

Hepatitis Delta Revival

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Hannover**

HEPATITIS VIRUSES

Hepatitis A	Feinstone	1973	RNA
Hepatitis B	Blumberg	1965	DNA
Hepatitis C	Houghton	1988	RNA
Hepatitis D	Rizzetto	1977	RNA
Hepatitis E	Balayan	1980	RNA

**EASL Monothematic
Conference:
Delta Hepatitis
September 24-26, 2010
*Istanbul, Turkey***

M Mans, M Rizzetto, C Yurdaydin

EASL | MONOTHEMATIC CONFERENCE

Delta Hepatitis
Istanbul, Turkey
September 24 – 26, 2010

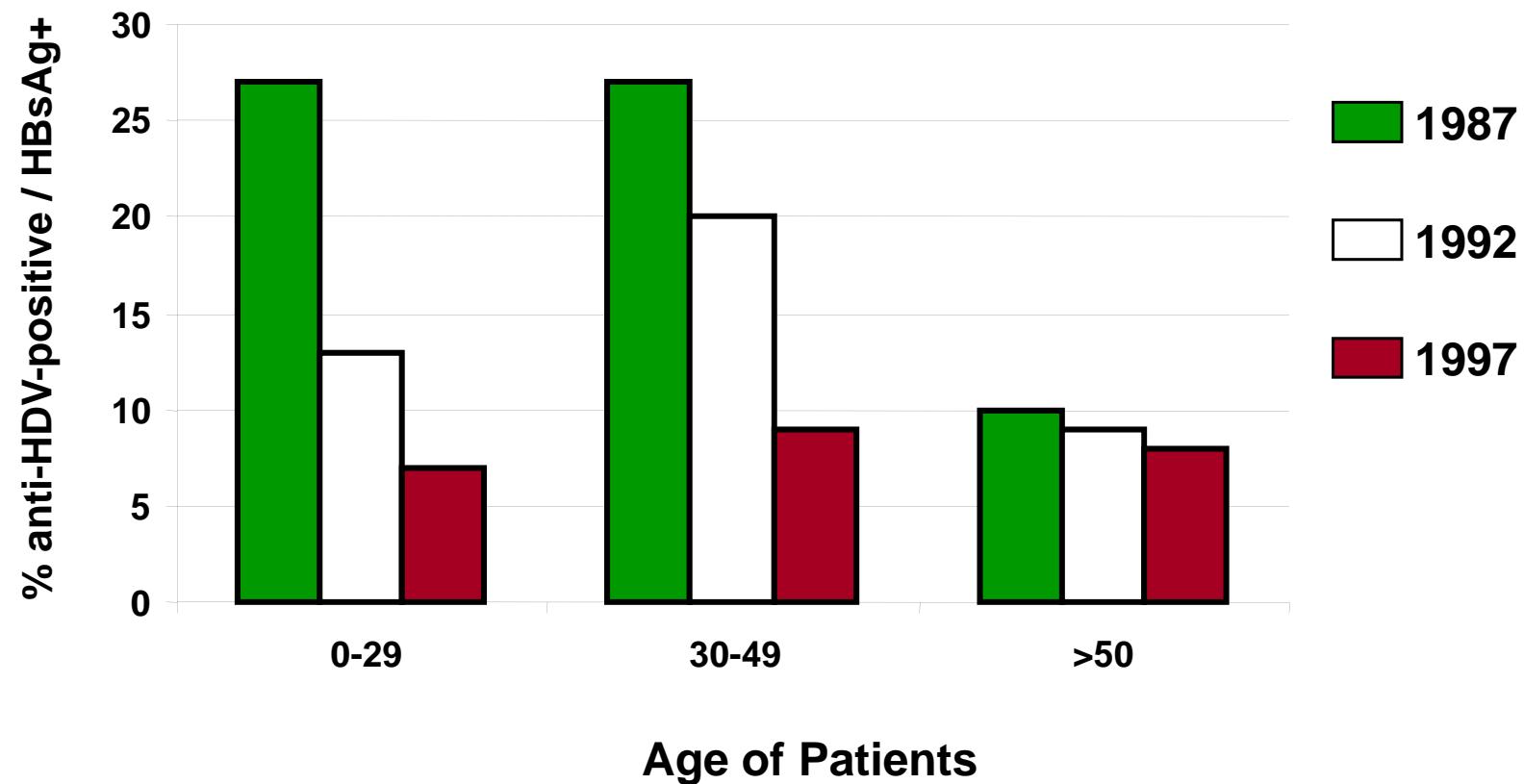


**ANNOUNCEMENT AND
CALL FOR POSTER ABSTRACTS**
Abstract Submission Deadline: May 25, 2010
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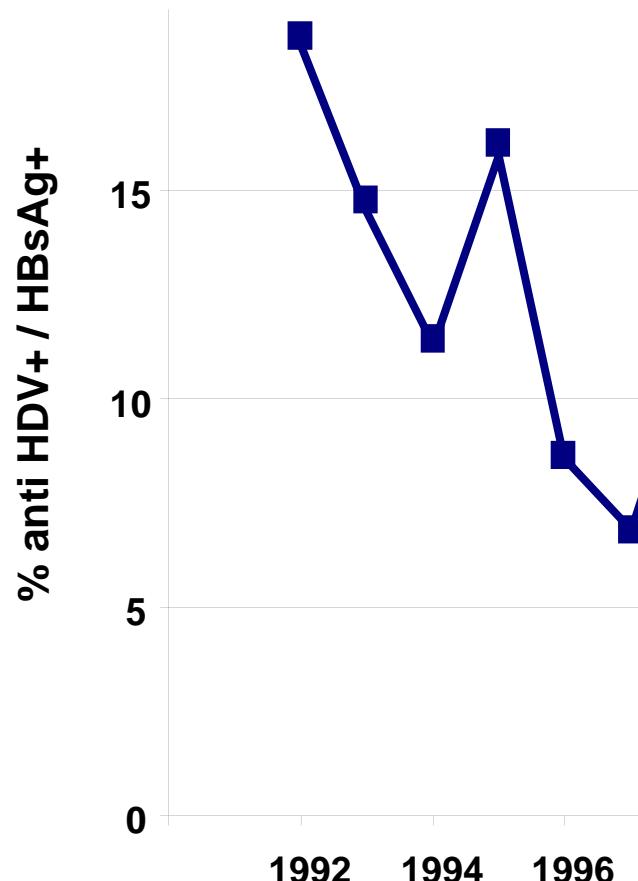
 GILEAD |  MSD |  Becton

Declining Prevalence of Hepatitis D Virus Infection in Italy



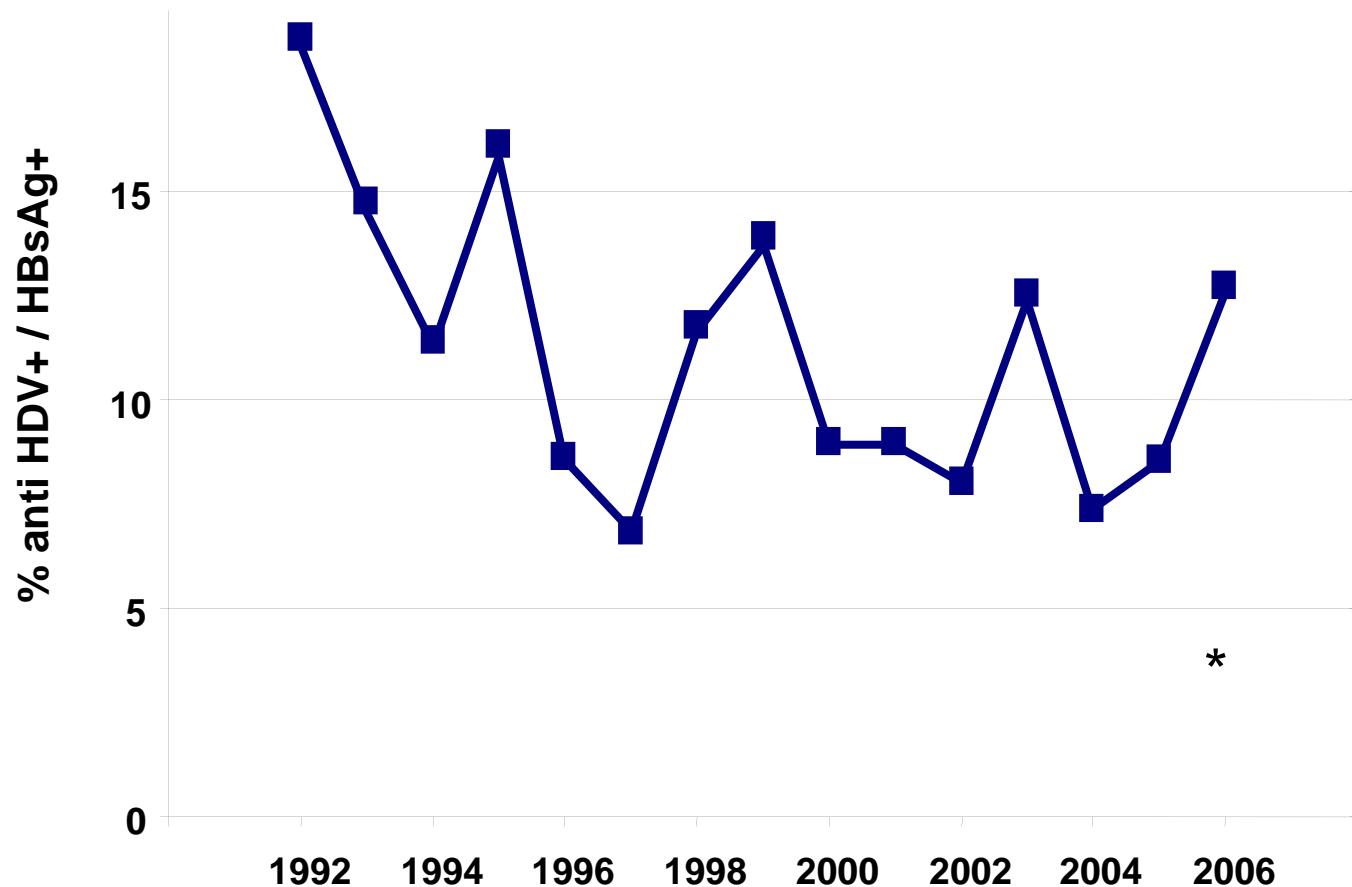
HDV-Infection in Germany

Anti-HDV-Prevalence in HBsAg+ patients
Hannover Medical School
(1-1992 bis 4-2006; n=2354)

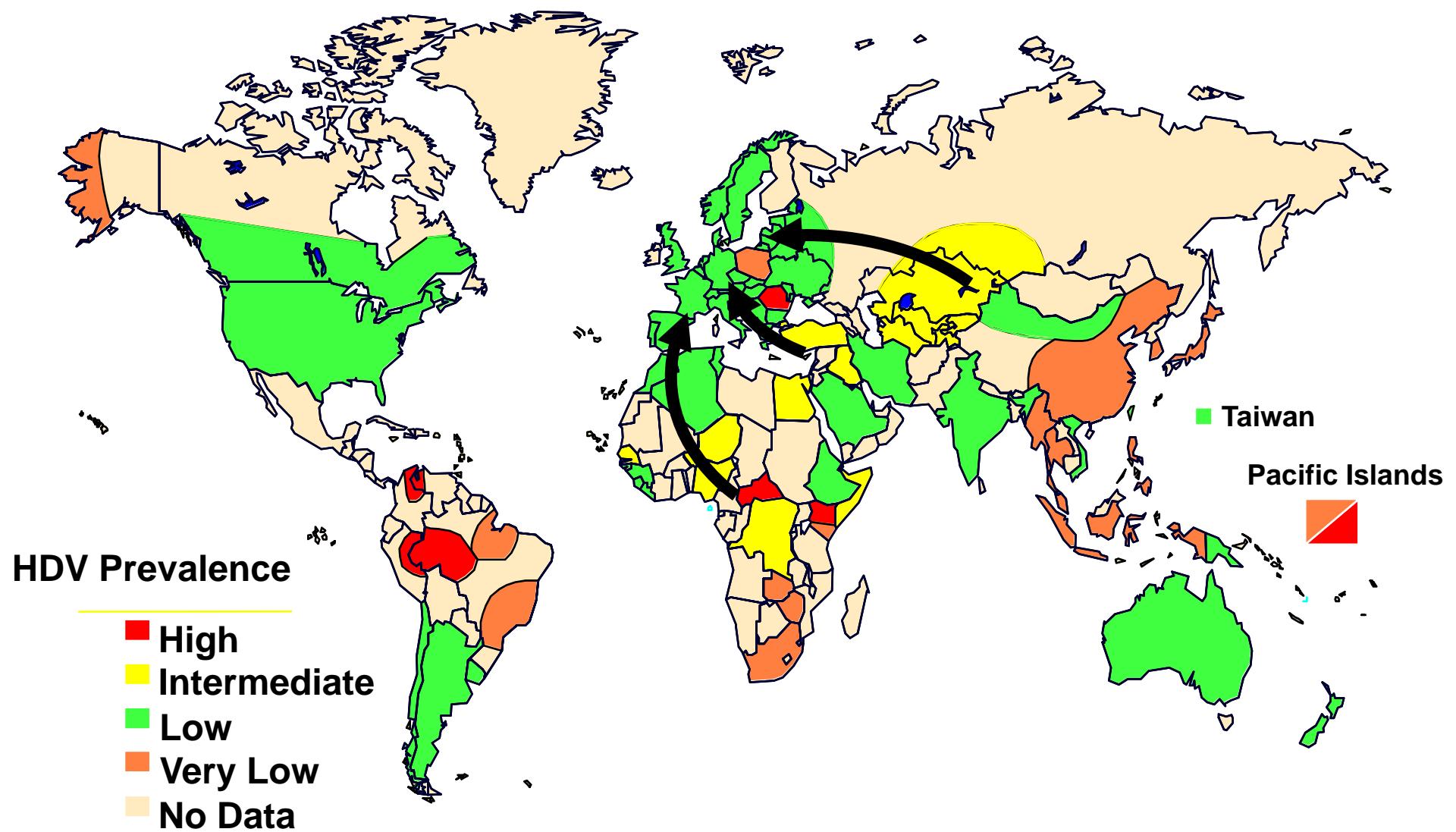


HDV-Infection in Germany

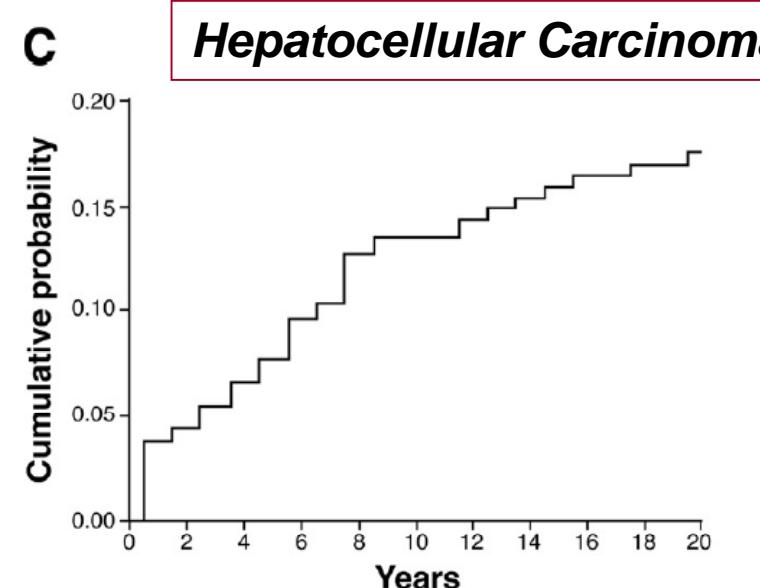
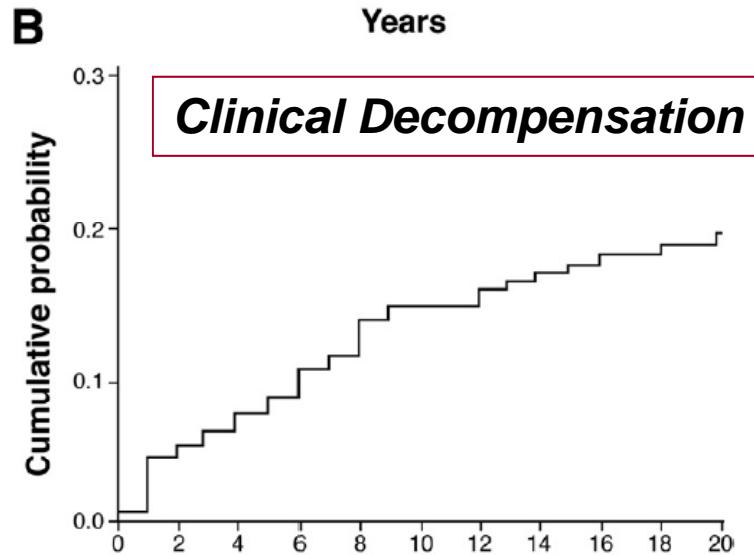
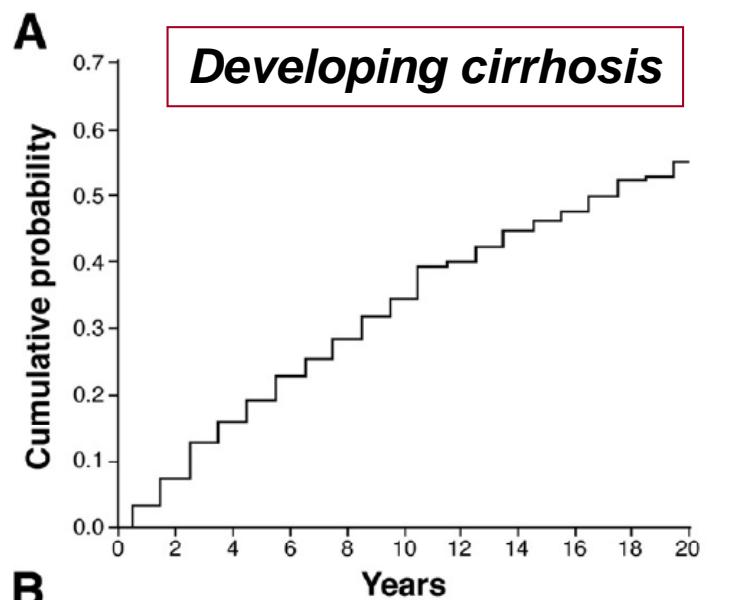
Anti-HDV-Prevalence in HBsAg+ patients
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Emerging HDV Epidemiology: Migration



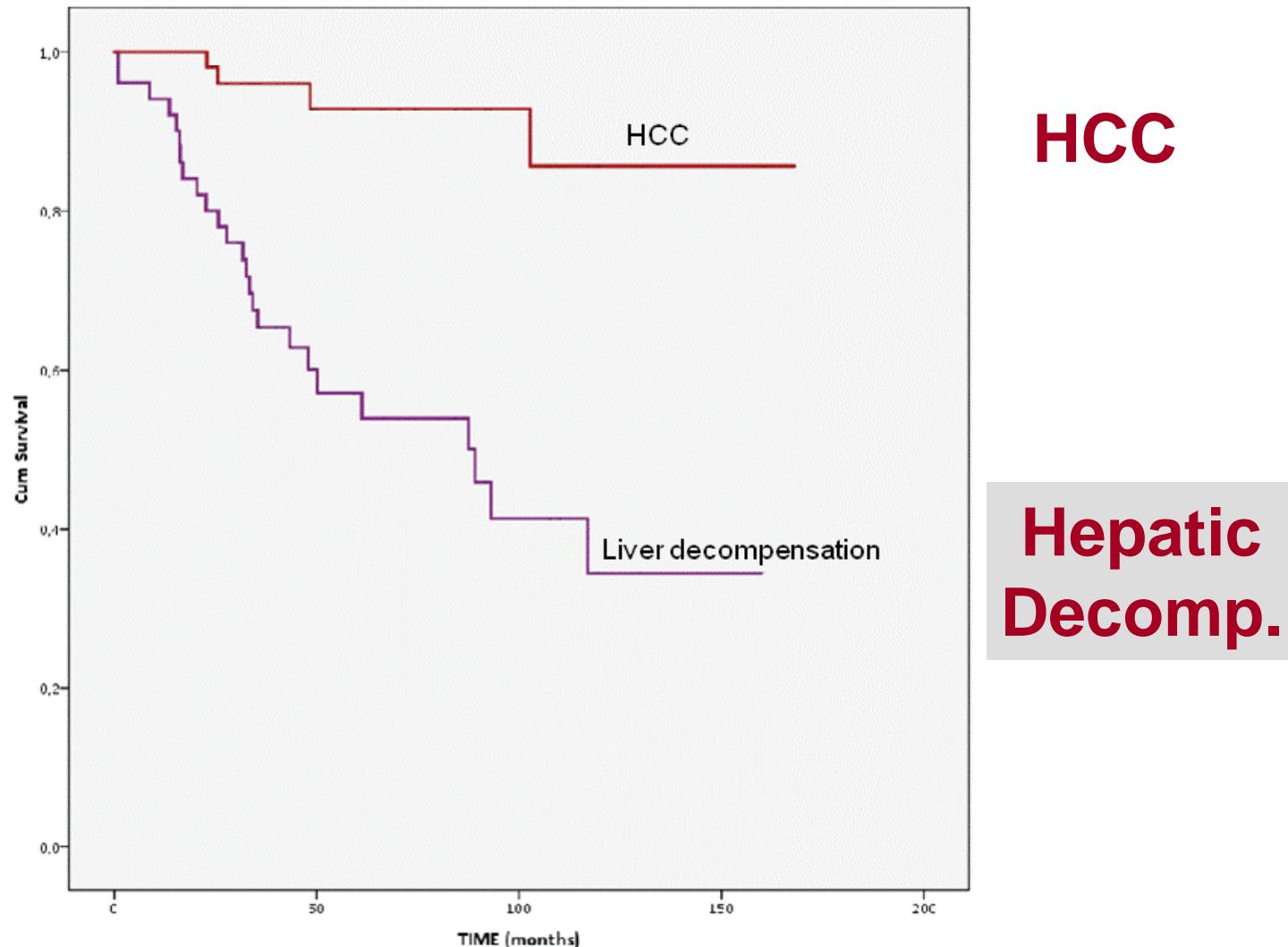
Long-term outcome of hepatitis D in Italy



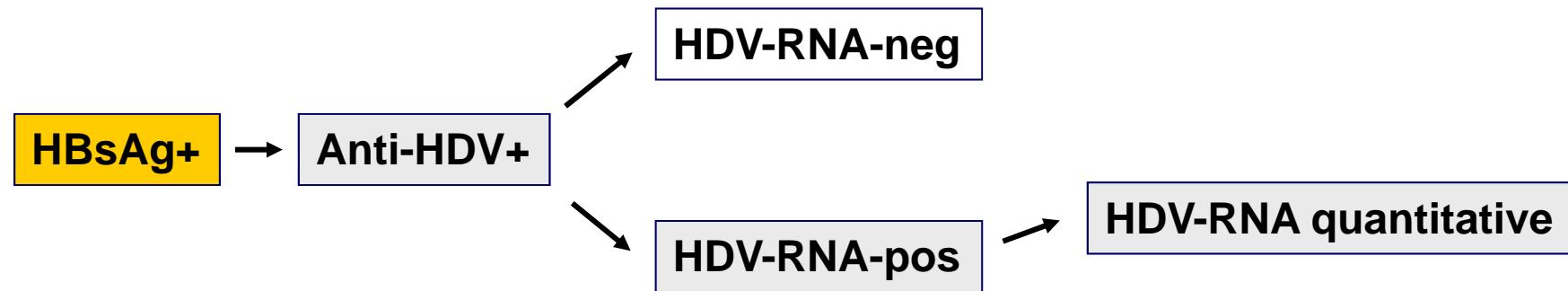
**Main Cause of Death:
Liver Failure (38%)**

**Only independent Factor of mortality:
HDV replication**

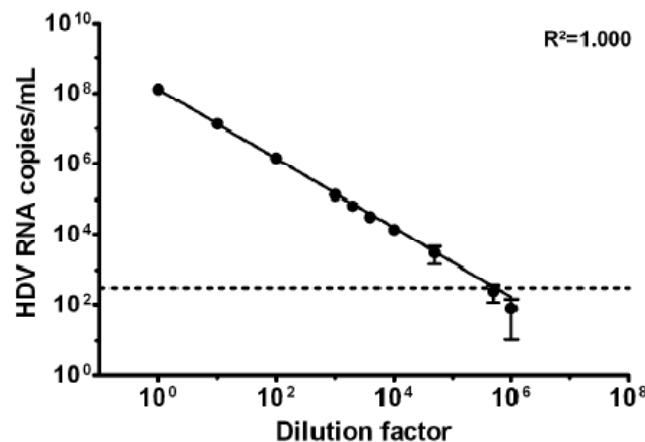
Hepatic Decompensation but not HCC development is the primary cause of mortality



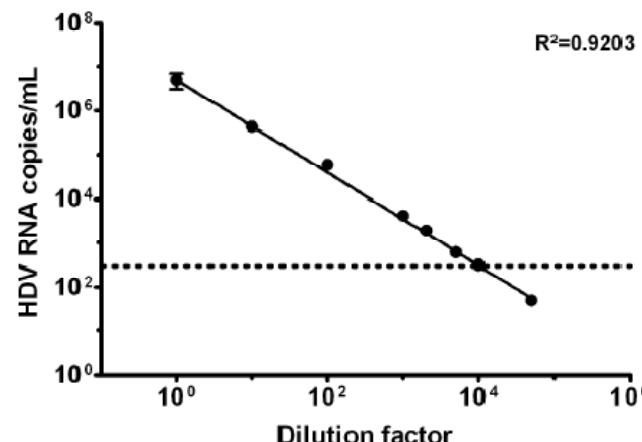
Diagnostic Steps in Delta Hepatitis



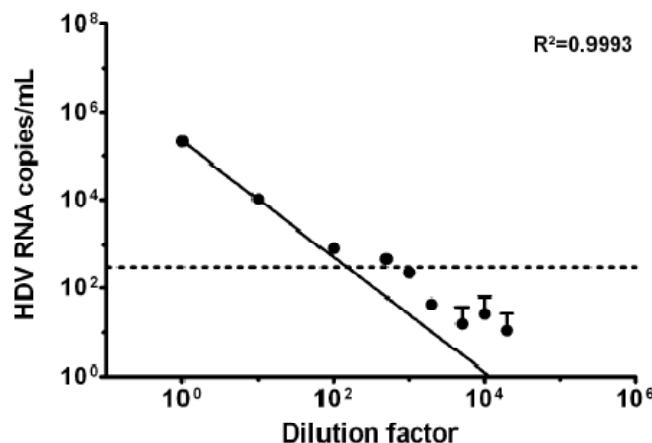
Quantitative HDV-PCR: Cobas-TaqMan Assay



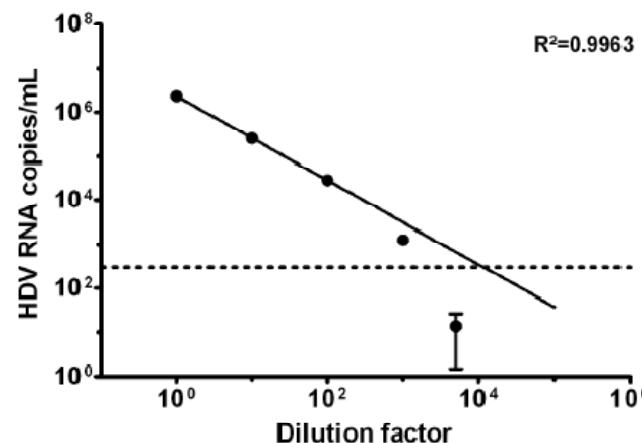
a) Plasmid as template



b) Patient sample 1

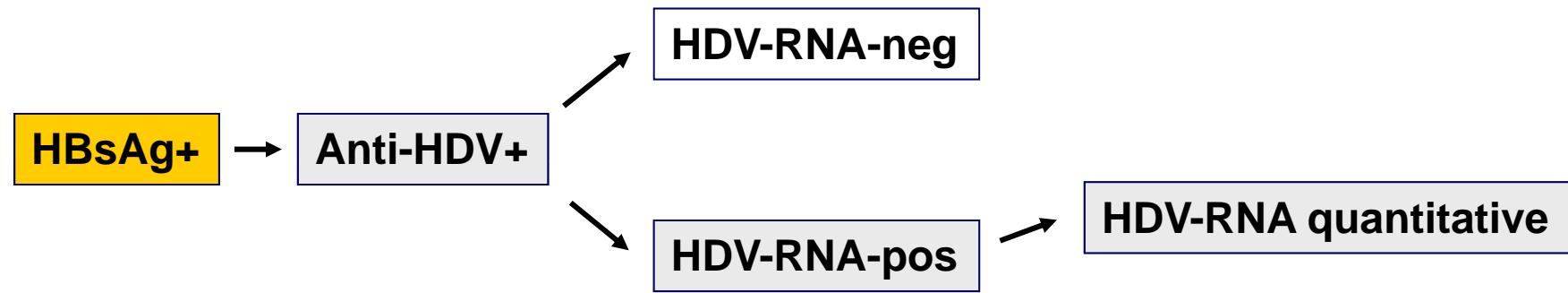


c) Patient sample 2



d) Patient sample 3

Diagnostic Steps in Delta Hepatitis

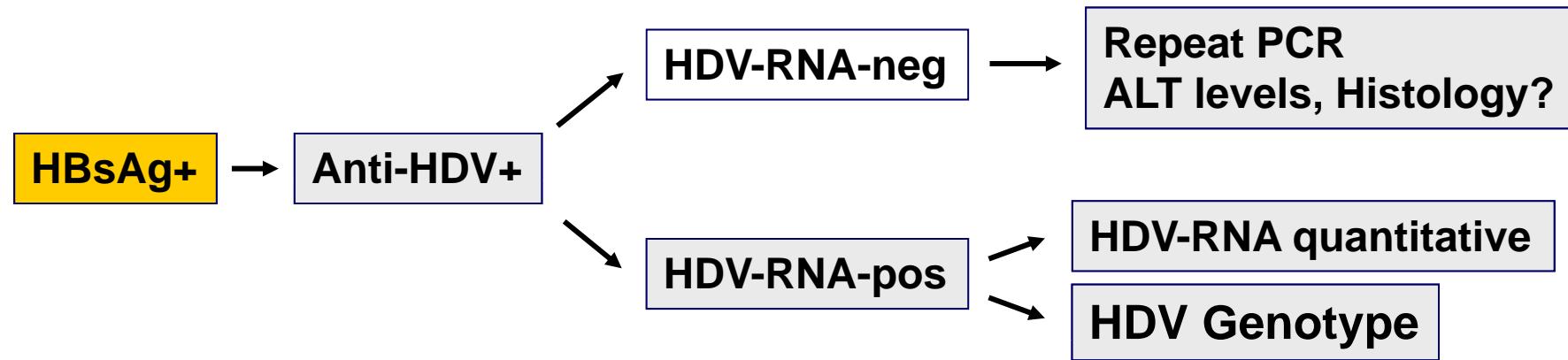


Does HDV viremia correlate with the stage/grade of liver disease?

HDV-RNA does NOT correlate with liver fibrosis

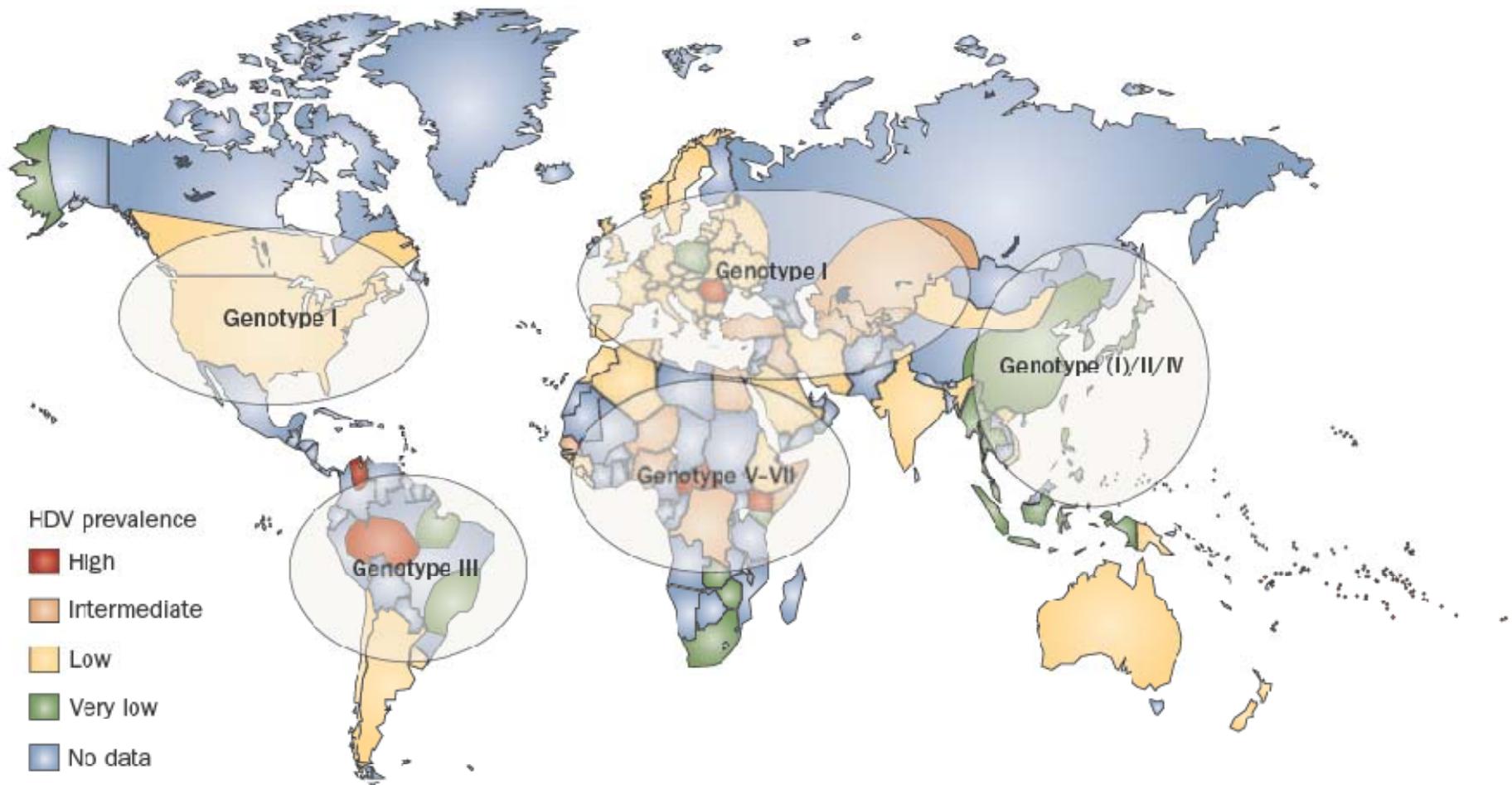
	HDV-RNA< 10^5 copies/ml (n=20)	HDV-RNA> 10^5 copies/ml (n=47)	p value
Ishak fibrosis score	3.4 ± 0.9	3.2 ± 1.4	NS*
Cirrhosis (Ishak 5-6) (%)	2 (10)	11 (23.4)	NS ^{§§}
Significant fibrosis (Ishak 3-6) (%)	16 (80)	31 (66)	NS [§]

Diagnostic Steps in Delta Hepatitis

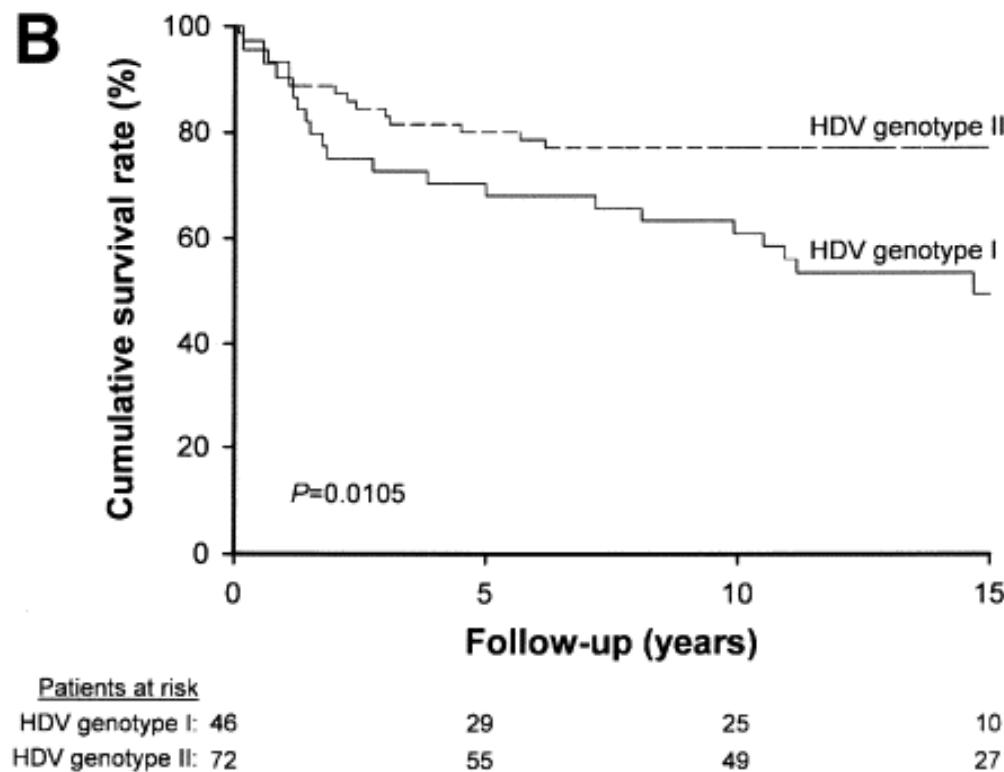


Does the course of Delta Hepatitis differ between different genotypes?

Different HDV genotypes in different regions

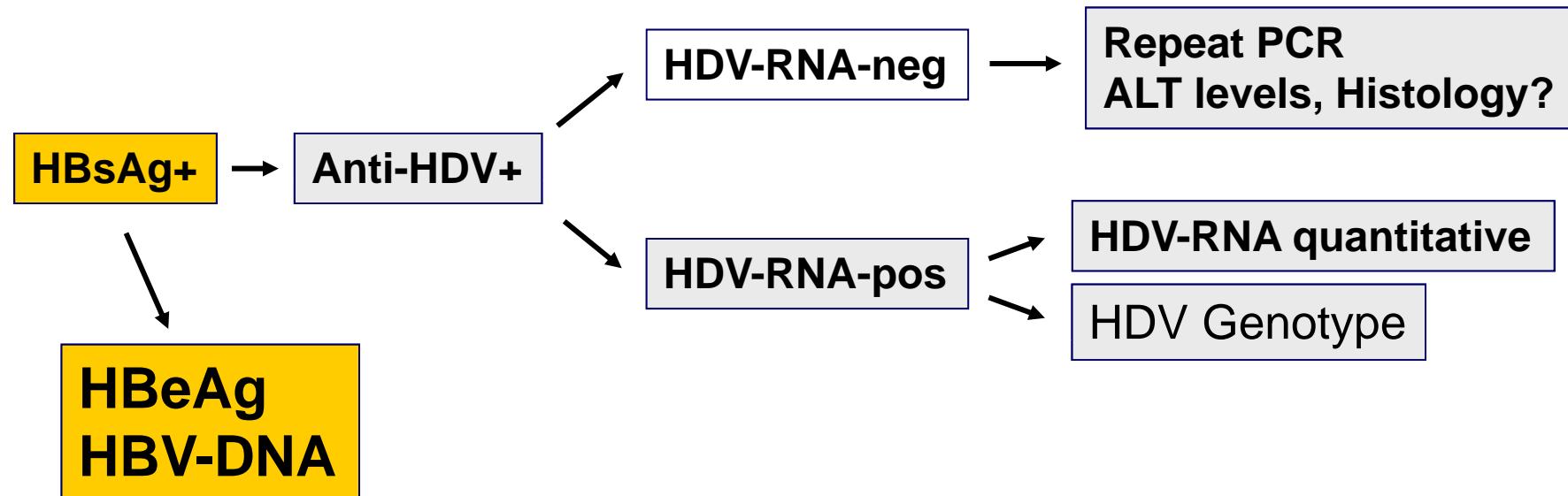


Different HDV genotypes are associated with different clinical outcomes



Su et al,
Gastroenterology 2006

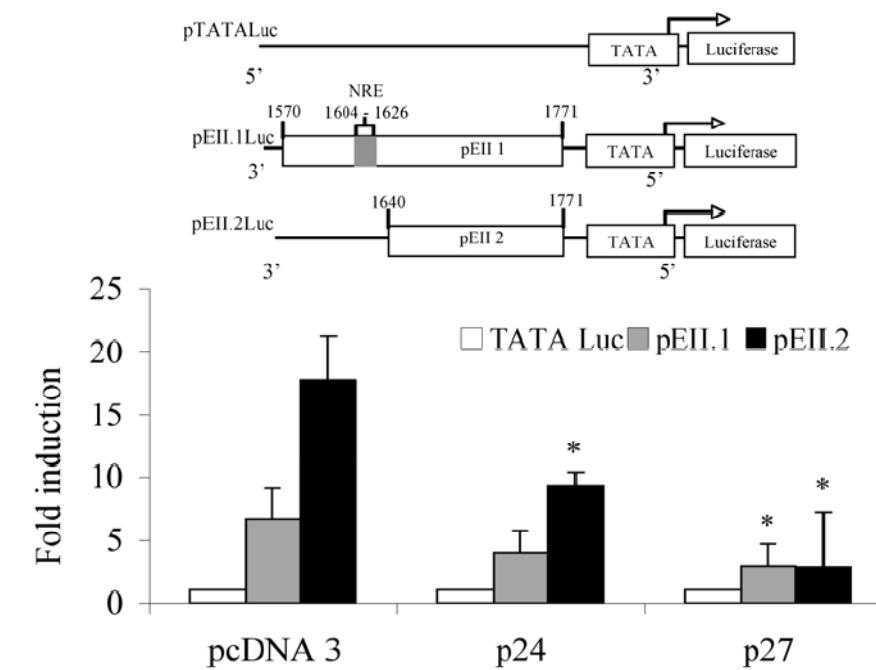
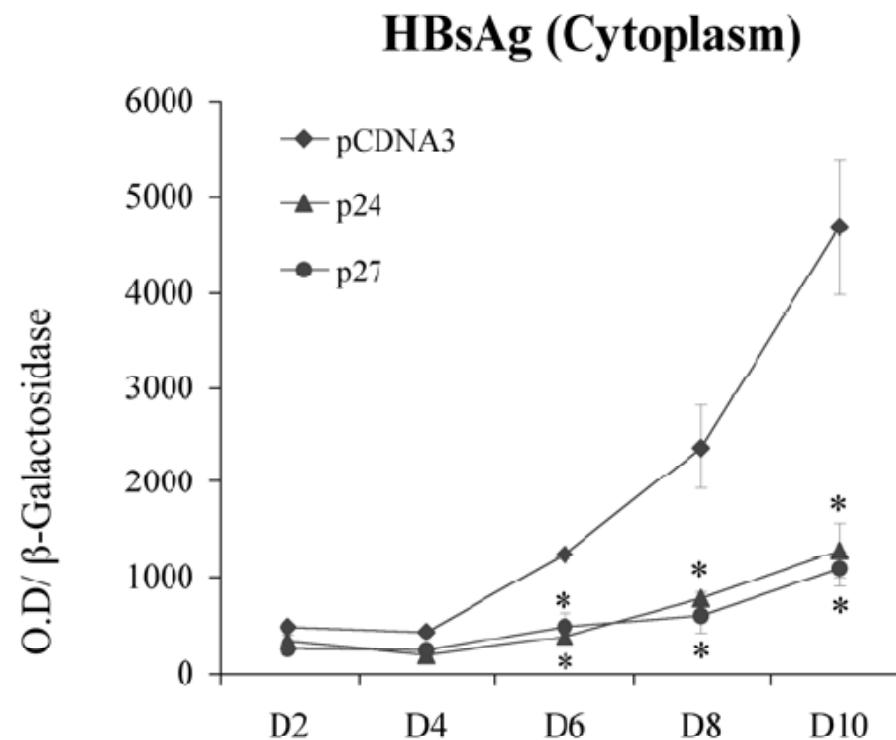
Diagnostic Steps in Delta Hepatitis



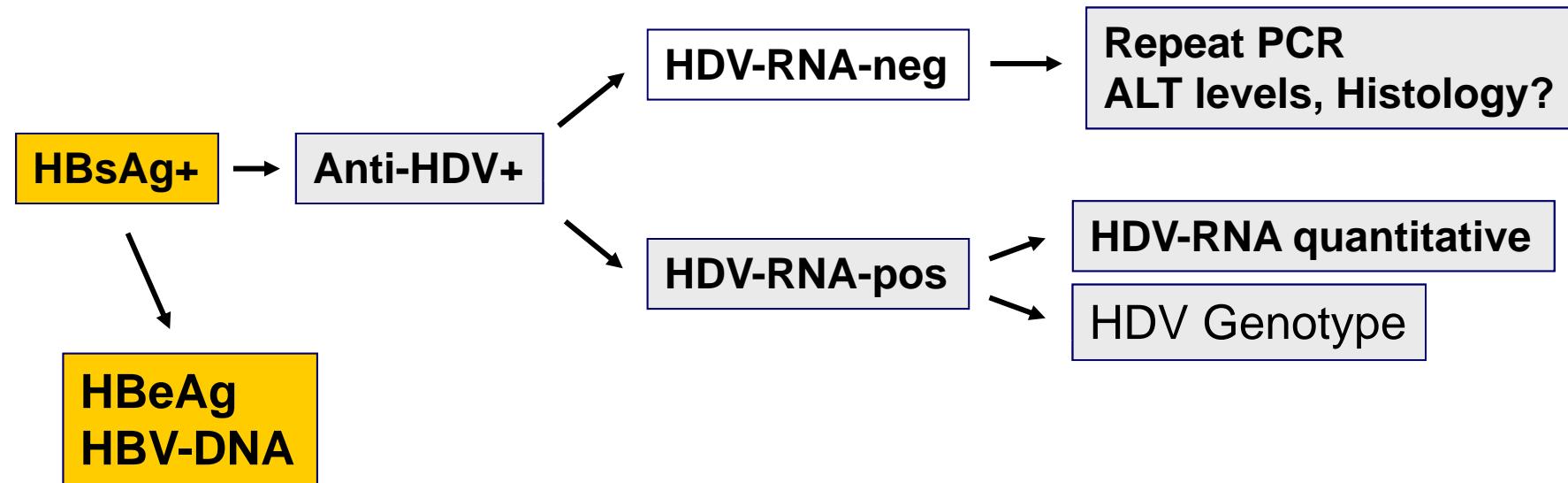
HBeAg and HBV-DNA are suppressed in Delta Hepatitis

	aHDV positive	HBsAg+ / aHDV negative	χ^2 p-level
HBeAg positive	44/ 257 (17%)	610/ 2024 (30%)	< 0.001
HBV-DNA positive	59/ 228 (25%)	708/ 1562 (45%)	< 0.001

HDV p24 & p27 repress HBV enhancers



Diagnostic Steps in Delta Hepatitis



**Fluctuating Patterns of Viral Dominance
maybe observed over time**

Fluctuating Patterns of Viral Dominance in Hepatitis D

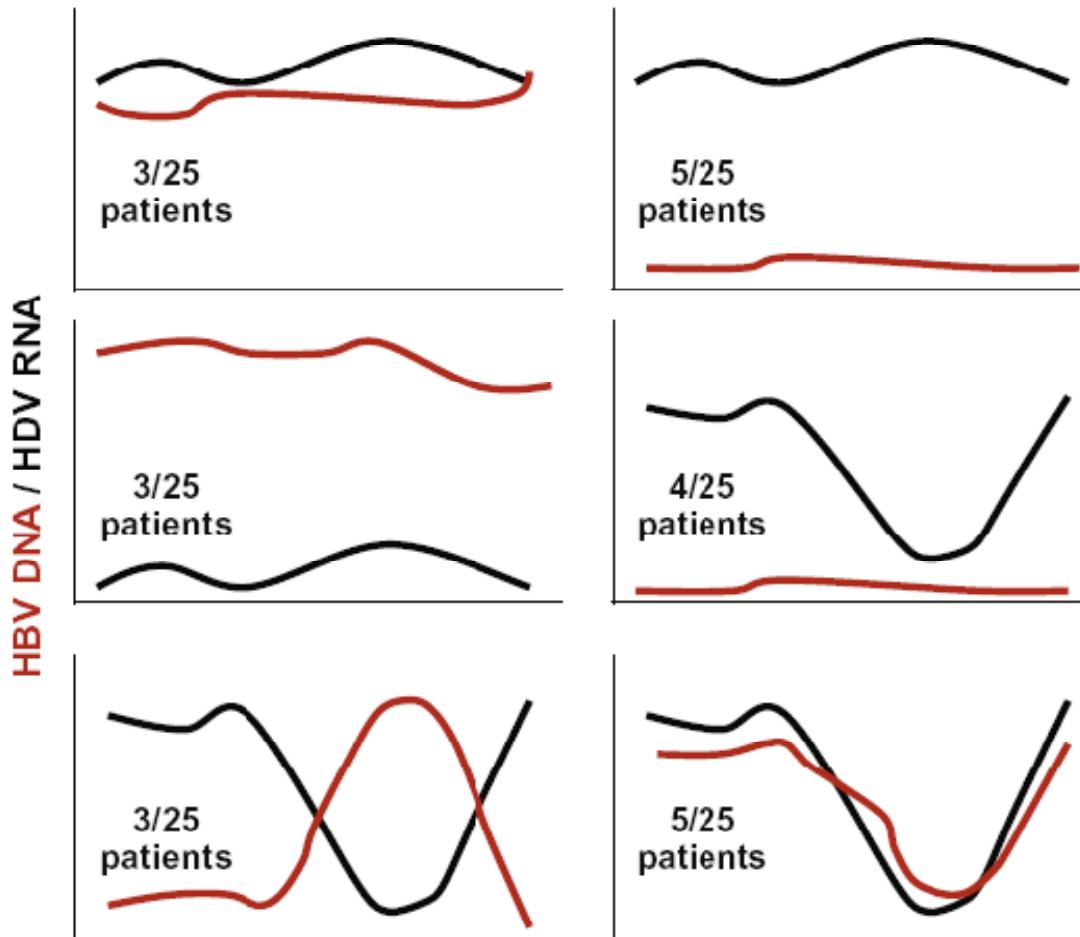


Fig. 1. Schematic representation of HBV DNA and HDV RNA patterns over time observed in the study by Schaper et al. [19].

Treatment of Delta Hepatitis?

HDV-Infection Treatment Options

Nucleos(t)ide Analogues

- Famciclovir ineffective
- Lamivudine ineffective
- Ribavirin ineffective

Yurdaydin et al., J Hepatol 2002

Wolters et al., J Viral Hepatitis 2000

Niro, Aliment Pharmacol Ther. 2005 ; Niro et al., J Viral Hepatitis 2008

Yurdaydin et al., J Viral Hepatitis 2008

Niro et al., Hepatology 2006

Garripoli et al., Liver 1994

Gunsar et al., Antiv Therapy 2005

Interferon alpha

- Sustained biochemical responses in 0-36% of patients
Few Studies with virological endpoints
treatment >12 months may be required

Farci et al., NEJM 1994

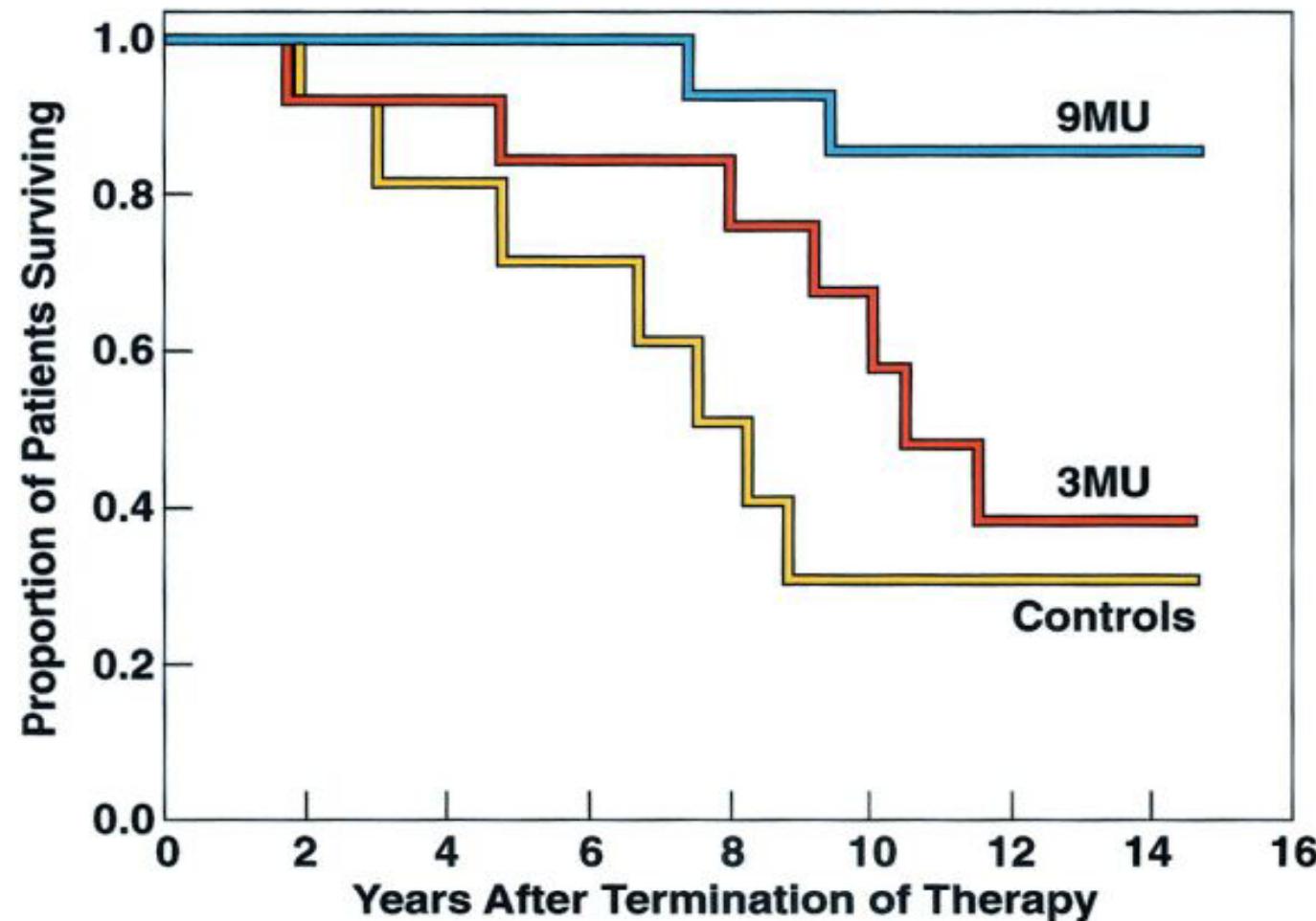
Di Marco et al., J Viral Hepatitis 1996

Niro et al., J Viral Hepatitis 2005; Yurdaydin et al., J Viral Hepatitis 2008

- Higher IFN doses were associated with better survival in small study cohort

Farci et al., Gastroenterology 2004

Farci et al., IFNa for HDV infection
(NEJM 1994 / Gastroenterology 2004)



Trials using PEG-IFN in Delta Hepatitis

3 studies published in September 2006

Castelnau, Marcellin, Gault et al. Hepatology 2006

14 patients, 12 months of PEG-IFN α -2b

SVR in 6 patients (43%)

Niro, Rizzetto et al. Hepatology 2006

38 patients, 72 weeks PEG-IFN α -2b

16 pts monotherapy

22 pts + ribavirin (first 48 weeks)

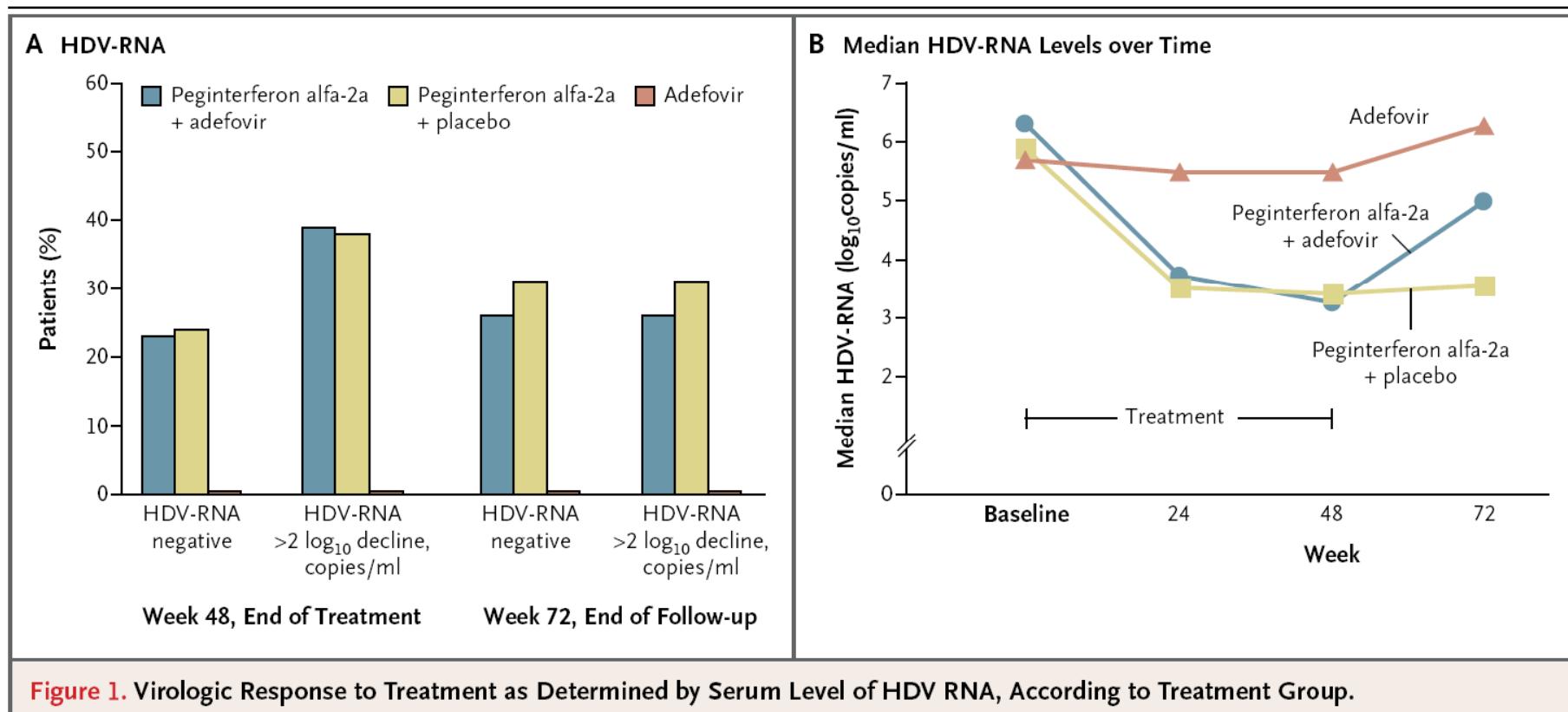
SVR: 8 patients (21%)
Ribavirin had no additional effect

Erhardt, Häussinger et al. Liver Int 2006

12 patients, 48 weeks of PEG-IFN α -2b

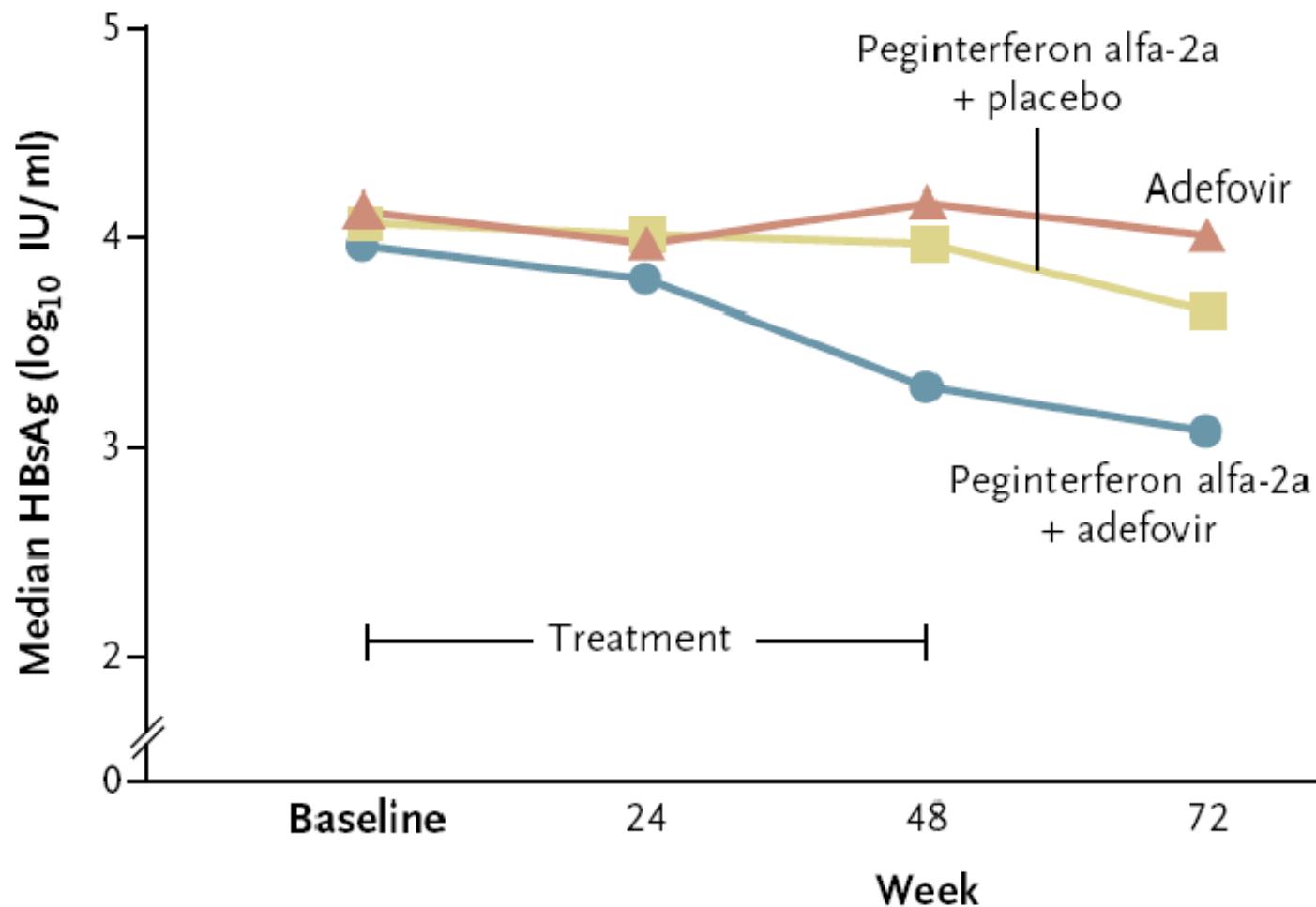
SVR in 2 patients (17%)

Treatment of Hepatitis Delta with PEG-IFNa-2a: ~25% Sustained HDV RNA clearance



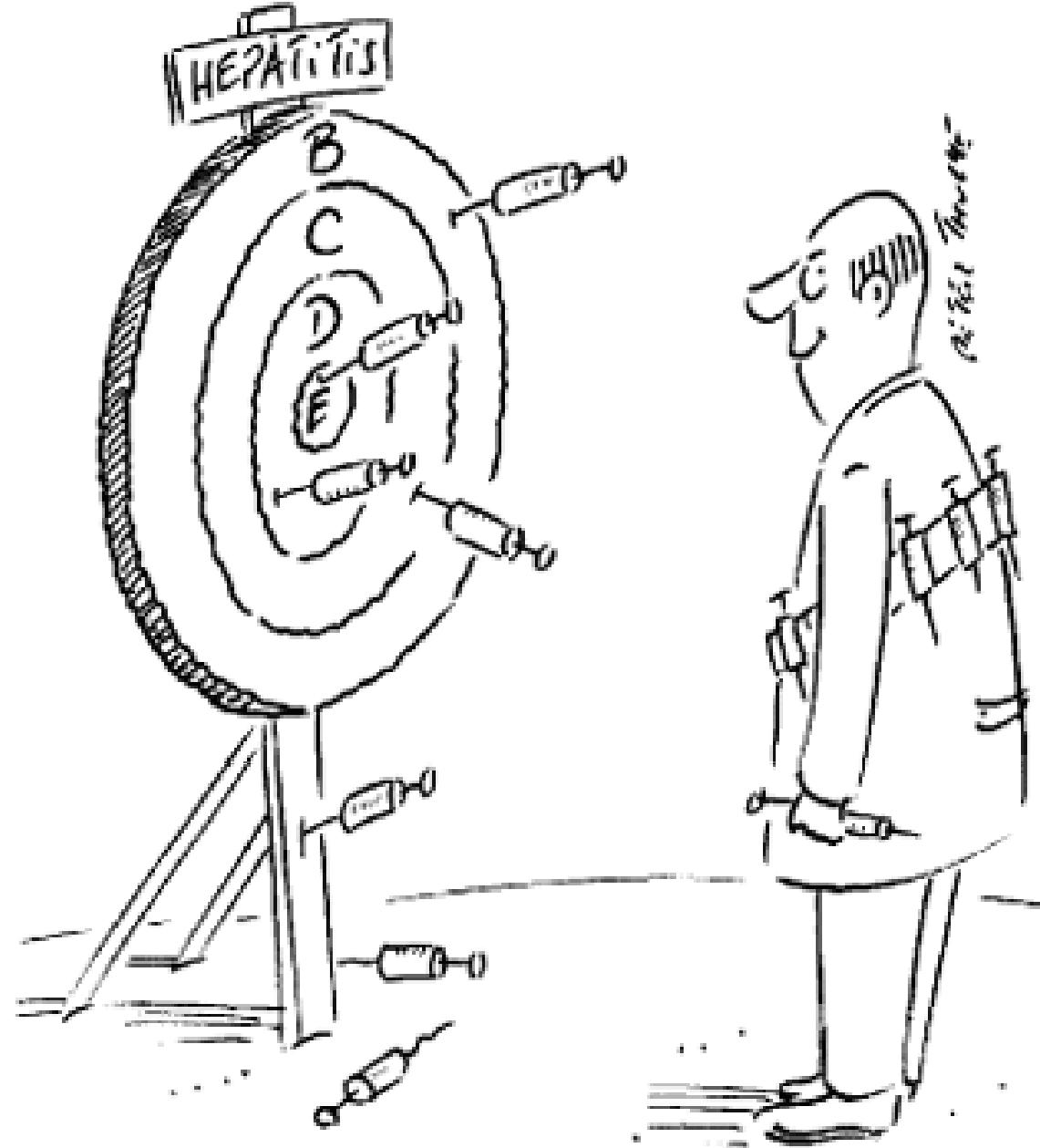
Combination Therapy shows more pronounced HBsAg decline!

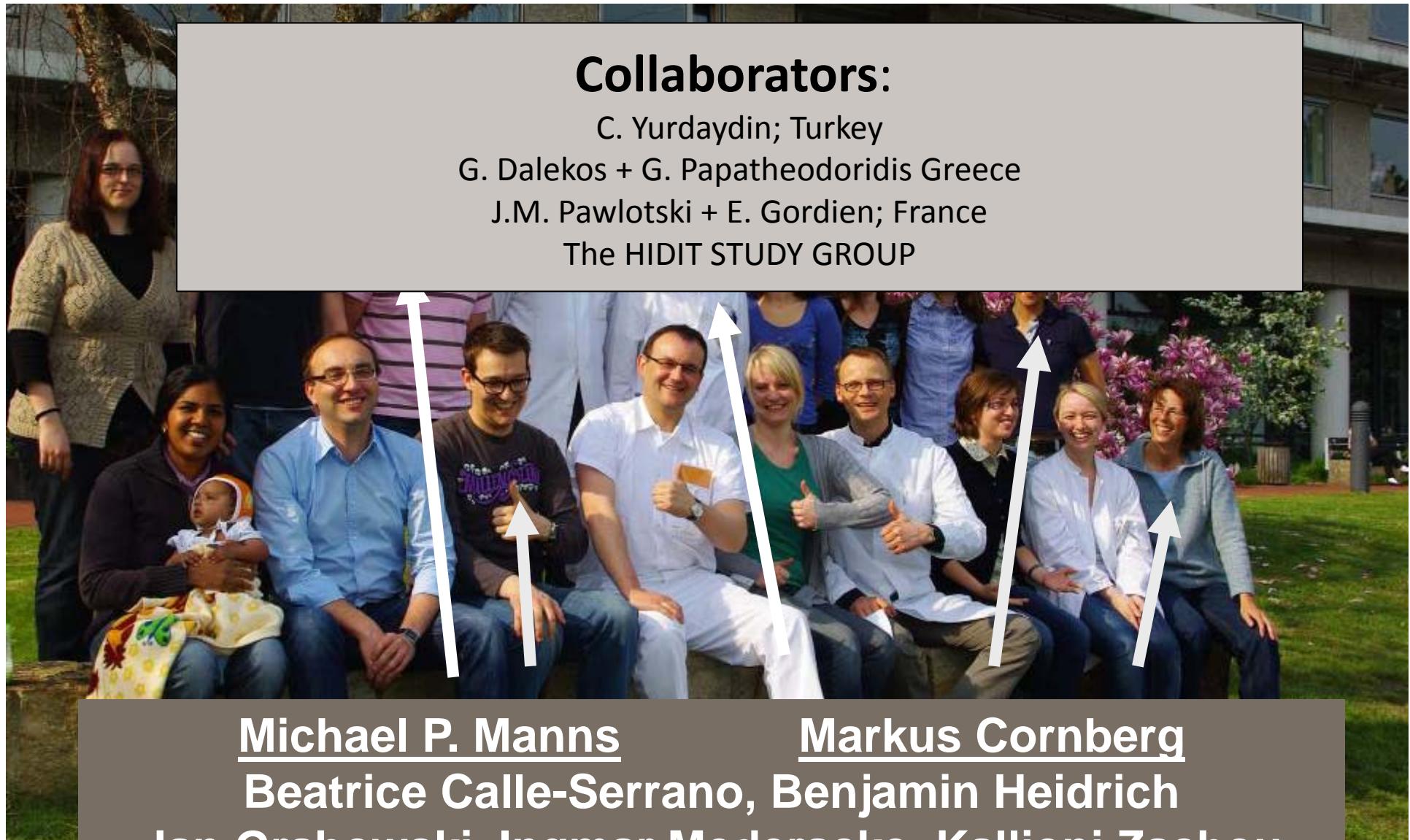
B HBsAg Levels over Time

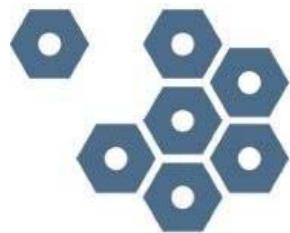


Alternative Treatment options?

Liver Transplantation for Hepatitis D?







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