

Acute HCV infection in Young Injectors: the Acute UFO Study

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Project Description: This study is a four-year continuation of the Acute UFO study. Young injection drug users (IDU) constitute a distinctive high risk and understudied group with high rates of hepatitis C virus (HCV) infection. The Acute UFO study has identified 22 incident HCV infections, 19 of whom are being followed prospectively. We will continue immunological studies of the spectrum of cytotoxic T lymphocyte (CTL) responses and evolution within CTL targets (“epitopes”) in early infection, to identify early correlates of viral resolution, critical for defining correlates of protective immunity and thus future vaccine development. We will now include genotype 3 infection in these analyses. We will expand our investigation of factors that may be associated with determining candidacy for early antiviral treatment. Finally, we will incorporate epidemiological and molecular virology methods to study HCV infectivity and transmission dynamics of acute HCV between young IDU in injecting and sexual partnerships using phylogenetic analyses coupled with epidemiologic data.

Interesting Findings: Beginning 1997, young (<30 years) injectors in San Francisco have been offered participation in multiple studies under the shared title of the 'UFO study'. Younger IDU have higher parenteral and sexual risk behaviors and higher incidence rates of HIV, HBV and HCV infection than older injectors.

The UFO Study 1997-1999: The first UFO Study was a cross sectional study conducted over the period 10/97 – 11/99. The aims of that study were to assess prevalence of HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) infections. We established high seroprevalence of HCV among young IDU. In addition we published on HIV prevalence and risk factors, high overdose rate and HBV vaccine adherence. In total 706 individuals participated.

The UFO study 1999--2002: UFO-1 and UFO-2: The first longitudinal *UFO study* was a 3-year NIDA funded study of HIV and HCV infections (*UFO-1*) and HBV immunization schedules (*UFO-2*). We established high rate of HCV seroconversion (25% ppy) and risk factors for HCV seroconversion, tested adherence to and efficacy of accelerated HBV vaccine schedules in a randomized controlled trial and documented high rates of overdose and risk factors for overdose. We also established the utility of using nucleic acid amplification testing for the early identification of HCV infections.

The UFO-3 Study: 2002-2004: The *UFO-3 study* was a NIDA-funded longitudinal study and extends our successful research focused on HCV infection. The primary aims of this two year study were to study incident HCV infection, confirm the utility of NAT testing for identifying acute and serosilent HCV infection, and examine immunological correlates of viral clearance in newly infected young injectors by enrolling them into a sub-study of acute HCV infection (named *Acute UFO study*). HCV incidence was 25% per 100 person years of observation. As of August

Continued on the next page

Acute UFO Study continued

Continued from the previous page

2004, we enrolled 19 persons acutely infected with HCV in the longitudinal study. The median number of return visits has been four. Incidence of HCV infection remains high at an annualized rate of 25% per year.

Acute UFO Study: We have enrolled 163 HCV antibody (anti-HCV) negative young IDU in a longitudinal study (UFO-3 Study) and identified 22 incident HCV infections, 19 of whom are being followed prospectively. Using transcription mediated amplification (TMA) testing we successfully detect acute HCV infection (10 of 22 new infections) during the seronegative window period. HCV incidence is estimated at 27.8% to 40.7% per year. One of seven (14%) new genotype 1 HCV infections with completed RNA tests six months apart has spontaneously resolved infection and liver function tests (LFT) as measured by liver transaminase (ALT) levels are normal. Two of eight (25%) genotype 3 infections appear to be resolving. Preliminary immunological analyses have shown broad HCV-specific T cell responses in resolvers.

AFFILIATED UFO Studies:

UFO-VAX: (PI Paula Lum) A Randomized trial of vaccine adherence in Young IDU.

This trial will examine strategies to deliver a promising preventive HIV vaccine candidate-employing hepatitis B vaccine as a surrogate to a cohort of high-risk young injection drug users (IDU) and young male IDU that have sex with men (MSM-IDU).

ORBIT: (PI Judith Hahn) This study tests the feasibility of following young IDUs who travel, using ATM cards for instant incentives and online interviewing systems for follow up interviews. We are also determining young IDUs' rate of accessing services "on the road" for future research that might include collecting biological samples or delivering immunizations in this mobile group. This approach if successful, could be used to increase the ability to test the effectiveness of interventions to prevent HIV, HBV, HCV in this crucial at-risk population.

Project Web Site: www.caps.ucsf.edu/ufostudy/

Project End Date: June 30 , 2009