C. PRELIMINARY STUDIES

1. The ALIVE Study. The ALIVE (AIDS Linked to Intravenous Experience) Study began in February 1988 under the direction of the Infectious Disease Epidemiology Program at the Johns Hopkins School of Hygiene and Public Health. The study's principle objective was to monitor the development of HIV-1 infection and assess risk factors associated with seroconversion in a cohort of injection drug users. The population was recruited and screened for anti-HIV-1 in 1988 and early 1989. They were recruited through word of mouth from a variety of community agencies including drug abuse treatment centers, city health department clinics for STDs, local emergency rooms, state probation and parole offices, HIV/AIDS clinics, and the street outreach AIDS prevention program (SOAP) of a local community education program (HERO). Word-of-mouth spread was encouraged. ALIVE recruited adults with a history of IDU in the past 10 years without an AIDS defining illness. Over 90% of those that were screened returned to receive their test results. ALIVE recruited an average of 240 persons per month. Baseline recruitment resulted in 2,921 IDUs screened for anti-HIV; 703 were HIV-1 seropositive and 553 participants were female. Of the total, 630 positives and 160 negatives were enrolled for semiannual follow-up. Another round of recruitment resulted in a total of 2,960 IDUs screened and 713 HIV seropositives. Of the 2,247 seronegatives identified, 1,532 have returned at least once for serologic rescreen, and 275 seroconverters were identified and receive follow-up. Return rates for the follow-up clinic have consistently exceeded 85% per 6 month period. Follow-up rates for participants under 25 years may be lower. Details on methods employed in the ALIVE study have been described elsewhere. (94)

a) Risk of Seroconversion: Recent analysis of the seroconversion rates in ALIVE injecting drug users showed persistently high rates and differential trends by sex and age. (3) The overall crude seroconversion rate equaled 3.86 per 100 person years of observation. The incidence was two times greater in younger (< 35 years) as compared to older IDUs, and in females compared to males. (3) These results served as impetus that lead to our interest in studying **adolescent** and young adult injectors and further assess the factors surrounding initiation as it relates to HIV infection.

b) Trends in Initiates: In an effort to examine HIV seroprevalence data by duration of reported injection drug use, Vlahov et al. analyzed drug use patterns for 2,921 IDUs by year of initiation into injecting drug use. (15) A 15% seroprevalence was found among injecting drug users that initiated use within 18 months of enrollment into the ALIVE cohort study. Subsequently, Vlahov et al. (1991) reported on drug injection practices specific to the year of initiating intravenous drug use. (5) New injectors reported that during the first three months after initial injection, they shared less and had fewer injecting partners.

Due to the cohort study design, the researchers have not been able to document injection patterns and rates of HIV seroprevalence of injectors initiating use after 1988. This can now be addressed through recruitment of the proposed new initiate cohort.

c) Interaction of HIV and Sexually Transmitted Diseases: ALIVE reported an association between STDs and HIV seropositivity among **IDUs.** (95) At baseline, 24.1% of all IDUs were HIV seropositive and 60% reported a history of an STD. A history of treatment or diagnosis of syphilis was noted by 16.8% of HIV positives and 11.3% of HIV negatives, and both were more frequent among homo/bisexual man. Being female, however, was not significantly associated with history of syphilis. Cocaine use was associated with HIV seropositivity but not with syphilis. These results indicated that the exchange of sex for drugs or money may not have been an important transmission mode in this population as measured at baseline. However, in a more recent analysis of female IDUs, the odds of HIV infection was increased three fold for women who reported a frequency of trading sex for money or drugs with more than 50 partners. (25) Although the investigation of specific STDs through STD testing is beyond the scope of this study, we will investigate the role of detailed, self-reported sexual histories among new injectors.

The exchange of sex for drugs or money will be further explored in this young population. A popular drug choice for young people is crack or "rock" cocaine. The association of crack and injectable cocaine use and trading sex for money or drugs has been previously described. (11,28) **However, we aim to clarify the role of 'sex for money or drugs' transactions in relation to initiating an injecting career and HIV transmission among young NIUs and initiates.**

d) Hepatitis C Virus (HCV) among Recent Initiates: Infection of HCV **has also been** found to be correlated with high risk behaviors within the enrolled cohort of young IDUs. (4) At enrollment 38.4% were HCV seropositive and 14% seroconverted to HCV at the 6-month follow-up. (4) Of those who were HIV seropositve, 60% were also co-infected with HCV. Factors bivariately associated with first injection were younger age ($\leq$ 19), injecting cocaine, and never watching other inject prior to initiation. (4) Current injection risks included using needles that appeared dirty inside and injecting $\geq$5 times daily in the last six months, while injecting cocaine versus heroine only and injecting at least once daily during peak use were significant lifetime factors for being HCV seropositive. (4) Unlike HIV risk, current and lifetime risky sexual practices were not associated

with HCV. (4) Using logistic regression analysis, initiates injecting for ≥3 years (OR=3.3), injecting at least daily (OR=2.8), injecting cocaine (OR=4.3), being >5 years younger than the person assisting at initiation (OR=2.8), and never watching others inject before initiation (OR= 3.3) were all significantly associated with being HCV seropositive. (4) Among the newest initiates (injecting for ≤ 1 year), HCV was only associated with high risk injecting variables and there was no association with high risk sexual practices. (4)

e) Studies on Physical/Sexual Abuse: In the HERS Study, Dr. Vlahov analyzed cross-sectional data on history of physical and sexual abuse as it related to HIV infection, social supports, drug use and sex practices. In this population of 1093 adult women with HIV infection or at risk for HIV from four cities, physical or sexual abuse as a child and as an adult was common (40%), but was not significantly associated with HIV infection; these data suggested that among high risk women, childhood abuse did not explain HIV infection above and beyond established risk behaviors. Another concern is that disclosure of HIV seropositivity might be associated with violence against women. Given the similarity of rates of abuse as an adult by HIV serostatus, the data suggest **that either** violence with disclosure might be uncommon or that disclosure to partners is uncommon (for fear of violence). The data did not probe this issue further. Interestingly, recent violence was less common in HIV seropositives than seronegatives and this was related to lower CD4 cell counts. This suggested that as women with HIV infection become more ill, they are less likely to be in situations that lead to violence (i.e., drug use, multiple sex partners). Data to examine these associations in young IDUs are sparse. Similarly, the role of psychiatric condition(s) following a history of abuse and its relationship to type and frequency of risk behavior remain to be clarified. **Additionally, interaction between social networks/social support and history of physical abuse/violence (or violence as a result of disclosure) on HIV can be explored in this proposed study.**

f) Studies on Social Networks: A recent study of ALIVE participants utilized social network analysis to study patterns of drug use among Baltimore IDUs. Concepts of social integration, social network structure and relationship content (adapted from Hall and Wellman, 1985) served as the framework for examining the structural and relationship characteristics of social networks of IDUs, and the relation of social network characteristic to high risk injection practices. (89) In a sample of 293 IDUs, 89% reported at least one family member in their social network, and 44% listed their mother or step-mother, yet presence of a family member in personal social networks was not associated with patterns of drug use. (86) Network density and size of drug subnetworks were positively associated with frequency of drug injection and those who reported presence of a partner in a personal social network injected less often than those reporting the absence of a partner. (86) These results suggested that social network analysis may be of use in understanding the social context of risky injections behaviors.

An additional ALIVE study, 330 sampled IDUs were interviewed twice approximately 5.2 months apart to examine the association between personal networks characteristics at baseline and needle-sharing at follow-up. (87) This analysis revealed that higher total network density and larger drug subnetwork size were positively associated with reports of needle sharing. Attending shooting galleries was positively associated with size of positive feedback network (social network members identified as people you would go to for positive advice or tell you good things), and negatively associated with size of material aid network (social network members identified as people that would lend you or you could borrow money/valuable things from). These findings suggest the potential utility of network-oriented strategies for reducing high risk injection practices among IDU. Given that these findings represent a population of long-term injection drug users with a mean age of 42 years, further studies of young adult injectors are warranted due to the high seroprevalence among this group.

2. The REACH Study. The REACH (Risk Evaluation and Assessment of Community Health) Study was implemented in 1994 under the direction of the Infectious Disease Epidemiology Program at the Johns Hopkins School of Hygiene and Public Health and Centers for Disease Control and Prevention, Division of HIV/AIDS. The purpose of the study was to identify the prevalence and correlates of HIV infection among 400 recent initiates between the ages of 18 and 25 years of age. Injection status was verified by presence of injection stigmata (scar tissue or "tracks") and through a series of questions aimed at identifying the plausibility of the individual's experience injecting drugs. Participants were recruited from a variety of community based sources such as street outreach, young adult treatment programs, local emergency rooms, and health clinics in Baltimore City. Flyers were distributed throughout the community and word-of-mouth was encouraged. Those who agree to participate underwent a baseline interview, venipuncture, and HIV testing with pre- and post-test counseling. All participants were scheduled to return two to three weeks after baseline to receive HIV test results and six months later for a follow-up interview and HIV test for seronegative participants. As of June 1996, 335 participants were screened, 250 recent initiates were enrolled (75%), and 13.2% initiates were HIV positive at baseline with 4.5% seroconverting. The follow-up rate for the 2-week visit was 87%, the 6-month visit was 73%. and the 6-month result visit was 90%. Beginning October 1996, enrollment re-opened for recruitment and follow-up of an additional cohort of similar initiates (REACH II) using the same recruitment methods and eligibility criteria as stated in this proposed study. If given funding from the National Institute on Drug Abuse (NADA), this new cohort will complement this proposed cohort and will potentially generate the necessary power to detect risk factors of HIV seroconversion.

a) HIV Infection among Recent Initiates: Over the past 3 years of the REACH study, we have conducted various analysis for peer review describing characteristics of young adult initiates. Specifically, high risk behaviors at first initiation and currently were assessed in addition to high risk behaviors associated with being HIV seropositive. Among recent initiates enrolled in REACH, both risky injecting and sexual practices were important for HIV infection (Table 3). Factors associated with HIV among initiates were having >100 lifetime sex partners, identifying as gay/bisexual, sexual assault, trading sex post-initiation, ≤ 18 years old at initiation, injecting cocaine or speedball at initiation, having ≥ 2 "trainers" before being able to self-inject, smoking crack ≥ 1 per day, injecting ≥ 5 times per day, and "backloading". (38) These results suggest that immediate steps should be taken to prevent new infections among young IDUs. In the proposed study, examining reasons for deciding to initiate injection drug use and engage in risky sexual and injection behaviors can be explored through a more careful assessment of physical/sexual abuse, the role of psychiatric condition and the characteristics of social networks/social support among young initiates.

b) Circumstances of Initiation: One hypothesis tested through the REACH study was possible gender differences with respect to the gender and age of the primary initiator. It was though that young women may be more likely to be introduced to injection drug use by an older male. Yet, the enrolled cohort demonstrated that young women and men were more likely to have a primary initiator of the same sex who tended to be around the same age (64% of young women had a female primary initiate and 83% of the young men had a male initiate; 56% of the women and 60% of the men had a primary initiate with <5 year age difference) (Table 1). These factors can be more closely addressed in the proposed study through analysis of social support and social networks.

Additional hypotheses addressed using the REACH cohort included gender differences with respect to sex and drug behaviors (Table 2.) Young women initiates were 3.98 times more likely than young male initiates to report <10 lifetime sex partners. Young women were also 4.33 and 2.85 times more likely than young men to trade sex before initiation and after initiation, respectively. Consistent with previous research linking crack use and sex for drugs or money, young women initiates were also 5.98 times more likely than young men to report recent crack use one or more times per day. A startling finding within this cohort showed young women to be 15.7 times more likely than young men to self-report previous sexual assault. (96) This 41% reporting of sexual assault among women compared to 6% among young men created the need to further address this issue as a specific aim of the proposed study.

Table 1. Characteristics of Primary Initiators (n=153) at IDU Initiation.

Characteristic	**Primary Initiator**	**Women (n=88)**	**Men (n=65)**
		(%)	**(%)**
Gender	Female	64	17
	Male	36	83
Role	Hitter	9	8
	Introducer & Hitter	82	79
Race	African American	86	74
Relationship	Friend	60	57
	Other relative	17	18
	Sex partner	15	11
Age Difference	< 5 years	56	60
Years Acquainted	< 5 years	41	51
Years Injected	< 5 years	56	54

(Doherty et al, APHA 1995)

Table 2. Preliminary Data of Sex and Drug Behaviors Associated with Gender among Young Adult IDU (n=164).

Characteristic	**Women (n=93)**	**Men (n=71)**	**OR**	**[95% C.I.]**

Lifetime sex partners	(%) 49	(%) 20	3.98	[1.98-8.00]
Sexually assaulted	41	4	15.7	[5.72-42.9]
Trade sex				
Before initiation	35	11	4.33	[1.92-9.76]
After initiation	47	24	2.85	[1.46-5.58]
Recent crack use	31	7	5.98	[2.36-15.2]

(Doherty et al, APHA 1995)

Table 3. Final Data of Factors Associated with HIV Seroprevalence Among 229 Young Adult IDUs.

Characteristic	**HIV+ n=32 (14%)**	**OR**	**[95% C.I.]**
	N		
Age first inject ≤ 18	18	2.87	[1.37-6.02]
Ever inject cocaine/speedball	31	17.9	[3.97-80.4]
Number "trainers" before can self inject ≥ 2	20	2.77	[1.31-5.88]
Past 6 months:			
Smoke crack ≥ 1x/day	11	3.03	[1.36-6.77]
Injected ≥ 5x/day	16	2.57	[1.10-6.04]
Backloaded	12	2.88	[1.32-6.29]
Female	20	1.49	[0.69-3.21]
Lifetime sex partners >100	7	5.84	[2.2-15.49]
Gay/bisexual	7	3.96	[1.53-10.3]
Sexually assaulted	15	2.40	[1.13-5.07]
Trade sex post-initiation	19	3.18	[1.51-6.69]
trade anal	5	7.11	[2.26-22.4]
trade oral	14	3.60	[1.69-7.67]
trade penile/vaginal	15	2.12	[0.99-4.47]