Epidemiology of hepatitis C virus infection among injecting drug users in Australia

Nick Crofts, Damien Jolley, John Kaldor, Ingrid van Beek, Alex Wodak

Abstract

Study objective—To review the epidemiology of hepatitis C virus (HCV) infection among injecting drug users (IDUs) in Australia, and consider needs for further research and prevention policies and programmes.

Design—(1) Review of the results of surveillance for HCV; (2) review of published literature on prevalence, incidence, and risk factors for HCV among IDUs; and (3) reconstruction of incidence rates from prevalence studies of HCV in IDUs.

Setting and Participants—Field and clinic based studies of IDUs in Australia.

Main results—HCV has been present at high prevalences (of the order of 60–70%) in populations of Australian IDUs since at least 1971. Duration of injecting and main drug injected were the main predictors of seropositivity, the latter possibly a surrogate for frequency of injecting and both together as surrogate for cumulative numbers of times injected. Risk of infection begins with first injection and continues as long as injecting does. Current incidence is approximately 15 per 100 person years, and up to 40 per 100 person years in some subpopulations. Incidence may have decreased through the 1980s as a result of behaviour change in relation to HIV, as it has for hepatitis B, but not significantly so.

Conclusions—Control of HCV infection in Australia will depend on effectiveness of measures to control HCV spread among IDUs. This will be a greater challenge than the control of HIV in this population has been. Needs identified include improved surveillance, especially for recently acquired infection, better understanding of exact transmission modes, and urgent improvement in prevention strategies.

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Since the identification of hepatitis C virus (HCV) in 1989¹ and the availability of assays for the detection of antibody to HCV in 1990,² the epidemiology of HCV infection has been investigated in many populations. The major group infected and at risk of continuing infection with HCV in Australia, as in other developed countries, is people who currently or previously injected or had been injected with illicit drugs.³ This increased risk is associated with the practice of sharing of equipment used in injecting; especially needles and syringes, as

is the case also with hepatitis B virus (HBV) and human immunodeficiency virus (HIV).

Other exposures that have been found to be important are the receipt of contaminated blood or blood products,⁴ tattooing,⁵ and dental procedures.⁶ Since the introduction of universal donor screening for HCV antibody in 1990, transmission through the blood supply has become rare.⁷

It is currently estimated that over 80% of those exposed to HCV will become carriers,⁸ at risk of long term disease including cirrhosis and hepatocellular carcinoma.⁹ While actual rates are still unclear, it is possible that 20% or more of those chronically infected will develop such disease over 20 years or more.¹⁰ The only available treatment, alpha interferon, is ineffective in most patients and is specifically not available to current injecting drug users (IDUs) in Australia.¹¹ Prospects of a vaccine against HCV are not promising in the short-term.¹²

There have been a number of surveys of different populations of IDUs in Australia for HCV exposure. Surveillance for diagnosed HCV infection at a national level was introduced and has been gradually refined since testing began in 1990. To establish as complete a picture as possible of the pattern of HCV infection among IDUs in Australia, we undertook a review of available epidemiological data. We have also sought to identify research needs and opportunities, and effectiveness of and requirements for further prevention programmes to decrease its spread in these populations.

Methods

NATIONAL SURVEILLANCE

There are two national surveillance systems for communicable diseases that collect information on the occurrence of HCV infection: the National Notifiable Diseases Surveillance System (NNDSS), which receives notification data from State and Territory Health Departments; and the Communicable Diseases Intelligence Laboratory Reporting Scheme (LabVISE), which receives reports of laboratory diagnoses from sentinel laboratories. Reports of HCV infections were available for the years 1991 to 1994 for the first system, and for the period 1990 to September 1995 for the second. The NNDSS collects information on age, sex, and postcode of residence of cases, but not on possible route of exposure; since 1994, cases have been classified as incident or otherwise. The LabVISE system collects data on age, sex, postcode, risk factor (a combination of

The Macfarlane
Burnet Centre for
Medical Research,
Fairfield, Victoria,
Australia
N Crofts
D Jolley

National Centre in HIV
Epidemiology and
Clinical Research,
Darlinghurst,
New South Wales,
Australia
J Kaldor

Kirketon Road Centre,
Darlinghurst,
New South Wales,
Australia
I van Beek

Alcohol and Drug
Services, St Vincent's
Hospital,
Darlinghurst,
New South Wales,
Australia
A Wodak

Correspondence to:
Dr N Crofts, The
Macfarlane Burnet Centre
for Medical Research, PO
Box 254, Fairfield, Victoria,
Australia 3078.

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Table 1 Contributions to the overall log likelihood

Status	Observed	Log-likelihood terms
Always negative	<i>u</i> only	$-\lambda (u - s)$
Entered positive	<i>v</i> only	$\log [1 - \exp \{-\lambda (v - s)\}]$
Seroconverted	both <i>u</i> & <i>v</i>	$-\lambda (u - s) + \log [1 - \exp \{-\lambda (v - u)\}]$

s = date of starting to inject; *u* = date of last negative test; *v* = date of first positive test.

exposure factors and personal characteristics), outcome, and method of diagnosis.

PREVALENCE AND INCIDENCE STUDIES
Published reports on prevalence, incidence, and predictors of HCV seropositivity among IDUs in Australia were also reviewed. Studies based on self reported HCV status were not included, because of evidence of uncertainty about reliability and validity of such data,¹³ but those using self report to assess whether subjects had had a test for HCV were included. Published reports were identified by MedLine search and contact with researchers known to be working in this field.

RECONSTRUCTED INCIDENCE
To assess the impact of programmes introduced from 1987 in Australia to decrease the spread of HIV among IDUs on the spread of HCV in the same populations, we modelled the incidence of HCV over the 1980s, using prevalence data. Data from two studies were used. The first was a longitudinal prospective study of field recruited IDUs in Victoria, the full method for which has been published elsewhere.¹⁴ The second was of IDUs attending a primary care clinic in inner Sydney, New South Wales, the method for which has also been published elsewhere.¹⁵ We estimated a seroconversion rate as the subject's risk of testing positive (even at first test) as a function of the number of years of exposure since first injecting, assuming zero risk for HCV infection before starting to inject. The full method is presented in table 1.¹⁶

Ninety five per cent confidence intervals for incidence rates were calculated using an exponential error factor for incidence rates.¹⁷

Results

The earliest evidence of HCV infection among Australian IDUs came from a study of stored serum samples from IDUs admitted to Fairfield Hospital in Victoria in 1971.¹⁸ Of all 53 IDUs admitted in that year, all with a diagnosis of acute hepatitis, 44 (83%) had at least one (including 28 with more than one) serum specimen stored and available for second generation anti-HCV EIA testing. Of these, 25 (57%) had antibody to HCV on admission, and a further three of 15 initially seronegative seroconverted during admission.

NATIONAL SURVEILLANCE
Four years of data (1991 to 1994) were available from the National Notifiable Diseases Surveillance System. Nationally, there was a total of 29 353 notifications of hepatitis C for the four years, with a male:female ratio of 1.6:1.7 and 84–88% in the age range 20–44

years in each year. Incident cases were so classified in 1993–4, making up 0.4% of notifications (73 of 16 424).
There were data available from the LabWISE system for six years (1990 to 1995), but only to September in the last year. The total number of reports for the period was 18 124, with annual totals rising from 115 in 1990 to 6118 in 1994. Details on risk factors were available only for the years 1992 to 1995, but over these years only 11.8% of cases had such information. Of the 2137 cases with such data, 1847 (86.4%) were classified as having a history of IDU, this proportion remaining constant over the years.

PROPORTION OF AUSTRALIAN IDUS TESTED FOR ANTI-HCV
Most of the reported clinic based studies of seroprevalence did not report the participation rate of clients in anti-HCV testing. One retrospective study on the stored serum samples of methadone clinic attenders reported testing samples from 172 IDUs of a total of 783 people (22%), based apparently on the availability of stored serum samples.¹⁹ Of 234 young drug users, which included an unstated proportion with no history of drug injecting in Perth in 1993, 57 (24%) reported having had a test for HCV; 29% (51 of 176) of those who reported a history of injecting drug use (mean duration 1.9 years) had been tested.¹³ A similar study of 275 young IDUs (mean duration of injecting 2.5 years) in Melbourne in 1994 found 59% reported having had an HCV test.²⁰ Of 872 respondents of all ages interviewed in four cities in 1994, 79% reported having been tested for hepatitis C antibodies at least once.²¹

HCV PREVALENCE IN AUSTRALIAN IDU POPULATIONS (TABLE 2)
A variety of IDU populations has been surveyed for prevalence of HCV antibody including those from whom serum samples have been collected for other purposes, IDUs in hospital, IDUs attending clinics (methadone, primary care, and STD), and IDUs participating in field studies. A variety of antibody tests with different sensitivities and specificities were used in the different studies.²² Overall, the prevalence among male IDUs ranged from 47% to 88%; among female IDUs, from 51% to 85%; and overall from 8% to 94%, when studies that did not specify sex are included. The lowest rate recorded was among young IDUs who began injecting within two years of being tested,¹³ and the highest was among IDUs entering methadone programmes in South Australia.²³

RISK FACTORS FOR HCV PREVALENCE IN IDUS
In most studies of risk factors for HCV exposure among IDUs the strongest association was with length of time from the first injection (fig 1).^{14 15 19 21} Age was also found to be associated with HCV seroprevalence in two studies, but primarily through its association with duration of injecting.^{14 15} Three studies also found an association with opioid (especially heroin) compared with stimulant

Table 2 Prevalence of hepatitis C virus antibody among populations of injecting drug users (IDUs) in Australia, 1971–1994. (n=sample size; *† refer to whether first or second generation enzyme linked immunosorbent assay was used in the testing)

Populations of IDUs	Site	Source	Year(s)	Prevalence			Reference no
				Male % (no)	Female % (no)	Total % (no)	
Hospital inpatients*	Victoria	Fairfield Hospital	1971			56.8 (44)	18
Hospital in/outpatients*	Victoria	Fairfield Hospital	1979–89			61.9 (431)	32
Methadone clients*	Sydney	Westmead Hospital	1986–89	88.4 (112)	81.7 (60)	86.1 (172)	19
All prison entrants*	Victoria	Victorian prisons	1991–92	64.0 (1437)	84.8 (125)	65.0 (1562)	24
Broad spectrum†	Victoria	Field-recruited	1991–92	70.0 (183)	65.0 (120)	68.0 (303)	14
Primary care†	Sydney	Clinic attenders	1991–92	55.3 (94)	62.2 (107)	59.2 (201)	15
STD clinic†	Adelaide	Clinic attenders	1991–93	26.0 (684)	36.1 (305)	30.0 (989)	26
Methadone clients†	S Australia	Clinic attenders	1992–93			94.3 (87)	23
Young IDUs†	Perth	Field-recruited	1993			8.0 (75)	13
Primary care†	Sydney	Clinic attenders	1992–94	46.5 (351)	51.3 (387)	48.7 (749)	25
Broad spectrum†	Sydney	Field-recruited	1994			69.5 (139)	21
	Perth	"	"			41.1 (76)	21
	Adelaide	"	"			50.5 (102)	21
	Melbourne	"	"			57.2 (115)	21

Figure 1 Prevalence (per cent seropositive) of HCV infection among current injecting drug users by the length of time since first injection.

(especially amphetamine) injection,²¹ and higher prevalences among heterosexual compared with homosexual IDUs. This latter association did not reach significance in one study¹⁴ and may have been confounded by drug of choice or injecting practice in another.¹⁵ HCV exposure was found to be associated with HBV exposure but not a good predictor of HIV infection in two studies.

INCIDENCE OF HCV IN IDU POPULATIONS (TABLE 3)
The first published report of HCV incidence among IDUs in Australia came from a cohort study of IDUs, which on the basis of five seroconversions observed in 1991–2 indicated an incidence of almost 20 per 100 person years (95% CI 2.3, 36.8).¹⁴ A rate of 18.3 per 100 person years (95% CI 9.8, 34) was observed in a cohort of prison entrants, with a rate of 41 per 100 person years (95% CI 20.5, 82) among young male IDUs entering prison in Victoria in 1991–2.²⁴ Similarly high rates have been

observed among attenders at a primary health care clinic that targets IDUs in Sydney, of about 15 per 100 person years over the years to 1994.²⁵ A much lower incidence (3.5 per 100 person years) was reported from an STD clinic in South Australia, but the population followed up was those attenders who reported “ever having injected drugs”, rather than current IDUs.²⁶ Overall, of 236 initially HCV seronegative current IDUs followed up serologically for any length of time in various populations around Australia, 25 (10.6%) have been observed to seroconvert, with incidence rates varying from 14 to 38 per 100 person years. Only two (see table 3) of these studies have produced incidence rates based on routine monitoring of the group being observed, but even with these there are selection and participation biases. Incidence rates produced by the other studies are potentially even more biased because of selection for follow up and testing.^{14 24} In particular, clinic based studies may overestimate incidence because of re-testing on the basis of illness thought to be associated with new HCV infection.

RISK FACTORS FOR INCIDENT HCV IN IDUS
In the cohort study, the five observed seroconverters to HCV were more likely to be men, older, to have been injecting longer, and to have a rural base.¹⁴ In the study of prison entrants, seroconverters were all men and younger than non-seroconverters.²⁴ In the Sydney clinic based study, seroconversion rates were higher among transgender IDUs (one observed seroconversion, 39 per 100 person years) than among male IDUs (six seroconversions, 25 per 100 person years), and in both were much higher than among female IDUs (two seroconversions 5.8 per 100 person years).¹⁵

Table 3 Seroincidence of hepatitis C virus infection among populations of injecting drug users in Australia, 1991–94. (py: person-years; CI: confidence intervals). (All sera were tested with second generation enzyme linked immunosorbent assays)

Population of IDUs	Years	No initially seronegative	Seroconverters No (%)	Incidence per 100 py (95% CI)	Reference no
Field recruited IDUs, Victoria	1991–92	32	5 (15.6%)	19.6 (2.4, 36.8)	14
Prison entrants, Victoria	1991–92	47	8 (17.0%)	38.2 (19.1, 76.4)	24
STD clients, “ever injected”, Adelaide	1991–93	73	2 (2.7%)	3.5 (0.4, 12.7)	26
Methadone clients, South Australia	1991–93	3	1 (33.3%)		23
Primary care, Sydney	1992–94	81	9 (11.1%)	15	25

Table 4 Seroconversion hazard rates and mean times to infection with HCV and HBV among injecting drug users in two independent studies in Victoria and Sydney, by time period of having started injecting (see table 1 for method)

	Injecting drug use		Total	Mean time to infection (y) (95% CI)	p value for difference
	Started before 1987	Started since 1986			
Hepatitis C					
Victoria:					
Hazard rate (95% CI)	0.171	0.129	0.146 (0.126, 0.169)	6.9 (5.9, 7.9)	0.27
Rate ratio (95% CI)	1.32 (0.82, 2.14)				
Sydney:					
Hazard rate (95% CI)	0.258	0.129	0.148 (0.115, 0.188)	6.8 (6.0, 8.7)	0.31
Rate ratio (95% CI)	1.56 (0.67, 3.28)				
Combined:					
Hazard rate (95% CI)	0.178 (0.103, 0.159)	0.129 (0.133, 0.229)	0.147 (0.129, 0.166)	6.8 (6.0, 7.8)	0.31
Rate ratio (5% CI)	1.37 (0.90, 2.05)				
Hepatitis B					
Victoria:					
Hazard rate (95% CI)	0.119	0.038	0.078 (0.066, 0.092)	12.8 (10.9, 15.2)	<0.001
Rate ratio (95% CI)	3.1 (1.75, 4.9)				

INCIDENCE OF HCV AMONG IDUS THROUGH THE 1980s
Assuming that a constant risk of infection applies uniformly to each IDU from the time of starting injecting (see table 1), the hazard rate estimated by maximum likelihood is 14.6 per 100 person years for the Victorian sample and 14.8 for the Sydney group, corresponding to a mean time to infection of almost seven years. The model gives a hazard ratio of 1.32 in Victoria and 1.56 in Sydney comparing those beginning to inject before 1987 with those beginning to inject after 1986; but these estimates are not significantly different from 1.0, or constant uniform risk (table 4). Combining the Sydney and Melbourne data gives a hazard ratio of 1.37, with a decline in hazard from 0.178 to 0.129, but again the change did not reach statistical significance.

There was however a significant difference in both Sydney and Melbourne in hazard between those who started injecting heroin and those who started with amphetamines, corresponding to a difference in mean time to infection of about three years in Victoria (opioids 5.8 years, stimulants 8.7 years; $p=0.016$) and over 10 years in Sydney (opioids 6.0 years, stimulants 16.7 years; $p=0.022$).

For comparison, using the same method, hazard rates were calculated for HBV exposure in the Victorian sample, and a decline from 0.119 to 0.038 between the two time periods was observed, giving a ratio of 3.1, which was significantly different from 1.0 (table 4).

CURRENT ESTIMATES OF NUMBERS OF HCV INFECTED IDUS
On the basis of one sample, it has been estimated that there were about 80 000 current and former IDUs carrying HCV in Australia.¹⁴ This estimate is based on a carriage rate of 50% among those who are HCV antibody positive, and as more recent estimates have indicated that in fact approximately 80% of those antibody positive are chronically infected⁸ it should perhaps be raised to around 130 000 or 0.75% of the Australian population. It was further estimated, on the basis of an annual incidence of between 20% and 25% per annum that between 8000 and 10 000 new infections with HCV were occurring per year among IDUs. If, more conservatively and in line with

the data reviewed here, annual incidence is of the order of 15% this figure should be revised to around 6000 new HCV infections per annum in Australian IDUs.

Discussion
The results of these studies of hepatitis C infection in IDUs in Australia show a consistent pattern in different populations of IDUs recruited using different strategies in different settings over the last few years, of high incidences of infection beginning with the start of injecting and continuing through the career of the drug injector. Furthermore, it seems that spread of HCV has been occurring among Australian IDU populations for more than two decades. The most important association of HCV infection in these studies is duration of injecting. Demonstrated associations of HCV prevalence with heroin injecting more than with amphetamine injecting suggest that the association is with frequency of injecting (heroin on average being injected more frequently than amphetamines), though this has not yet been demonstrated. This would explain continuing risk over the IDU's injecting career—each injecting event poses a finite risk of exposure—so with increased numbers of injections over time risk of infection increases. If so, there may be little relevant difference between the behaviours of those infected and those not yet infected, except perhaps frequency of those behaviours.

The epidemiology of HCV among Australian IDUs is very similar to that reported among IDUs in the other major longitudinal study of HCV among IDUs, in Amsterdam, where prevalence of antibody in one study was 65% and incidence was 10 per 100 person years, and where HIV risk was found to be more closely related to HBV than to HCV status.²⁷

It might be expected that if the sharing of needles and syringes were the major mode of transmission of hepatitis viruses there would have been a decline in HCV and HBV transmission rates among IDUs in Australia since the late 1980s, with the introduction of programmes (particularly sterile needle and syringe distribution) for the prevention of HIV transmission.²⁸ Our analysis shows that this has been the case from these data for hepatitis B but not for hepatitis C, and this second finding

is reinforced by the findings of high current incidences in several different populations of IDUs in different settings. Behavioural research carried out since the introduction of these programmes suggests that most IDUs in Australia do not now knowingly share injecting equipment most of the time.²⁹ It is probable therefore that the carriage rate of HBV, and indeed of HIV, in these populations has been low enough for further spread to have been decreased by changes in relation to needle and syringe use. Against this, the prevalence of carriage HCV is so high that transmission will continue at a high rate even with infrequent sharing of needles and syringes.

It is also plausible, however, that HCV is being transmitted in injecting situations by means other than the sharing of needles and syringes—by the sharing of other injecting equipment, for instance, such as spoons, filters, water or tourniquets, or by spread on surfaces or the hands of IDUs. While this is still speculative, examination of videotapes of IDUs injecting illustrates opportunities for such spread (Crofts N, unpublished observations); and there numerous anecdotal cases of IDUs who have been exposed to HCV who are certain that they have never used a needle or syringe that has been previously used by someone else. This is similar to the situation of outbreaks of HCV infection in haematology or haemodialysis units where there is no reuse of equipment, but where there is the opportunity for some form of environmental contamination.³⁰

The national surveillance data do not yet totally reflect the prevalence rates implied by the studies reviewed here. In particular, acute infection is necessarily substantially underreported because most people acutely infected are asymptomatic or have only non-specific symptomatology. Only about 30 000 people have been diagnosed as having antibody to HCV in Australia to the end of 1994; if the estimate of about 160 000 infected as a result of IDU alone is at all accurate, then at most 15% or less of those infected have been diagnosed. Furthermore, while it is probable that most people infected with HCV were infected through injecting drugs, only one eighth have such a history recorded by the Laboratory Reporting Scheme, implying significant under ascertainment.

Several conclusions can be drawn from the data presented here. Firstly, further research is indicated to specifically describe those exact behaviours involved in the spread of HCV among IDUs, and provide a basis for the development of strategies for prevention of that spread; secondly, surveillance systems must be refined to systematically monitor prevalence and incidence in these populations; and thirdly, it will be difficult to control the HCV epidemic, where spread is occurring at such high rates in a context of seemingly highly successful HIV prevention programmes, even among IDUs who are gaining access to those programmes.

Furthermore, it must continue to be recognised and emphasised that such a continuing epidemic could not last and such high rates

KEY POINTS

- The major group at risk and the core group for HCV in Australia is IDUs.
- There is no evidence that incidence of HCV among IDUs in Australia has decreased significantly since the introduction of harm reduction programmes.
- Environmental contamination may account for a significant proportion of transmission among IDUs, necessitating new approaches to prevention.

would not continue without continued recruitment of susceptibles into the population at risk—that is, that there are continued substantial numbers of new drug injectors in Australia each year.

Control of the continuing spread of HCV among IDUs will be much more difficult than control of spread of HIV has been in this population. In the long term, control of HCV among IDUs will rest on control of the epidemic of injecting drug use; in the medium and short terms, multiple strategies including enhancement of availability of sterile injecting equipment and specific targeted education programmes must be brought to bear as soon as possible to stem the tide of this continuing major epidemic.³¹

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