NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Acute Hepatitis C in HIV-infected Patients

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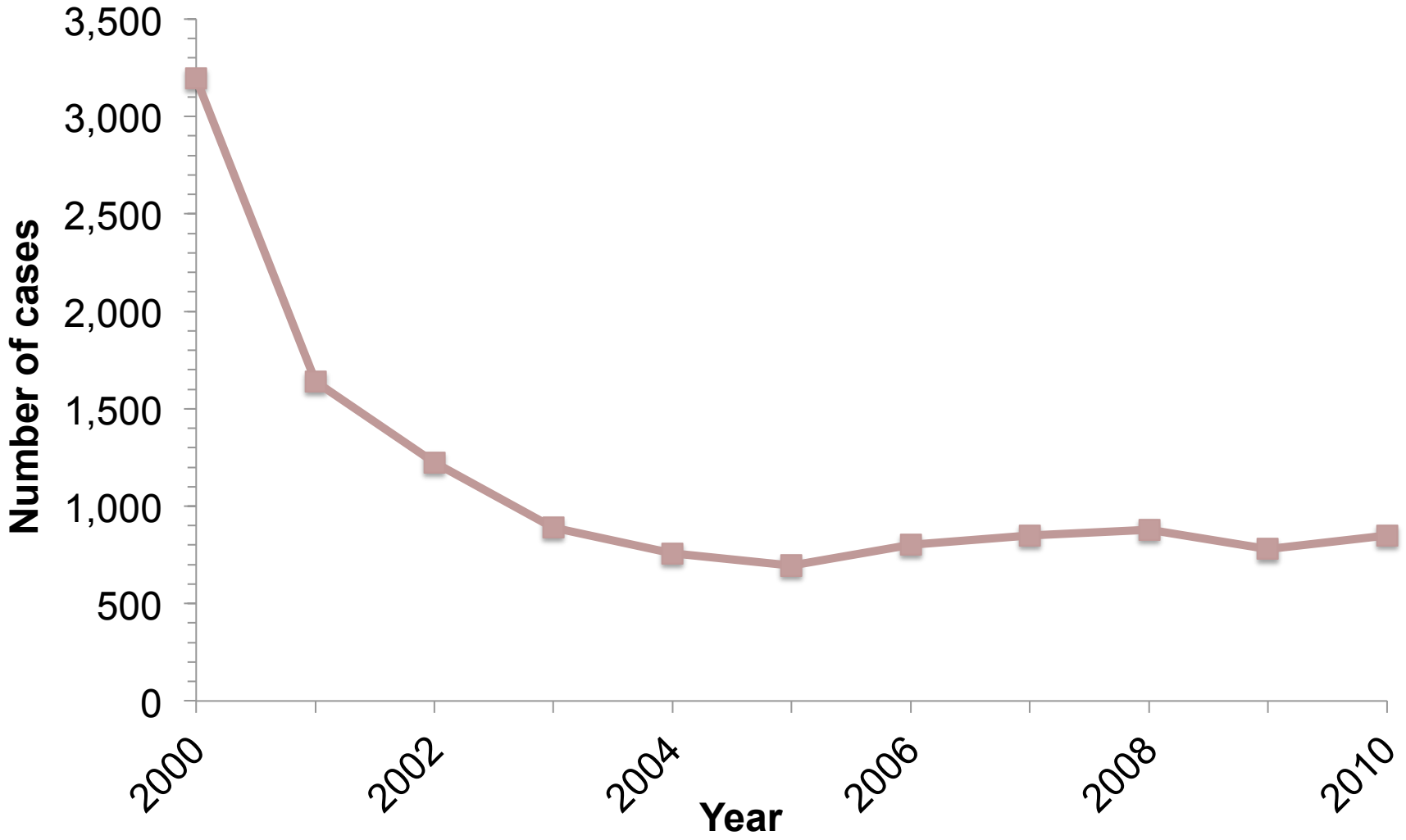
Acute Hepatitis C

- Epidemiology: Recent Trends (among HIV+ MSM)
- Risk factors for acute HCV acquisition
- Screening
- Natural History & Clinical Features
- Case Definition: Challenges to Diagnosis
- To Treat or not to Treat?
- Management

Reported number of acute HCV cases U.S., 2000-2010



www.cdc.gov/hepatitis

Hepatitis C Transmission

- HCV most efficiently transmitted parenterally
- Sexual transmission in general population considered rare
  - Among cohort of 895 heterosexual HCV-serodiscordant couples, only 3 transmissions occurred → incidence 0.37/1000 person-years
  - Strain analysis did not support sexual transmission
- Barrier protection not mandated for HCV prevention
- Historically, HCV prevalence among HIV-infected tracked closely with injection drug use (IDU)
  - 1-7% among MSM without IDU versus 25-50% among MSM + IDU

Vandelli C, *Am J Gastroenterol* 2004; 99:855-59.

Rising Hepatitis C Incidence among HIV-infected MSM

- 2004-2005: Increased HCV incidence in multiple countries in Europe → US/Canada, Australia, Asia
  - Netherlands – HCV prevalence among HIV-infected MSM rose from 1-4% in 2000 to 21% in 2008
  - Swiss HIV cohort – noted 18-fold increase in HCV incidence (1998-2011) in 23,707 person-years of follow-up.
- Many of these cohorts reported low rates of IDU
- Phylogenetic comparisons show HCV transmission clusters among sexual networks of MSM
- Alarming patterns of reinfection occurring among those patients who clear, either spontaneously or with tx.

Urbanus, *AIDS* 2009; 23:F1-F7.
Wandeler, *Clin Infect Dis* 2012; 55:1408-16.
Ingiliz, CROI 2012, Abstract 752.

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 60 / No. 28
July 22, 2011

World Hepatitis Day — July 28, 2011

July 28, 2011, marks the first official World Hepatitis Day established by the World Health Organization

Sexual Transmission of Hepatitis C Virus Among HIV-Infected Men Who Have Sex with Men — New York City, 2005–2010

www.cdc.gov/mmwr

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Acute HCV in HIV-infected MSM in New York City

- 2005-2010, total of 74 HIV-infected MSM with recently acquired HCV referred to Mt Sinai Medical Center
- None had reported hx IDU
- Phylogenetic analysis of HCV strains revealed five clusters of closely-related HCV variants
- Clinical Features of 74 men:
  - Mean CD4 count 483 cells/mm^3. Median age 39 years.
  - 60 (81%) **asymptomatic** – new HCV infection detected solely by new ALT elevation.
  - 14 (19%) had jaundice.
  - Median peak ALT level 665 U/L (range 72-5,291 U/L).

www.cdc.gov/mmwr - July 22, 2011 Report

Acute HCV in HIV-infected MSM in New York City

- Cases and matched controls (also HIV+ MSM but no HCV)
- Completed self-administered surveys re sexual practices & drug-use behaviors during preceding 12 months.
- Multivariate analyses:
  - Receptive anal intercourse with no condom & with ejaculation of partner (adjusted odds ratio [aOR] = 23)
  - Sex while using methamphetamine (aOR = 28.6) → most strongly associated with HCV acquisition

www.cdc.gov/mmwr - July 22, 2011 Report

Risk Factors for HCV Acquisition among HIV+ MSM

- Behavioral Factors:
  - "Serosorting" → concordant unprotected anal receptive intercourse
  - Mucosally traumatic sex practices: group sex, use of sex toys, fisting
  - Use of drugs during sex: methamphetamine (not IDU)
- Biologic Factors:
  - HIV infection: higher serum HCV viral levels
  - Sexually transmitted infections
    - Syphilis
    - Lymphogranuloma venereum proctitis
    - Gonorrhea, Chlamydia

Danta, et. al. *AIDS* 2007; 21:983-91.
Bradshaw, et. al. *Curr Opin Infect Dis* 2013; 26:66-72.

Screening High-risk Patients
Quarterly ALT

- Urban HIV care center: a third of all HIV-infected patients were HCV-coinfected
  - 34% of HCV-HIV patients reported MSM as primary risk factor
  - 25% reported IDU; 2% both
- Completed survey re risk behaviors & perceptions of risk
- HCV-susceptible high-risk patients screened with q3 mon ALT:
  - MSM with unprotected traumatic anal sex, STI, or stimulant/drug use
  - MSM with >5 sex partners within prior 6 months
  - MSM with HCV-infected partner
  - Intranasal or injection drug
- Elevated ALT (>45 U/L or >1.5 X baseline) triggered HCV RNA testing (pooled for uninsured patients)

Taylor, AIDS Pt Care STDS. 2011;25:571-77.

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Screening High-risk Patients
Quarterly ALT

- Majority (54%) of MSM did not perceive traumatic sexual or drug practices increased their risk for HCV
- Unprotected sex often occurred w/ drugs or alcohol
- Decent rollout: 88% participants had at least one ALT in 9-month follow-up.
- 2% annual incidence (n=1 among 58 participants)

Taylor, AIDS Pt Care STDS. 2011;25:571-77.

Natural History of Acute HCV Infection

- Incubation period = 10-14 weeks.
  - Clinical illness occurs a mean 7 weeks from exposure
- HCV RNA (+) as early as 1 week post-infection.
- HCV Ab seroconversion detected 2-6 months post-infection.
- Only ~10-20% clinically ill – rarely fulminant.
- ALT typically 400-1000 U/L; Bilirubin rarely >12 mg/dl.
- Spontaneous clearance – estimated 20-25%, may be lower in HIV-infected.

Low, et. al. AIDS Reviews 2008; 10:245-53.

Diagnosis of Acute Hepatitis C

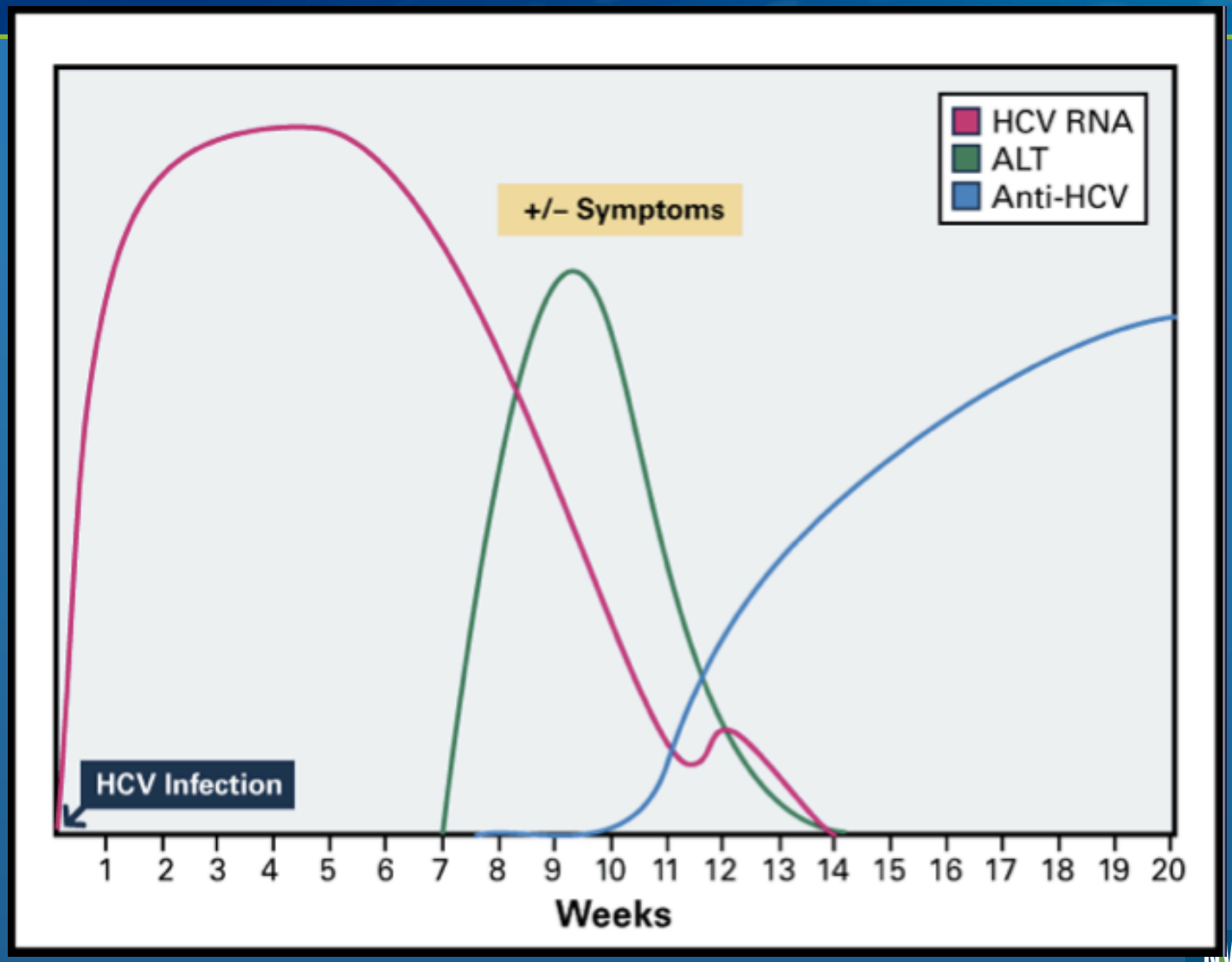
- Diagnosis of acute HCV can be challenging:
  - Most cases asymptomatic
  - No reliable or specific IgM-based HCV antibody test

- CDC case definition:
  - Acute illness compatible w/ hepatitis or serum ALT >400 AND
  - Antibodies to HCV (either by EIA or RIBA) *or*
  - HCV RNA positive by nucleic acid testing *AND*
  - Exclusion of acute HAV or HBV – negative anti-HAV IgM and anti-HBV core IgM

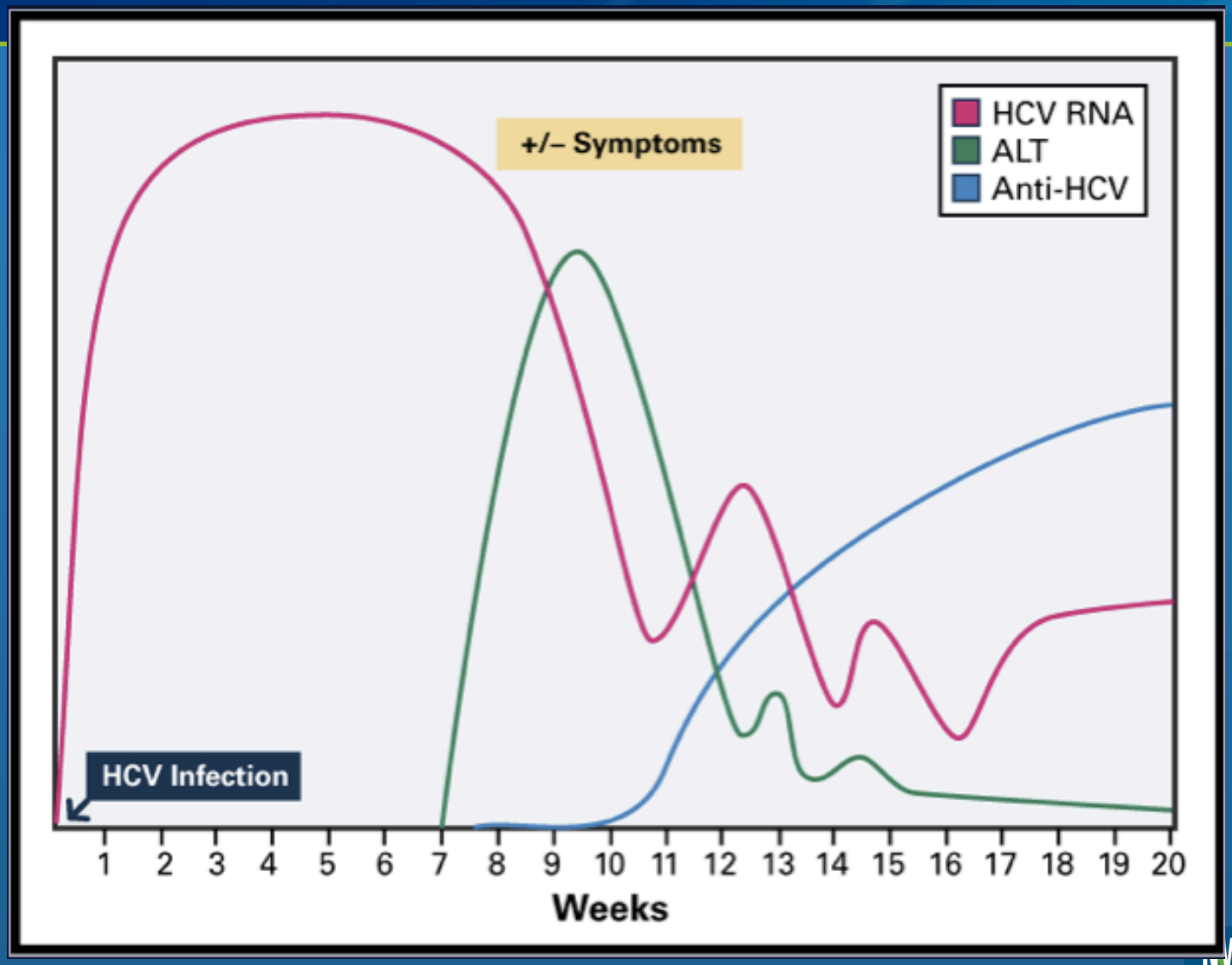
- HCV RNA levels can fluctuate widely in early infection.

- Seroconversion can be delayed
  - About 2/3 (+)Ab by 3 months
  - 5% can still be Ab negative by 12 months

Spontaneous Clearance after Acute Infection



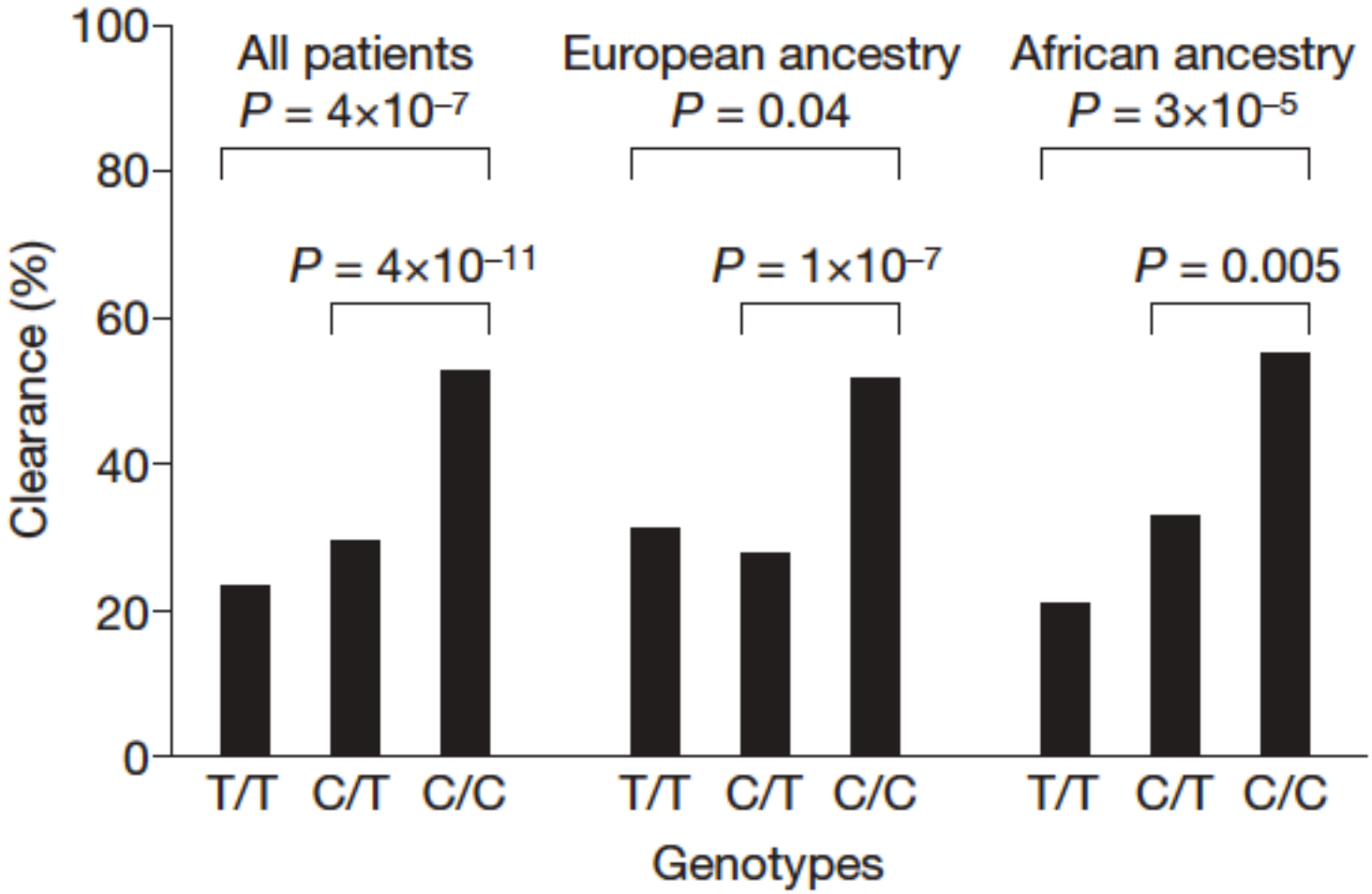
HCV Persistence after Acute Infection



To Treat or not to Treat
Predictors of Spontaneous HCV Clearance

- Higher CD4 cell counts
- Lower peak HCV RNA levels
- Rapid early decline in HCV viral level
- High ALT
- Presence of jaundice
- Female gender
- Younger age
- Non-black race
- Coinfection with chronic hep B (+HBsAg)
- *IL28B* CC homozygous genotype

HCV Clearance by *IL28B* Genotype



Thomas, et. al. *Nature* 2009; 461:798-802.

When to Treat?
Acute Hepatitis C

- Treatment of acute HCV shown to reduce risk of chronic persistent infection with improved rates of SVR compared with established infection:
  - SVR 30% for genotype 1 in chronic HCV with dual therapy vs
  - SVR 60-80% for genotype 1* with dual therapy in acute HCV
- Weigh the decision to treat carefully:
  - To avoid unnecessary therapy in those who will clear and
  - To achieve highest possible SVR for those who will not

(* SVR >90% for genotype 2 or 3)

AASLD Guidelines on HCV 2009.

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When to Treat?
Viral Monitoring & Timing

- Important to monitor HCV RNA q4 weeks in acute HCV
- Indications for treatment:
  - Absence of a 2 $\log_{10}$ drop in HCV RNA x 4 weeks
  - Persistent HCV viremia at 12 weeks
- Most experts agree best to wait at least 8-12 weeks before starting therapy for acute HCV
- A short delay of 12 weeks is unlikely to compromise SVR rates but a delay of >12 months halves the likelihood of SVR

NEAT Acute Hep C Consensus Panel. AIDS 2011; 25:399-409.

How to Treat?
Acute Hepatitis C

- Optimal regimen remains unclear
- Most studies of acute HCV are case series, small cohorts and use both peg-interferon & ribavirin (wt-based or fixed)
- Duration also unclear
  - Studies heterogeneous with duration ranging from 12 to 48 wks (most of them 24 wks)
  - Our clinic opts for peginterferon + ribavirin of 24 weeks duration esp. for patients who achieve a rapid virologic response
  - Consider 48 weeks in patients with suboptimal early viral response

Acute Hepatitis C
Role of Direct-acting Antivirals (DAAs)

- Remains to be seen…
- Current DAAs (telaprevir, boceprevir): no data in acute HCV
- DAAs to revolutionize HCV management for both acute & chronic infection
- Real potential for
  - All oral (IFN-free) regimens
  - Short duration courses (<12 weeks?)*
  - Enhanced tolerability
  - High efficacy (>90% SVR)

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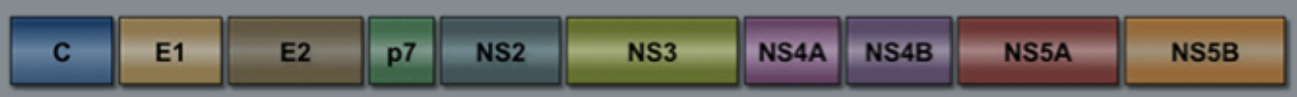

Thanks!