

# Co-infected health-care workers

Y.Yazdanpanah

Service Universitaire des Maladies Infectieuses et du  
Voyageur

C.H. Tourcoing, Faculté de Médecine de Lille  
CNRS U362, Lille, France

Co-infected health-care workers =  
HBV + HCV

HBV + HDV

**HBV + HCV**

# Prevalence of co-infection

- HBV and HCV share several modes of transmission
- Co-infection by the two viruses is not uncommon.
  - In patients with chronic HBV infection : 10 -20% anti-HCV +

Fattovich et al. J Infect Dis 1991.

Crespo et al. Am J Gastroenterol 1994.

Di Marco et al. Hepatology 1999.

Gaeta et al. Infection 1990.

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**Selection bias: Hospital based patient groups**

Fattovich et al. J Infect Dis 1991.  
Crespo et al. Am J Gastroenterol 1994.  
Di Marco et al. Hepatology 1999.  
Gaeta et al. Infection 1990.

# Co-infection associated with a more severe histological liver disease

- **Fibrosis score**                           VHB&VHC > VHC  
  VHB&VHC > VHB
- **Prevalence of cirrhosis:**           VHB&VHC > VHC  
  VHB&VHC > VHB
- **Hepatocellular carcinoma:**       VHB&VHC > VHC  
  VHB&VHC > VHB
- **Repeatedly elevated ALT:**         VHB&VHC > VHB

Sagnelli et al. Infection 2004  
Zarski et al. J Hepatol 1998  
Gaeta et al. J Hepatol 2003  
Kirk et al. Hepatology 2004

# Prevalence of co-infection

- HBV and HCV share several modes of transmission
- Co-infection by the two viruses is not uncommon.
  - HBsAg chronic carriers : 7% anti-HCV + (59/837)
    - 14 liver units throughout Italy
    - Patients routinely tested irrespective of the presentation modalities
    - 12 month period

Gaeta et al. J Hepatol 2003.

# Prevalence of co-infection

- HBV and HCV share several modes of transmission
- Co-infection by the two viruses is not uncommon.
  - HBsAg positive or anti-HBs positive HCWs : 3.1%  
anti-HCV + (42/1357)
    - Five hospitals personnel, Latium region, Italy  
(n=5813)
    - HCWs' pre-vaccination screening for HBsAg +



# Impact of HBV on HCV

# Impact of HBV on spontaneous HCV clearance

- **Objective:** factors associated with HCV clearance
- **Study population:**
  - 203 spontaneously HCV-recovered subjects (HCV Ab+/RNA-)
  - 293 chronically HCV-infected patients (HCV Ab+/RNA+)
- HIV co-infection negatively associated with HCV clearance (OR 0.37; 0.16-0.83)
- **HBV co-infection positively associated with HCV clearance (OR 5.0; 1.26-28.6).**

# Impact of HBV on spontaneous HCV clearance

**Table 4. HBV and HIV Coinfections: Differences in the Seroprevalence of Markers for HBV and HIV Exposure in Recovered and Chronically HCV-Infected Male Veterans**

Serological Groups	Chronic (n = 293)	Recovered (n = 203)	Unadjusted OR	95% CI	P Value*
HbsAg <sup>+</sup>	3/276 (1.1%)	10/192 (5.2%)	5.0	1.26-28.6	.008
HbcAb <sup>+</sup> †	166/251 (66.1%)	117/168 (69.6%)	1.17	0.75-1.83	.452
HbsAb <sup>+</sup>	98/272 (36%)	74/184 (40.2%)	1.19	0.80-1.79	.365
HIV <sup>+</sup> among those tested	39/153 (25.5%)	9/78 (11.5%)	0.38	0.15-0.87	.014

NOTE. Percentages are based on all available data. Numbers shown are those subjects for which data was available from the total for each group.

\*Chi-square test for categorical variables.

†HbcAb positive also tested for HBsAb.

# Impact of HBV on HCV replication

- Serum HCV RNA:
  - In 41%–65% anti-HCV + and HBsAg+
  - In 90%–98% anti-HCV +

VHB&VHC

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graph TD; A[VHB&VHC] --> B[With Active HCV replication]; A --> C[Without active HCV replication]
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With Active HCV replication

Without active HCV replication

Wang et al. J Gastroenterol 1999  
Mathurin et al. J Viral Hepatol 2000  
Sagnelli et al Hepatology 2000

# Impact of HBV on HCV replication

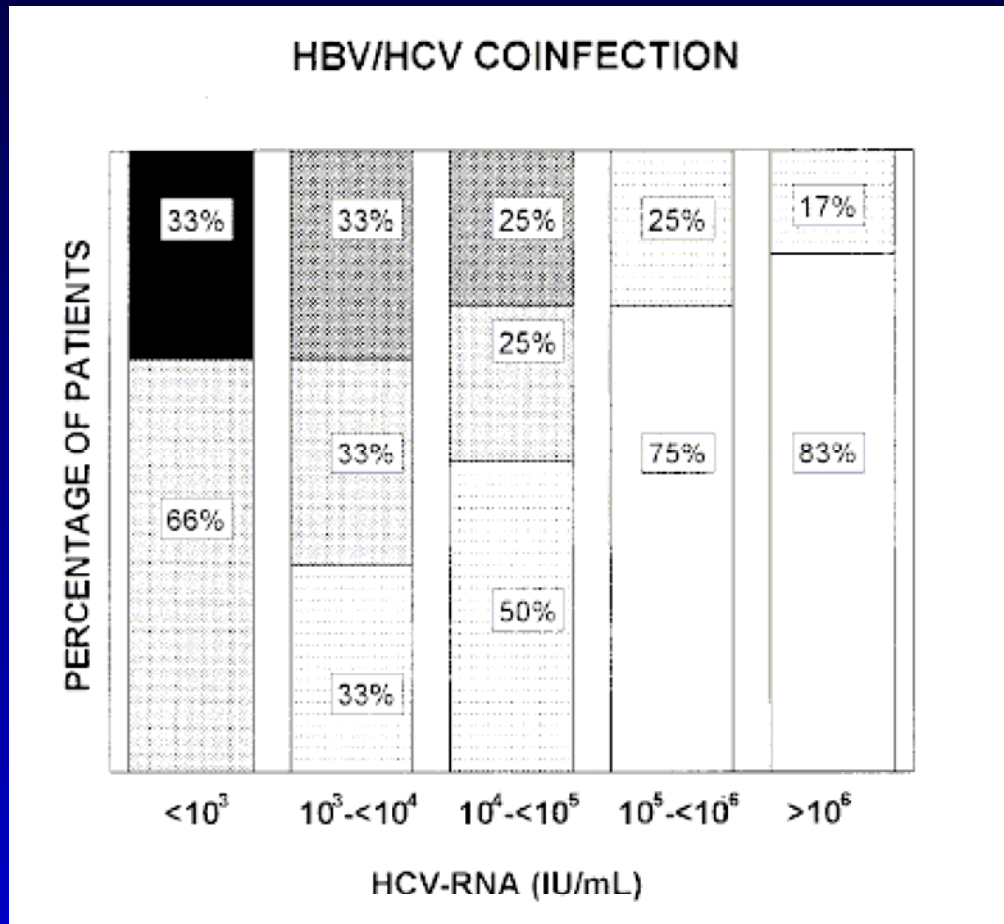
- HCV-RNA levels lower in HBV&HCV co-infections than in HCV infection:
- HCV RNA level lower in HBV DNA positive than in HBV DNA negative patients

Jardi et al. Hepatology 2001

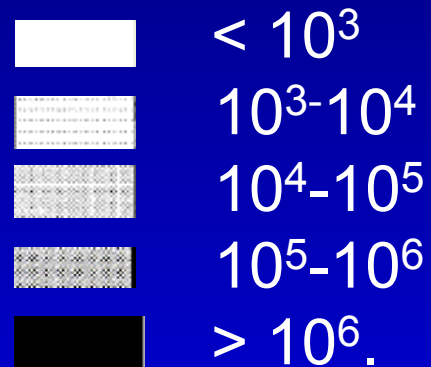
Chu et al. Scand J Gastroenterol 2004

Zarski et al. J Hepatol 1998

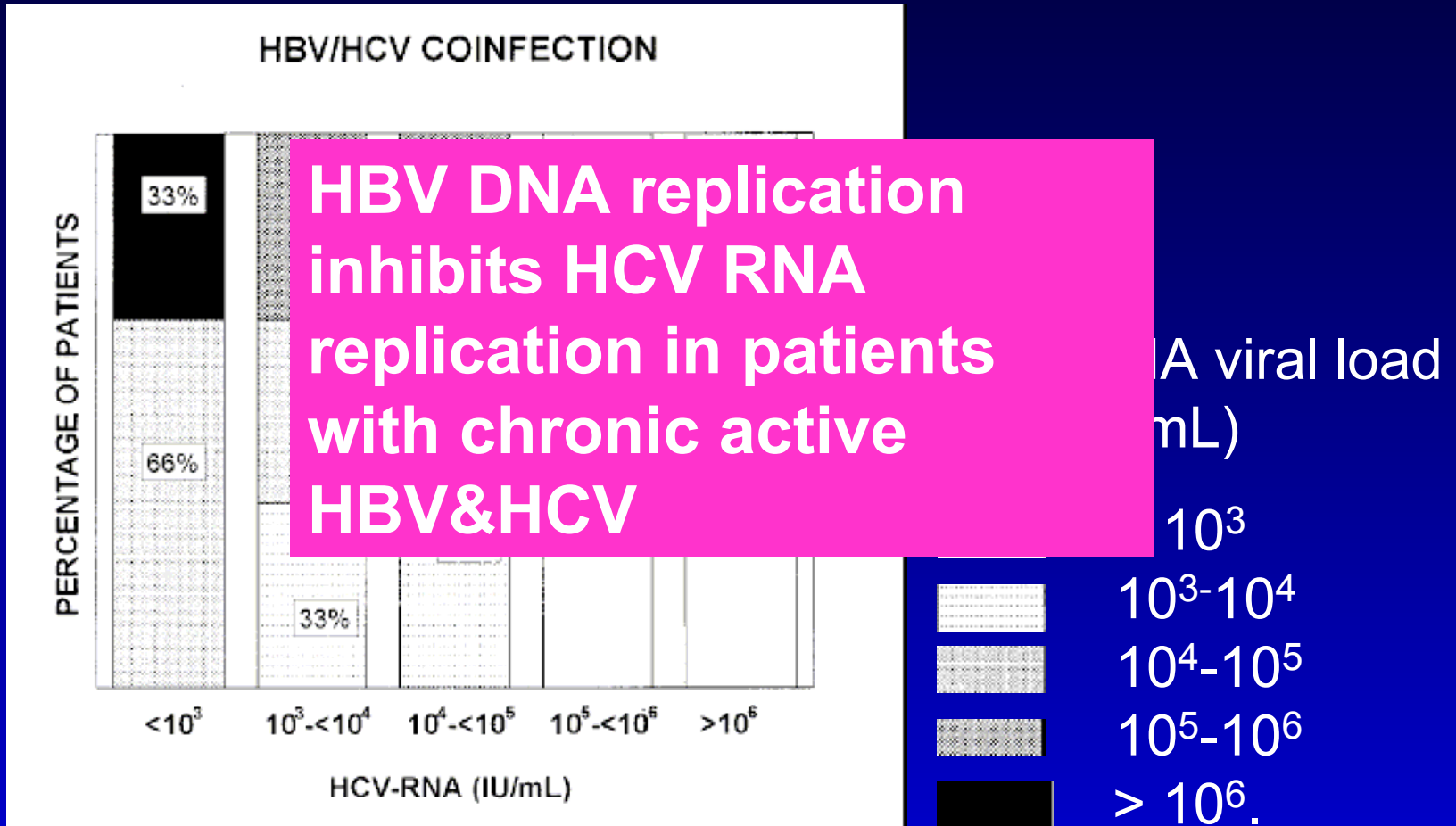
# Impact of HBV on HCV replication



HBV-DNA viral load  
(copies/mL)



# Impact of HBV on HCV replication

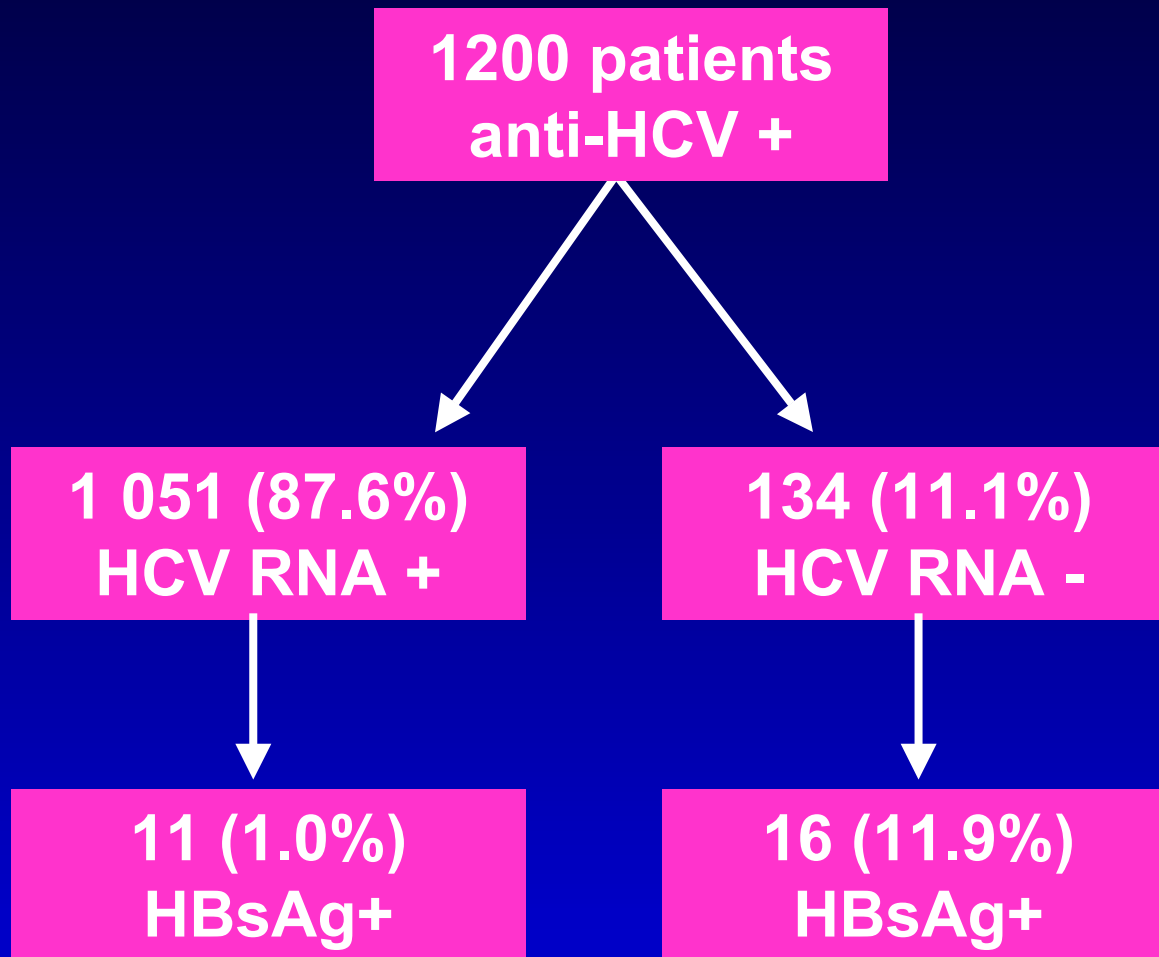


# **Impact of HCV on HBV**



# Impact of HCV on HBV replication

Haushofer et al. J Clin Virol 2002



# Impact of HCV on HBV replication

Haushofer et al. J Clin Virol 2002

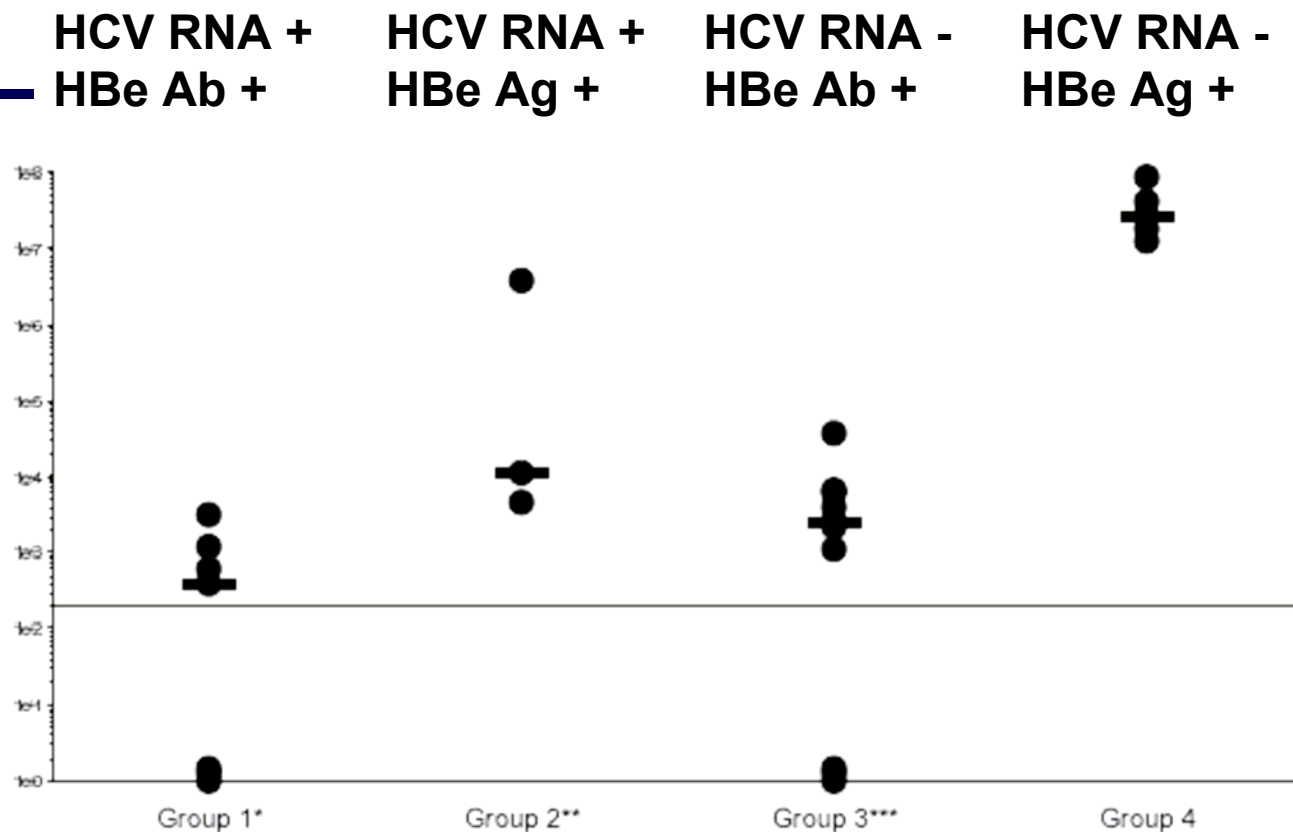


Fig. 1. Serum HBV DNA levels (copies per ml) in patients with serum HCV RNA positivity and HBeAg seroconversion (group 1), in patients with serum HCV RNA positivity and without HBeAg seroconversion (group 2), in patients with serum HCV RNA negativity and HBeAg seroconversion (group 3), and in patients with serum HCV RNA negativity and without HBeAg seroconversion (group 4). \*,  $P < 0.05$  compared with group 2. \*\*,  $P < 0.05$  compared with group 4. \*\*\*,  $P < 0.005$  compared with group 4.

# Impact of HCV on HBV replication

Dai et al. J Gastroenterol Hepatol 2001

**Table 1** Comparison of demographic, clinicopathological and virological features of chronic hepatitis B patients with and without concurrent HCV and HBV infection

	Chronic hepatitis B		<i>P</i>
	HCV infection positive N (%)	HCV infection negative N (%)	
Patients' no.	18	82	
Sex (male/female)	12/6	67/15	NS
Age (year)*	42.8±11.5	33.4±10.5	< 0.05
ALT* (IU/L)	83.8±25.9	200.3±30.3	0.08
HBeAg			< 0.01
Positive	➔ 2 (11%)	➔ 61 (74%)	
Negative	16 (89%)	11 (26%)	
HBV DNA			< 0.05
Positive	➔ 6 (33%)	➔ 65 (79%)	
Negative	12 (67%)	17 (21%)	
HBV-DNA levels* (log Meq/mL)	➔ 6.00±0.63	➔ 7.65±0.38	< 0.001
Histopathology			NS
Chronic persistent hepatitis	4 (22%)	22 (27%)	
Chronic active hepatitis	12 (67%)	51 (62%)	
Liver cirrhosis	2 (11%)	9 (11%)	

\*The continuation variables were represented as mean ± standard deviation.

# Impact of HCV on HBV replication

Dai et al. J Gastroenterol Hepatol 2001

**Table 3** Stepwise logistic regression analysis of factors significantly associated with hepatitis B e antigen seroconversion in chronic hepatitis B virus carriers

Factors	Comparison	Odds ratio (95% CI)
Age	Per year increase	0.932 (0.886–0.980)
Concurrent HCV and HBV infection	Positive versus negative	0.057 (0.012–0.298)

**HCV-core protein can bind to HBV-RNA and suppress HBV gene expression and replication**

**HBV replication would be more effectively inhibited by HCV genotypes 1 and 3 than the remaining HCV genotypes** (HBV core protein and the 101-102 core domain of HCV genotypes 1 and 3 share an important Arg-rich motif)

Shih et al. J Virol 1993

Pontisso et al. Antiviral Therap 1998

## **Interplay of HBV and HCV in cases of combined infection:**

Decreased replication level (or  
supressed activity) of one or both  
viruses: decreased risk of  
transmission?

# **Risk factors for HCV transmission after occupational exposure in health care workers (HCWs): a European case-control study (ANRS)**

Y.Yazdanpanah, G.De Carli, B.Miguères, F.Lot, M.Campins, C.Colombo, T.Thomas, S.Deuffic, A.Tarantola, D.Abiteboul, P.Deny, S.Pol, J.C.Desenclos V. Puro, E.Bouvet.

GERES, Paris, France ; Istituto Nazionale per le Malattie Infettive, Rome, Italy ; InVS, Saint-Maurice , France ; Hospital Vall d'Hebron, Barcelona, Spain; Div.Infect Dis and Hospital Epidemiol, Zurich, Switzerland; HIV & STI Div CDSC, London, UK

# Impact of source patient viral load on HCV transmission - univariate analysis

	Cases (n = 60)	Controls (n = 204)	OR	95%CI
<b>Viral load (source)*</b>				
PCR +	100.0%	85.0%		
PCR -	0.0%	15.0%		
<b>HCV viral load*</b>				
<= 4 log <sub>10</sub> cop/mL	8.3%	40.7%	1.0	
4 < <= 6 log <sub>10</sub> cop/mL	41.7%	37.0%	5.5	0.6-55.5
> 6 log <sub>10</sub> cop/mL	50.0%	22.2%	11.0	1.1-114.1

\*cases = 12, controls = 27

Yazdanpanah ICAAC 2003



# Higher prevalence of occult HBV in patients with HCV

- Study population:
  - 396 patients with HCV-related chronic liver disease and HBsAg-
  - 50 patients with liver disease anti-HCV- HBsAg-
- Liver biopsy and HBV DNA extraction from liver specimens

# Higher prevalence of occult HBV in patients with HCV

TABLE 2. PREVALENCE OF OCCULT HBV INFECTION IN PATIENTS WITH AND WITHOUT CHRONIC HCV INFECTION AND WITH AND WITHOUT ANTIBODIES TO THE HBV CORE ANTIGEN (ANTI-HBc).

PATIENT STATUS	HBV-POSITIVE PATIENTS/ TOTAL
HCV-positive	
Anti-HBc-positive	46/100*
Anti-HBc-negative	20/100
Total	66/200†
HCV-negative	
Anti-HBc-positive	2/7‡
Anti-HBc-negative	5/43
Total	7/50

# HBV DNA levels in patients with occult HBV

- Quantification possible with the development of real-time highly sensitive PCR assays
- 160 anti-HBc-positive/HBsAg-negative sera collected in the diagnostic setting.
- HBV DNA detected in 12.5% of the samples.
  - 70% < 500 geq/ml
  - 30% 500 and 63 000 geq/ml.
- Risk of detecting HBV DNA was increased by a positive HCV serostatus (OR: 5.0, 1.6–15.7)

- Risk of HBV transmission from patients (HCWs) with occult HBV?
  - reported in the past via organ and blood donations from anti-HBc-positive/HBsAg-negative donors

Matsumoto et al., Transfusion 2001  
Chazouilleres et al., Lancet 1994

- Risk of HBV transmission from patients (HCV) Should HBV DNA be performed in  
– re anti-HBc-positive/HBsAg-negative d  
don HCWs infected with HCV? g-  
negative donors

Matsumoto et al., Transfusion 2001  
Chazouilleres et al., Lancet 1994

**HBV + HDV**

# Impact of HDV on HBV replication

- Cases: 65 patients with dual or triple chronic viral hepatitis
  - 25 (38%) by HBV and HCV
  - 18 (28%) by HBV and HDV
  - 22 (34%) by HBV, HCV, and HDV
- Controls: 110 patients with single virus infection:
  - 55 by HBV
  - 55 by HCV
- HBV/HDV coinfection was associated with lower HBV viremia ( $2.5 \times 10^4$  copies/mL) than that found in HBV infection ( $1.2 \times 10^7$  copies/mL) ( $P < .05$ ).

# Conclusion

- Scarce data on co-infection by the HBV HCV viruses in HCWs
- Co-infection by the two viruses is not uncommon.
- In general, decreased replication level of one or both viruses in cases of combined infection

“Publication bias”: decreased replication resulting in none transmission and therefore no case reports published?



# Conclusion

- HBV DNA detection in HCV-infected HCW with isolated antibody to hepatitis B core should be discussed
  - High rate of positivity
  - Risk of transmission

- **Anti-hepatitis B vaccination**