Natural History of Hepatitis C Infection

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Outline

- Spontaneous clearance versus chronic infection
- Variable outcomes of chronic infection
- Predictors related to rate of progression of fibrosis
Spontaneous Clearance Versus Chronic Infection
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- Outcome of acute infection
  - Clearance of hepatitis C virus (HCV): 10%-35%
  - Development of chronic HCV infection: 65%-90%

- Predictors affecting outcome of acute infection
  - IL28B genotype
  - Quasispecies diversification
  - Size and source of inoculum
  - Immune status
  - Clinical features
    - Development of jaundice
IL28B

IL28B: Percentage of HCV Clearance by rs12979860 Genotype

All patients: $P = 4 \times 10^{-7}$
European ancestry: $P = 0.04$
African ancestry: $P = 3 \times 10^{-5}$

Clearance (%)

- OR 3.0
- OR 2.6
- OR 3.1
Genetic Variation in IL28B Explains Differences in HCV Recovery Rates in Diverse Ethnicities

Different frequencies in IL28B variants explain ethnic differences in HCV recovery rates

Acute Hepatitis C

Chronic Hepatitis
75%-85%

Cirrhosis 20%

Decompensated 20%

HCC 1%-4% per year

20 years

Variable Outcomes of Chronic Infection
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- Mild
- Moderate
- Severe fibrosis
- Cirrhosis: mild
- Cirrhosis: severe
- HCC

20%-33%
15%-33%

Years
20 30 40

Factors Impacting Rate of Progression of Fibrosis
Predictors Related to Rate of Progression of Fibrosis

- Older age at infection
- Male sex
- Alcohol
- HIV infection
- Post-transplant
- Quasispecies complexity
- Presence of comorbid liver diseases
Clinical Outcomes of Cirrhosis

- Portal hypertension
  - Varices
  - Ascites
  - Hepatic encephalopathy
  - Splenomegaly
  - Thrombocytopenia
- HCC
HCV in Patients With Cirrhosis, Risk of Decompensation and HCC

Summary

- Most people who are infected with HCV progress to a chronic disease state.
- A variety of factors determines individual risk of clearance vs chronicity.
- Chronicity leads to variable rates of fibrotic progression.
- Cirrhosis leads to
  - End-Stage Liver Disease
  - HCC
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