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An Update on Hepatitis D

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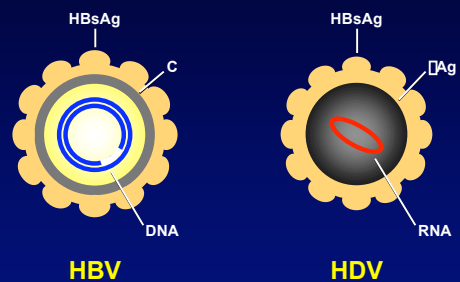
Outline

- Virology
- Epidemiology
- Natural course
- Diagnosis
- Therapy and Prevention
- Conclusions

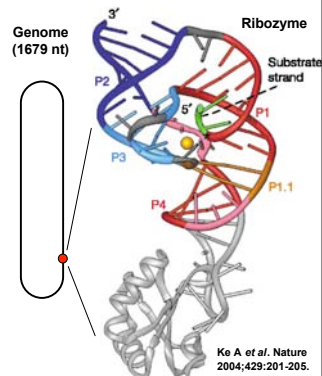
Hepatitis D Virology

- Discovered in 1977 and cloned in 1986
- Subviral agent
- HBV envelope proteins required for particle assembly
- Single-stranded circular RNA genome
- Genetic variability → 7 genotypes

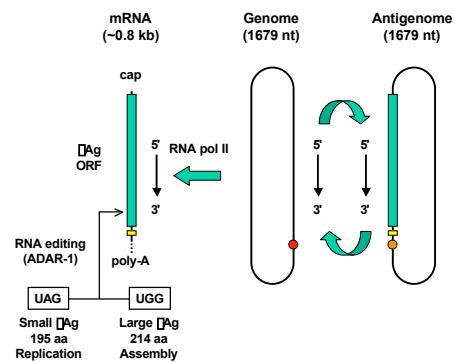
Taylor JM. *Virology* 2006;344:71-76.

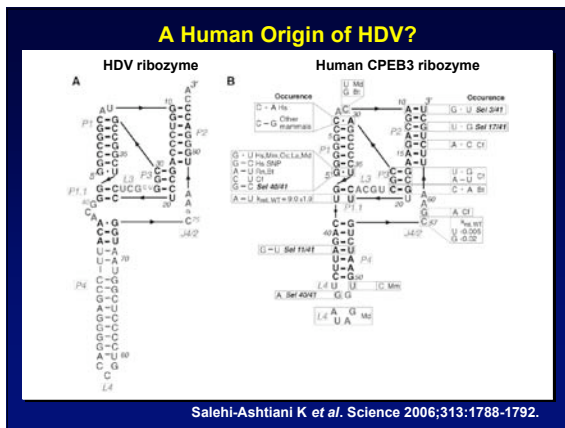


Genetic Organization of Hepatitis D Virus



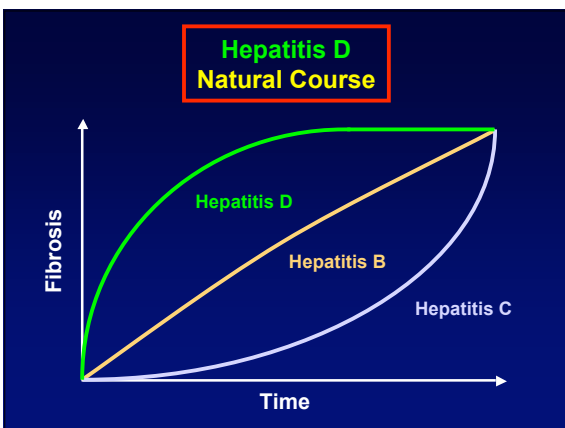
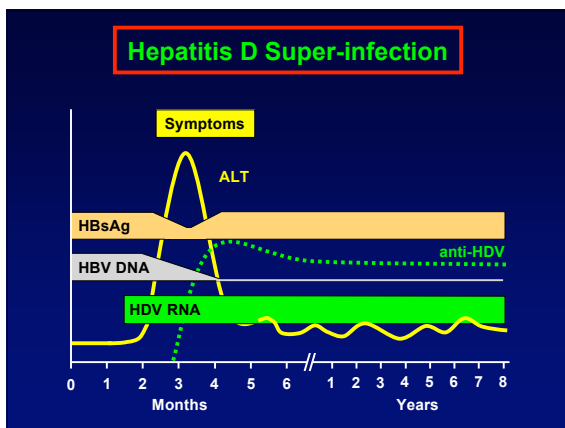
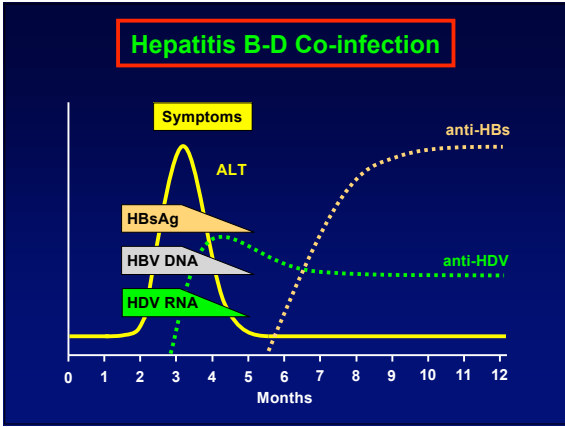
Genetic Organization of Hepatitis D Virus





- ### Hepatitis D Epidemiology
- 5% of HBsAg carriers worldwide → 20 mio chronically infected
 - Endemic in the Mediterranean basin, the Amazon basin and central Africa
 - Eastern Europe (Romania), former Soviet Union, Japan, India
 - Resurgence in northern Europe: IVDA → immigration

- ### Hepatitis D Natural Course
- Co-infection vs. super-infection
Fulminant course in 5%
Chronicity in 2% vs. 90%
 - Frequent and rapid progression to cirrhosis (up to 80%)
 - High risk of HCC development
 - OLT → latent infection

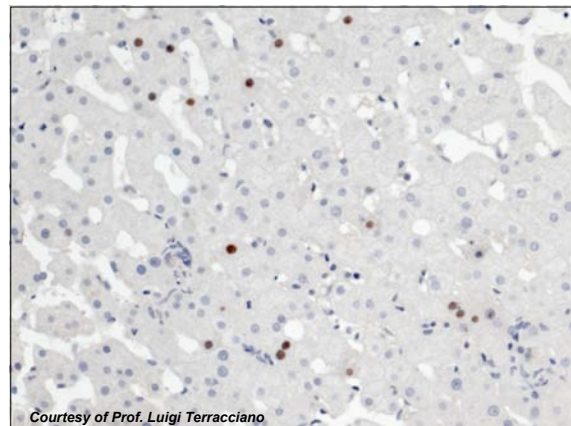
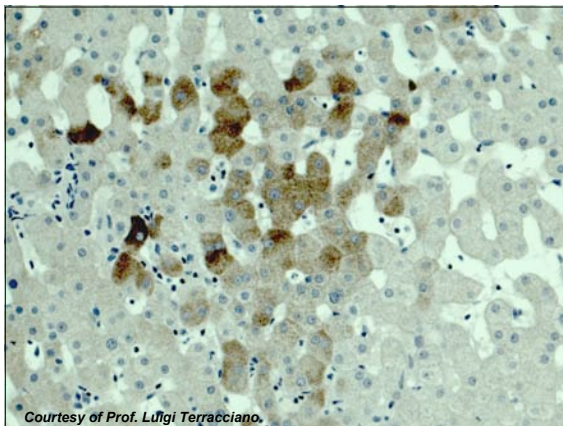


Hepatitis D Suspicion

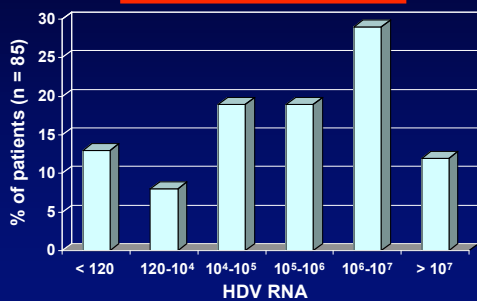
- Active hepatitis in HBsAg-positive patient with low or negative HBV DNA
- Anti-HBc IgM-negative exacerbation of chronic hepatitis B
- Severe or fulminant acute hepatitis B

Hepatitis D Diagnosis

- Anti-HDV
- Anti-HDV IgM
- Immunohistochemistry
- HDV RNA → quantitative RT-PCR

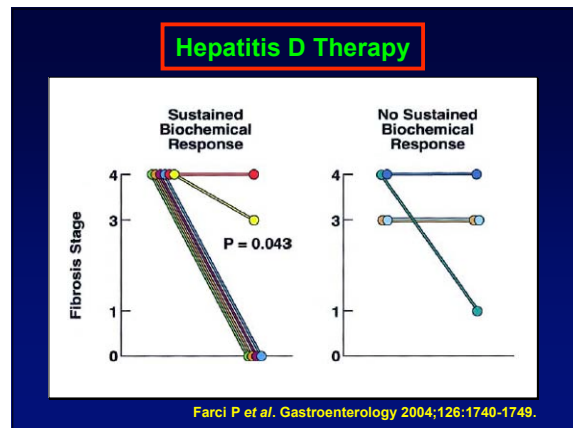
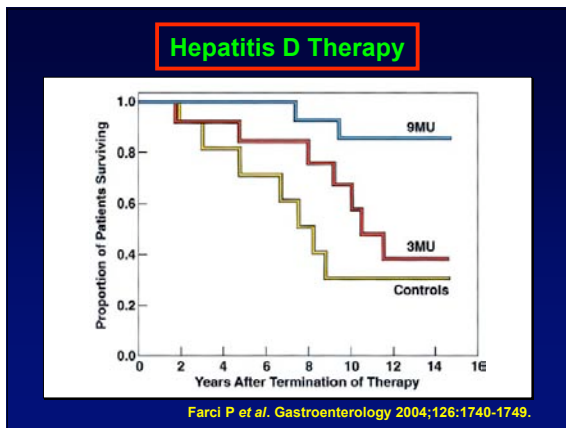
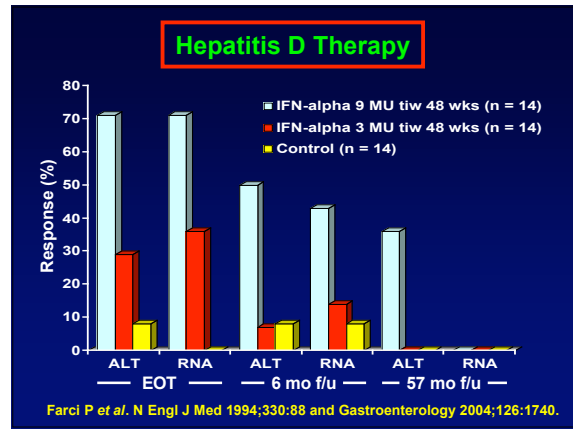
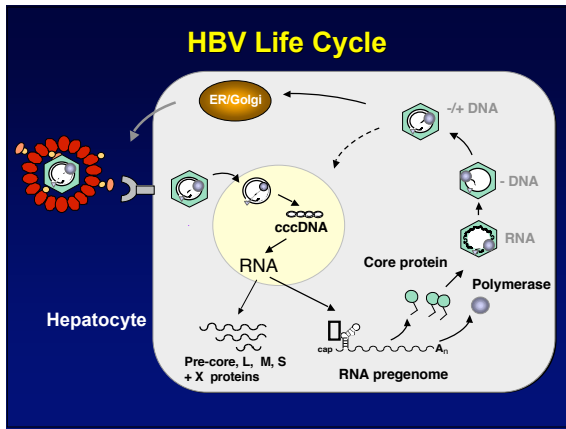


Hepatitis D Diagnosis Real-time RT-PCR

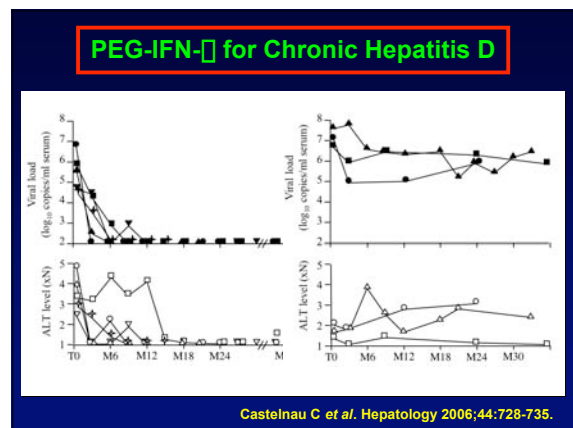


Chronic Hepatitis B Therapy 2006

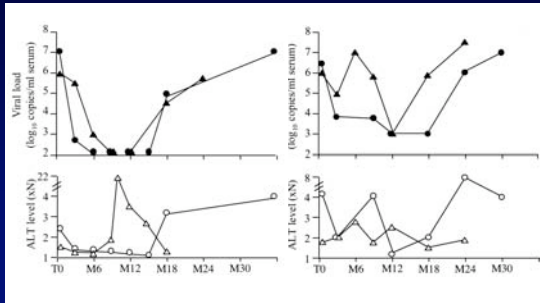
PEG-IFN-α	Pegasys® (PegIntron®)	registered
Lamivudine	LAM Zeffix®	registered
Adefovir	ADV Hepsera®	registered
Telbivudine	L-dT Sebivo®	registered
Entecavir	ETV Baraclude®	registered
Tenofovir	TDF Viread®	registered for HIV
Emtricitabine	FTC Emtriva®	registered for HIV
Clevudine	L-FMAU	phase II



- ### Hepatitis D Therapy PEG-IFN- α
- n = 14, 28% cirrhosis, PEG-IFN- α 2b 1.5 μ g/kg/wk for 48 wks, f/u 16 (1-42) months
 - Generally well tolerated (4/15 dose modification)
 - ETVR 8/14 (57%) \rightarrow SVR 6/14 (43%)
 - No HBV reactivation
 - No correlation of anti-HDV IgM and HDV RNA
 - ALT not sufficiently accurate to monitor treatment response \rightarrow quantitative HDV RNA
- Castelnau C *et al.* Hepatology 2006;44:728-735.



PEG-IFN- α for Chronic Hepatitis D



Castelnau C *et al.* Hepatology 2006;44:728-735.

Hepatitis D Therapy PEG-IFN- α

- n = 38, 74% cirrhosis, PEG-IFN- α 2b 1.5 μ g/kg/wk for 72 wks \pm RBV for 48 wks, f/u 24 wks
- 25% treatment discontinuation and 58% dose modification
- ETVR 19 vs. 9% \rightarrow SVR 25 vs. 18%
- No advantage of combination with RBV

Niro GA *et al.* Hepatology 2006;44:713-720.

Hepatitis D Current Therapy

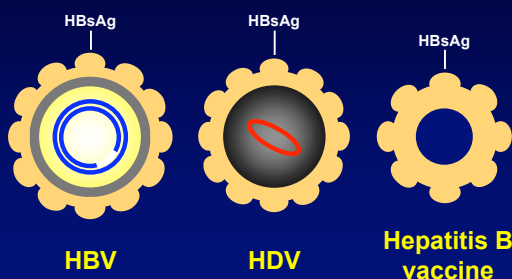
- PEG-IFN- α for at least one year current standard of care
- Combination therapies do not appear superior to monotherapy (studies in progress)
- HDV RNA monitoring during treatment
- Consider combination with nucleos(t)ide analog in patients with active HBV replication

Hepatitis D Liver Transplantation

- End-stage HDV cirrhosis represents an excellent indication to LT
- Very low risk of recurrence with appropriate prophylaxis

Samuel D *et al.* N Engl J Med 1993;329:1842-1847.
Samuel D *et al.* Hepatology 1995;21:333-339.

Hepatitis D Prevention



Hepatitis D Conclusions

- Least common but most severe form of chronic hepatitis
- Resurgence in the context of immigration
- PEG-IFN- α current standard of care
- HDV RNA for treatment monitoring
- New therapeutic strategies needed
- Role of hepatitis B vaccination