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Indications of Immune Protection from Hepatitis C Infection

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ABSTRACT *Hepatitis C affects many millions of people worldwide and is at very high prevalence among people who inject drugs. In our study of hepatitis C virus (HCV) in the social networks of injecting drug users (IDUs), five IDUs with injecting careers of 9 years or more were HCV antibody and RNA negative. All injected frequently with HCV RNA-positive IDUs, and two had recently injected with the syringe of an RNA-positive IDU. Our data suggest the existence of immune protection from HCV infection.*

KEYWORDS *Hepatitis C virus, Immunity, Vaccine development.*

The hepatitis C virus (HCV) affects hundreds of millions of people worldwide and is at very high prevalence among people who inject drugs. It is a major risk factor for cirrhosis and hepatocellular carcinoma and results in chronic infection in the majority of cases.[1] Nevertheless, clearance of a minority of HCV infections suggests that some individuals can mount an effective immune response, and demonstration of significantly reduced incidence in previously infected individuals implies that immunity against viral persistence can be acquired.[2] In this brief report, we present further evidence suggesting that human immunity to HCV infection exists.

In a study combining social network methods and molecular epidemiology to investigate HCV epidemiology, we recruited injecting drug users (IDUs) from a long-established street drug scene in a suburb of Melbourne, Australia. Each recruit nominated up to 10 IDUs with whom they had injected drugs (meaning injecting on the same occasion, in the same location) over the previous 6 months and were invited to introduce these network members to us for interview. Venous or fingerprick blood samples were collected from 198 IDUs in total, and participants completed an extensive questionnaire covering their sociodemographics, drug use and injecting histories, their social (injecting) networks, and drug-injecting and other behaviors practiced with network members.

The study operated with ethical approval from the Human Research Ethics Committee of the Department of Human Services, Victoria.

Of the 198 blood samples, 172 (86.9%) were HCV antibody positive; 138 (69.7%) contained detectable HCV RNA; 21 (10.6%) had neither anti-HCV nor

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HCV RNA. Of the 21 HCV RNA-negative IDUs, 5 had been injecting illicit drugs for 9 years or more (median 11 years, maximum 15 years). Examination of the relationships described by these 5 HCV RNA-negative individuals revealed that all had injected with HCV RNA-positive IDUs in the 6 months prior to interview, at frequencies ranging from once to daily (median 30 times, maximum 193 times). All had shared drug preparation equipment, including spoons, water, filters, and drug solutions, and 2 had injected with an HCV RNA-positive IDU's used needle and syringe (two and three times) during the 6 months before interview. As shown in the Table, the risk behavior described by these 5 HCV antibody and RNA-negative IDUs is very similar to that of the 171 participants whose blood samples contained evidence of current or previous infection.

Our study was unique in that, by taking account of relationships between IDUs as well as information about individuals, it enabled demonstration of risks of exposure of IDUs to HCV through injecting with HCV RNA-positive members of their social networks. Although it is impossible to be certain that these 5 HCV RNA-negative participants had been exposed to viable HCV, given the high-risk behavior they described and their membership of an extended network in which over 85% of IDUs had already been exposed to HCV, it is highly unlikely that RNA-negative participants avoided exposure during their years of injecting illicit drugs. We concur with the hypothesis of Mehta et al.[2] that some individuals have or acquire immune function that protects them from HCV infection or enables them to clear infection rapidly without producing persistent detectable antibodies. Our data imply that long-term IDUs lacking evidence of HCV infection should be regarded as an important resource for vaccine development.

TABLE. IDU risk behavior by HCV status

						95% CI of the difference	
	HCV status	N	Mean	SD	*P*	Lower	Upper
Age, years	Exposed	172	30.25	7.37	.29	−10.08	3.01
	AB−, RNA−	5	33.79	3.73			
Length of injecting career, years	Exposed	172	10.92	7.49	.24	−4.20	1.26
	AB−, RNA−	5	12.39	2.25			
Needle-sharing frequency, last 6 months	Exposed	172	1.63	3.59	.84	−2.86	3.52
	AB−, RNA−	5	1.30	1.30			
Injecting frequency, last month	Exposed	172	40.13	37.53	.20	−11.76	54.81
	AB−, RNA−	5	18.60	15.49			
Number of injecting partners	Exposed	172	10.91	12.80	.03	−24.21	−1.16
	AB−, RNA−	5	23.60	15.57			
Number of injections with HCV RNA + IDUs, last 6 months	Exposed	151	41.51	64.88	.68	−70.91	46.20
	AB−, RNA−	5	53.87	76.46	.74	−106.70	81.98
Number of times injected with an HCV RNA + IDU's needle and syringe, last 6 months	Exposed	153	0.49	1.96	.78	−1.99	1.50
	AB−, RNA−	5	0.73	1.30	.70	−1.83	1.34

AB, antibody; CI, confidence interval.

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