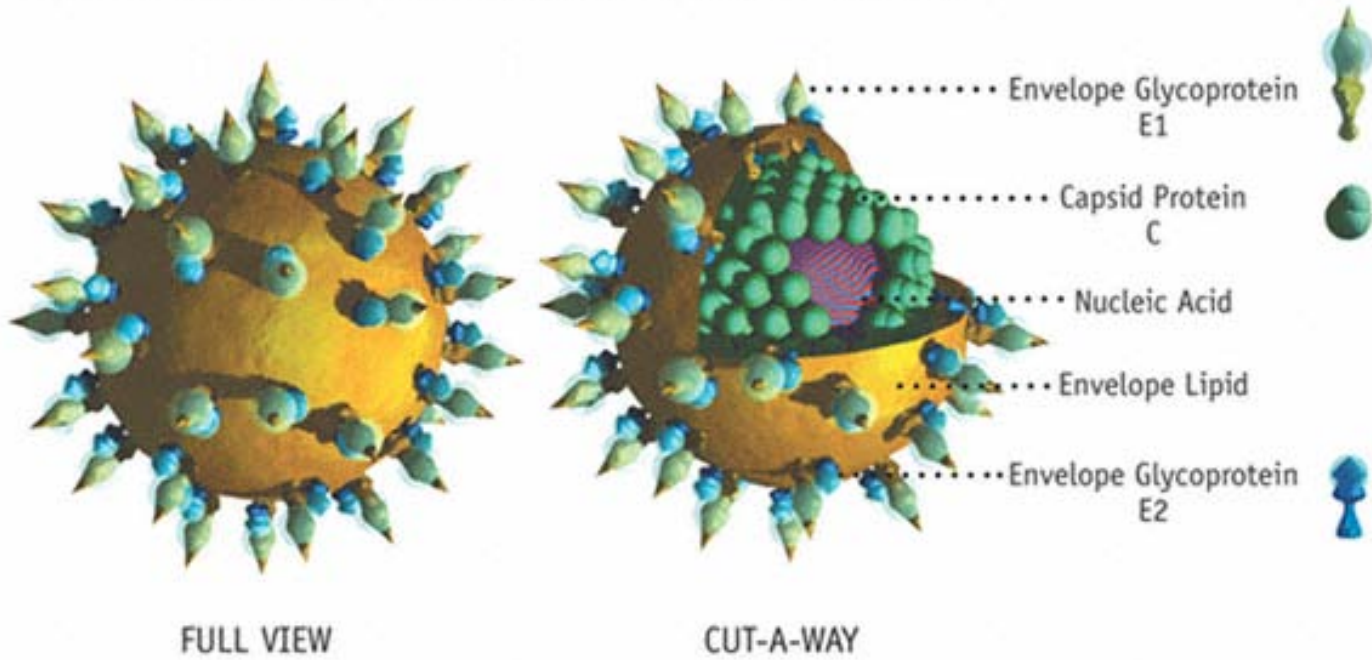




Choices, health and wellness
for people with long-term
disease.

Natural History of HCV Infection

MODEL OF THE HUMAN HEPATITIS C VIRUS



Hepatitis C Virus Facts

- *Flaviviridae* family; the prototype Hepacivirus
- Rapid replication rate
 - $>10^{12}$ virions/day
 - $T_{1/2} = 2.7$ hours
- High mutation rate
 - RNA-dependent RNA polymerase lacks proofreading mechanisms; predisposes to mutation

Features of Hepatitis C Virus Infection

Incubation period	ave. 6-7 weeks (range 2-26)
Acute HCV	60-70% asymptomatic 20-30% mild jaundice 10-20% nonspecific symptoms, e.g., malaise, abdominal pain, anorexia
Fulminant acute hepatitis	rare; reported only among those with pre- existing liver disease
Ave. time to seroconversion	8-9 weeks
Chronic infection	~55%-85%
Chronic active liver disease	60-70% (chronic or intermittent elevations in ALT and AST)

Adapted from Centers for Disease Control & Prevention Hepatitis C slide kit.



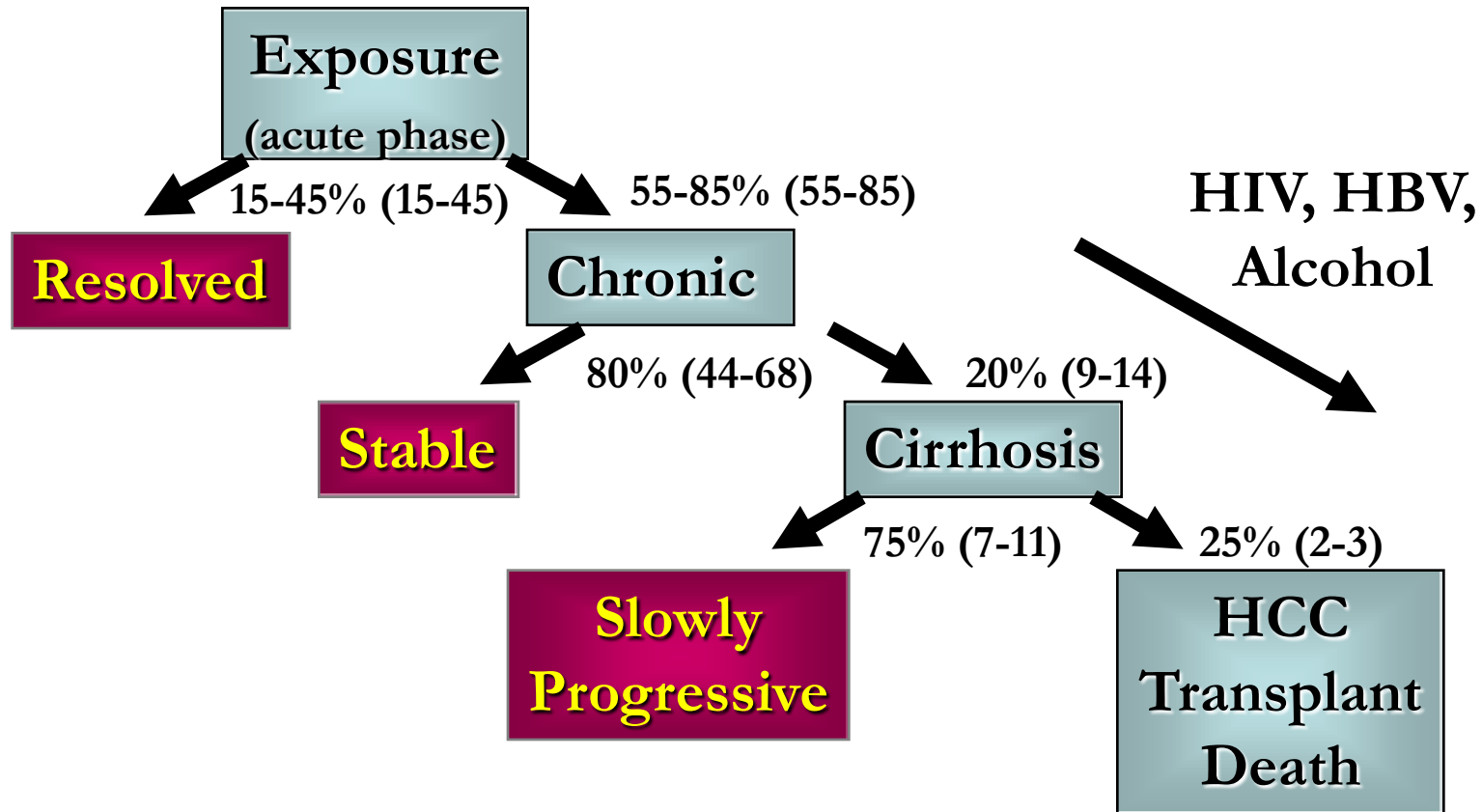
Features of Hepatitis C Virus Infection, cont.

Clinical course	insidious; asymptomatic or with non-specific symptomatology
Case finding	often incidental until cirrhotic signs and symptoms develop
Cirrhosis	10%-20% over a 20-30 year period
Hepatocellular carcinoma	1-4%
Mortality from chronic liver disease	1%-5%

Adapted from Centers for Disease Control & Prevention Hepatitis C slide kit.



Features of Hepatitis C Virus Infection, cont.



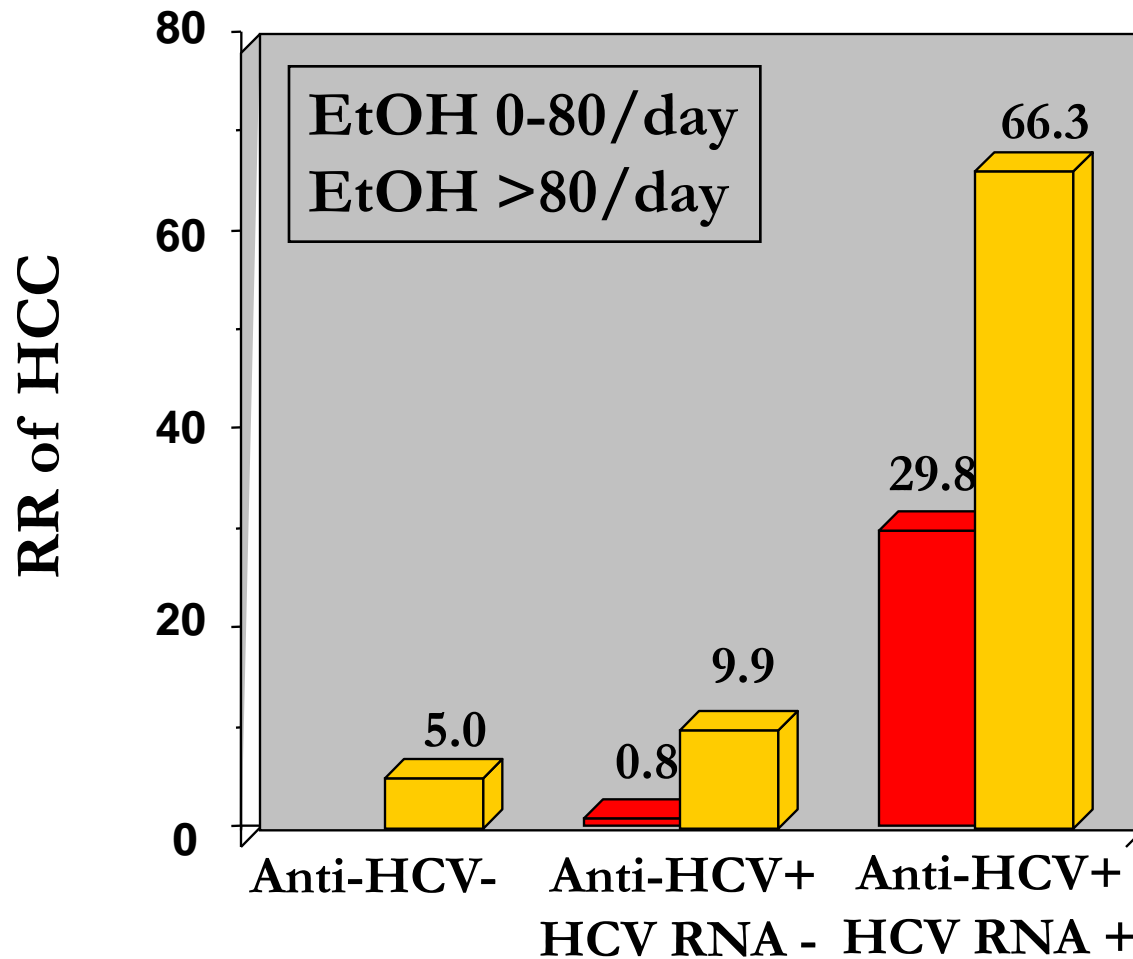
Factors Influencing HCV Disease Progression

- **Age** - People infected after age 35 appear to have more rapid disease progression compared to those infected at younger ages.
- **Sex** - Overall, women (especially those <50 years) fare significantly better than men with less severity of infection.
 - **Women may spontaneously clear the virus more frequently than men do.**
- **Alcohol consumption** exacerbates the damage caused by HCV and accelerates disease progression.
- The presence of **fat and/or excess iron in the liver** are associated with higher degrees of fibrosis.
- **Coinfection** with HIV and/or HBV may accelerate disease progression.

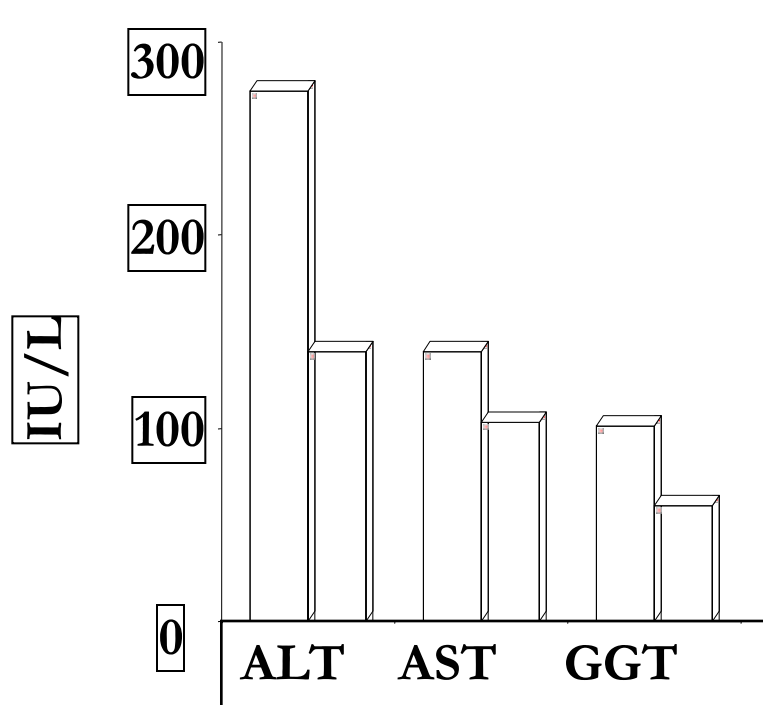
Impact of Alcohol on HCV Disease

- Persons consuming ≥ 30 -50g/day have increased rates of fibrosis.
 - women higher risk than men for alcohol-associated liver injury
 - there is no known “safe” level of alcohol consumption
- Risk of cirrhosis is increased in patients using alcohol (studies focused on >50 -80 g/day).
- Risk of HCC is increased in those using alcohol.
 - effects may be more than additive at 80 g/day or higher
- Alcohol consumption lowers the likelihood of response to IFN therapy.
 - mechanism unknown - effect on viral load? quasispecies?

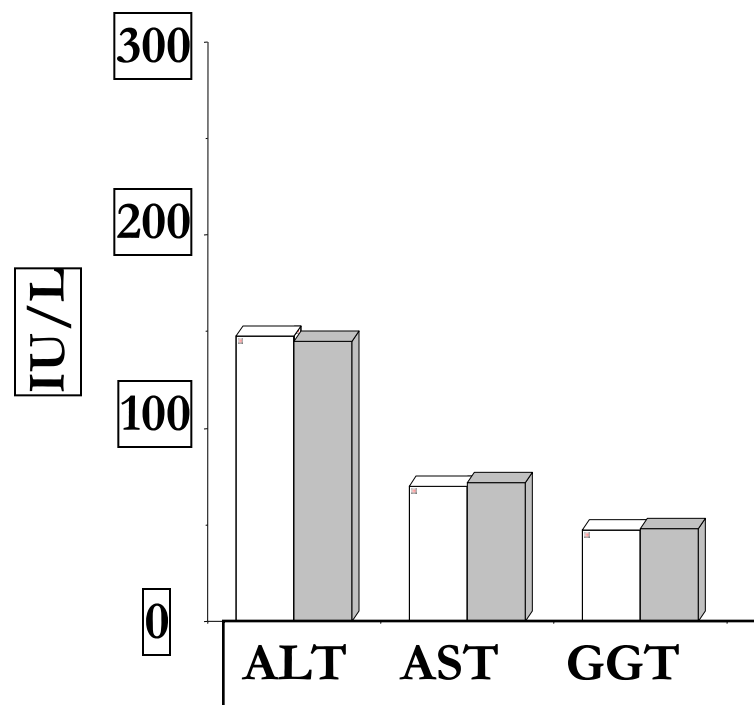
Are HCV & Alcohol Effects Synergistic?



Reduced Alcohol Intake Associated with Improved Liver Enzymes



Alcohol intake decreased mean 13 ± 2 g/d (range 0-50) in mean follow-up 4.4 months



Alcohol intake ≤ 10 /g before and after

Common Symptoms of Hepatitis C in the Absence of Cirrhosis

- fatigue
- impaired cognitive functions
- low grade fevers
- abdominal discomfort
- appetite disturbances
- abdominal pain
- digestive disturbances
- migratory arthralgia or myalgia
- depression
- anxiety
- many others

Signs of HCV-Related Advanced Liver Disease with Cirrhosis

vascular spiders

jaundice

caput medusae (abdominal venous engorgement)

hepatomegaly

splenomegaly

ascites

parotid enlargement

encephalopathy

muscle loss

sexual dysfunction



Compensated Cirrhosis

Due to Chronic HCV Infection

- 5-year probability for development of hepatocellular carcinoma (HCC) $\sim 10\%$ ¹
 - other studies suggest $\sim 1-5\%$ incidence HCC per year in the context of cirrhosis
- a long-term (median 7.8 yrs) follow-up study (n=254):²
 - 21% developed HCC
 - 18% developed ascites
 - 5% developed bleeding
 - 16% died of liver-related causes

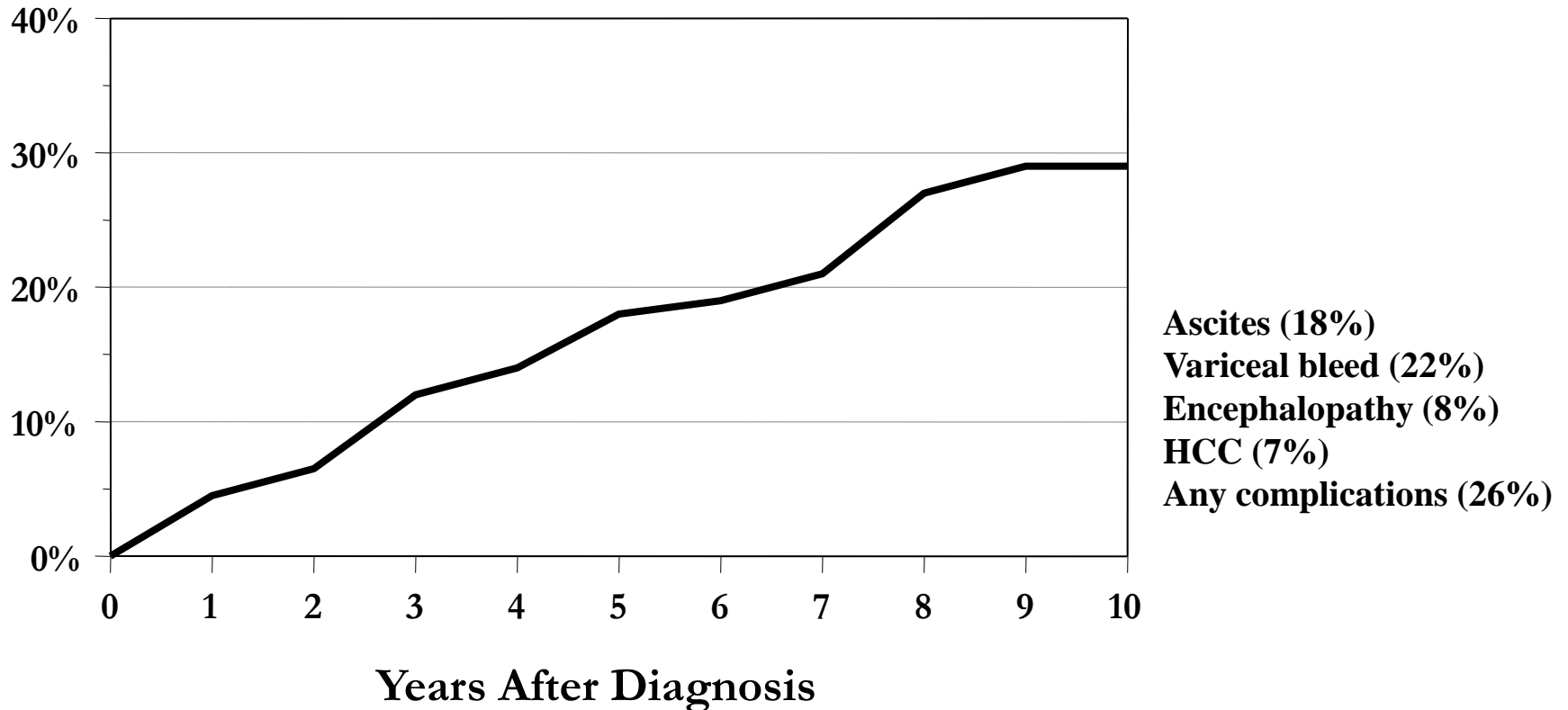
¹ Fattovich, et al. Am J Gastroenterol. 2002;97

² Benvegnù et al. Gut. 2004;53



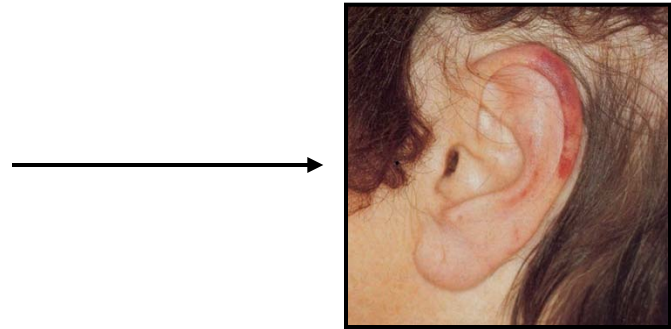
Natural History of HCV Cirrhosis

Risk of Decompensation



Extrahepatic Manifestations of Hepatitis C

- hematologic
 - mixed cryoglobulinemia (10-25% of HCV patients)
- renal
 - glomerulonephritis
- dermatologic
 - porphyria cutanea tarda
 - lichen planus
 - cutaneous necrotizing vasculitis
- metabolic
 - insulin resistance
 - lipid abnormalities
- mood and sleep disorders
- others



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