

## **Hepatitis C virus infection in Iceland: a recently introduced blood-borne disease**

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### SUMMARY

This study demonstrates a very high prevalence of antibodies to hepatitis C virus among Icelandic intravenous (i.v.) drug users. Of 152 identified i.v. drug users 95 (63%) were shown to have antibodies to the hepatitis C virus. In contrast the seroprevalence in the general Icelandic population is low, (0·2%). Almost all cases of hepatitis C virus infection in Iceland are due to i.v. drug use or to use of infected blood or blood products. Sporadic cases with unexplained modes of transmission, a significant portion of hepatitis C infections elsewhere, are virtually non-existent in Iceland. The results of this study are consistent with the hypothesis that the sporadic community-acquired cases could be caused by blood transfer due to bites from insect vectors such as mosquitoes which are not found in Iceland.

### INTRODUCTION

Iceland, one of the Nordic Countries, is an island situated in the North-Atlantic Ocean. The population is about 260 000, and more than half of the people reside in the capital city, Reykjavík and surrounding area. The population is white and the life style is similar to the other Nordic countries. At present, travel to the outside world is easy, a great contrast to the pre-World War II period when Iceland was relatively isolated. Intravenous (i.v.) drug use was considered rare in Iceland until the early 1980s when a great increase in the use of drugs especially i.v. amphetamines was observed both by physicians and police. There are, however, no systematic studies on the prevalence of drug use in Iceland.

With the advent of diagnostic tools for the newly discovered hepatitis C virus (HCV), diagnosis of the infection, prevalence studies for antibodies to the virus and identification of modes of viral transmission have been made possible [1, 2]. In this study the diagnosis of HCV infection in Iceland is reported, and the prevalence of HCV in the general Icelandic population is assessed. In addition the prevalence of HCV among known i.v. drug users and anti-HBc positive individuals is studied and an attempt is made to estimate the initial entry of HCV among the i.v. drug users in Iceland. The modes of transmission of HCV in Iceland are discussed.

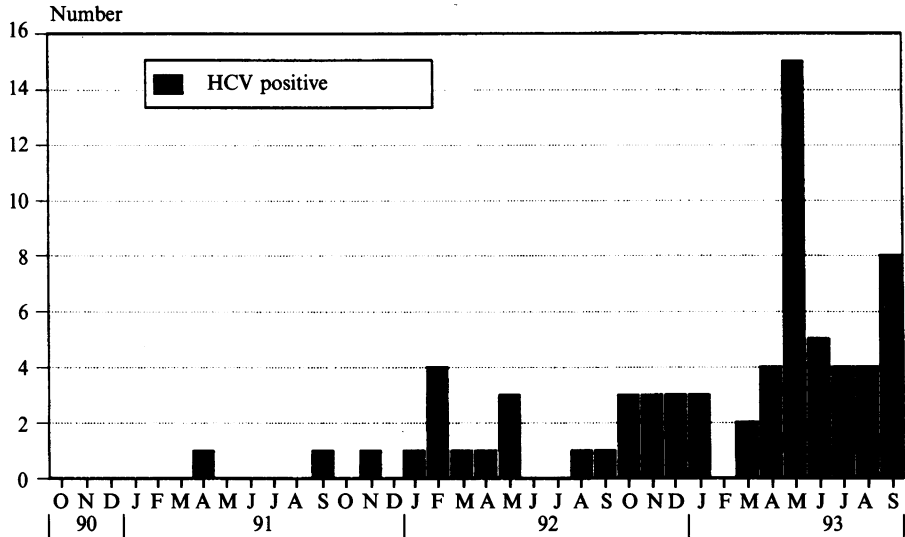


Fig. 1. Time of identification of 69 hepatitis C infected individuals among 925 assay requests.

## MATERIALS AND METHODS

### *General diagnosis*

The Department of Medical Virology at the University of Iceland serves as a diagnostic unit for virus diseases for hospitals and practising physicians. Hepatitis C antibody determinations were started in October 1990. The requests for analysis were due to various reasons, such as known i.v. drug use or elevated liver enzymes. The Department of Medical Virology performs all confirmatory tests necessary for the Icelandic Blood Bank which started screening for antibody to HCV in the autumn of 1992. Before screening, prevention of HCV through blood donation was done by filling out a questionnaire about drug use. A total of 9–10000 individuals donate blood at the Blood Bank each year, some donate more than once. In the first phase of this study the results from the initial 3 years of HCV diagnoses at the Department of Medical Virology are presented.

Antibody to HCV was measured by use of the 2nd generation enzyme linked immunosorbent assay (ELISA) from Ortho. Positive results were confirmed with the recombinant immunoblot assay (RIBA) (Ortho, 2nd generation) [3]. Cut-off values in the ELISA and RIBA results were determined according to criteria given by the manufacturer.

### *Prevalence among the population*

The second phase of the study was to assess the prevalence of antibodies to HCV among the general Icelandic population. For this phase blood samples from 1537 individuals, representing 0.6% of the total Icelandic population, were examined. The blood samples were obtained from two sources, the Icelandic Heart Association, and the Department of Medical Virology, University of Iceland. The samples from the Icelandic Heart Association were from individuals, randomly

selected, undergoing a long term surveillance study on cardiovascular diseases and from individuals requesting a physical examination. The serum samples from the Department of Medical Virology were sent by various physicians for viral antibody determinations. None had requested HIV or hepatitis analyses. The blood samples used in this part of the study were collected early in 1991.

#### *Prevalence among i.v. drug users and anti-HBc positive individuals*

In the third phase of this study serum from patients with known i.v. drug use were examined for antibody to HCV. The information on i.v. drug use was obtained from the written request for analysis or directly from the patients' physicians.

In addition, 160 serum samples from individuals whose previous analysis had demonstrated anti-HBc antibodies were tested for antibody to HCV. If an assay was found to be positive, information on i.v. drug use was sought when it had not been previously recorded. In this part of the study blood samples, collected during the period of October 1990 to October 1993, were analyzed.

#### *Time of introduction of HCV*

Finally, an attempt was made to estimate retrospectively the introduction of HCV virus into Icelandic i.v. drug users. Stored serum samples from presently known HCV infected individuals born before 1965, were sought. These samples had been kept frozen at  $-20^{\circ}\text{C}$  at the Department of Medical Virology from the time of collection. Sera were found from 18 individuals collected during the years 1977–90. These represent 12% of the known HCV infected individuals.

## RESULTS

#### *General diagnosis*

Among 925 HCV assay requests from various hospitals and physicians 69 individuals were found to be antibody positive. Their time of diagnosis is shown in Figure 1. This demonstrates an increasing frequency of HCV diagnoses in the later months of the study. This may be a reflection both of the ongoing epidemic and also physicians' increasing awareness of this virus infection. The peak of positive HCV diagnoses in May 1993 was the result of a search for blood recipients who were thought to have received blood from HCV antibody positive blood donors. During the first year of screening of antibody to HCV at the Icelandic Blood Bank eight antibody positive donors were detected. All eight had a history of i.v. drug use. Five were still active drug users. Red blood cells, plasma and thrombocytes were shown to transmit HCV infection. At the end of this period of observation 19 individuals had been found whom 6 of these 8 donors had previously infected through blood donation. A few more HCV infected blood or blood factor recipients were detected at a later time (Löve et al., submitted).

Only 4 of the 69 patients that proved to be antibody positive to HCV exhibited acute jaundice. The mother of the HCV antibody positive newborn was a known i.v. drug user.

Table 1. *Age of 1537 individuals (724 males and 813 females) tested for antibody to HCV*

Decade of birth	Number of samples source			HCV infected
	Heart-association	Department of virology	Total	
1900-09	8	16	24	—
1910-19	107	42	149	2*
1920-29	169	31	200	—
1930-39	200	17	217	—
1940-49	291	1	292	—
1950-59	302	10	312	—
1960-69	101	138	239	1†
1970-79	14	89	103	—
1980-		1	1	—
Total	1192	345	1537	3

\* One male, one female.

† Male.

Table 2. *Age and sex distribution of 152 IVDUs and number of individuals positive for antibody to HCV*

Decade of birth	Sex	No of IVDUs	HCV infected	(%) infected
1930-39	M	2	2	100
	F	—	—	—
1940-49	M	6	4	67
	F	2	2	100
1950-59	M	35	22	63
	F	10	7	70
1960-69	M	52	31	60
	F	17	14	82
1970-79	M	13	4	31
	F	15	9	60
Total		152	95	63

*Prevalence among the population*

In the prevalence study among the 1537 randomly selected individuals 3 samples positive for antibody to HCV were identified and 4 were weakly indeterminate. The age distribution of the individuals tested is shown in Table 1. The prevalence of antibody to HCV in Iceland is thus 0.2%.

*Prevalence among i.v. drug users and anti-HBc positive individuals*

Among 152 individuals identified with known i.v. drug use 95 (63%) had antibody to HCV. The age and sex distribution and percentage with antibody to HCV shown in Table 2 clearly demonstrates that young adult males predominate among the HCV-infected individuals. The high percentage of infection among young female i.v. drug users is also striking.

Of 160 individuals with antibodies to HBc 48 (30%) also had antibody to HCV as shown in Table 3. All of the individuals positive for antibody to HCV identified

Table 3. Age distribution of 160 anti-HBc positive individuals and number of HCV infections

Decade of birth	Anti-HBc positive	HCV positive	HCV positive (%)
1900-49	40	6	15
1950-59	38	14	37
1960-69	62	20	32
1970-79	20	8	40
Total	160	48	30

Table 4. Suggested modes of transmission among 125 individuals positive for antibody to HCV

Modes of transmission	Sex	Number	Per cent
i.v. drug users	M	62	76
	F	33	
Blood recipients	M	12	16.8
	F	9	
Blood factor recipients	M	4	4
	F	1	
Congenital	M	1	0.8
Unknown	M	2	2.4
	F	1	
Total	—	125	100

in this part of the study as previously known i.v. drug users or retrospectively proven to have used drugs intravenously are included in the total number of i.v. drug users in Table 2.

Table 4 shows all 125 identified HCV antibody positive individuals according to mode of transmission. It is noticeable that i.v. drug users constitute the great majority of the HCV infected individuals although blood and blood product recipients make up a significant portion. Very few of the infected individuals do not have a clear mode of transmission. The age and sex distribution of the 125 HCV infected individuals shown in Figure 2 demonstrates clearly that young male adults form the majority of the infections, concurring with Table 2 showing the age and sex distribution of the i.v. drug users. Most of the HCV infected individuals over 50 years of age were infected by blood or blood products. Of the 95 i.v. drug users with antibody to HCV 44 were among the initial 69 antibody positive individuals detected according to physicians' request. In addition 30 others were found among known i.v. drug users and 21 previously unidentified among individuals with antibody to HBc.

#### *Time of introduction of HCV*

The results from the retrospective analysis of stored sera for antibody to HCV taken from currently infected individuals are shown in Table 5. The first serum positive for antibody to HCV was from the year 1984, but during 1985-6 only 1 of 7 sera was positive for antibody to HCV. Thus until 1986 the spread of the virus

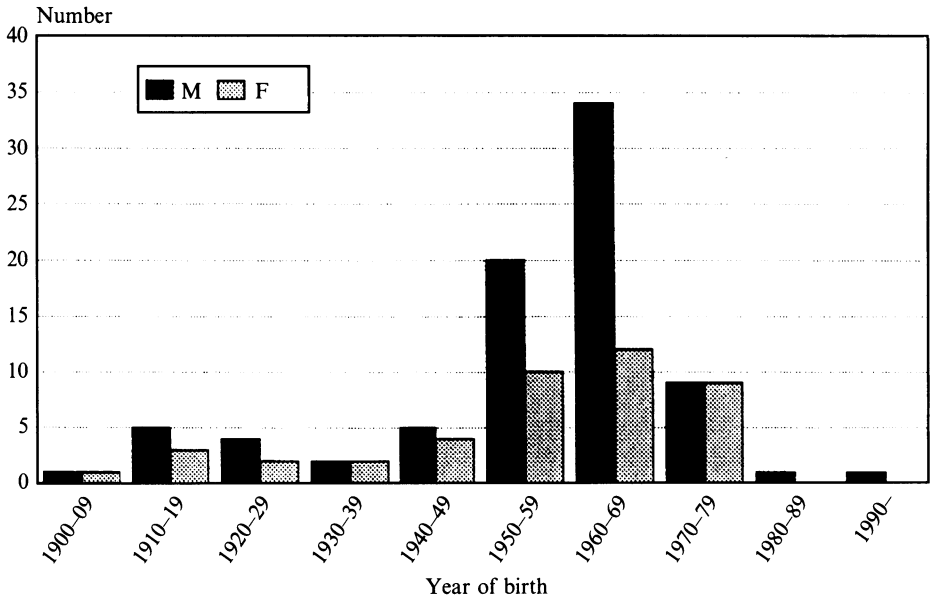


Fig. 2. Age and sex distribution of all 125 hepatitis C infected individuals.

Table 5. Retrospective analysis of 18 previously collected sera from individuals presently positive for antibody to HCV

Year of collection:	77/78	79/80	81/82	83/84	85/86	87/88	89/90
HCV positive	0	0	0	1	1	1	2
HCV negative	1	2	1	2	6	1	0

seems to have been slow. Subsequently, it has taken only approximately 5 years to reach a prevalence of 63% among known i.v. drug users.

#### DISCUSSION

This study demonstrates that HCV is a common infection among Icelandic i.v. drug users. It is evident that the HCV was introduced into the population of i.v. drug users in Iceland before 1984, the year from which the first HCV antibody positive serum was found in the retrospective study. This probably happened shortly after the undocumented upsurge of i.v. drug use in Iceland in the early 1980s. Since that time the virus has spread steadily among this vulnerable population.

This study also demonstrates a prevalence of antibody to HCV of 0.2% among the Icelandic population. This is lower than reported in most other countries [4-9]. It should be pointed out that the sera for the prevalence study for antibody to HCV were collected early in the year 1991. Most of the HCV infected individuals were identified after this time and the virus continued to spread significantly among the i.v. drug users. However, due to the limited number of i.v. drug users this should not affect significantly the prevalence of HCV infection in the general population. Table 4 shows that three HCV antibody positive individuals had no known mode of transmission. Two of these were found in the prevalence study. One had received blood transfusions, the other individual was an immigrant from

Central Europe where the HCV prevalence is much higher than in Iceland. The third individual positive for antibody to HCV without a clear history of blood-borne infection was living abroad with a spouse who had a history of jaundice. Therefore, virtually all cases of HCV infection in Iceland are of a known blood-borne origin and other modes of transmission are insignificant. Elsewhere, sporadic community-acquired cases where no detectable mode of transmission can be found constitute a significant, although variably large portion of HCV cases [10–13].

These data raise two questions concerning the modes of transmission of HCV. Since both sexual and perinatal transmission seem to exist but are rare and epidemiologically not significant, [14–21] the questions are, first, are the sporadic HCV cases described blood borne through some means and, secondly, is there possibly an unknown vector, perhaps an arthropod, involved in some or all sporadic community-acquired cases? The latter view is supported by the fact that the HCV is a member of the *Flaviviridae* and thus its closest relatives are arthropod-borne viruses [22]. However, blood sucking mosquitoes are non-existent in Iceland so this mode of transmission is impossible there [23, 24]. Infection may be acquired this way overseas. This is consistent with the data presented in this paper where the mode of transmission is known in almost all cases of HCV infection.

We believe that an arthropod vector responsible for the transmission of HCV should be extensively sought by utilizing sensitive methods such as the polymerase chain reaction for detection of viral nucleic acids in blood sucking arthropods particularly mosquitoes [25–29].

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