

ACUTE HCV IN HIV-INFECTED PATIENTS

Kenneth E. Sherman, MD, PhD
Gould Professor of Medicine
Director, Division of Digestive Diseases
University of Cincinnati College of Medicine/UCHealth

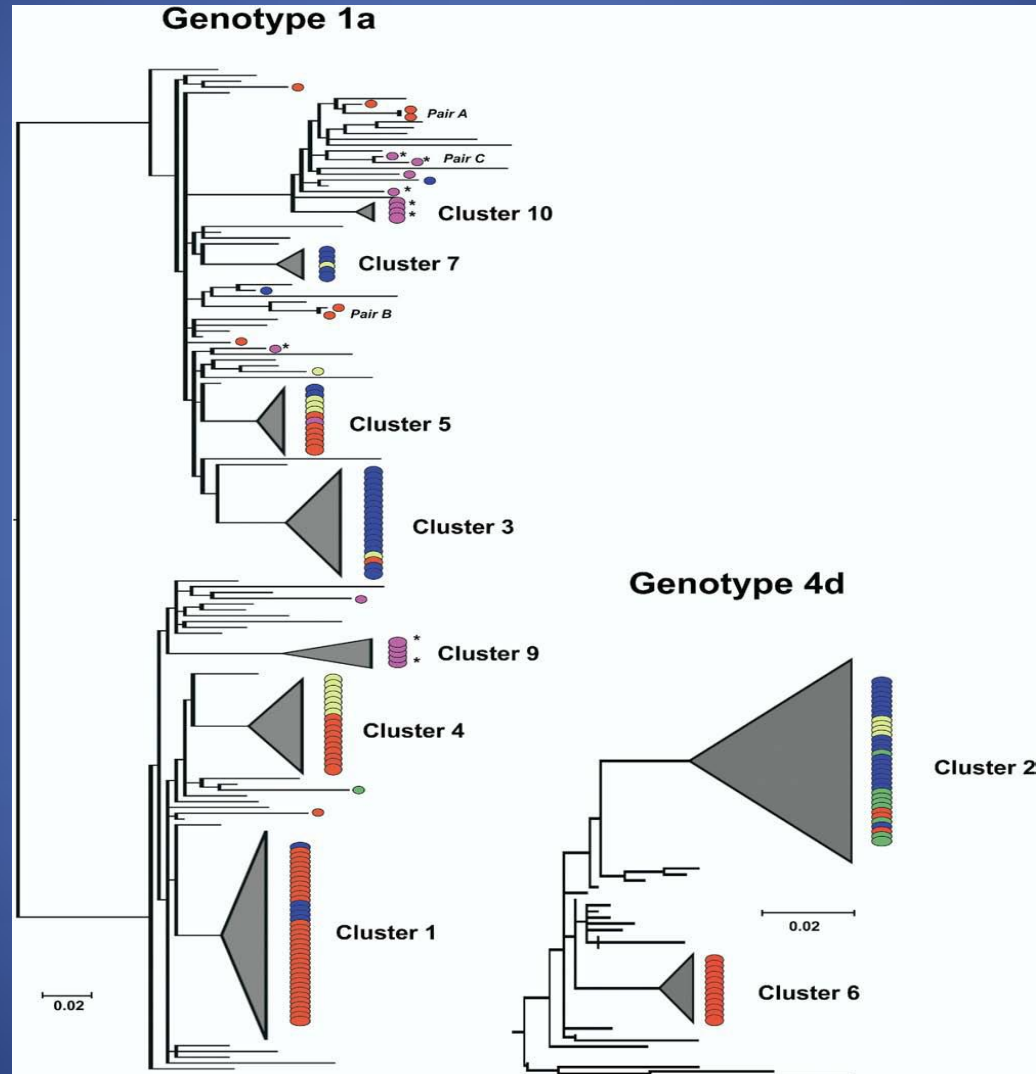
EPIDEMIOLOGY

- New Patterns of Acute Infection Observed
- Mini-Outbreaks of Acute HCV Described
 - Urban Areas
 - MSM
 - High Risk Sexual Practices

HCV OUTBREAKS IN MSM

- (1) Paris, N=29 Gambotti L et al., Euro Surveill, May 2005
High-risk behavior: anal sex, fisting, concomitant STI, bleeding during sex
- (2) San Francisco, N=9 Luetkemeyer et al., JAIDS, Jan 2006
- (3) Paris, N=25 Dominguez S et al. AIDS, May 2006
- (4) Paris, N=6 Ghosn J et al., Sex Transm Infect, Dec 2006
- (5) Paris, N=12 Serpaggi et al., AIDS, Dec 2006
- (6) London, N=111 Danta M, AIDS, May 2007
7 clusters, RFs: sex with 3+ partners, hi-risk sexual behavior
- (7) New York, N=11 Fierer D et al., J Infect Dis, 2008
histology with inflammation and septal fibrosis
- (8) Madrid, N=4 Montoya-Ferre, Emerging Inf Dis, 2011

Phylogenetic Analysis



Changing Epidemiology



MSM



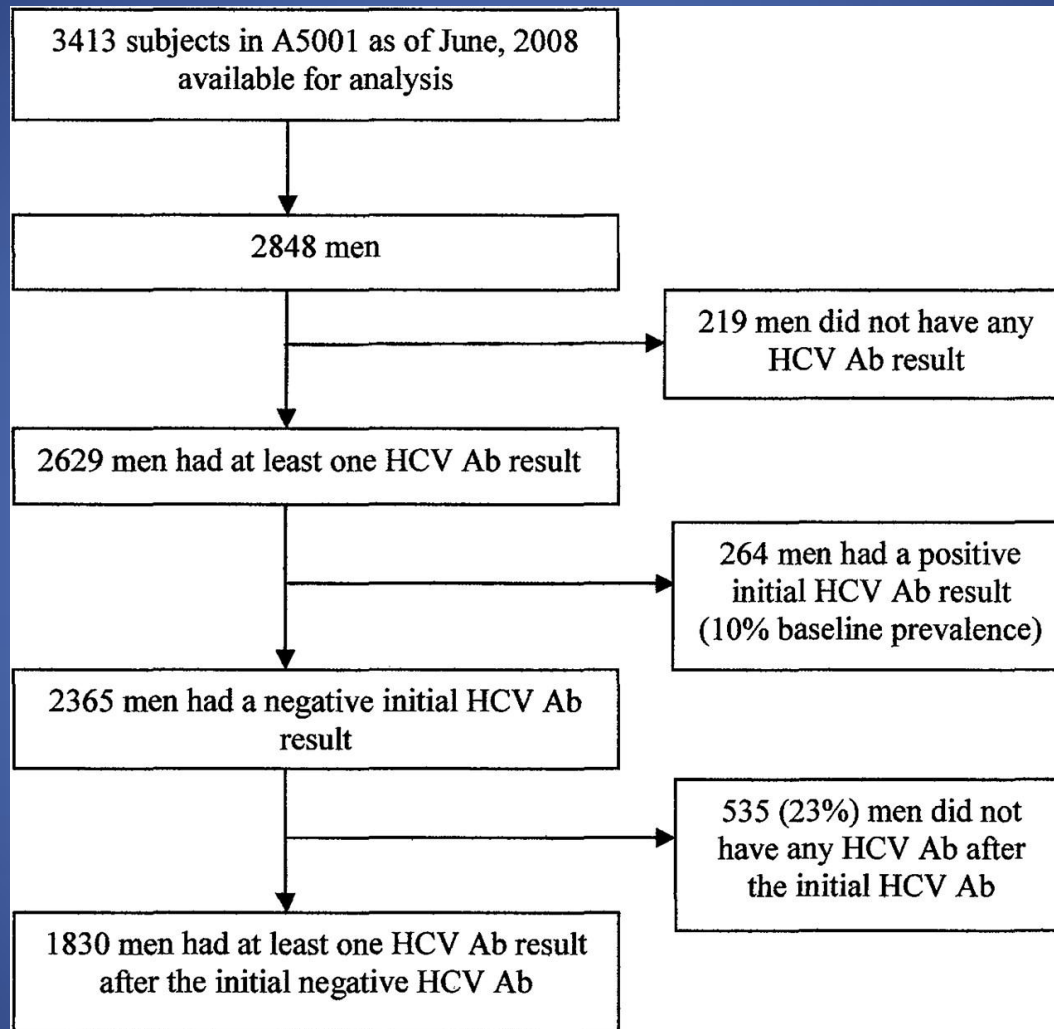
IDU

Post-HAART

Factors in Changing Epidemiology

- Unprotected (Receptive>Insertive) Anal Sex
- Use of Gamma Hydroxybutyrate (GHB)
- Fisting and Use of Sex Toys
- Group Sex
- Other Sexually Transmitted Diseases
 - Syphilis
 - Gonorrhea
 - LGV
- Internet-based Social Networks

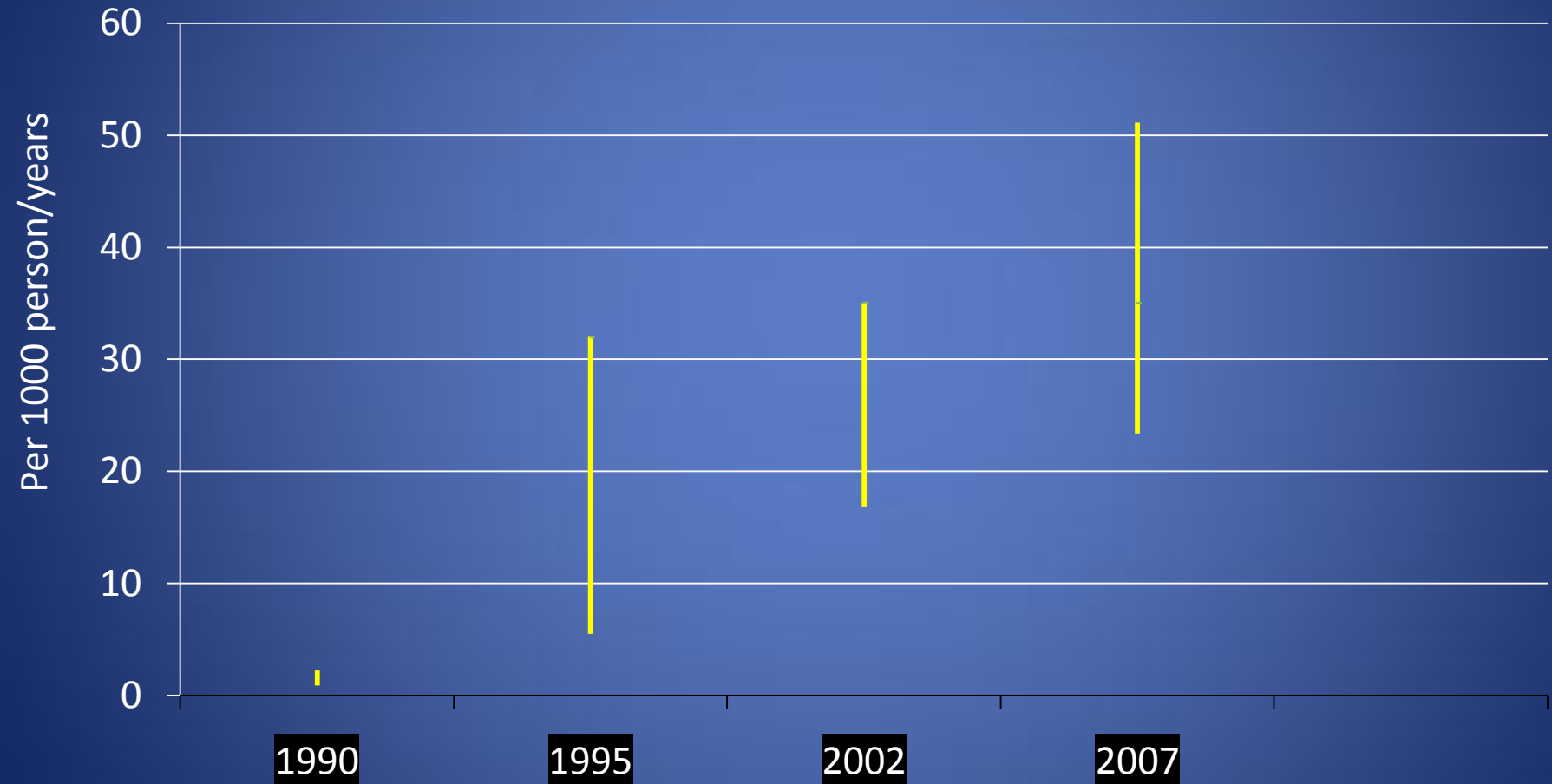
ACUTE HCV INCIDENCE



INCIDENCE HCV SEROCONVERSION=

.51 cases per 100 person-years (95% confidence interval [CI], .36 - .70).

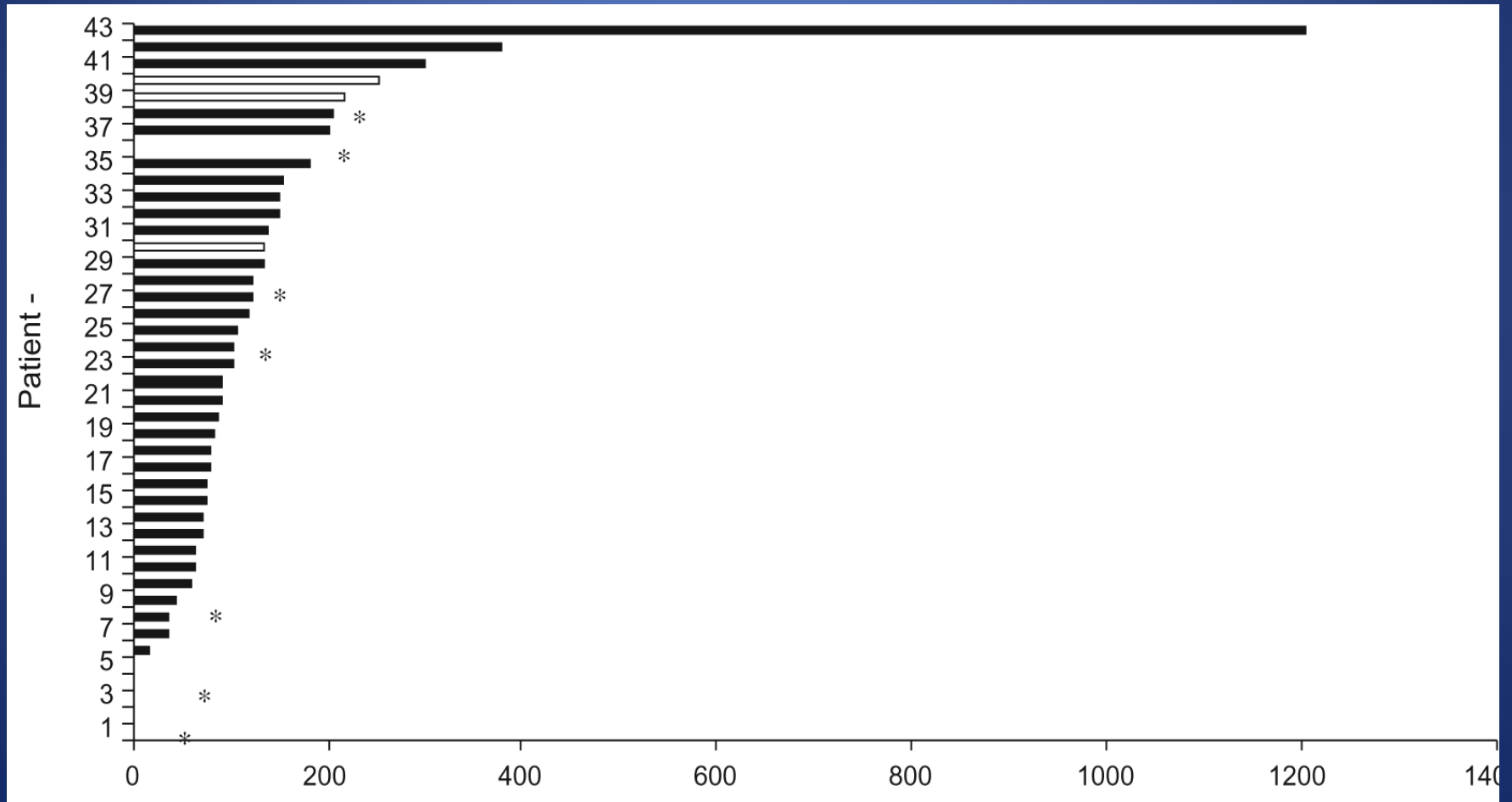
CHANGING INCIDENCE OF ACUTE HCV in MSM with HIV-INFECTION Amsterdam



Surveillance

- Method
 - ALT
 - HCV Antibody
 - HCV RNA
- Frequency
 - 6 months
 - 12 months
 - Other

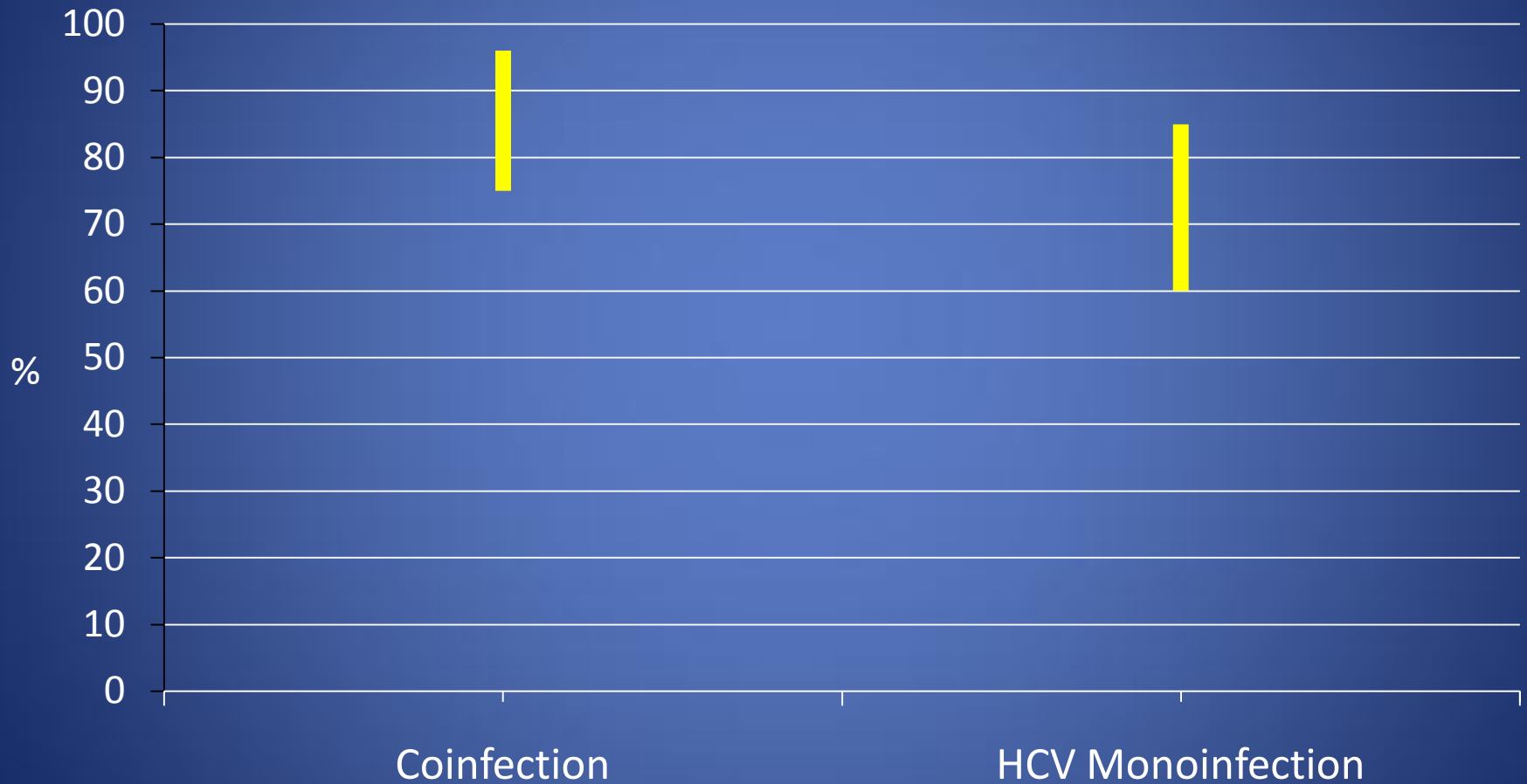
Delayed HCV Antibody Conversion



HCV EIA vs. ALT

- ALT elevation more sensitive than antibody testing ($p= 0.017$)
- When $ALT < 30$ used sensitivity 79% at baseline and 82% 3 months later
- 93% had $ALT > 30$ at initial or 3 month timepoint
- ALT did not distinguish those who cleared from those who didn't

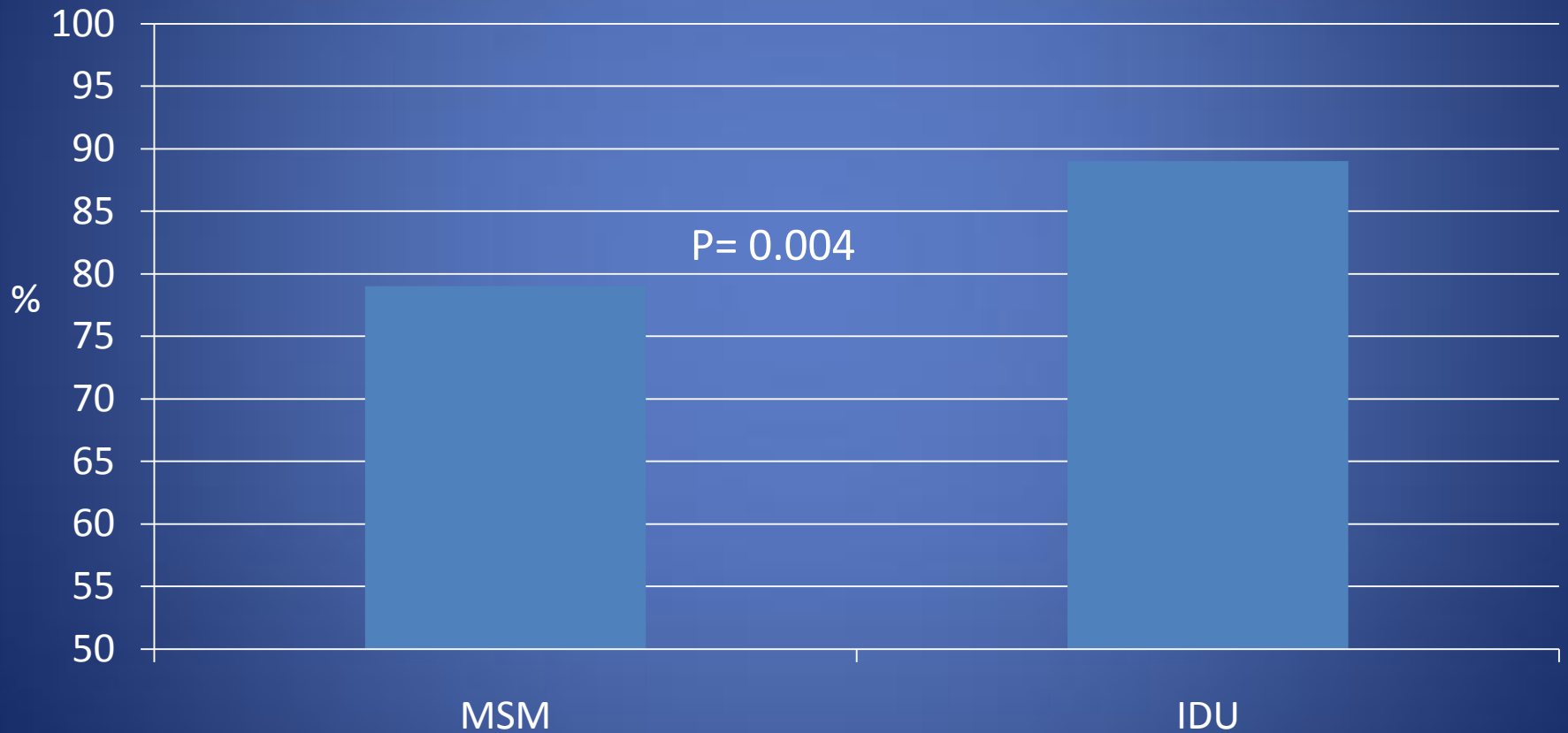
Risk of Chronicity



Arends et al, ANTIVIRAL THERAPY, 2011

Thompson et al., J GEN VIROL, 2011

Risk of Chronicity of HCV in HIV MSM vs. IDU

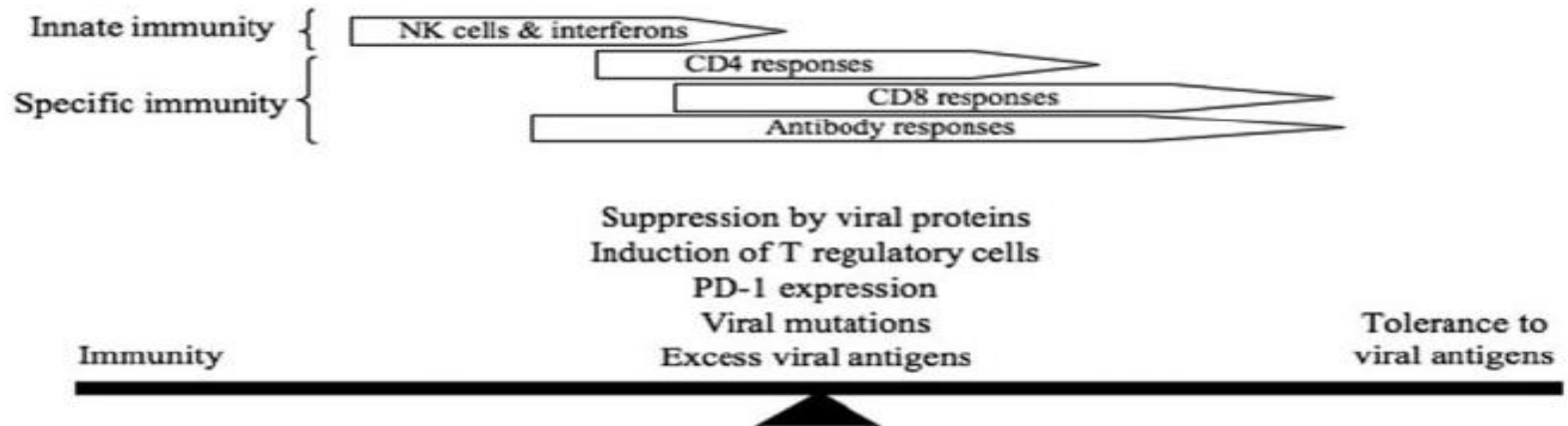
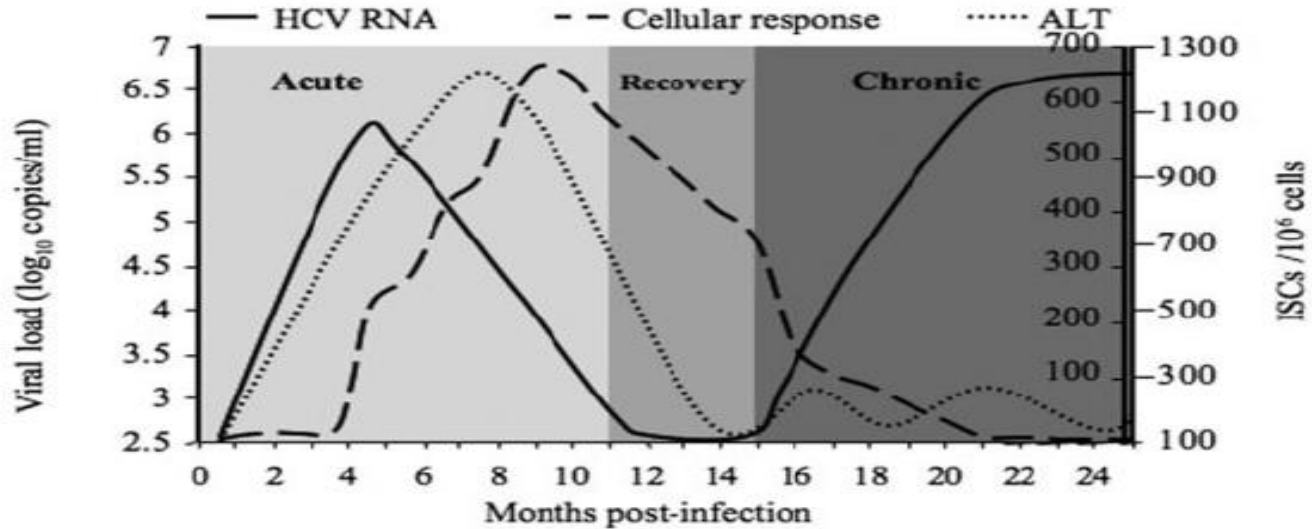


Clinical Features

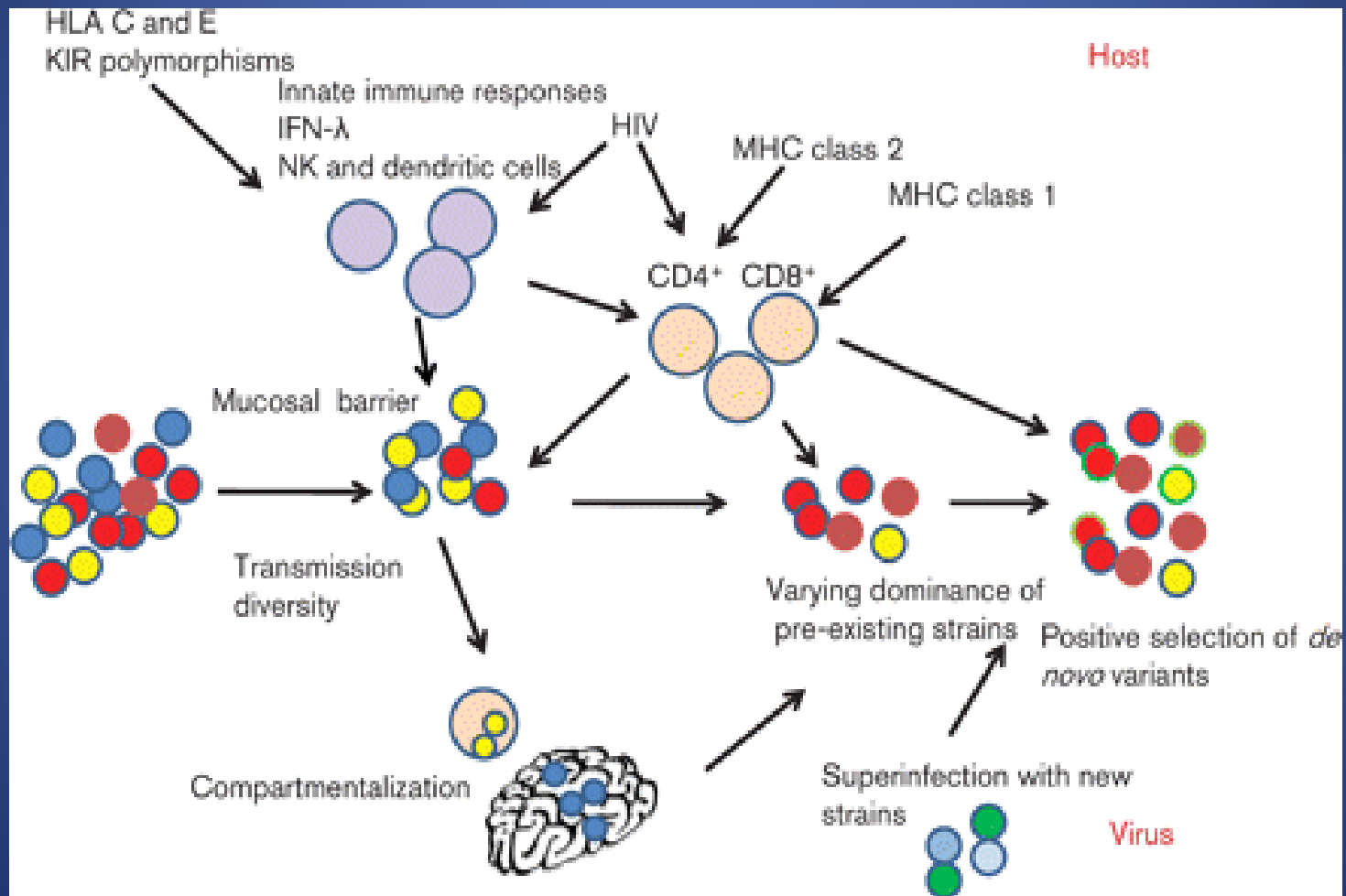
Clearance vs. Chronicity

- Poorly Characterized in Setting of HIV
- Factors Favoring Clearance
 - High ALT
 - High CD4
 - Rapid Kinetics of Viral Decline
 - Less Quasispecies Complexity
 - Jaundice

ACUTE HCV COURSE



Model of HCV Chronicity in HIV

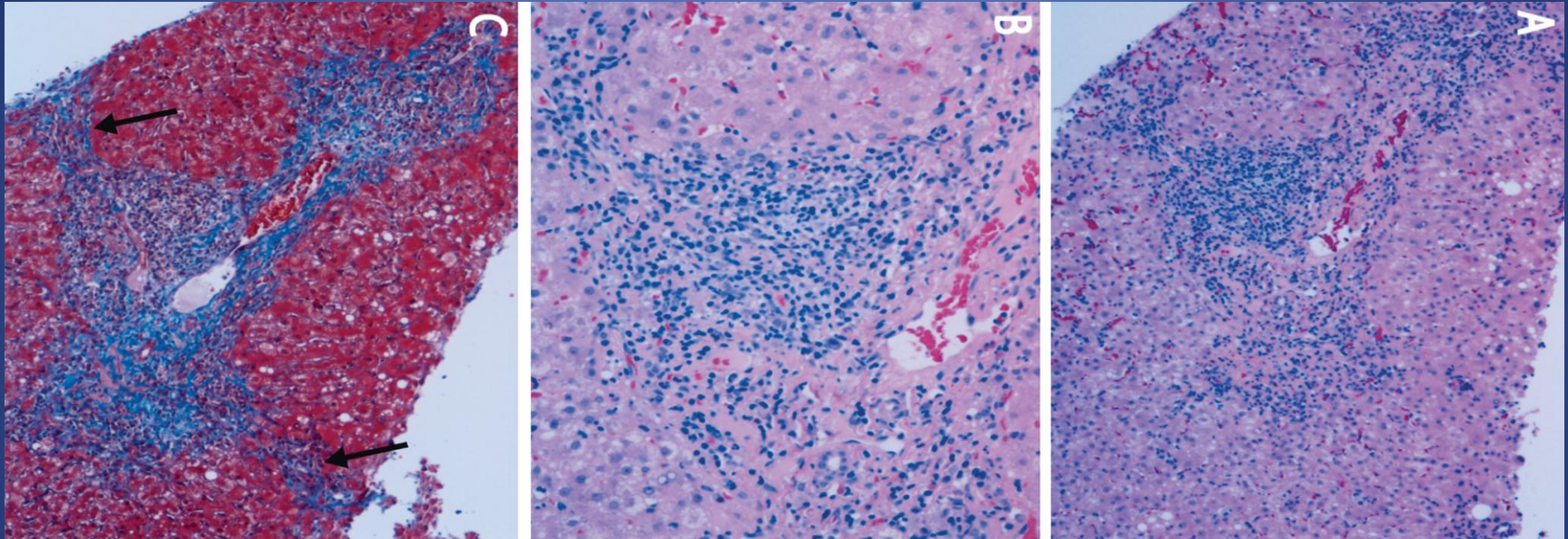


SPONTANEOUS CLEARANCE OF ACUTE HCV IN HCV/HIV

Role of IL28b

- 80 Patients with Acute HCV
 - CC n=38
 - Non-CC n= 42
- Spontaneous Clearance Could be assessed in 38 (others started treatment too early)
- 8/38 had spontaneous clearance
 - 5 CC (CC was present in 47.5% of population)
 - 3 CT/TT

Rapid Fibrotic Progression



Periportal Fibrosis with Focal Bridging: 8 Weeks After Onset of Hepatitis
--82% (9/11) Patients with Acute HCV in Setting of HIV had Stage 2 Fibrosis

TREATMENT ALGORITHM

Unrecognized exposure



Evaluate symptoms and/or ALT elevation with HCV RNA, HCV Ab

if HCV RNA/Ab positive



12 week observation



Evaluate for HCV RNA

HCV RNA negative (PCR or TMA)

Confirm HCV RNA negative

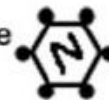
Monitor HCV RNA, HCV Ab, ALT every 4 weeks x 6 months



Known or suspected exposure

if HCV RNA/Ab negative, no further evaluation necessary

HCV RNA positive (PCR or TMA)

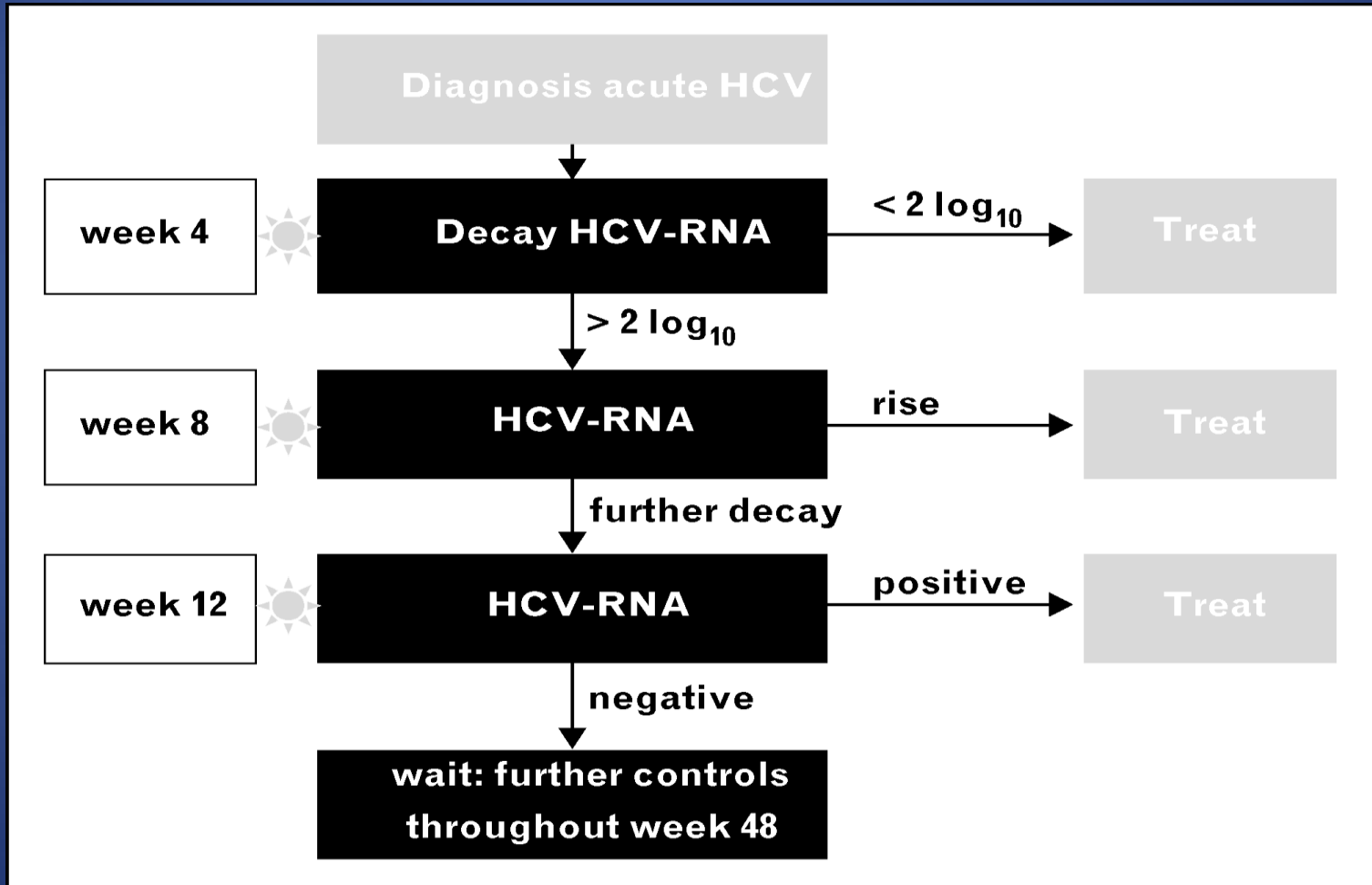


individualized therapy based on race, weight, HCV genotype (24 weeks)

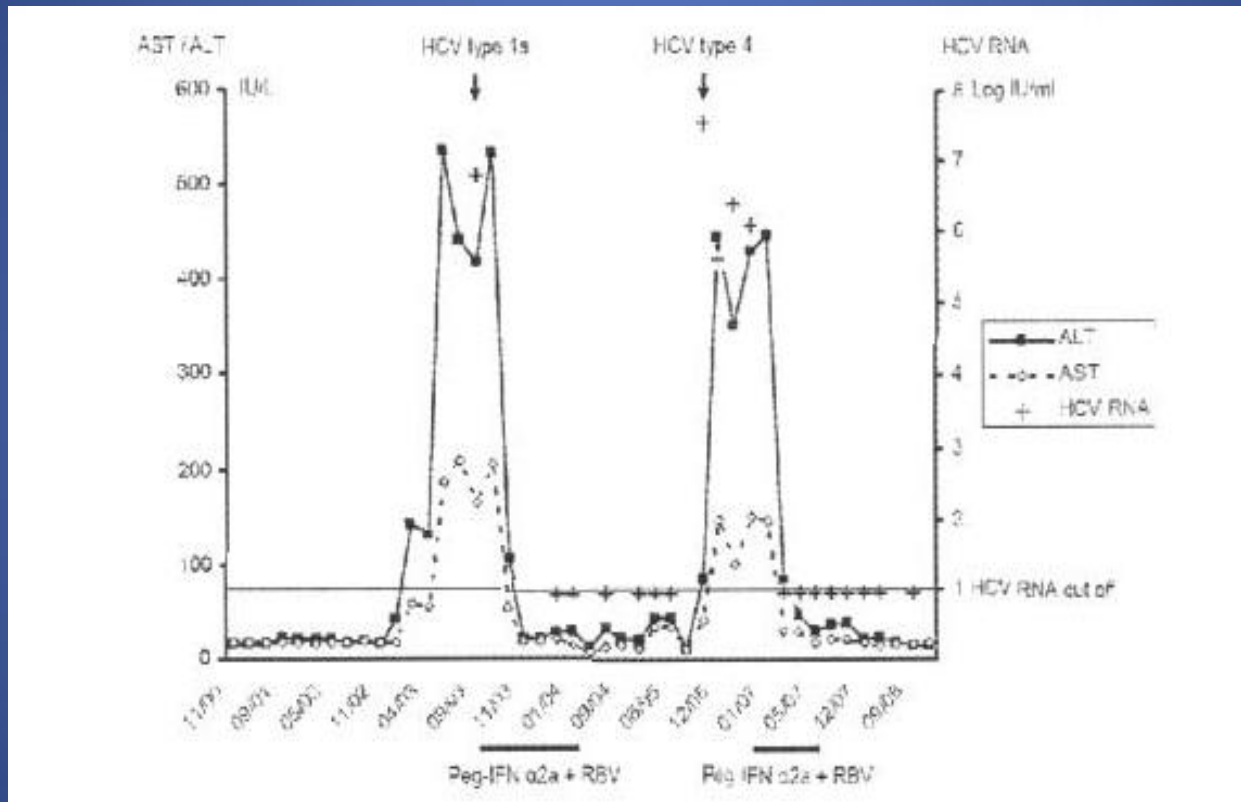
Peg-IFN + RBV_{300mg}

Peg-IFN

ALTERNATIVE ALGORITHM FOR ACUTE HCV IN HIV



Serosorting and Reinfection



Reinfection rate of nearly 10% reported in followup of 227 patients
Jones et al, CROI, 2008

Cotte et al, Gastroenterologie Clinique et Biologique, 2009

Conclusion

- Acute HCV Infection Occurs at Rate of $>5/1000$ cases per year among HIV-positive persons with highest risk among MSM engaged in high-risk behaviors
- Surveillance with ALT recommended in at risk individuals- Optimal duration ?4-6 months
- Earlier treatment intervention may be needed compared to those with HCV mono-infection
- Reinfection rates poorly defined but serosorting may increase risk