

# Hepatitis C In The Native Community

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## Chronic Liver Disease in Aboriginal North Americans

- **Aboriginal North Americans**
  - American Indians/Alaska Natives(AI/AN)
  - Canadian First Nations
  - Native Greenlanders
- **Disproportionately affected by chronic liver disease (CLD)**
- **USA mortality chronic liver disease**
  - Twelfth leading cause of death in general population
  - Fifth leading cause of death in AI/AN
- **USA mortality rate(1990-1998)**
  - 4.5% decrease in general population
  - 11% increase in AI/AN
  - Second leading cause of death AI/AN 25-44

## Epidemiology of Chronic Liver Disease

- Alcohol
- Viral Hepatitis
  - Hepatitis B
  - Hepatitis C
- Non Alcoholic Fatty Liver Disease (NAFLD)
- Autoimmune Liver Disease
- Primary Biliary Cirrhosis (PBC)

## HCV Infection: Magnitude of the Problem

- Approximately 3.9 million persons in United States infected
  - Approximately 35,000 new cases yearly
  - 85% of new cases become chronic
- 10,000-20,000 HCV-related deaths per year
  - Number expected to triple in next 10-20 years
- Leading cause of
  - Chronic liver disease
  - Cirrhosis
  - Liver cancer
  - Liver transplantation

CDC. MMWR Morb Mortal Wkly Rep. 1998;47;1-39.  
NIH Consensus Conference Statement. Available at: <http://consensus.nih.gov/2002/2002HepatitisC2002116html.htm>. Accessed August 19, 2008.  
Rustgi VK. J Gastroenterol. 2007;42:513-521.

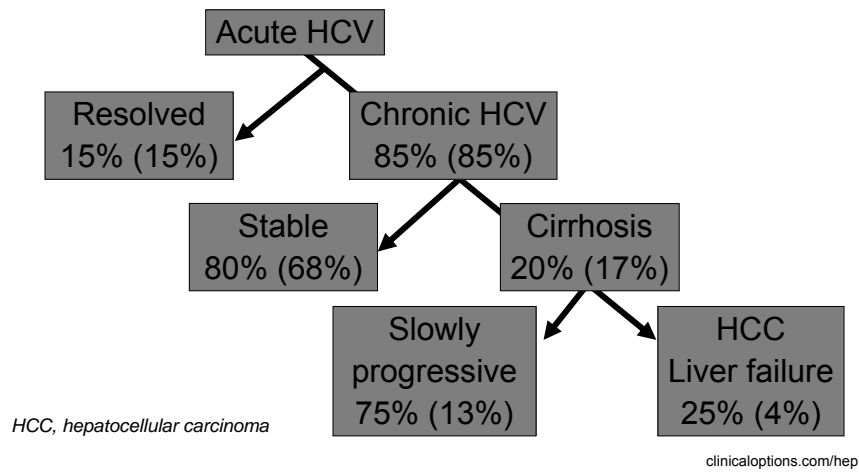
## Hepatitis C in AI/AN

- Common cause of CLD
- Incidence varies with population studied
  - .8%-32%
- Route of transmission similar to general population
- Genotype distribution
  - Type 1 60%(72% in general pop.)
  - Type 2 23%(15% in general pop.)
  - Type 3 14%(6% in general pop.)
- Treatment response data is limited due to small numbers of AI/AN in studies

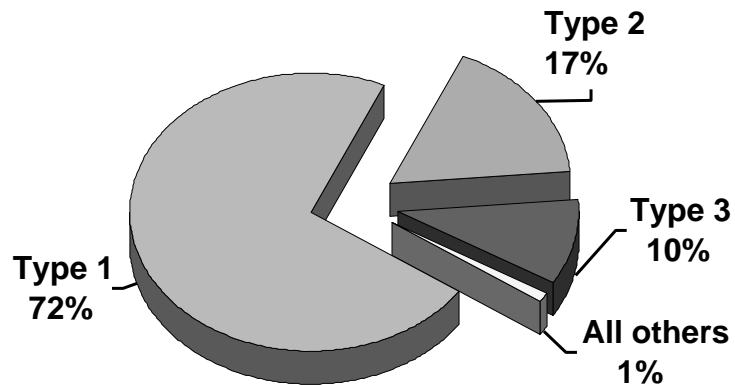
### **Hepatitis C Virus Infection** ***Population at Risk***

- Transfusion of blood products before 1992
- Intravenous drug use
- Nasal inhalation of cocaine
- Chronic renal failure on dialysis
- Incarceration
- Occupational exposure to blood products
- Transplantation of an organ/tissue graft from an HCV-positive donor
- **Body piercing and potentially tattoo**

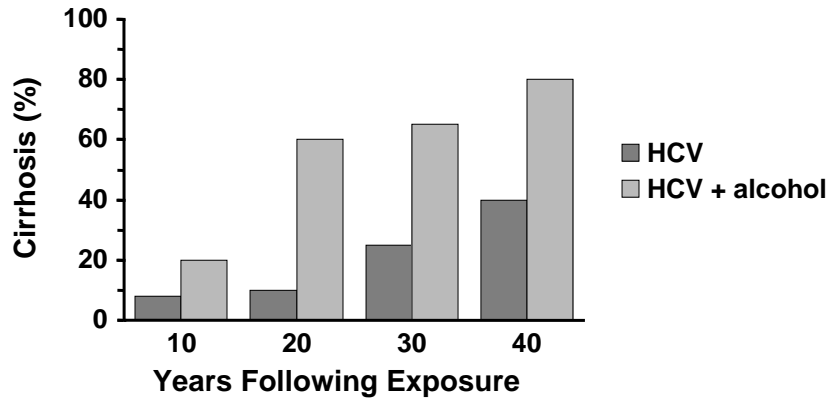
## Hepatitis C Virus Infection *Natural History*



## Hepatitis C Virus *Genotypes in the USA*



## HCV and Alcohol Risk of Cirrhosis



Excessive alcohol intake characterized as > 40 g/day for women and > 60 g/day for men.

Wiley TE, et al. Hepatology. 1998;28:805-809.

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## Goals of HCV Therapy

- Primary goal of treatment is to eradicate the virus
- Additional goals
  - Slow disease progression
  - Minimize risk of HCC
  - Improve liver histology
  - Enhance quality of life
  - Prevent transmission of virus
  - Reduce extrahepatic manifestations

Lindsay KL. Hepatology. 2002;36(suppl 1):S114-S120.

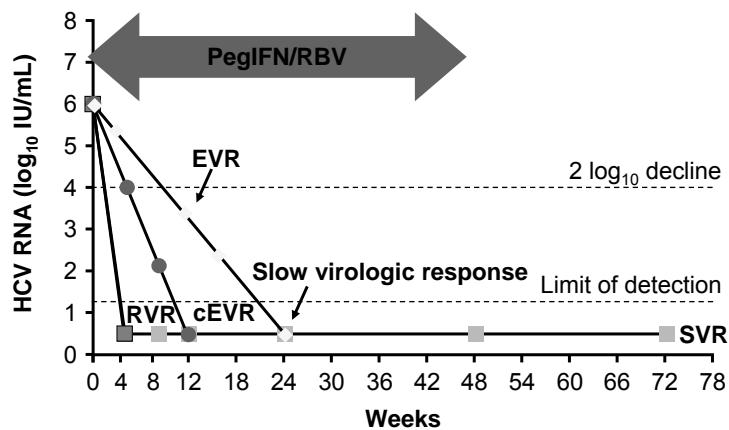
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## Important Definitions Used in Treatment of Hepatitis C

- RVR (rapid virologic response)
  - Absence of virus by PCR 4 weeks after starting therapy
  - Indicates better prognosis for SVR (cure) and perhaps shorter course of therapy (genotype 1)
- EVR (early virologic response)
  - Absence of virus by PCR 12 weeks after starting therapy
  - IF no EVR chance for SVR less than 5% and therapy is stopped
  - If partial response ie. At least a 2 log drop can continue for 24 weeks if virus is then absent can continue for 48 weeks? 72 weeks
- ETR (end of treatment response)
  - Absence of virus at end of treatment
  - Associated with high SVR
- SVR (sustained virologic response)
  - Cure !!

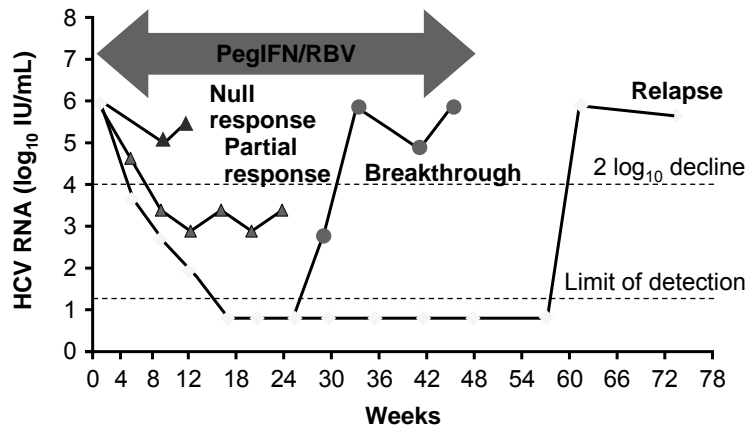
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## Virologic Responses



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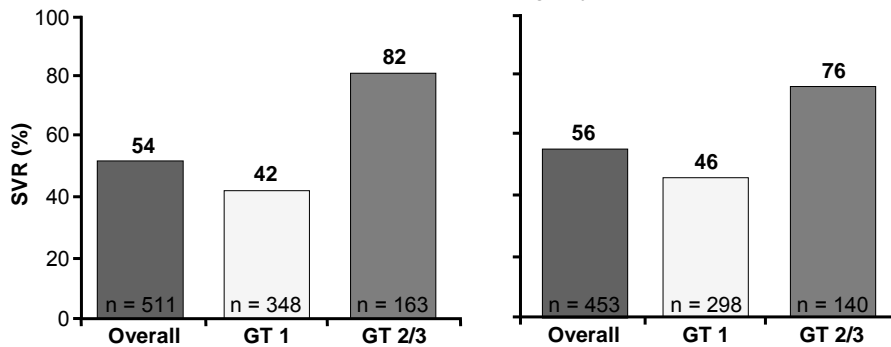
## Suboptimal Virologic Responses



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## SVR With PegIFN: > 50% of GT 1 Patients Do Not Respond

- PegIFN alfa-2b 1.5 µg/kg/week + RBV 800 mg/day for 48 weeks<sup>[1]</sup>
- PegIFN alfa-2a 180 µg/week + weight-based RBV (1000 or 1200 mg/day) for 48 weeks<sup>[2]</sup>



1. Manns M, et al. Lancet. 2001;358:958-965.  
2. Fried MW, et al. N Engl J Med. 2002;347:975-982.

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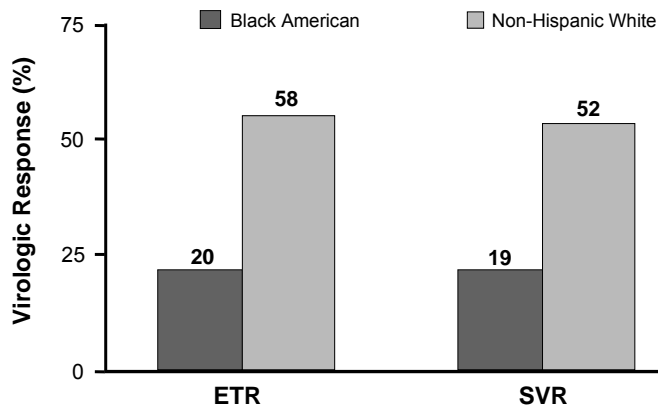
## Black Americans and HCV Infection

- HCV infection more common in black Americans than in whites
  - Risk factors the same
- Predominantly genotype 1
- Disease severity or progression may be different
- Rate of HCC increased
- Lower response rate
- Mechanism unknown

## HCV Treatment Considerations in Black Americans

- Two prospective, clinical trials of peginterferon and ribavirin were undertaken to better determine actual response rates in African Americans.
- Patient groups were balanced for genotype and histologic severity

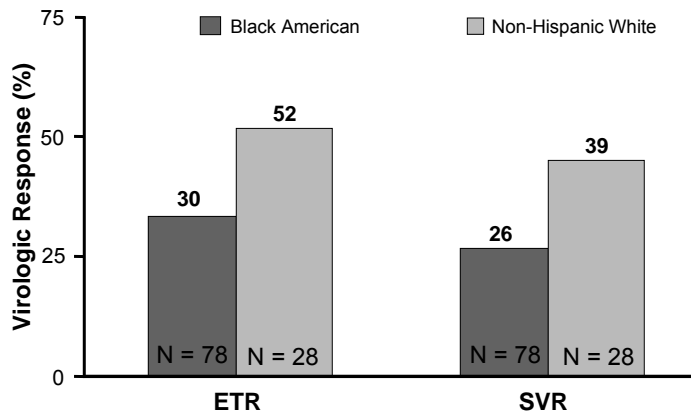
## Virologic Response: PegIFN Alfa-2b + RBV



Muir AJ, et al. N Engl J Med. 2004;350:2265-2271.

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## Virologic Response: PegIFN Alfa-2a + RBV



Jeffers L, et al. Hepatology. 2004;39:1702-1708.

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## Obesity, Metabolic Syndrome, and HCV

- Patients with BMI > 30 more likely to have steatosis and fibrosis
- Steatosis is common in HCV (20% to 60%)
  - Related to insulin resistance in genotype 1
  - Related to HCV replication in genotype 3
- Steatosis may lead to progressive fibrosis
- Obesity and steatosis decrease response to HCV treatment
- Weight loss may improve insulin resistance and steatosis
- *Few data on weight loss before treatment to improve results but patients may benefit*

Swain M, et al. AASLD 2005. Abstract 1244. Cesario K, et al. DDW 2005. Abstract M953. Poynard T, et al. Hepatology. 2003;38:75-85. Fartoux L, et al. Gut. 2005;54:1003-1008. Matos C, et al. J Gastro Hepatology. 2006;21:1236-1239. Hourieux C, et al. Gut. 2007;56:1302-1308. Romero-Gomez M, et al. Gastroenterology. 2005;128:636-641. Sanyal AJ, et al. AASLD 2004. Abstract 179A. Younossi ZM, et al. J Clin Gastroenterol. 2004;38:705-709. Hui JM, et al. Gastroenterology. 2003;125:1695-1704. Conjeevaram H, et al. Hepatology. 2007;45:80-87. Tarantino G, et al. Gut. 2006;55:585. [clinicaloptions.com/hep](http://clinicaloptions.com/hep)

## HIV/HCV Coinfection

### HIV-infected

- 1 million people have HIV
- Incidence: 40,000/yr
- 15,000 deaths/year
- ~45% are HCV-infected

### HCV-infected

- 4 million people have HCV
- Incidence: 40,000/yr
- 8000-10,000 deaths/year
- ~10% are HIV-infected

Verucchi G, et al. Infection. 2004;32:33-46.

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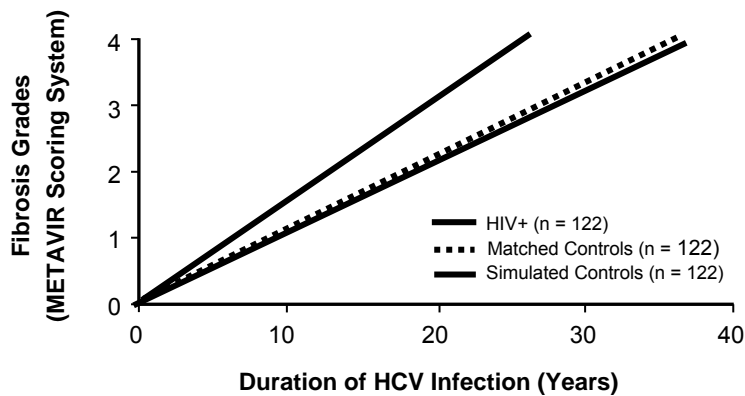
## Impact of HCV on HIV Disease Progression

- Prospective cohort study of 3111 patients on HAART between 6/96 to 5/99
- 37% were HCV+
- HIV-related progression and death higher in active IVDU with HCV infection
- HCV associated with blunted CD4 recovery
- Deaths from liver disease 3-fold higher

Greub G, et al. Lancet. 2000; 356:1800-1805.

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## Effect of HIV/HCV Coinfection on Fibrosis Progression Rates



Benhamou Y, et al. Hepatology. 1999;30:1054-1058.

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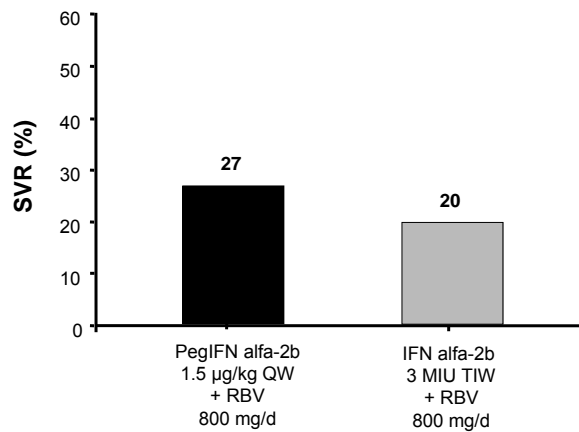
## HIV/HCV Coinfection Trials: PegIFN/RBV

Study	Treatment Regimen
<b>RIBAVIC</b> France (N = 412)	PegIFN alfa-2b 1.5 µg/kg QW + RBV 800 mg/d IFN alfa-2b 3 MIU TIW + RBV 800 mg/d
<b>ACTG 5071</b> USA (N = 133)	PegIFN alfa-2a 180 µg QW + RBV 600 mg → 1 g/d IFN alfa-2a 6 MIU TIW → 3 MIU + RBV 600 mg → 1 g/d
<b>APRICOT</b> International (N = 868)	PegIFN alfa-2a 180 µg QW + RBV 800 mg/d IFN alfa-2a 3 MIU TIW + RBV 800 mg/d PegIFN alfa-2a 180 µg QW + placebo QD

Carrat F, et al. JAMA 2004;292:2839-2848. Chung RT, et al. N Engl J Med. 2004;351:451-459. Torriani FJ, et al. N Engl J Med. 2004;351:438-450.

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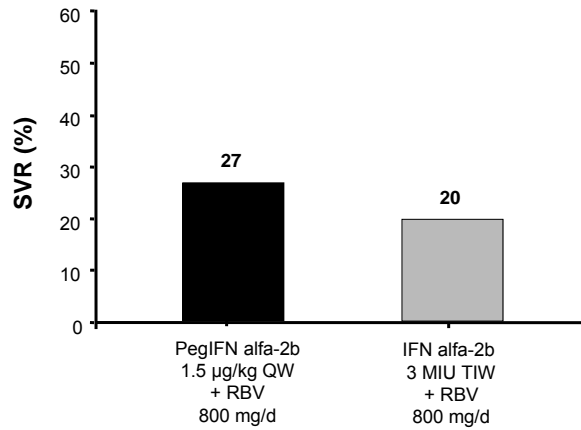
## RIBAVIC Study: SVR



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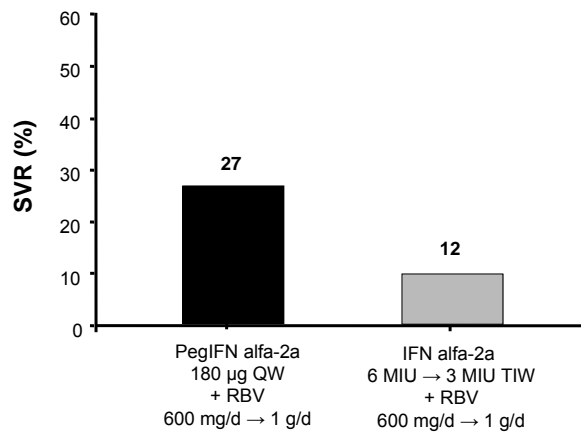
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Carrat F, et al. JAMA 2004;292:2839-2848.

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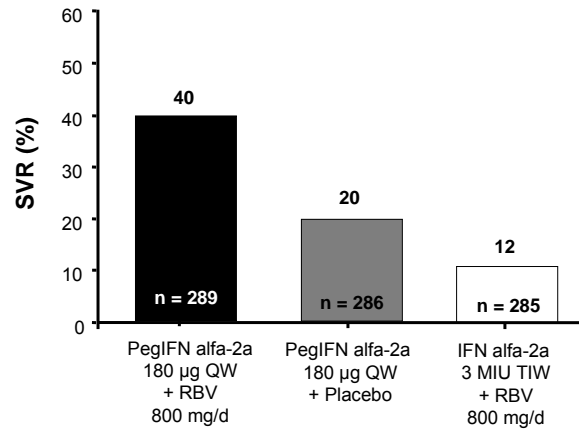
## ACTG 5071 Study: SVR



Chung RT, et al. N Engl J Med. 2004;351:451-459.

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## APRICOT Study: SVR



Torriani FJ, et al. N Engl J Med. 2004;351:438-450.

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## HIV/HCV Co-infection

- In 2005, the FDA approved peginterferon alfa-2a and ribavirin as treatment for HCV disease in HCV/HIV coinfection

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## Potential New Treatments For Hepatitis C

- Not all patients have an SVR (19%-70%)
  - Multiple variables
    - Race
    - Genotype
    - Viral load
    - Liver histology
    - BMI
    - Compliance
- We need better treatment options

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## Telaprevir Treatment For HCV

- Complicated regimen
  - 12 week lead in with 3 medications
  - High dropout rate due to side effects
    - Severe dermatitis
    - GI intolerance
- SVR only 60-70% (Genotype 1)

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## Potential New treatments For Hepatitis C

- Protease Inhibitors
  - Telaprevir
    - Complicated regimen
    - Severe side effects
- Helicase inhibitors
- Polymerase inhibitors
- Other agents that interfere with viral replication
- Vaccine against Hepatitis C

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## Hepatitis C Infection In AI/AN

- Major cause for Morbidity and Mortality
- Treatment is available
  - Preliminary data suggests response rates comparable to non Hispanic Caucasians
  - We need more data to confirm this
  - Comorbidities need to be addressed
    - Coinfection with HIV
    - Alcoholism
    - Obesity
- Prevention
  - Education
  - Addiction services
- Increase availability of treatment(ECHO)

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