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More Rare Birds, and the Occasional Swan

Brian R. Edlin, MD[1,2,3], **Marla A. Shu, MPH**[1], **Emily Winkelstein, MSW**[1], **Don C. Des Jarlais, PhD**[4], **Michael P. Busch, MD, PhD**[3,5], **Barbara Rehermann, MD**[6], **Thomas R. O'Brien, MD, MPH**[7], **Andrew H. Talal, MD, MPH**[2], **Leslie H. Tobler, DrPH**[5], **Marija Zeremski, PhD**[2], and **Ann B. Beeder, MD**[8]

[1]Department of Medicine, State University of New York (SUNY) Downstate College of Medicine, Brooklyn, NY.

[2]Center for the Study of Hepatitis C, Department of Medicine, Weill Cornell Medical College, New York, NY.

[3]University of California San Francisco, San Francisco, CA.

[4]Baron Edmond de Rothschild Chemical Dependency Institute, Beth Israel Medical Center, New York, NY.

[5]Blood Systems Research Institute, San Francisco, CA.

[6]Immunology Section, Liver Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health (NIH).

[7]Division of Cancer Epidemiology and Genetics, National Cancer Institute (NCI), NIH.

[8]Departments of Public Health and Psychiatry, Weill Cornell Medical College, New York, NY.

Dear Sir:

Your January Comment from the Editor[1] described several North American acute hepatitis C cohorts. We describe here two additional cohorts (Table 1). In both studies, infections have been identified prospectively, avoiding the selection bias inherent in studying patients who have sought medical attention.

Urban Health Study

The Urban Health Study recruited semiannual cross-sections of persons who injected illicit drugs from the streets and other natural settings in inner-city neighborhoods in the San Francisco Bay area.[2] Of nearly 14,000 persons enrolled from 1986 through 2002, nearly 5,000 participated more than once (mean, 4.5 visits), comprising a passive, embedded cohort.[3] Participants were interviewed, tested for HIV antibody, and given harm reduction counseling and referrals to needed services. Data from the interviews, blood samples, and add-on studies were used to study health and illness among persons who inject illicit drugs and evaluate interventions. Findings from this cohort have been published in more than 100 articles, describing basic biological, clinical, immunological, and epidemiologic investigations; social and behavioral studies; and research on health services, health policy, and legal policy.[2-7] From 1998 through 2002, 4,018 study participants received hepatitis B and C serologic testing, of whom 3548 (88%) tested positive for antibodies to the hepatitis C virus (HCV). Of those testing negative, 84 returned for a subsequent visit, and 24 tested positive for HCV antibody, representing prospectively identified seroconversions.

Conflicts of interest The authors disclose no conflicts.

Retrospective testing of stored serum identified an additional 43 seroconversions during 1986-1998. Ongoing analyses are examining HCV prevalence, incidence, and risk factors, and genetic factors associated with resistance to viral infection and persistence.

Swan Project

The Swan Project began recruiting injection drug users (IDUs) aged 18-35 on the Lower East Side of Manhattan in 2005; > 500 IDUs have been interviewed and tested for HIV and HCV antibody, and 150 who have tested HCV antibody-negative have enrolled in a prospective cohort. Cohort members undergo biweekly risk behavior interviews and HCV RNA testing to detect new HCV infections as soon as possible after they are acquired, along with counseling and referrals to needed services. Biweekly interviewing and testing has proved feasible, reveals more risk behavior than quarterly or semiannual interviewing, and identifies the timing of risk behavior and infections more precisely, providing increased power to detect associations between specific injection practices and contexts and HCV acquisition. Identifying these risk factors is urgent because HCV still spreads rapidly among IDUs even where access to sterile syringes has dramatically reduced transmission.[5] The incidence of new infections in Swan participants during follow-up fell three-fold from 2005 to 2007, while the incidence during the period immediately preceding enrollment, calculated using data on window period infections,[8] did not fall, suggesting that the reduction might have resulted from our intervention. We are prospectively studying the clinical features, immunology, and virology of acute infection, and comparing those who clear infection, those who develop chronic infection, and those who remain uninfected. We have found HCV-specific cellular responses in nearly 50% of seronegative, HCV RNA-negative persons in this cohort.[9] Our study provides the rare opportunity to analyze blood specimens collected before infection and then from the same persons weekly during acute infection. Participants who do not clear infection within 90 days are offered antiviral treatment through a unique multidisciplinary program.[10] To date, we have identified 21 prospectively observed infections, 18 persons in the seronegative window period on enrollment, 3 recent seroconverters, and 12 possible reinfections.

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Abbreviations

HCV	hepatitis C virus
NCI	National Cancer Institute
NCRR	National Center for Research Resources
NIDDK	National Institute of Diabetes and Digestive and Kidney Diseases
NIDA	National Institute on Drug Abuse
NIH	National Institutes of Health

SAMHSA	Substance Abuse and Mental Health Services Administration
SFDPH	Department of Public Health of the City and County of San Francisco
SUNY	State University of New York
UCSF	University of California, San Francisco

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Table 1

Additional Acute Hepatitis C Cohorts in North America

Study	Urban Health Study	Swan Project
Principal Investigator:	Brian R. Edlin, MD	Brian R. Edlin, MD
Co-Investigators:	Thomas R. O'Brien MD MPH, Michael P. Busch, MD, PhD, Barbara Rehermann, MD, and others	Don C. Des Jarlais, PhD, Michael P. Busch, MD, PhD, Barbara Rehermann, MD, Leslie H. Tobler, DrPH, Andrew H. Talal, MD, MPH, Marija Zeremski, PhD, Ann B. Beeder, MD, Thomas R. O'Brien MD MPH, and others
Cities:	San Francisco, Oakland, and Richmond, California	New York, NY
Institutions:	UCSF	SUNY Downstate College of Medicine, Weill Cornell Medical College, and Beth Israel Medical Center
Contact:	Brian R. Edlin, MD	Brian R. Edlin, MD
Inception:	1986 (retrospective), 1998 (prospective)	2005
Risk group:	Persons who inject illicit drugs	Persons who inject illicit drugs
No. acute infections identified:	24 (prospective), 43 (retrospective)	42
Treatment:	referral	offered
Funding:	NIDA (R01-DA09532, R01-DA12109, R01-DA13246), NCI (contracts NO1-CO-12400 and N02-CP-91027), SAMHSA (H79-TI12103), SF DPH, and the intramural research programs of NCI and NIDDK, NIH	NIDA (R01-DA03574, R01-DA16159, R01-DA021550), NCRR (M01-RR000047, UL1-RR024996), and the intramural research program of NIDDK, NIH
Ongoing research:	Prevalence, incidence, and risk factors for infection and clearance of infection; genetic factors associated with resistance to infection and chronicity.	Prevalence, incidence, and risk factors for infection and clearance of infection; immunology, viral kinetics, viral evolution, and natural history of acute infection; treatment outcomes, treatment decision-making; cost-effectiveness of screening and early treatment.