Aspects of chronic viral infections and their interactions

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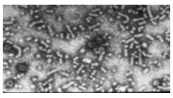
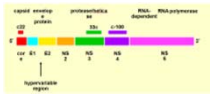
The viruses are quite different

- HIV
- Hepatitis B
- Hepatitis C



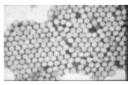


ALL are able to be measured accurately

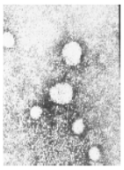
Treated quite differently

Other hepatitis viruses

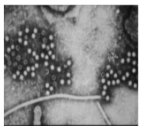
- Hepatitis A
  - Vaccine exists ; acute infection but potentially serious in HIV infected



- Hepatitis D
  - Co-virus with hepatitis B

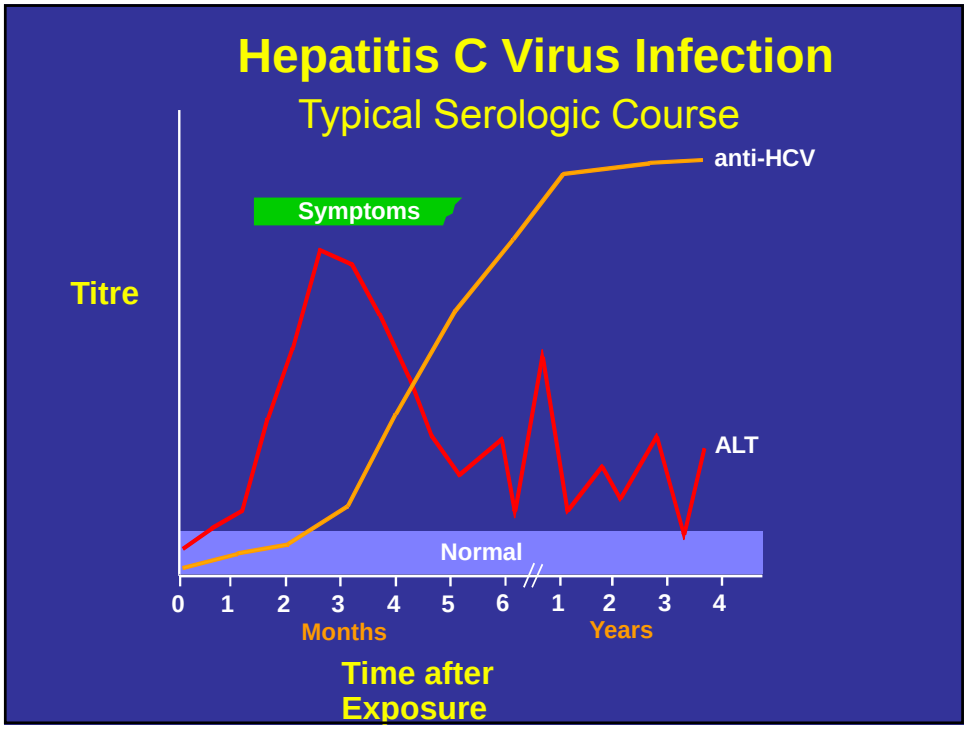


- Hepatitis E



Virus response to treatment

	Treatment (Rx)	Effect of Rx	Outcome without Rx
HIV	Lifelong	suppression	Usually AIDS
Hep B	Variable	Suppression or cure	Chronic hepatitis/ (Cirrhosis)
Hep C	24 – 72 weeks	cure	Chronic hepatitis/ (Cirrhosis)



Timing treatment

- Best time to start Rx is an individualised complex parameter
- Factors considered are many and include
  - Viral activity / speed of damage occurring
  - Target organ effects (liver for hep viruses) – whether fibrosis of liver
  - Likelihood of success of Rx
  - Sensitivity of virus / new drug availability

Interactions of viruses

- HIV
  - Allows Hep B and Hep C to progress more rapidly
  - Treatment responses of Hep B and Hep C are moderately inferior if HIV present
- Treating HIV
  - Improves long term outcome of Hep B/ Hep C
  - May lead to a temporary flare in Hepatitis

Implications of effects of hepatitis Rx with interferon / ribavirin

- Rx for Hep C usually temporarily depresses CD4 T-cell level , a marker of immune competence
- Best to either treat hepatitis virus prior to decline in CD4 T-cells OR after immune reconstitution
- During hepatitis Rx need to enhance monitoring of HIV and CD4 T-cell level
- Interferon injections can affect mood/ thinking / adaptability

Natural history of hepatitis C

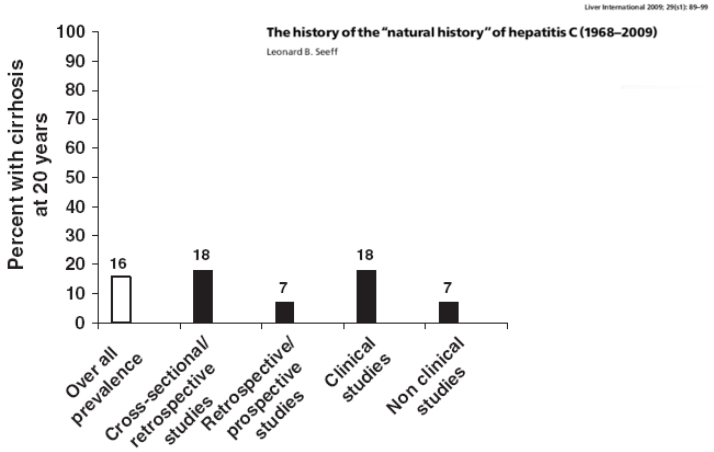
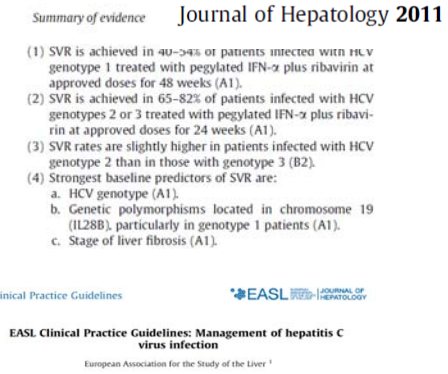


Fig. 2. Estimated prevalence of cirrhosis at 20 years after infection according to strategy of case identification. Meta-analysis and metaregression based on 111 reported natural history studies (105).

Response rates for hepatitis C in HIV co-infections

Without HIV


Summary of evidence Journal of Hepatology **2011**

(1) SVR is achieved in 40–54% of patients infected with HCV genotype 1 treated with pegylated IFN-α plus ribavirin at approved doses for 48 weeks (A1).
(2) SVR is achieved in 65–82% of patients infected with HCV genotypes 2 or 3 treated with pegylated IFN-α plus ribavirin at approved doses for 24 weeks (A1).
(3) SVR rates are slightly higher in patients infected with HCV genotype 2 than in those with genotype 3 (B2).
(4) Strongest baseline predictors of SVR are:
a. HCV genotype (A1).
b. Genetic polymorphisms located in chromosome 19 (IL28B), particularly in genotype 1 patients (A1).
c. Stage of liver fibrosis (A1).

Clinical Practice Guidelines EASL JOURNAL OF HEPATOLOGY

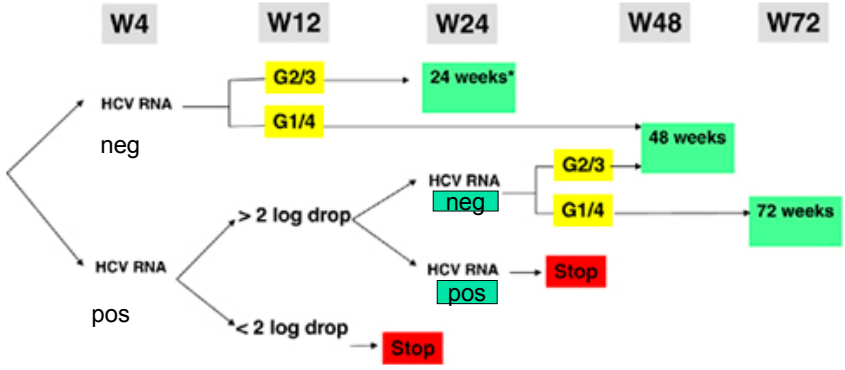
EASL Clinical Practice Guidelines: Management of hepatitis C virus infection

European Association for the Study of the Liver [1]

With HIV

- Lower success rates
- Longer Rx needed
- More drug interactions to consider
- Even more important to intervene as outcome more threatening

Therapy for HCV / HIV co-infected patients: IFN-α and ribavirin (RBV)



Adapted from Rockstroh JK et al. *HIV Med* 2008;9:82–88.

Other considerations

- Parenthood aspirations
  - Fertility impact of viruses
  - Fertility issues with treatments
  - Side effects of Rx
- Other haemophilia related issues
  - Joints / surgery needs / analgaesia
  - Opiates for bad chronic pain

Fertility and HIV

- Untreated HIV may reduce fertility by reducing sperm numbers and fitness
- Treating HIV does NOT adversely affect the sperm quality
- During 1990s and 2000s in vitro fertilization (ICSI) was widely used to commence pregnancy using HIV seropos male sperm
- Treated male with very low (i.e. undetectable) viral load in blood is very unlikely to transmit to female during vaginal sex (African data) / Swiss statement of risk
- Practitioners differ in recommendations with many units now recommending post-ovulation timed intercourse from HIV treated partner as “safe enough”
- It is likely but not proven that IVF from treated male is safer than natural intercourse mediated fertilisation
- IVF allows pre-implantation genetic screening and selection of healthiest embryo

Fertility and Hepatitis virus

- Sexual transmission much more likely for Hep B than Hep C
- Hep B can be prevented by vaccination
- Hep C risk to female is low from pos male
- Liver disease may affect fertility via effects on – libido, androgen/ oestrogen metabolism, testicular function

Co-infected Haemophilia patients in Australia

- Almost all are now aged > 25 years with most in the 30- 60 age group
- Many with co-infection have controlled HIV and have already failed to clear Hep B or Hep C with current Rx
- Great interest in prospects of response to new Hep C protease inhibitors with retreatment
- Hep C / Hep B are now looking to be the dominant cause of premature death in adult haemophilia patients in Australia
- Liver transplant may potentially salvage late stage heptatis B or hepatitis C and cure haemophilia
- No cases of OLTx in Australia for haemophilia but success reported from overseas

The future

- Better agents for HIV (less adverse effects)
- Early availability of new classes of Rx for hepatitis virus
- Hopefully an effective hepatitis C and HIV vaccine ….will protect partners and generations of HIV/ Hep C/ B uninfected haemophilia patients