital, Munich, Germany
Erika von Mutius, *paediatrician*
Thomas Nicolai, *paediatrician*

Respiratory Sciences Center, Department of Pediatrics, University of Arizona, Tucson, Arizona, USA
Fernando D Martinez, *paediatric pulmonologist*

University Children's Hospital, Leipzig, Germany
Christian Fritzsch, *paediatrician*

Research Centre for Environment and Human Health, Medis Institute, Munich, Germany
Peter Reitmeir, *statistician*

University Children's Hospital, Halle, Germany
Hans-Heinrich Thiemann, *paediatrician*

Correspondence and reprint requests to:
Dr E von Mutius, Universitätskinderklinik, Lindwurmstr 4, D-8000 München 2, Germany.

BMJ 1994;308:692-5

Abstract

***Objective*—To investigate the relation between skin test reactivity in children and number of siblings.**

***Design*—Cross sectional survey among schoolchildren aged 9-11 years. Skin prick tests in the children and self completion of written questionnaire by their parents.**

***Subjects*—5030 children in Munich and 2623 children in Leipzig and Halle, Germany.**

***Main outcome measures*—Atopic status assessed by skin prick tests.**

***Results*—After possible confounders were controlled for, the prevalence of atopic sensitisation decreased linearly with increasing number of siblings (odds ratio = 0·96 for one sibling, 0·67 for five or more siblings; P = 0·005). In atopic children the severity of the skin test reaction as assessed by the weal size was not associated with the number of siblings.**

***Conclusions*—Factors directly or indirectly related to the number of siblings may decrease the susceptibility of children to become atopic. Thus, declining family size may in part contribute to the increased prevalence of atopic diseases reported in Western countries over the past few decades.**

Introduction

A strong inverse association between the number of siblings and the prevalence of hay fever in British children was reported by Strachan.[1] As the presence of older siblings had a stronger effect than the presence of younger siblings, the author suggested that factors such as viral infections early in life may prevent the development of allergic sensitisation. His observations, however, were based on parents' answers to a questionnaire. It could be argued that the effects observed may have been affected by recall bias, as parents with many children may not remember a relatively mild disease such a hay fever as accurately as parents with only one or two children.

The aim of this report was to investigate the relation between the number of siblings and an objective measure of atopic sensitisation in children living in eastern and western Germany. We performed skin prick tests in 9-11 year old schoolchildren in a survey in Leipzig and Halle, East Germany, and Munich, West Germany, and related these findings to answers to a parental questionnaire on household size, socioeconomic status, and occurrence of disease.

Methods

STUDY AREAS AND POPULATIONS

In former West Germany, all fourth grade pupils (n = 7445) at all primary schools in Munich, a city of about 1·3 million inhabitants located in the southwestern part of the country, were included in the study. All schoolchildren (n = 3105) attending the fourth grade of a random sample of 39 schools in Leipzig and of 23 schools in Halle were studied in former East Germany. Leipzig, a city of about 535 000 inhabitants, is located in the southeastern part of the country in close proximity (35 km) to Halle, a city of about 300 000 inhabitants. These two cities are heavily polluted due to private coal burning and industrial emissions, whereas Munich has moderate industry but

heavy car traffic.[2] In all three study areas, climatic conditions are very similar.

Children in Munich were studied between September 1989 and July 1990 and children in Leipzig and Halle were studied between October 1991 and July 1992. The main purpose of both surveys was to determine the prevalence of asthma and allergies in western and eastern Germany.[6] Therefore, field workers performing the skin prick tests were blind to the hypotheses being tested.

QUESTIONNAIRE

A self administered questionnaire was distributed through the schools to the parents. The questionnaire had been developed according to international recommendations.[3] Questions concerning diagnoses and typical symptoms of respiratory and allergic disorders in the child and the parents were included. In addition, the sociodemographic characteristics of the family, such as the number of siblings, the parents' education, and the presence of pets at home, were assessed by questionnaire.

Parents were asked how many siblings their child had; how many years of education the mother and the father of the child had; whether there were pets at home; who smoked in the household; and whether a member of the family had ever had asthma, hay fever, or eczema (atopic dermatitis). Children with one or more first degree relatives with any of these diseases were defined as having a family history of asthma or atopy.

SKIN PRICK TESTS

The sensitivity to six common aeroallergens (*Dermatophagoides pteronyssinus*, grass, birch and hazel pollen, cat and dog dander) was assessed by skin prick tests; the same multitest device (Stallerkit) was used in all three study areas. Results obtained with this device had been validated in a pilot phase in Munich.[4] In this pilot study, weal reactions obtained with the multitest were compared with weal reactions elicited by the puncture method using the same allergen extracts in 31 atopic and 33 non-atopic children. Validation of results of skin tests by radioallergosorbent testing has been reported and discussed elsewhere.[4]

A child was considered sensitised to a specific allergen if a weal reaction of 3 mm or more to this allergen was present, the reaction to the negative control being previously subtracted from that to the respective allergen. Children with a weal reaction $\geqslant 3$ mm to one or more of the six allergens tested were considered to be atopic.

STATISTICAL ANALYSIS

The prevalence of atopic sensitisation was calculated for numbers of siblings in both West and East Germany. The Mantel-Haentzel statistic was computed to estimate statistical significance over all strata. A regression analysis was used to assess the effects of the number of siblings on the weal size of skin prick test reactions in atopic and non-atopic subjects. A categorical logistic regression model[5] was used to assess the independent effect of the number of siblings on atopic sensitisation after possible confounders such as a family history of asthma or atopy, sex, the socioeconomic status of the family, the presence of pets at home, and the study area were simultaneously controlled for. To assess a linear trend for the predictor variable, the logarithms of the odds ratio obtained from the logistic regression were plotted against the different levels of the predictor variable. Furthermore, linearity was tested by comparing the goodness of fit χ^2 of the categorical and linear model. If the fit of the data did not deviate significantly from the linear model, the slope of the regression line was obtained from a logistic regression model that included the same predictor variables plus the number of siblings as a scored ordinal term. The 95% confidence intervals around the regression line for each odds ratio were calculated on the logarithmic scale using the technique proposed by Rothman.[6] Calculations of confidence intervals from logistic regression when the risk decreases with increasing "exposure" may be problematic.[6] For this reason, odds (and their confidence intervals) of being "non-atopic" were first calculated from the logistic model. To make results more intuitively understandable, reciprocals of these odds and their confidence intervals are reported. The SPSS software package version 4.0 was used for all computations.[7]

All study methods had been approved by the ethics committee of the Bavarian Medical Association. Informed consent for skin prick tests was obtained from the parents.

Results

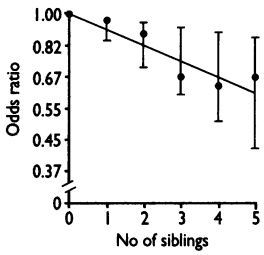
The questionnaire was distributed to 1854 children in Leipzig, 1251 children in Halle, and 7445 children in Munich. Parents of 1500 (80·9%) children in Leipzig, 1134 (90·6%) children in Halle, and of 6537 (87·8%) children in Munich returned the questionnaire. The proportion of children without German nationality was 0·5% (eight) in Leipzig, 0·3% (three) in Halle, and 23·0% (1507) in Munich. To keep the study populations as similar as possible with regard to ethnic background, the analysis was restricted to children with German nationality. As children in Leipzig and Halle were very similar with respect to sociodemographic characteristics, prevalence of respiratory and allergic disorders, and results of skin prick tests, data for these two populations were pooled. Of the eligible German children for whom the questionnaire was returned, skin prick tests were obtained in 2335 (89·0%) children in East Germany and 4451 (88·5%) children in Munich. Subjects not tested for skin reactivity to allergens did not differ in their family size nor in their family history of atopy from subjects undergoing skin prick tests.

Atopic sensitisation is about three times as prevalent in West Germany as in East Germany.[8] Skin test reactivity decreased significantly with age and was more prevalent when the tests were performed in the months January to May than in June to December (data not shown). The table shows the prevalence of atopic sensitisation in children with different numbers of siblings in both study areas. After the study area was adjusted for, the prevalence of atopic sensitisation decreased significantly with increasing numbers of

*Prevalence (%) of atopy among children with different numbers of siblings in East and West Germany**

	No of siblings					
	0	1	2	3	4	≥5
Prevalence (No/group) of atopy:						
West Germany	36·1 (405/1122)	38·0 (859/2263)	36·5 (271/742)	31·7 (65/205)	28·6 (18/63)	25·0 (6/24)
East Germany	19·4 (77/396)	17·7 (177/1001)	15·5 (44/284)	15·4 (14/91)	16·7 (5/30)	11·1 (3/27)

$\chi^2 = 4·0$, $P < 0·05$ (Mantel-Haenszel test statistic over both strata).
*A complete data set was not available for every subject.



Odds ratios (95% confidence intervals) of being atopic by number of siblings after correction for other risk factors in a multivariate logistic regression analysis (logarithmic scale)

siblings. This relation between number of siblings and atopic sensitisation was similar in boys and girls (data not shown). When cut off points of 4 mm and 5 mm were used a similar, significant relation was found, but when a weal size of ≥ 2 mm was defined as atopy the association disappeared. This finding may be attributable to a better discrimination of atopic from non-atopic children when a larger weal size is used as cut off point. In atopic and non-atopic children, no association was found between the weal size of the skin prick test reaction and the number of siblings.

The relation of household size to atopic sensitisation was further assessed in a multivariate logistic regression analysis. The prevalence of atopic sensitisation was significantly correlated with the number of siblings ($P=0{\cdot}005$; figure) when various factors were controlled for: family history of asthma or atopy (odds ratio = 1·6; 95% confidence interval 1·4 to 1·8; $P<0{\cdot}0001$); male sex (1·2; 1·1 to 1·4; $P=0{\cdot}0005$); higher maternal education (1·1; 0·9 to 1·2; $P=0{\cdot}4$); maternal smoking (0·8; 0·7 to 0·9; $P=0{\cdot}02$); the presence of pets at home (0·9; 0·8 to 1·0; $P=0{\cdot}1$), and the West German study area (2·6; 2·1 to 3·2; $P<0{\cdot}0001$). Controlling for age and month of testing did not change the results.

Discussion

Our results suggest that factors directly or indirectly related to the number of siblings decrease the susceptibility of children to becoming atopic. These factors do not affect the severity of atopic sensitisation as assessed by the weal size of the skin prick test reaction in atopic subjects.

Our findings are consistent with an earlier report by Strachan, who found a strong inverse correlation between the number of siblings and the prevalence of hay fever in British children.[1] He speculated that declining family size, improvements in household amenities, prevention of viral infectious diseases, and higher standards of personal cleanliness—which are characteristics of what has been called Western lifestyle —may be associated with the increase of atopic diseases seen over the past few decades. The association was stronger for older siblings than younger siblings. Our data do not allow us to disentangle the effect of having older or younger siblings on the development of atopic sensitisation, since parents were asked only how many siblings their children had. Therefore, if children with older siblings are less susceptible to becoming atopic than are children with younger siblings, our results would probably have shown stronger effects had we been able to study the association between sensitisation and number of older siblings separately from that between sensitisation and number of younger siblings.

The factors that cause a decrease in the prevalence of atopic sensitisation with increasing numbers of siblings are not known. However, firstborn children are usually exposed to common infections after their enrolment in kindergarten or school, whereas children born subsequently are often exposed much earlier, through their siblings. Thus, having more siblings may be associated with an increased exposure to viral infections early in life.[9] Recent immunological studies support the hypothesis of a downregulation of IgE production by viral and bacterial infections.[10-12] It has been shown that two mutually exclusive patterns of cytokine release are produced by different clones of T helper cells, and it has been suggested that a predominant activation of TH1-like T helper cells in the course of recurrent viral or bacterial infections may prevent the proliferation of TH2 clones and the development of allergic disease.[10] Our results suggest that having more siblings may prevent the development of atopic sensitisation. Once atopy is present, the number of siblings does not affect the size of the skin reaction. It is thus possible that factors associated with a larger number of siblings may interfere with the process of allergic sensitisation in early life. The size of the weal, on the other hand, may depend on other genetic and environmental factors such as degree of exposure to allergens.

A higher number of siblings may not only reflect an increased exposure to viral infections early in life but may be related to other factors such as the socioeconomic status of larger families, nutrition, household amenities, or personal cleanliness.[1] In addition to these environmental factors, inborn differences between children of increasing birth order may be important. Increasing parity is associated with changes in levels of sialic acid on neonatal lymphocytes.[13] Immunogenicity of these cells can be altered by removal of sialic acid residues.[14] It is not known whether these immunological changes are associated with any changes in disease prevalence.

Several reports have shown an increase in the prevalence of hay fever[15-18] and eczema[15 17 19] over the past few decades. Our results suggest that factors such as declining family size and subsequent decreased exposure to common infectious diseases may indeed be associated with the increase in the prevalence of atopic diseases in Western countries.

Public health implications

- The prevalence of atopic diseases is on the increase
- The development of hay fever has been linked to decreasing number of siblings
- This study shows that an objective measure of atopy (skin test reactivity) decreases with increasing numbers of siblings
- Increased exposure to infections early in life through siblings or socioeconomic factors related to the family size may explain these findings
- The increase in the prevalence of atopic diseases over the past few decades may in part be associated with decreasing family size and higher socioeconomic status

This work was supported by the Bundesministerium für Forschung und Technologie (German Ministry for the Sciences and Technology). Dr Martinez was supported by a SCOR grant (HL14136) from the National Institutes of Health.

1 Strachan DP. Hay fever, hygiene, and household size. *BMJ* 1989;**299**: 1259-60.
2 Von Mutius E, Fritzsch C, Weiland SK, Roell G, Magnussen H. Prevalence of asthma and allergic disorders among children in united Germany: a descriptive comparison. *BMJ* 1992;**305**:1395-9.
3 Ferris BG. Epidemiological standardisation project. *Am Rev Respir Dis* 1978;**118**(suppl):7-53.
4 Berbig B, von Mutius E, Nicolai T, Stiepel E, Adam D. [Comparing the multitest to a conventional skin prick test.] *Allergologie* 1991;**14**:51-7. (In German.)
5 Breslow NE, Day NE. *Statistical methods in cancer research.* Vol 1. *The analysis of case control studies.* Lyons: International Agency for Research on Cancer, 1980:192-246. (IARC scientific publication No 32.)
6 Rothman KJ. *Modern epidemiology.* Boston: Little, Brown, 1986:327-49.
7 *SPSS statistical algorithms.* 2nd ed, Chicago: SPSS Inc, 1991.
8 von Mutius E, Martinez FD, Fritzsch C, Nicolai T, Reitmeir P, Thiemann HH. Differences in the prevalence of asthma and atopic sensitization between East and West Germany. *Am Rev Resp Dis* (in press).
9 Martinez FD, Wright AL, Holberg CJ, Morgan WJ, Taussig LM. Maternal age as a risk factor for wheezing lower respiratory illnesses in the first year of life. *Am J Epidemiol* 1992;**136**:1258-68.
10 Romagnani S. Human TH1 and TH2 subsets: regulation of differentiation and role in protection and immunopathology. *Int Arch Allergy Immunol* 1992;**98**: 279-85.
11 Parronchi P, De Carli M, Manetti R, Simonelli C, Sampognaro S, Piccinni MP, *et al.* IL-4 and IFNs exert opposite regulatory effects on the development of cytolytic potential by TH1 or TH2 human T cell clones. *J Immunol* 1992;**149**:2977-83.
12 Maggi E, Parronchi P, Manetti R, Simonelli C, Piccinni F, Rugiu FS, *et al.*

Reciprocal regulatory effects of IFN-gamma and IL-4 on the in vitro development of human TH1 and TH2 clones. *J Immunol* 1992;148:2142-7.
13 Komlos L, Landmann J, Notmann J, Dulitzky F, Kyzer S, Hart J, *et al.* Sialic acid level in maternal and neonatal lymphocytes and sera correlated to birth order and sex of the neonate. *Biol Neonate* 1992;62:379-84.
14 Shearer WT, Gottlieb C, Kornfeld S. Humoral immunostimulation. VII. Sialic acid masks antigenic sites on antibody-selected variant cell line. *J Immunol* 1977;119:614-7.
15 Varonier HS, de Haller J, Schopfer C. [Prevalence of allergies in children and adolescents.] *Helv Paediatr Acta* 1984;39:129-36. (In French.)
16 Fleming DM, Crombie DL. Prevalence of asthma and hay fever in England and Wales. *BMJ* 1987;294:279-83.
17 Ninan T, Russell G. Respiratory symptoms and atopy in Aberdeen school-children: evidence from two surveys 25 years apart. *BMJ* 1992;304:873-5.
18 Wüthrich B, Schneyder UW, Henaue SA, Heller A. [Incidence of pollinosis in Switzerland. Results of a representative demographic survey with consideration of other allergic disorders.] *Schweiz Med Wochenschr* 1986; 116:909-17. (In German.)
19 Taylor B, Wadsworth J, Wadsworth M, Peckham C. Changes in the reported prevalence of childhood eczema since the 1939-45 war. *Lancet* 1984;i: 1255-7.

(Accepted 16 November 1993)

Chronic hepatitis in United Kingdom blood donors infected with hepatitis C virus

W L Irving, K R Neal, J C E Underwood, P N Simmonds, V James, on behalf of Trent Regional Hepatitis C Virus Study Group

University Hospital, Queen's Medical Centre, Nottingham NG7 2UH
W L Irving, *senior lecturer in clinical virology*
K R Neal, *lecturer in public health medicine and epidemiology*

Royal Hallamshire Hospital, Sheffield S10 2JF
J C E Underwood, *professor of pathology*

Medical School, University of Edinburgh, Edinburgh EH8 9AG
P N Simmonds, *lecturer in medical microbiology*

Trent Regional Blood Transfusion Centre, Sheffield S5 7JN
V James, *consultant haematologist*

Other members of the Trent Regional Hepatitis C Virus Study Group are listed at the end of the paper.

Correspondence to:
Dr Irving.

BMJ 1994;308:695-6

Routine screening for antibodies to hepatitis C virus in blood donations was introduced in Britain in 1991. It showed that 1 in 2000 donors was positive for antibodies. The natural course and importance of hepatitis C virus infection in apparently healthy people are unclear. We assessed the value of clinical and laboratory data in predicting the need for liver biopsy in blood donors with antibodies to hepatitis C virus.

Patients, methods, and results

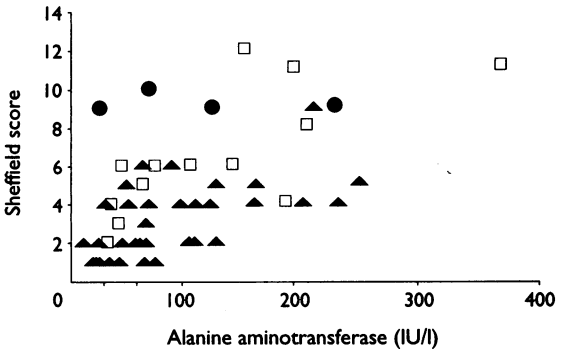
Blood donors in the Trent region are screened for antibodies to hepatitis C virus by second generation enzyme linked immunosorbent assay, and results are confirmed by a four antigen recombinant immunoblot assay. Donors with positive results are interviewed and referred to a consultant for further management. We studied all 52 donors who had had a liver biopsy by 1 May 1993 (30 men, 22 women; aged 21-57 (mean 35) years).

We collected data on risk factors for hepatitis C virus infection, duration of infection (assuming that infection was acquired on the first exposure to a risk factor), and alcohol intake. Alanine aminotransferase concentrations (three measurements), GOR antibodies,[1] hepatitis C virus RNA,[2] and hepatitis C virus serotype[3] were measured. Biopsy specimens were scored blind by the Knodell and Sheffield[4] schemes; the Sheffield scheme includes assessment of histological features characteristic of hepatitis C. We used the statistical package SPSS-PC to analyse data with Spearman rank correlation, Mann-Whitney, and logistic regression analyses. Predictive values for severe liver disease (chronic active hepatitis or cirrhosis) were calculated by using the standard definition and 95% confidence intervals by the program Confidence Interval Analysis.

The histological diagnoses were cirrhosis (four patients), chronic active hepatitis (13), chronic persistent hepatitis (32), fatty change (one), and normal (two). Hepatitis C virus RNA was detected in sera from 51 donors. The biopsy specimen from the donor without viral RNA was normal. Hepatitis C virus RNA was assayed twice in 31 donors: 28 had positive results in both samples, one had negative results in both, and two had a positive result in the first sample but a negative second result. The biopsy specimens from the donors with discordant results were reported as normal in one and chronic persistent hepatitis with features of α_1 antitrypsin deficiency in the other. A negative test result was significantly associated with lower severity scores for biopsy specimens (Knodell score $P=0{\cdot}006$; Sheffield score $P=0{\cdot}005$).

Peak alanine aminotransferase concentration was correlated with both severity scores (Knodell score $r_s=0{\cdot}59$, $P<0{\cdot}001$; Sheffield score $r_s=0{\cdot}66$, $p<0{\cdot}001$, figure). The predictive value for chronic active hepatitis or cirrhosis was 0·42 (13/31 donors, 95% confidence interval 0·25 to 0·61) for an alanine aminotransferase concentration above 60 IU/l and 0·47 (9/19, 0·24 to 0·71) for a concentration above 100 IU/l. The predictive value of an alanine aminotransferase concentration under 60 IU/l for chronic persistent hepatitis, fatty change, or a normal biopsy result was 0·81 (17/21, 0·58 to 0·95).

Liver damage was more severe in men than women (median Knodell score 4 *v* 2, $P=0{\cdot}03$; Sheffield score 5 *v* 3, $P=0{\cdot}02$). Logistic regression models found no other significant predictor for histological change.



Correlation between Sheffield score of severity of disease in liver biopsy specimen and peak alanine aminotransferase concentration.
▲=*Chronic hepatitis or normal,* ●=*cirrhosis,* □=*chronic active hepatitis*

Comment

Fifty of 52 biopsy specimens from apparently healthy blood donors infected with hepatitis C virus were abnormal, with a third having evidence of chronic active hepatitis or cirrhosis. Although peak alanine aminotransferase concentration and biopsy scores were strongly correlated, alanine aminotransferase concentration was a poor predictor of serious liver disease.

Possible explanations for the discordant results with the test for hepatitis C virus RNA include intermittent viraemia,[5] low level viraemia, false positive or negative results, and clearance of viraemia between sampling. Larger studies are needed to determine whether variable results for viral RNA are associated with less severe liver disease.

We found no useful predictors of the severity of liver disease. Our estimates of age at, and duration of, infection, however, had obvious limitations. Our data suggest that donors who have repeated positive results for hepatitis C virus RNA require liver biopsy as a large proportion will have serious liver disease that cannot be predicted by measuring alanine aminotransferase concentration.

Members of the Trent Regional Hepatitis C Virus Study Group were D A Jones, P Nuttall (Trent Regional Blood Transfusion Service); S Day (Nottingham University); D