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Household members of hepatitis C virus-infected people in Hafizabad, Pakistan: infection by injections from health care providers

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SUMMARY

Household members of people with hepatitis C are at increased risk of HCV infection. The prevalence and routes of transmission of HCV to household members in Hafizabad, Pakistan were investigated. Household members of 24 index cases were given a risk factor questionnaire, tested for HCV infection, and the risk factors between the infected and uninfected were compared. Twelve of 74 household members (16·2%) were seropositive for HCV antibody. This was $2\frac{1}{2}$ times the rate of infection in the general population (OR = 2·8; $P = 0{\cdot}01$). None of the routes of transmission studied within the household was associated with an increased risk. Household members who received more than 4 injections per year were 11·9 times more likely to be infected than those who had not ($P = 0{\cdot}016$). In Hafizabad, the greatest risk for HCV infection to household members of infected people is injections given by health-care workers rather than household contact with infected persons.

Transmission of hepatitis C virus (HCV) can occur through intravenous drug use, blood and blood product transfusion and haemodialysis [1]. HCV is present in seminal fluid [2] and vaginal secretions [3] suggesting the possibility of sexual transmission. However, results of epidemiological studies have been inconsistent [4–6] suggesting low frequency sexual transmission. Identical HCV-RNA has been found in children born to HCV-RNA-positive mothers, confirming perinatal transmission of HCV [7]. Even in studies which assume that every HCV-infected person who reports a known exposure was infected by the reported exposure, the route of acquisition of the virus remains unknown in up to 50% of cases [1]. HCV infection rates in populations not at overt risk for infection range from 0·06 to 14·5% [8, 9].

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The rates of infection in household contacts of HCV-infected persons are higher than the infection rates in people who do not have household exposure. HCV prevalence is reported to be from two [8] to ten [10] times higher in family members of HCV-infected patients than in the general population. However the physical routes of viral transmission are not known [11]. Proposed routes of spread within families include sexual [8] and vertical [9] transmission, as well as speculation that other practices which may transfer blood, e.g. sharing of razors [12] or microtrauma incurred during daily life [3] may be responsible.

During a community-based survey in Hafizabad, a rural marketing town with a population of 125000 people in the province of Punjab in central Pakistan, an anti-HCV antibody prevalence of 6·5% was found in the general population. This rose from 2·7% in the 0–19 years age group to 35·3% in the population > 59 years of age [13]. We undertook the present study

to measure the risk of infection in household contacts of people who were HCV-antibody-positive and to investigate the routes of transmission of HCV within the household.

We conducted the study in Hafizabad in December 1994. Most houses in Hafizabad have 2 or 3 rooms and households typically include 7–9 members of an extended family.

In November 1993, 36 people in Hafizabad were identified who had antibodies to HCV [13]. We attempted to contact the infected persons and to enumerate all the people living in their households. We requested permission to interview the household members and to test them for anti-HCV antibody. We administered a questionnaire and obtained serum from all the consenting members of the households who were available on our first visit or could be located within two subsequent visits [13].

Age-specific prevalence of HCV infection was calculated for the household contacts tested in 1994 and compared to those obtained for the general population of Hafizabad during the 1993 community survey [13]. We calculated the relative risk for infection of those who were exposed compared to those not exposed to each of the risk factors. We used Cornfield's approximation to estimate confidence intervals, Fisher exact test where appropriate to test for statistical significance, and Epi-Info for statistical analysis [14].

During the initial survey in 1993 [13] we identified 36 people who had evidence of HCV infection in Hafizabad. Of these 36 people 24 were re-located in November 1994 and recruited for the current study. These 24 people ranged 11–75 years in age (mean 40·4 years); 58% were males. These were the index cases who were used to identify our study population. Assays for anti-HCV antibodies were repeated in December 1994 and all were positive.

We identified 86 household contacts of these 24 HCV-infected persons, 74 (86%) of whom consented to participate in the study, ranging 2–65 years of age, including 39 males (53%). Seventeen were spouses of index cases, 38 were offspring and 19 were other household members.

Twelve (16%) of the contacts had anti-HCV antibodies. Compared with the prevalence of 6·5% in the general population [13], household contacts of people with HCV infection were $2\frac{1}{2}$ times more likely to be infected with HCV (OR = 2·8; 95% CI 1·2–6·4; $P = 0{\cdot}01$). After adjusting for age the difference in rate of infection between the general population and the household members persisted (Mantel–Haenszel OR = 2·9; 95% CI 1·2–7·2; $P = 0{\cdot}02$) (Table 1).

Table 1. *Anti-HCV antibody prevalence rates in the general population in November 1993, compared to household contacts of HCV-infected persons in December 1994, in Hafizabad, Pakistan*

	Anti-HCV prevalence	
Age group (years)	Family members ($n = 74$)	General population ($n = 309$)*
0–19	7·1% (2/28)	2·7% (4/149)
20–39	14·8% (4/27)	5% (5/101)
40–59	25% (4/16)	12·2% (5/41)
> 60	66·7% (2/3)	35·5% (6/17)

* From Luby et al. [13].

Seven (29%) of the 24 families of index cases had at least one family member, other than the index case, who was anti-HCV positive. Two families demonstrated clustering; 1 with 4 of 6 members tested having HCV infection, and 1 family with 3 of 4 members tested. Of the 12 household members found to be infected, 3 were wives of index cases, 3 were mothers of index cases, 2 were fathers of index cases, 2 were children of index cases, 1 was the brother of an index case and 1 was the sister-in-law of an index case.

Three of the 12 people (25%) who were infected had sexual contact with the index cases compared to 14 out of 62 of the uninfected (23%). None of the 12 infected people were offspring of female cases compared to 15 of the 62 uninfected people (24%) (Table 2). None of the 12 cases shared tooth brushes with their household members whereas 4 of the 62 (6%) uninfected people shared their tooth brushes. We asked only adult males questions about sharing razors. Amongst the 12 infected people 4 were adult males and 2 of them share razors with household members (50%) whereas amongst the non-infected 51 were adult males and 4 of them shared razors (8%). Only 1 of the 12 (8%) infected people had handled syringes or blood of the index case whereas 11 of the 57 uninfected persons had such contact (19%). None of these intra-familial risk factors were significantly associated with HCV infection status amongst household members (Table 2).

Assessing personal risk factors, there was no difference in hospitalization (0/12 *vs.* 7/62) or transfusion (1/12 *vs.* 0/62). Persons who were HCV infected were 8·6 times more likely to receive > 4 injections in the preceding year (82 *vs.* 34%, $P < 0{\cdot}01$)

Table 2. *Postulated routes of household transmission of HCV and the relationship to anti-HCV antibody, Hafizabad, Pakistan in December 1994*

Risk factors	Rates of exposure in infected	Rates of exposure in uninfected	Odds ratio	*P* value Fisher's exact test
Intrafamilial				
Spouses of index cases	3/12	14/62	1·1	0·56
Offspring of female case	0.12	15/62	0	0·06
Sharing toothbrush	0/12	4/51	0	0·42
Sharing razor*	2/4	5/23	3·6	0·27
Contact with needles or syringes†	0/12	6/57	0	0·30
Contact with blood	1/12	11/57	0·4	0·33
Personal				
Blood transfusion	1/12	0/62	U§	0·16
Hospital admission	0/12	7/62	0	0·27
> 4 health-provider-dispensed infections (last 1 year)	9/11	21/61	8·6	< 0·01
> 4 health-provider-dispensed injections per year (1988–93)	6/8	21/58	5·3	0·04
> 4 health-provider-dispensed injections per year (1983–93)	7/8	17/46	11·9	0·01
Shaved by a barber at least once a month*	3/4	13/23	2·3	0·45
Dental work	7/12	22/59	2·4	0·15
High risk sexual behaviour‡	0/10	10/35	0	0·06

* Only adult (i.e. age more than 15 years) males were asked this question.
† The denominator in this case is 57 instead of 62 as 5 subjects did not know if they had contact or not.
‡ Lifetime multiple partner heterosexual/homosexual contacts (only adults were asked this question).
§ U, undefined.

5·3 times more likely to receive > 4 injections in the preceding 5 years (75 *vs.* 36%, $P = 0{\cdot}04$) and 11·9 times more likely to receive > 4 injections in the preceding 10 years (88 *vs.* 37%, $P = 0{\cdot}01$). Thus, receiving more than 4 health-care-provider-dispensed injections in the last 1 year was a significant risk for household members. Those who were infected were 8·6 times more likely to have received more than 4 injections in the preceding year than those who were not infected ($P = 0{\cdot}005$). Similarly, the household members who were infected were 5·3 and 11·9 times more likely to have received more than 4 health-care-provider-dispensed injections in the 5-year period 1988–93 and in the 10-year period 1983–93 respectively than those that were not infected.

To establish a route of transmission of an infectious agent it is necessary to demonstrate that a biologically credible mode for transfer exists and that people who are exposed to it have a higher rate of infection than an appropriate unexposed comparison group. The presence of HCV in body secretions [4] and sharing razors or toothbrushes, handling the needles and syringes used by the infected person and handling the blood of the infected person, make household transmission possible. That household contacts of HCV-infected persons in Hafizabad were more likely to be infected with HCV than the general population is consistent with previous observations [6, 10, 11]. All the people we looked at in our study were household contacts of HCV infected people. When we compared the rates of exposure to secretions containing the virus in infected and uninfected household members, there was no increased risk associated with any of these exposures. Thus having an HCV-infected person in the household was a risk factor for HCV infection however these data do not suggest that household contact was a route of transmission of HCV.

The household contacts of index HCV-infected people were at a greater risk for HCV infection if they received more than 4 health-care-provider-dispensed injections per year. In the general population in Hafizabad the most important route for HCV infection is through inadequately sterilized injections administered by health-care providers [13]. The present study shows that the risk for family members of HCV infected persons lies in the sharing of high-

risk health-care-seeking practices. The members of a family may be more likely to share similar attitudes and practices towards parenteral medication. The whole family may seek care from a particular health-care provider who has more unsanitary needle practices than usual, or a high proportion of HCV-infected patients, or both. Thus each individual in a family of an infected person has a higher individual risk of infection rather than a household risk.

These data do not prove that routes for intrafamilial transmission of the hepatitis C virus do not exist. In fact the increased risk of infection in those people who share razors with their household contacts may represent routes that we could not establish without a larger sample size. Regardless, in our study the increased risk that is associated with multiple health-care-provider-dispensed injections clearly outweighs any risk posed by intrafamilial modes of infection.

In Hafizabad, finding a person infected with HCV identifies a high risk family. The advice given to such a family must be based on known routes of transmission of the virus. In Hafizabad, and perhaps in many settings throughout the developing world [15] the most important advice is not about avoiding the infected household member but about avoiding unsafe health-care-provider-dispensed injections.

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