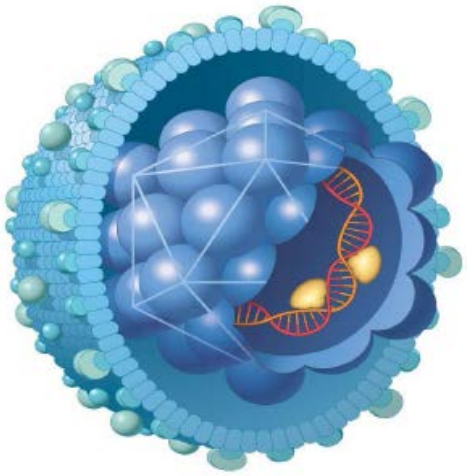
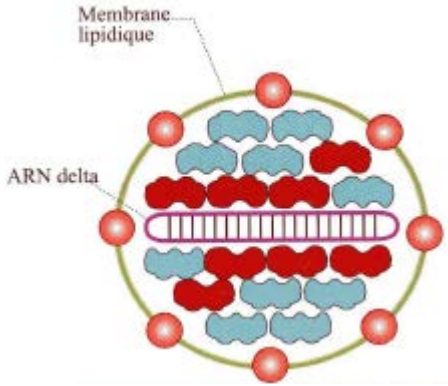
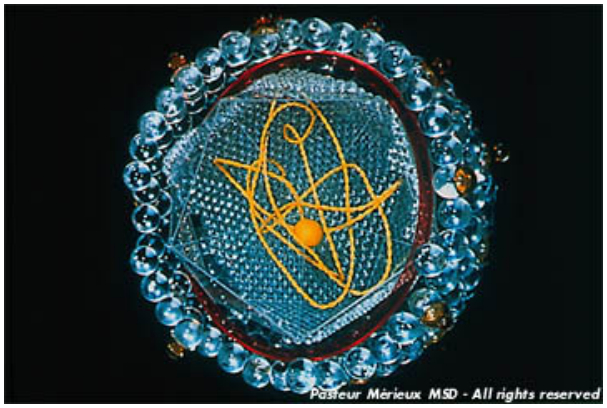
XX^e Journée Régionale de Pathologie Infectieuse
01/10/2013

Interactions virales dans le cadre de la co-infection VHB

Laurence Bocket Laboratoire de Virologie
CHRU de Lille







Replication status and histological features of patients with triple (B, C, D) and dual (B, C) hepatic infections

P. Mathurin,[1,2] V. Thibault,[3] K. Kadidja,[1] N. Ganne-Carrié,[5] J. Moussalli,[1] M. El Younsi,[1] V. Di Martino,[1] F. Lunel,[3] F. Charlotte,[4] M. Vidaud,[2] P. Opolon[1] and T. Poynard[1,2] [1]*Service d'HépatoGastroentérologie,* [2]*CNRS URA 1484 Paris,* [3]*Services de Virologie et* [4]*d'Anatomie-Pathologique, Hôpital Pitié-Salpêtrière and* [5]*Service d'HépatoGastroentérologie, Hôpital Jean Verdier Bondy, France*

Journal of Viral Hepatitis, 2000, 7, 15–22

Table 2 Case control study of patients with triple infection

	Patients with triple infection	Patients with HCV infection alone
No. of patients	16	16
No. of males/females	14/2	14/2
Median age (95% CI)	40.5 (28–46)	39 (30–44)
Alcohol consumption (g day^{-1}): mean ± SD (range)	6.67 ± 10.33 (0–20)	3.95 ± 9.6 (0–30)
Duration of infection (years): median (95% CI)	19.0 (4–22)	15.5 (6–20)
Ethnic origin		
Northern Europe	53%	54%
Mediterranean	47%	46%
Asia	0%	0%
Africa	0%	0%
Drug abusers (%)	60%	31%
Transfusion (%)	7%*	38%
Liver biopsy (no.)	12	16
Activity score: mean ± SD (range)	1.8 ± 0.79 (1–3)	1.13 ± 0.62 (0–2)
median (95% CI)	2 (1–3)†	1 (1–1)
Fibrosis score: mean ± SD (range)	3.3 ± 1.05 (1–4)	2.13 ± 0.8 (1–4)
median (95% CI)	4 (2–4)‡	2 (2–2)
No. with cirrhosis	7/12§	1/16
ALT (upper limit): mean ± SD	12.3 ± 31	2.9 ± 1.53
HBV DNA: mean ± SD (range)	324 ± 1143.6 (0–4130)	
median (95% CI)	0 (0–6)	
PCR HDV	11/11	
HCV RNA detected by amplicor PCR	2/16¶	13/13
HCV viraemia: mean ± SD (range)	3 ± 10.6 (0–42)	66.4 ± 66.3 (2–214)
median (95% CI)	0 (0–0)** ($P < 0.0001$)	54.7 (2.5–87.3)

*$P = 0.05$; †$P = 0.04$; ‡$P < 0.01$; §$P = 0.004$; ¶$P < 0.0001$; **$P < 0.0001$.

Replication status and histological features of patients with triple (B, C, D) and dual (B, C) hepatic infections

P. Mathurin,[1,2] V. Thibault,[3] K. Kadidja,[1] N. Ganne-Carrié,[5] J. Moussalli,[1] M. El Younsi,[1] V. Di Martino,[1] F. Lunel,[3] F. Charlotte,[4] M. Vidaud,[2] P. Opolon[1] and T. Poynard[1,2] [1]*Service d'HépatoGastroentérologie,* [2]*CNRS URA 1484 Paris,* [3]*Services de Virologie et* [4]*d'Anatomie-Pathologique, Hôpital Pitié-Salpêtrière and* [5]*Service d'HépatoGastroentérologie, Hôpital Jean Verdier Bondy, France*

Journal of Viral Hepatitis, 2000, 7, 15–22

Table 2 Case control study of patients with triple infection

	Patients with triple infection	Patients with HCV infection alone
No. of patients	16	16
No. of males/females	14/2	14/2
Drug abusers (%)	60%	31%
Transfusion (%)	7%*	38%
Liver biopsy (no.)	12	16
Activity score: mean ± SD (range)	1.8 ± 0.79 (1–3)	1.13 ± 0.62 (0–2)
median (95% CI)	2 (1–3)†	1 (1–1)
Fibrosis score: mean ± SD (range)	3.3 ± 1.05 (1–4)	2.13 ± 0.8 (1–4)
median (95% CI)	4 (2–4)‡	2 (2–2)
No. with cirrhosis	7/12§	1/16
ALT (upper limit): mean ± SD	12.3 ± 31	2.9 ± 1.53
HBV DNA: mean ± SD (range)	324 ± 1143.6 (0–4130)	
median (95% CI)	0 (0–6)	
PCR HDV	11/11	
HCV RNA detected by amplicor PCR	2/16¶	13/13
HCV viraemia: mean ± SD (range)	3 ± 10.6 (0–42)	66.4 ± 66.3 (2–214)
median (95% CI)	0 (0–0)** ($P < 0.0001$)	54.7 (2.5–87.3)

*$P = 0.05$; †$P = 0.04$; ‡$P < 0.01$; §$P = 0.004$; ¶$P < 0.0001$; **$P < 0.0001$.

16 pts VHC/VHB/VHD vs 16 pts VHC

triple infection: ↗ activité, ALT, fibrose, cirrhose

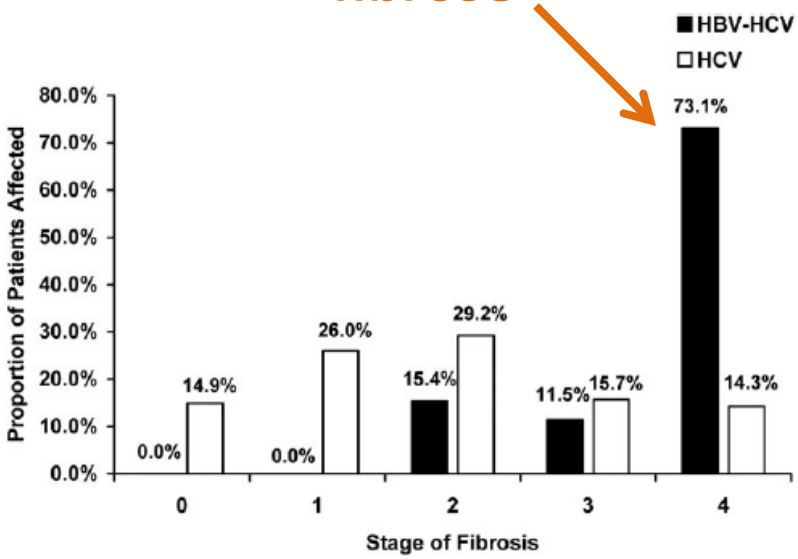
ARN-VHC moins souvent détectable et plus faible

Hepatitis B Virus Infection Among American Patients with Chronic Hepatitis C Virus Infection: Prevalence, Racial/Ethnic Differences, and Viral Interactions

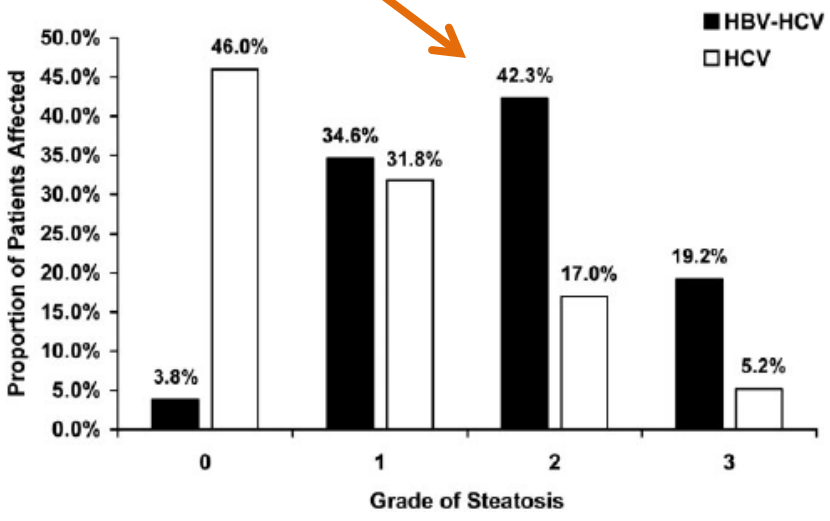
Edmund J. Bini and Ponni V. Perumalswami HEPATOLOGY, Vol. 51, No. 3, 2010

biopsies hépatiques chez 658 VHC+ et 26 VHC+VHB+

fibrose



stéatose



1257 pts VHC+ dont 73 VHB-VHC (5.8%)

ARN-VHC moins élevé

ARN-VHC élevé associé avec ADN-HB bas ou indétectable

VHB - VHD

VHB: 400 millions

VHD: 15 à 20 millions

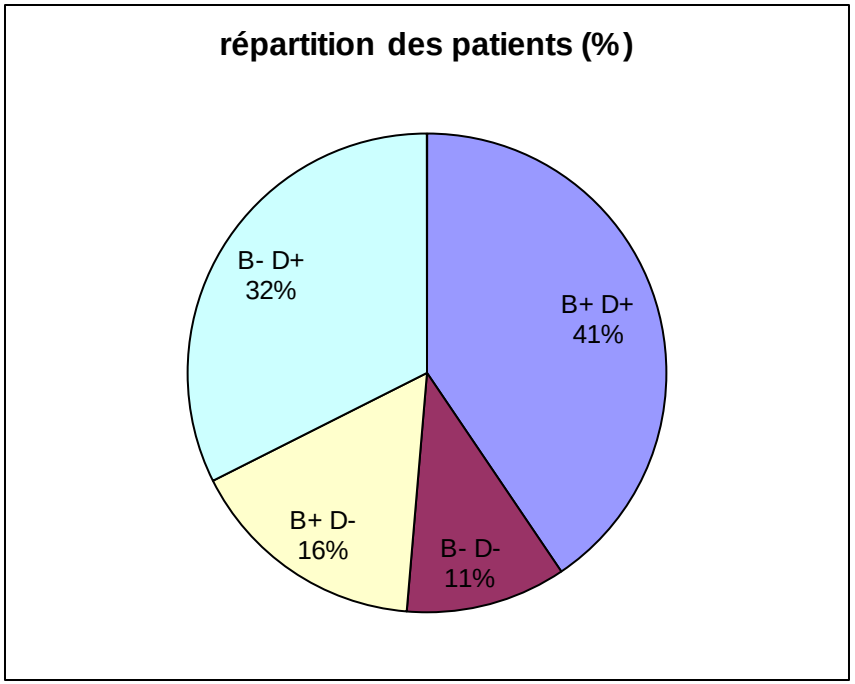
Co-infection VHB-VHD

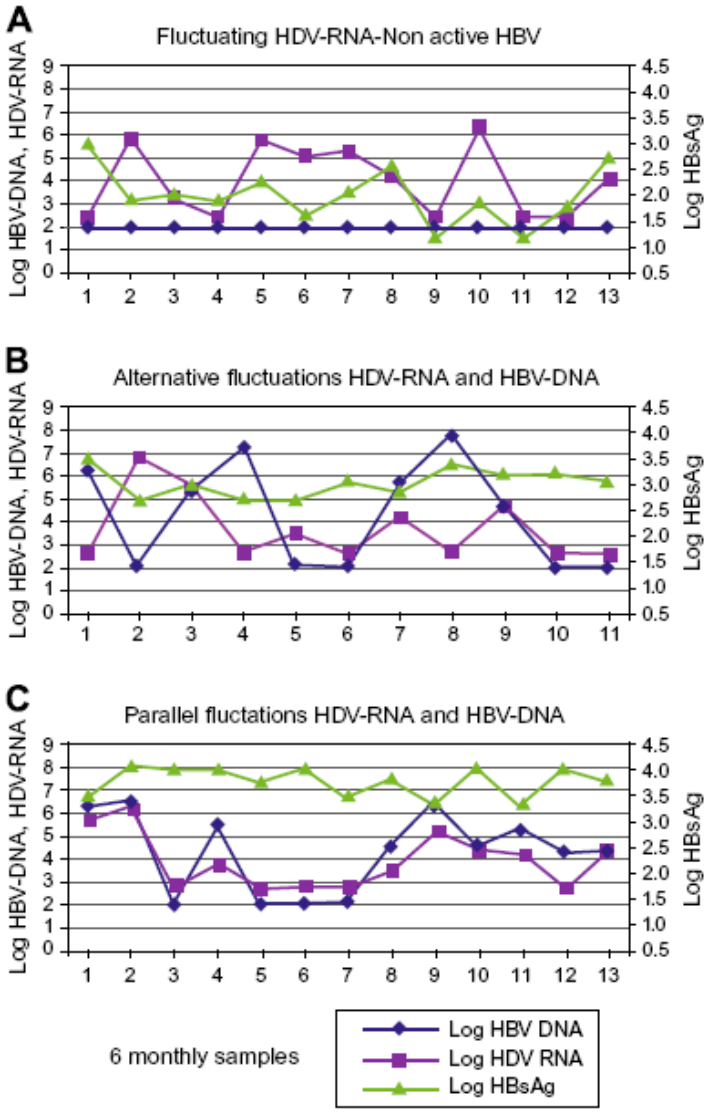
- 15 à 20 millions parmi les 400 millions infectés VHB sont coinfectés B-D
- **la plupart → formes sévères et «incurables»**
- classiquement coinfection B-D ⇒
  - ADN HBV faible ou indétectable mais parfois non (AgHBe +, ADN HB ++, associés à des formes aggressives)
  - et surtout état instable avec taux fluctuants, profil réplicatif complexe et dynamique
- **HDV augmente la chronicité VHB donc augmente le réservoir de virus B**

Quantitative longitudinal evaluations of hepatitis delta virus RNA and hepatitis B virus DNA shows a dynamic, complex replicative profile in chronic hepatitis B and D

Melanie Schaper[1], Francisco Rodriguez-Frias[1,3,*], Rosendo Jardi[1,3], David Tabernero[3], Maria Homs[3], Gerardo Ruiz[1], Josep Quer[2,3], Rafael Esteban[2,3], Maria Buti[2,3]

37 patients





Journal of Hepatology **2010** vol. 52 | 658–664

JOURNAL OF VIROLOGY, Jan. 2011, p. 432–439 Vol. 85, No. 1
0022-538X/11/$12.00 doi:10.1128/JVI.01609-10
Copyright © 2011, American Society for Microbiology. All Rights Reserved.

Replicative and Transcriptional Activities of Hepatitis B Virus in Patients Coinfected with Hepatitis B and Hepatitis Delta Viruses[▽]†

Teresa Pollicino,[1]* Giuseppina Raffa,[1] Teresa Santantonio,[2] Giovanni Battista Gaeta,[3] Giuliano Iannello,[4] Angela Alibrandi,[5] Giovanni Squadrito,[1] Irene Cacciola,[1] Chiara Calvi,[6] Giuseppe Colucci,[7] Massimo Levrero,[8] and Giovanni Raimondo[1]

Replicative and Transcriptional Activities of Hepatitis B Virus in Patients Coinfected with Hepatitis B and Hepatitis Delta Viruses[▽†]

TABLE 1. Demographic, virologic, and histological characteristics of patients with and without HDV infection

Parameter	Value		*P* value[a]
	HDV-positive patients	HDV-negative patients	
No. of males/total no. of patients	11/21	17/22	NS
Median (range) age (yr)	43.5 (30–58)	43 (14–62)	NS
No. of HBeAg-positive patients/no. of HBeAg-negative patients	3/18	8/14	0.007
No. of patients with HBV genotype			
D	20	18	NS
A	1	3	NS
C	0	1	NS
No. of patients with stage of fibrosis[b]			
0–1	5	6	NS
2	6	5	NS
3–4	10	11	NS
No. of patients with grade of activity[b]			
1	5	6	NS
2	11	15	NS
3	5	1	NS

[a] NS, not significant.
[b] Histological staging and grading were performed according to the classification method of Scheuer (25).

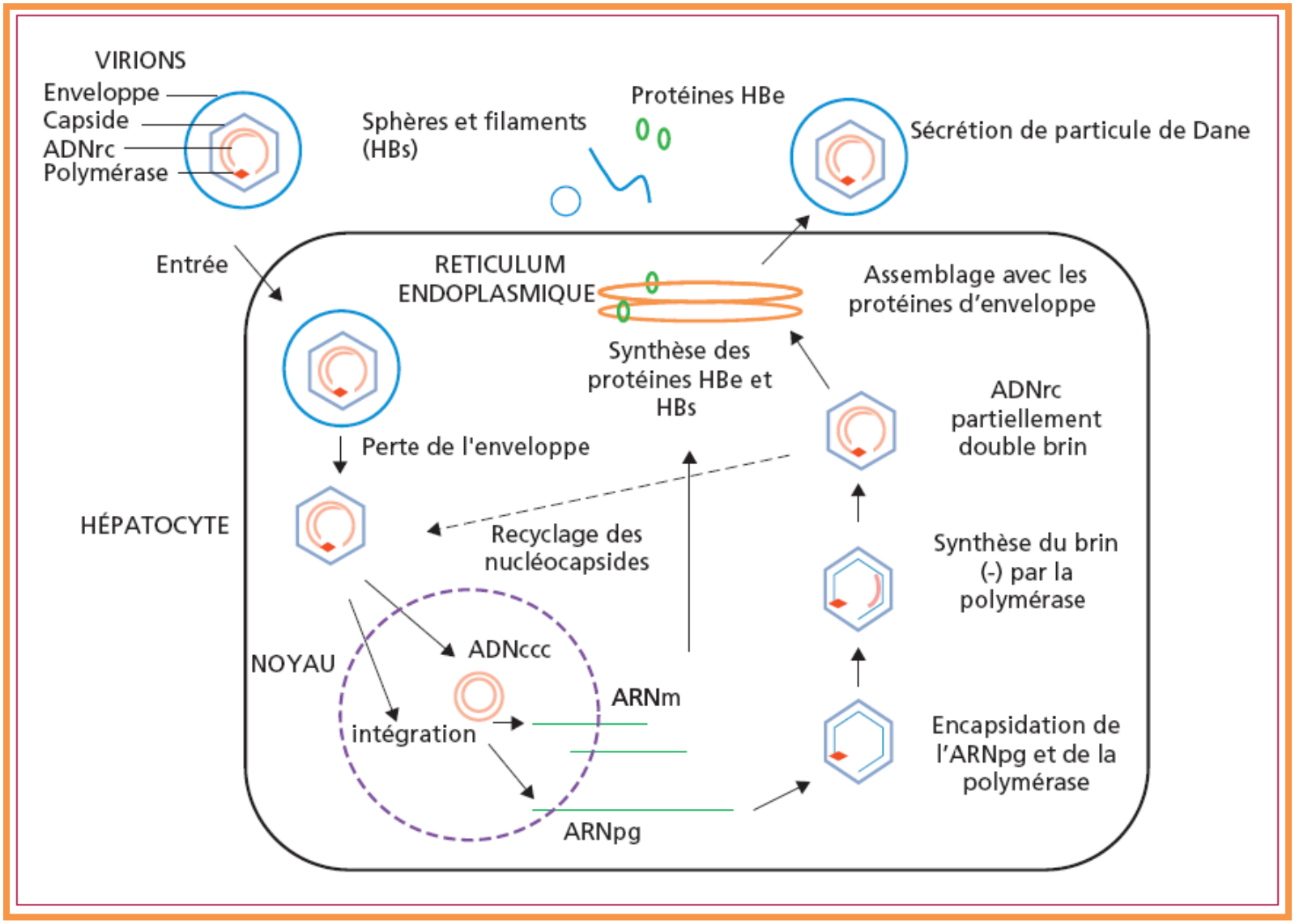
21 patients B-D comparés à 22 patients B

mesures / PCR

- tissus hépatique:
  - HBV DNA, cccDNA, pgRNA, préS/S mRNA, HDV RNA
    (→ HBV rc DNA : relaxed circular replicative DNA= HBVDNA – ccc DNA)
- serum
  - HBV DNA, qtHBs Ag, HDV RNA

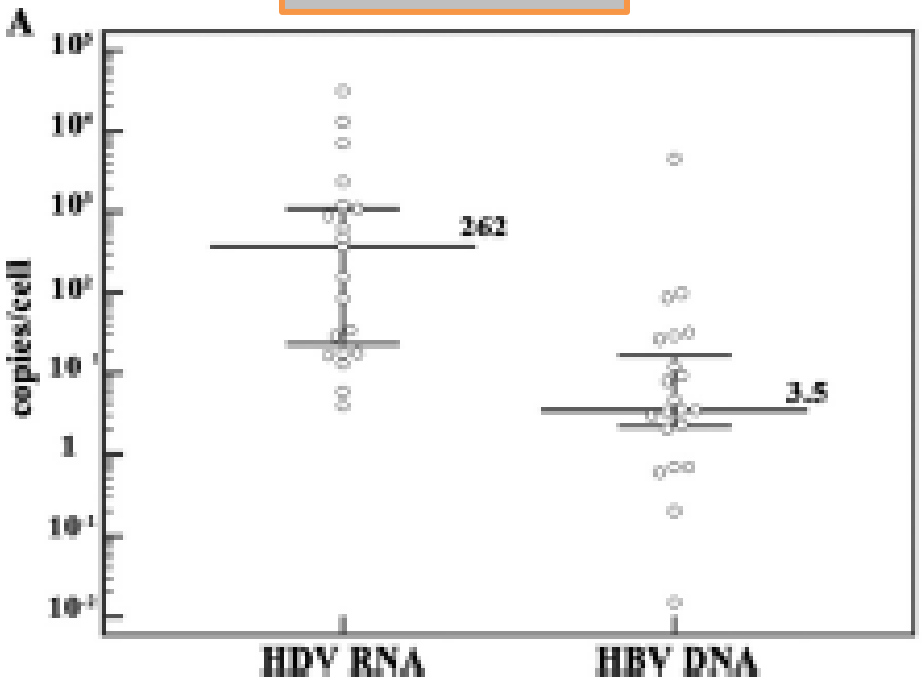
Hépatite B: le cycle viral

Lebossé et al Hépato Gastro 2012

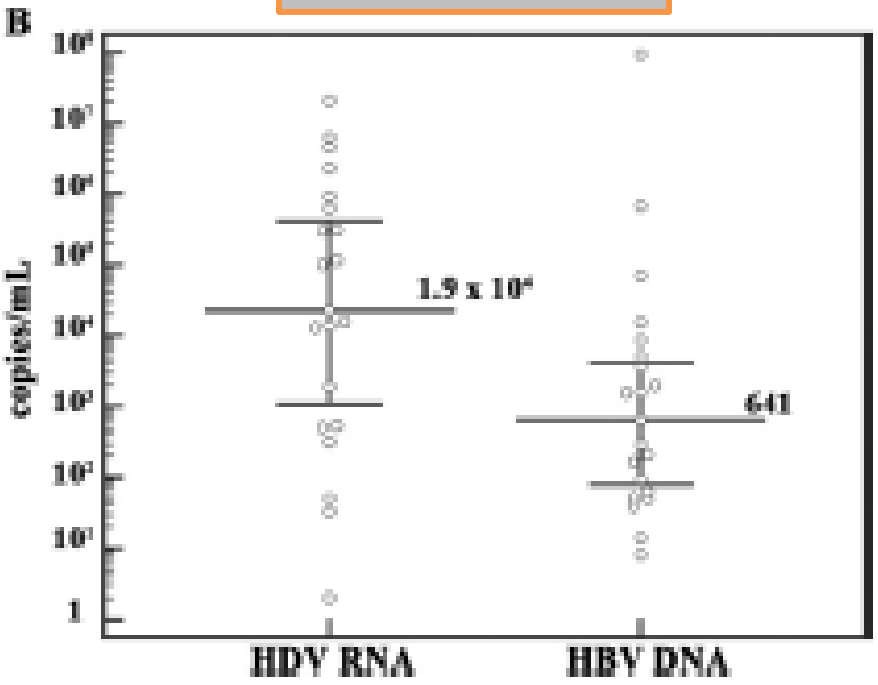


quantifications virales B et D

FOIE

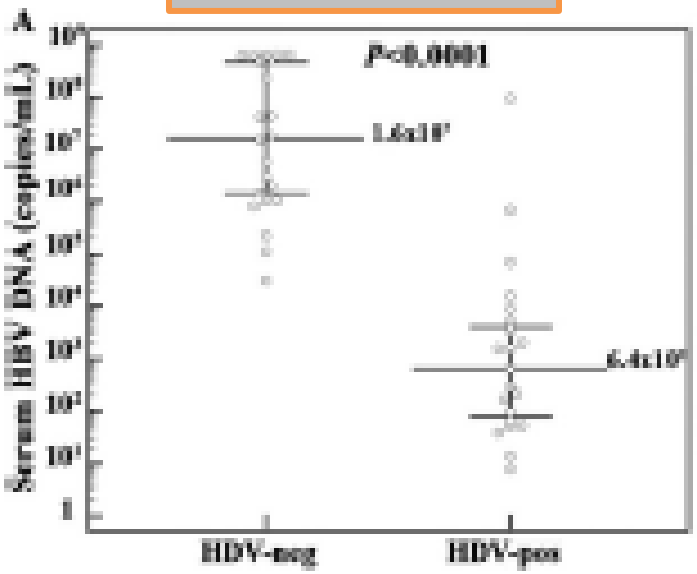


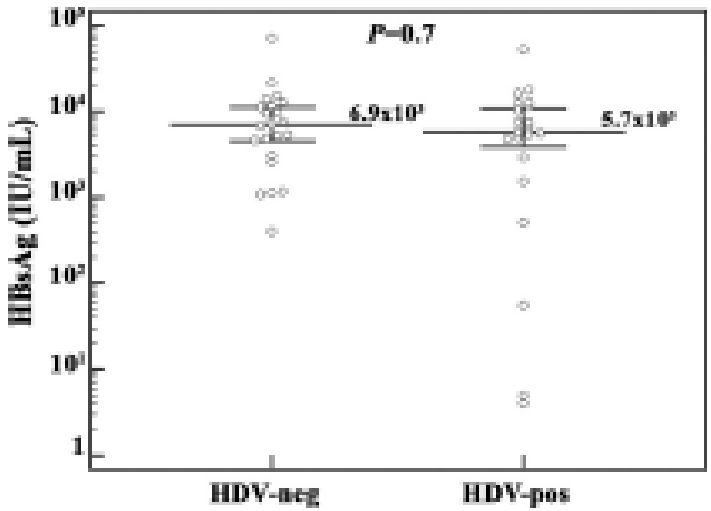
SERUM



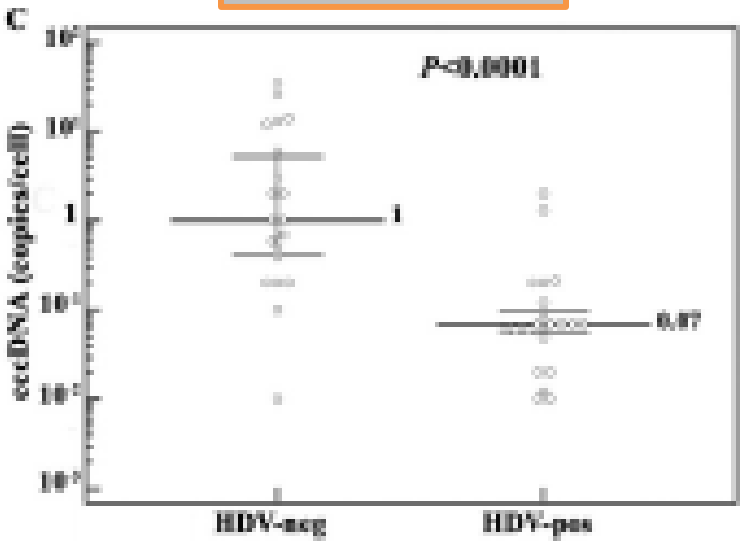
impact VHD / VHB

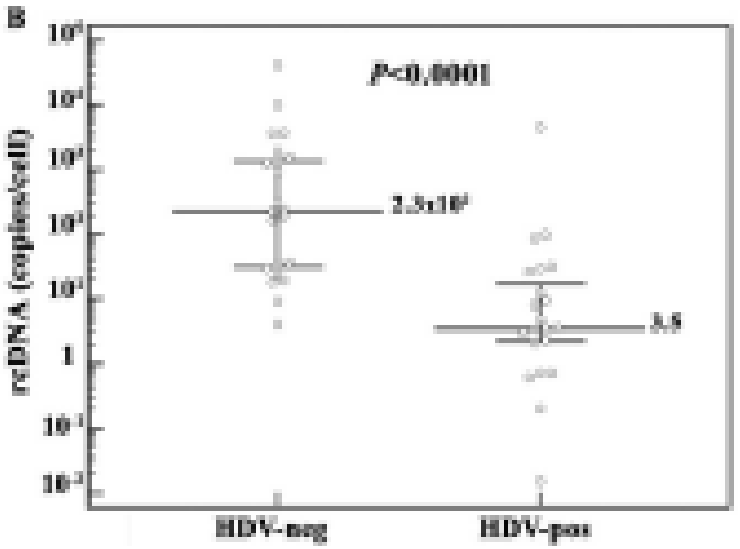
SERUM

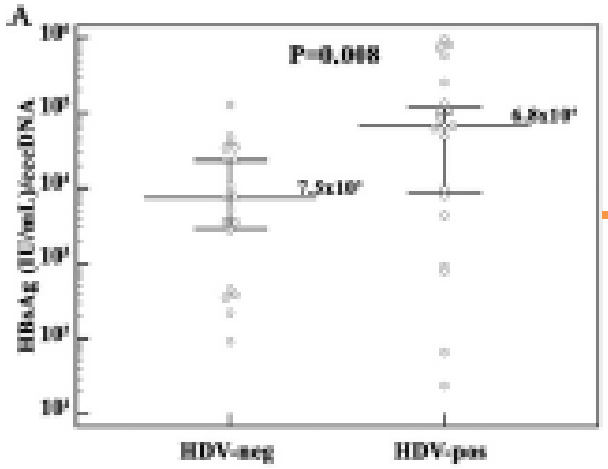


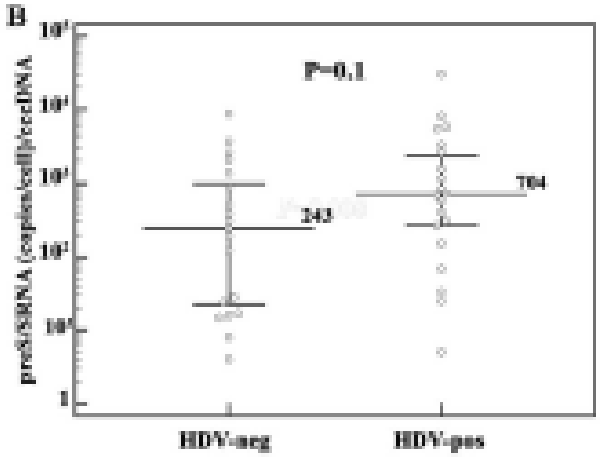


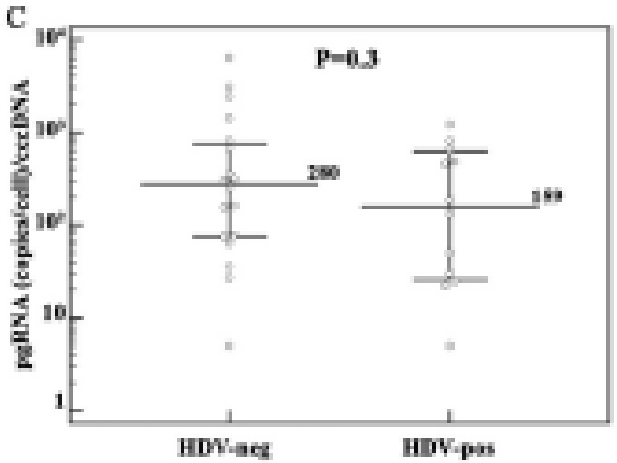
FOIE











impact VHD / VHB

- confirmation de la « domination » du VHD avec hypothèse d'une dissociation entre réplication et transcription VHB induite par VHD
- association significative entre HDV-RNA et cccDNA

⇒1/ suivi important (labilité et fluctuation HDV-RNA et AgHBs ds le sérum)

⇒2/ analogues nucléos(t)idiques antiVHB : peu d'effets sur cccDNA et AgHBs donc peu à même de lutter contre HDV

VHB - VHC

VHB: 400 millions

VHC: 170 millions

Current Concepts of HBV/HCV Coinfection: Coexistence, but Not Necessarily in Harmony

Shailaja Jamma, MD, **Ghazi Hussain, MD**, and **Daryl T.-Y. Lau, MD, MSc, MPH**
Liver Center, Division of Gastroenterology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA

Curr Hepat Rep. 2010 ; 9(4): 260–269.

- co-infection fréquente, mêmes modes de transmission, tous les scénarios possibles: co-infection aiguë, surinfection VHC/VHB ou VHB/VHC…
- prévalence VHC chez porteurs chroniques VHB: 7 à 22%

  $\Rightarrow$ 25 à 50 millions personnes concernées /monde
- prévalence marqueurs séro VHB chez patients VHC + aux USA: 25% soit 6 fois plus que chez VHC –
- fréquence accrue des infections HBV occultes et anti-HBc isolés:
  - 12 à 44% patients VHC+ sont ADN-HB + en absence d'AgHBs

  $\Rightarrow$ sous-estimation de la co-infection B-C
- risque d'hépatite fulminante majoré et développement accru cirrhose et HCC

co-infection VHB-VHC

- **observations précédentes:**
  - relation inverse entre les taux de réplication des 2 virus
  - patients VHB chroniques se surinfectant/VHC « guérissent » du VHB (l'inverse également)
  - réactivation VHB après guérison VHC chronique

⇒ interactions entre les deux virus

Fong et al, Hepatology 1991; Dai et al, J Gastroenterol Hepatol 2001, Liaw et al Gastroenterology 2004 , Potthoff et al J Hepatol 2008

co-infection VHB-VHC

- interactions difficiles à analyser en raison du manque de systèmes de culture
- études basées sur expression des protéines virales $\rightarrow$ résultats contradictoires: effet inhibiteur ou «enhancer» des protéines de core VHC et NS5a sur la réplication VHB
- immunité innée et/ou acquise (cytokines, IFN, facteurs de restriction …)

Schuttler et al J Hepatol 2002; Chen et al J Biol Chem 2003; Pasquinelli et al Hepatology 1997; Pan et al Biochem Biophys Res Commun 2007;Brass et al J Hepatol 2009

co-infection VHB-VHC

Hepatitis B virus and hepatitis C virus interaction in Huh-7 cells☆

Nicholas S. Eyre[1,2], Renee J. Phillips[1,2], Scott Bowden[3], Evelyn Yip[1,2], Ben Dewar[3], Stephen A. Locarnini[3], Michael R. Beard[1,2,*]

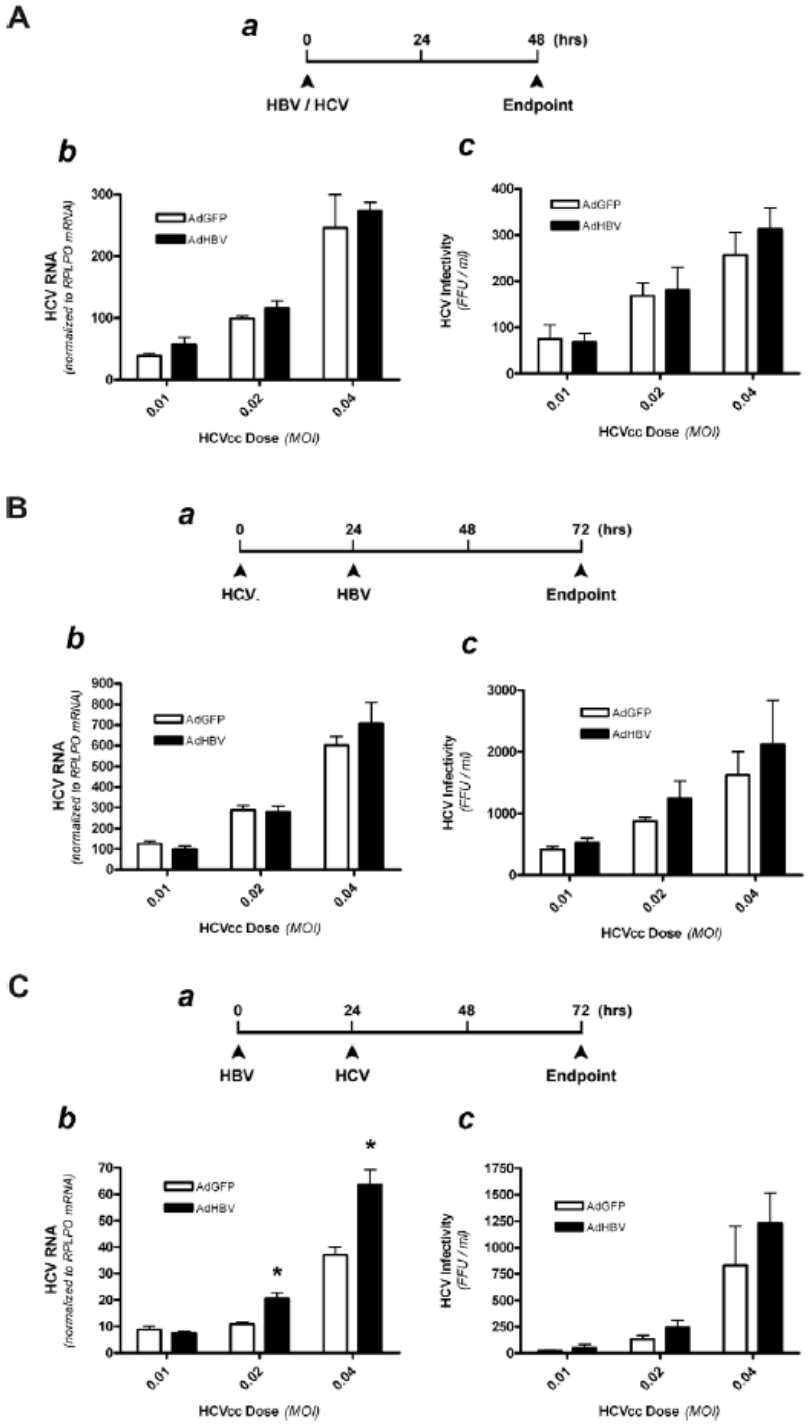
[1]*Infectious Diseases Laboratories, Institute of Medical and Veterinary Sciences, Adelaide, SA, Australia*
[2]*School of Molecular and Biomedical Science, University of Adelaide, Gate 8, Victoria Drive, Adelaide, SA 5005, Australia*
[3]*Victorian Infectious Diseases Reference Laboratories, North Melbourne, Vic., Australia*

Journal of Hepatology 51 (2009) 446–457

Hepatitis B and C Virus Coinfection: A Novel Model System Reveals the Absence of Direct Viral Interference

Pantxika Bellecave,[1] Jérôme Gouttenoire,[1] Markus Gajer,[2] Volker Brass,[2] George Koutsoudakis,[3] Hubert E. Blum,[2] Ralf Bartenschlager,[3] Michael Nassal,[2] and Darius Moradpour[1]

HEPATOLOGY, Vol. 50, No. 1, 2009



Hepatitis B virus and hepatitis C virus interaction in Huh-7 cells☆

Nicholas S. Eyre[1,2], Renee J. Phillips[1,2], Scott Bowden[3], Evelyn Yip[1,2], Ben Dewar[3], Stephen A. Locarnini[3], Michael R. Beard[1,2,*]

méthodes:

-¢ Huh-7 permettant co-réplication VHB et VHC

-virus recombinant Ad-VHB (vs Ad-GFP)

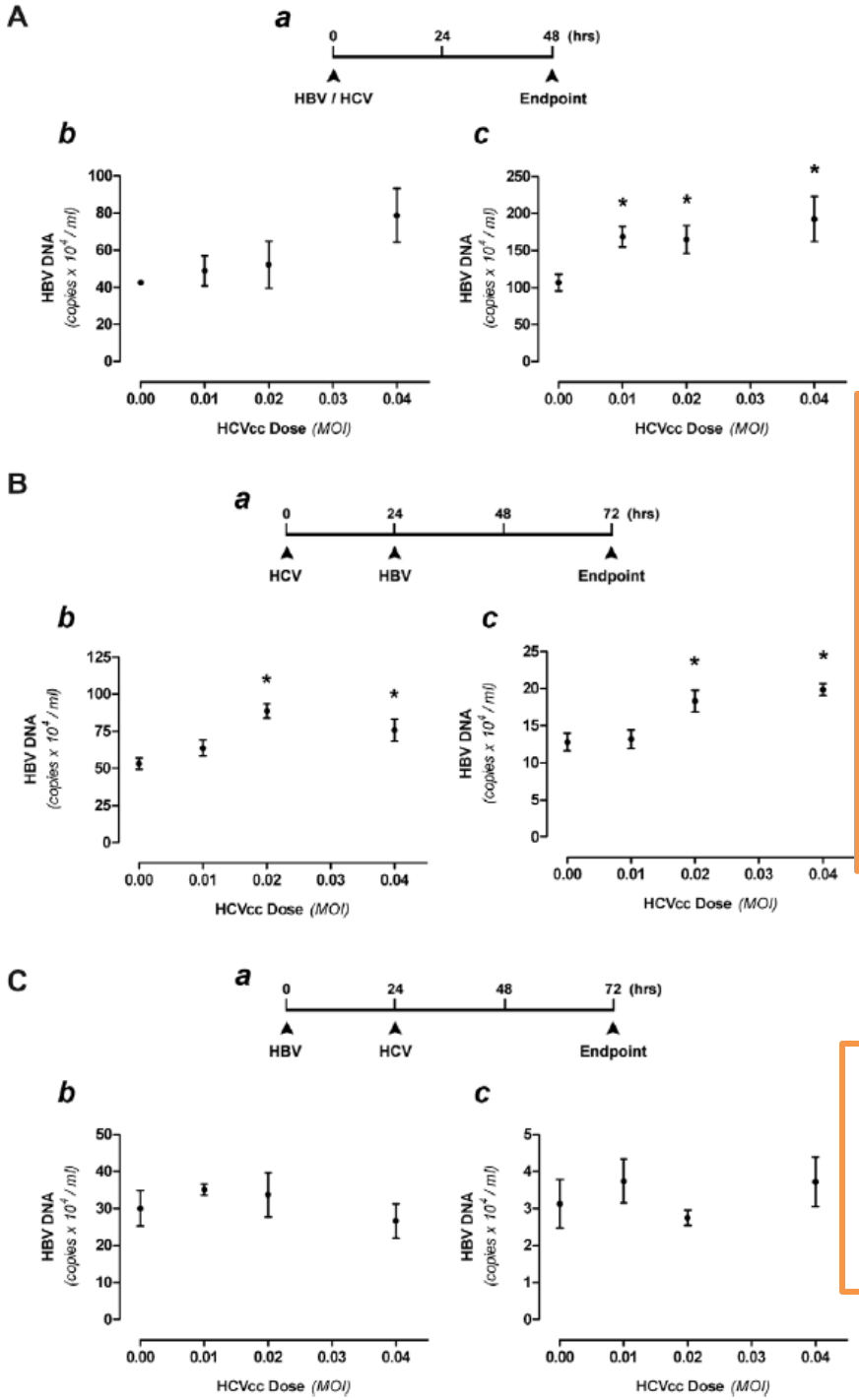
-détection production VHC / IF + PCR

-≠ scenarios testés (A B C)

résultat B sur C

pas d'effet de VHB sur réplication VHC (voire légère ↗ production VHC)

(b: ARN-VHC/surnageant c: infectivité (FFU))



Hepatitis B virus and hepatitis C virus interaction in Huh-7 cells☆

Nicholas S. Eyre[1,2], Renee J. Phillips[1,2], Scott Bowden[3], Evelyn Yip[1,2], Ben Dewar[3], Stephen A. Locarnini[3], Michael R. Beard[1,2,*]

méthodes:

-¢ Huh-7 permettant co-réplication VHB et VHC

- détection ADN-VHB intracellulaire et secrété/PCR

-≠ scenarios testés (A B C)

résultat C sur B

pas d'effet de VHC sur réplication VHB (voire légère ↗ production VHB)

(b: ADN HB intracellulaire c: ADN HB secrété)

Hepatitis B virus and hepatitis C virus interaction in Huh-7 cells☆

Nicholas S. Eyre[1,2], Renee J. Phillips[1,2], Scott Bowden[3], Evelyn Yip[1,2], Ben Dewar[3], Stephen A. Locarnini[3], Michael R. Beard[1,2,*]

- discussion
  - ni HBV ni HCV n'entravent directement le cycle réplicatif de l'autre virus dans les hépatocytes co-infectés
  - système permettant l'étude des potentielles interactions virales de façon « isolée » du système immunitaire et des cytokines produites par les hépatocytes infectés

  ⇒ **les «facteurs de l'hôte» sont très probablement les déterminants majeurs de suppression et/ou dominance d'un virus sur l'autre.**

Hepatitis B and C Virus Coinfection: A Novel Model System Reveals the Absence of Direct Viral Interference

Pantxika Bellecave,[1] Jérôme Gouttenoire,[1] Markus Gajer,[2] Volker Brass,[2] George Koutsoudakis,[3] Hubert E. Blum,[2] Ralf Bartenschlager,[3] Michael Nassal,[2] and Darius Moradpour[1]

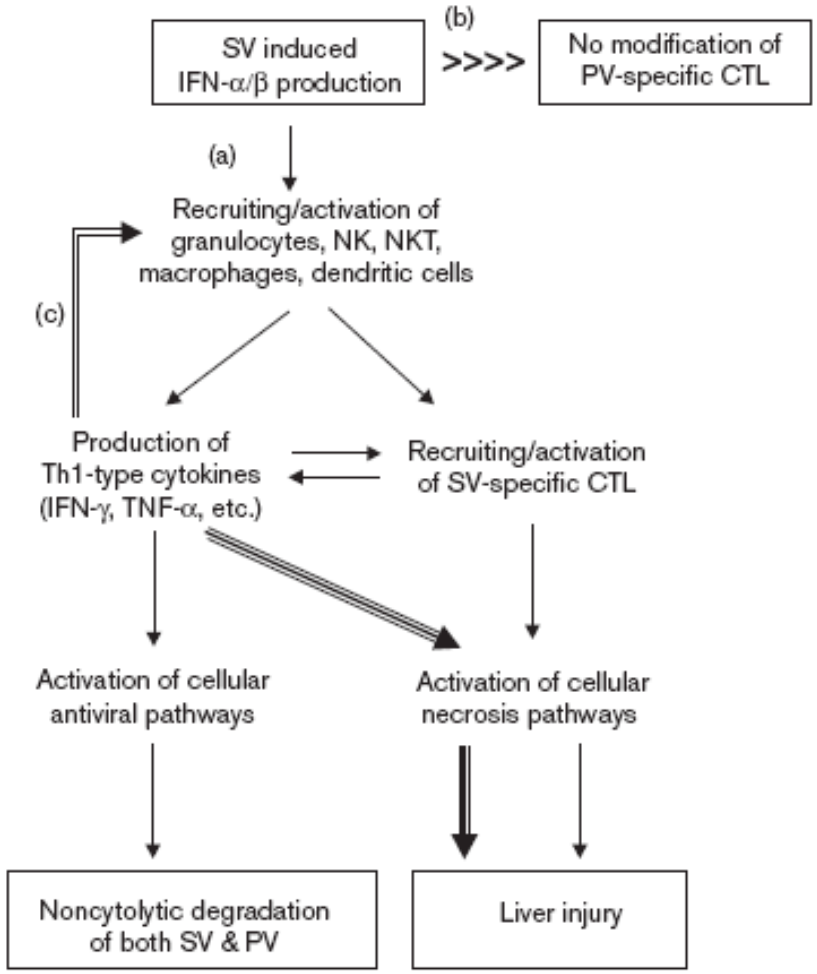
- même modèle in vitro: ¢ Huh-7, produisant VHC de façon constitutive et VHB de façon inductible (contrôle / tétracycline)
- test de ≠ inhibiteurs VHB ou VHC
- aucune interférence VHB-VHC
- pas d'interférence VHB sur l'effet antiviral anti-VHC de l'IFNα
- pas de conséquences sur la réplication de l'autre virus quand un des 2 est spécifiquement inhibé (Telaprevir, Lamivudine, Adefovir)

⇒ interférence in vivo liée aux facteurs de l'hôte, immunitaires et cellulaires (réponse innée et adaptive)

Viral interaction and clinical implications of coinfection of hepatitis C virus with other hepatitis viruses

Lan Lin[a], Chris Verslype[a], Jos F. van Pelt[a], Marc van Ranst[b] and Johan Fevery[a]

European Journal of Gastroenterology & Hepatology 2006, 18:1311–1319



HAV, HBV ± HDV sur HCV

- interactions virus-virus et virus-¢

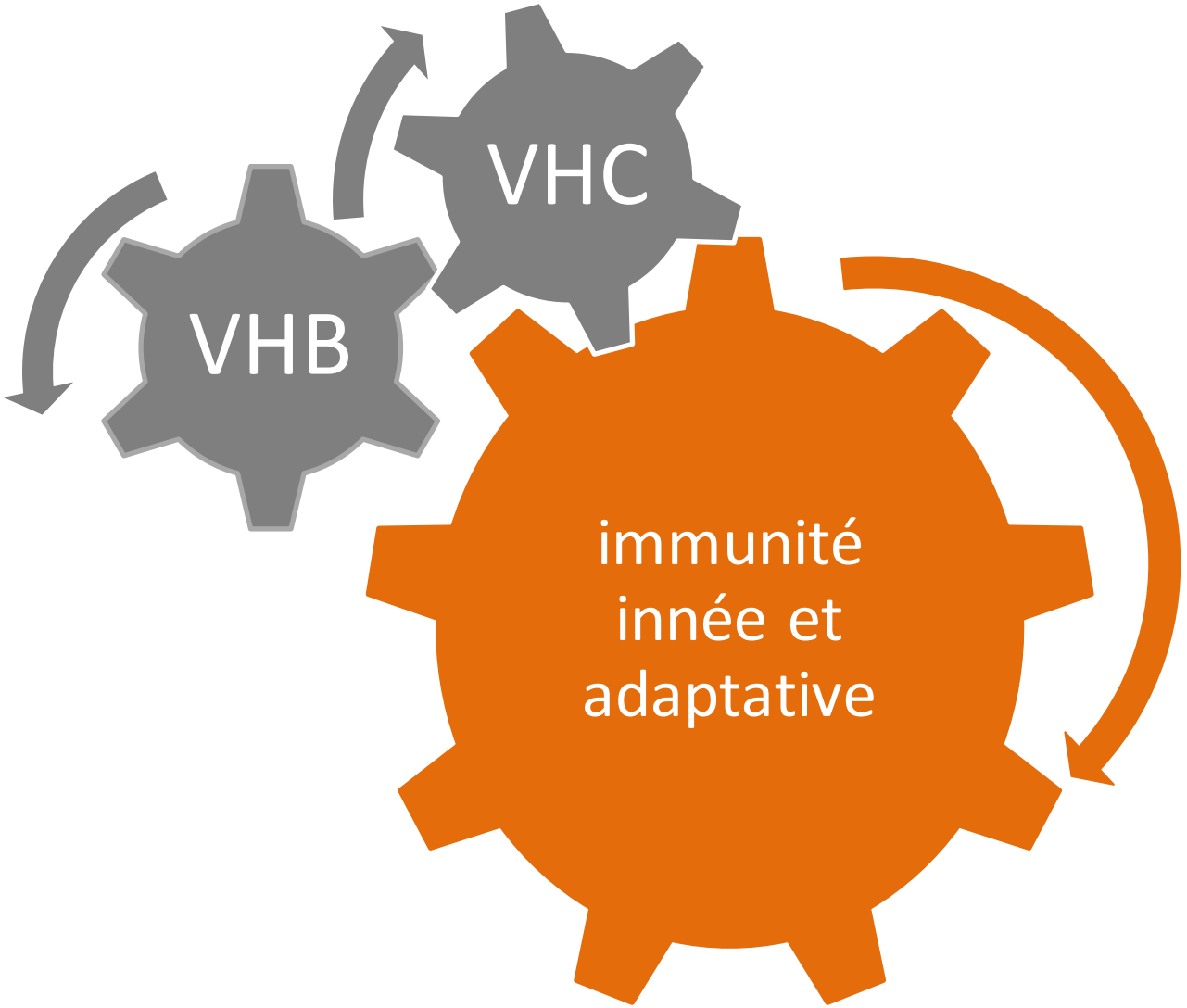
- majoration réponse immune

- voie commune nécro-inflammatoire

⇒ hépatocarcinogénèse

SV: virus surinfectant PV: virus pré-existant

immunité / facteurs de l'hôte



VHC ± VHB ± VHD ± VIH

Viral Interference Between Hepatitis B, C, and D Viruses in Dual and Triple Infections in HIV-Positive Patients

Giulia Morsica, Sabrina Bagaglio,* Paola Cicconi,† Maria R. Capobianchi,‡ Giampietro Pellizzer,§ Pietro Caramello,‖ Anna Orani,¶ Cristina Moioli,# Giuliano Rizzardini,** Caterina Uberti-Foppa,* Massimo Puoti,†† and Antonella d'Arminio Monforte,† for the Hepa I.C.o.N.A ‡‡ the Icona Foundation§§ Study Groups*

J Acquir Immune Defic Syndr 2009;51:574–581

TABLE 1. Characteristics of the HIV-Infected Patients With Concomitant HBV/HCV Infection (Group 1BC) and the Control Groups of Patients With HBV (Group 2B) or HCV (Group 3C)

	1BC	2B	3C	1BC vs 2B *P*	1BC vs 3C *P*
No. patients	21	18	33	—	—
Males	18	16	25	0.76	0.37
Age (yrs)	35 (31–38)*	40 (33–44)	35 (32–39)	0.009	0.22
Risk factors for HIV					
Man with man sex	2	7	2	<0.0001	0.78
Heterosexual contacts	2	9	2		
IVDU	17	2	29	—	—
AST (IU/L)	61 (31–100)*	37 (28–65)	38 (32–59)	0.13	0.08
ALT (IU/L)	83 (50–150)*	41 (32–97)	52 (35–65)	0.03	0.06
$CD4^+$ (cells/μL)	372 (214–565)*	372 (199–605)	261 (162–573)	0.39	0.33
$CD8^+$ (cells/μL)	1058 (851–1285)*	1177 (857–1454)	1027 (621–1366)	0.33	0.32

*Median values and IQR.
AST, aspartate aminotransferase.

ALT significativement ↗ dans le groupe VIH-VHB-VHC

Viral Interference Between Hepatitis B, C, and D Viruses in Dual and Triple Infections in HIV-Positive Patients

Giulia Morsica, Sabrina Bagaglio,* Paola Cicconi,† Maria R. Capobianchi,‡ Giampietro Pellizzer,§ Pietro Caramello,‖ Anna Orani,¶ Cristina Moioli,# Giuliano Rizzardini,** Caterina Uberti-Foppa,* Massimo Puoti,†† and Antonella d'Arminio Monforte,† for the Hepa I.C.o.N.A ‡‡ the Icona Foundation§§ Study Groups*

J Acquir Immune Defic Syndr 2009;51:574–581

TABLE 2. Virological Findings in HIV-Infected Subjects by Hepatitis Virus Coinfection

	1BC	2B	3C	1BC vs 2B *P*	1BC vs 3C *P*
No. patients	21	18	33	—	—
HIV RNA (log_{10} copies/mL)	3.9 (2.9–4.7)*	4.03 (3.7–4.7)	4.45 (3.6–4.9)	0.28	0.28
HBV DNA (pos/neg)	16/5	18/0	0/33	0.02	//
HBV DNA (log_{10} copies/mL)	3.9 (3.0–7.0)*	5.4 (4.6–8.9)	//	0.002	//
HBV genotype†				0.0071	//
A	1	1	//	—	—
D	12	4	//	—	—
G	—	6	//	—	—
HCV RNA (pos/neg)	12/9	//	33	//	<0.0001
HCV RNA (log_{10} copies/mL)	5.7 (2.7–6.3)*	//	6.1 (5.7–6.2)	//	0.10
HCV genotype				//	0.49
1	9/12‡	//	17/31§	—	—
2	0	//	1/31	—	—
3	3/12	//	9/31	//	—
4	0	//	4/31	—	—
HDV RNA (pos/neg)	9/12	2/16	//	0.028	//

*Median values and IQR.
†In group 1BC, HBV genotype was determined in 13 of 16 HBV DNA–positive specimens.
‡HCV genotype was determined in 12 of 18 specimens because 6 subjects were HCV RNA negative.
§In group 3C, 2 of 33 genotypings were unsuccessful.
Pos, positive; neg, negative.

Viral Interference Between Hepatitis B, C, and D Viruses in Dual and Triple Infections in HIV-Positive Patients

Giulia Morsica, Sabrina Bagaglio,* Paola Cicconi,† Maria R. Capobianchi,‡ Giampietro Pellizzer,§ Pietro Caramello,‖ Anna Orani,¶ Cristina Moioli,# Giuliano Rizzardini,** Caterina Uberti-Foppa,* Massimo Puoti,†† and Antonella d'Arminio Monforte,† for the Hepa I.C.o.N.A ‡‡ the Icona Foundation§§ Study Groups*

J Acquir Immune Defic Syndr 2009;51:574–581

TABLE 2. Virological Findings in HIV-Infected Subjects by Hepatitis Virus Coinfection

	1BC	2B	3C	1BC vs 2B *P*	1BC vs 3C *P*
No. patients	21	18	33	—	—
HIV RNA (log_{10} copies/mL)	3.9 (2.9–4.7)*	4.03 (3.7–4.7)	4.45 (3.6–4.9)	0.28	0.28
HBV DNA (pos/neg)				0.02	//
HBV DNA (log_{10} copies/mL)				0.002	//
HBV genotype†				0.0071	//
A				—	—
D				—	—
G				—	—
HCV RNA (pos/neg)				//	<0.0001
HCV RNA (log_{10} copies/mL)				//	0.10
HCV genotype				//	0.49
1				—	—
2				—	—
3				//	—
4				—	—
HDV RNA (pos/neg)				0.028	//

VIH + VHB + VHC vs VIH+VHB:

- **HB-DNA peut être négatif**
- **HB-DNA taux + faible**
- **HC-RNA peut être négatif**
- **HD-ARN plus souvent +**

*Median values and IQR.
†In group 1BC, HBV genotype was determined in 13 of 16 HBV DNA–positive specimens.
‡HCV genotype was determined in 12 of 18 specimens because 6 subjects were HCV RNA negative.
§In group 3C, 2 of 33 genotypings were unsuccessful.
Pos, positive; neg, negative.

Impact of Hepatitis D Virus Infection on the Long-Term Outcomes of Patients with Hepatitis B Virus and HIV Coinfection in the Era of Highly Active Antiretroviral Therapy: A Matched Cohort Study

Wang-Huei Sheng,[1] Chien-Ching Hung,[1] Jia-Horng Kao,[1,2] Sui-Yuan Chang,[3] Mao-Yuan Chen,[1] Szu-Min Hsieh,[1] Pei-Jer Chen,[1,2] and Shan-Chwen Chang[1]

[1]Department of Internal Medicine, National Taiwan University Hospital, [2]Graduate Institutes of Clinical Medicine, and [3]Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University College of Medicine, Taipei, Taiwan

Table 3. Hepatic, immunologic, virologic, and final outcomes for patients with HIV, hepatitis B virus (HBV), and hepatitis D virus (HDV) coinfection and patients with HIV-HBV coinfection.

Characteristic	HIV-HBV-HDV coinfected (n = 26)	HIV-HBV coinfected (n = 78)	Adjusted OR or HR[a] (95% CI)	P
Hepatitis flares	15 (57.7)	18 (23.1)	5.88 (1.96–17.54)	.002
Hyperbilirubinemia	9 (34.6)	11 (14.1)	3.40 (1.06–10.71)	.04
Cirrhosis	7 (26.9)	4 (5.1)	12.8 (1.78–72.89)	.009
Hepatic decompensation	6 (23.1)	4 (5.1)	9.68 (2.21–42.44)	.007
Hepatocellular carcinoma	1 (3.8)	2 (2.6)	1.57 (0.13–37.11)	.58
Increase in CD4$^+$ cell count				
Median cells/μL(range)	201 (4–768)	237 (2–835)	…	.69
≥100 cells/μL	20 (76.9)	63 (80.8)	0.69 (0.23–2.04)	.50
≥200 cells/μL	13 (50)	45 (57.7)	0.70 (0.28–1.79)	.45
New OI	7 (26.9)	10 (12.8)	1.93 (0.45–8.19)	.38
Undetectable HIV-PVL <400 copies/mL	17 (65.4)	69 (88.5)	0.37 (0.12–1.18)	.09
Virological failure[b]	6 (23.1)	12 (15.4)	2.45 (0.67–8.89)	.17
Death				
Any cause	6 (23.1)	4 (5.1)	5.41 (1.39–23.85)	.02
Liver related	4 (15.4)	2 (2.6)	6.49 (1.16–6.85)	.03

Impact of Hepatitis D Virus Infection on the Long-Term Outcomes of Patients with Hepatitis B Virus and HIV Coinfection in the Era of Highly Active Antiretroviral Therapy: A Matched Cohort Study

Wang-Huei Sheng,[1] Chien-Ching Hung,[1] Jia-Horng Kao,[1,2] Sui-Yuan Chang,[3] Mao-Yuan Chen,[1] Szu-Min Hsieh,[1] Pei-Jer Chen,[1,2] and Shan-Chwen Chang[1]

[1]Department of Internal Medicine, National Taiwan University Hospital, [2]Graduate Institutes of Clinical Medicine, and [3]Department of Clinical Laboratory Sciences and Medical Biotechnology, National Taiwan University College of Medicine, Taipei, Taiwan

« flares »

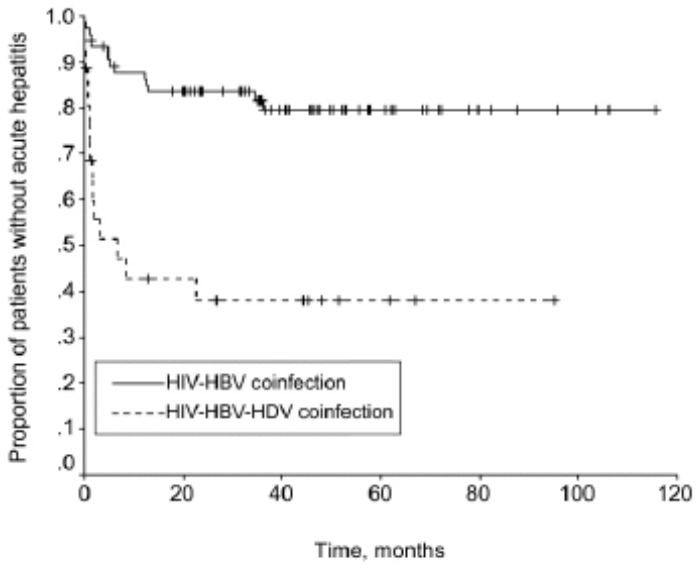


Figure 1. Kaplan-Meier estimates of hepatitis flares in patients with HIV, hepatitis B virus (HBV), and hepatitis D virus (HDV) coinfection and patients with HIV-HBV coinfection. $P = .001$, by log-rank test.

mortalité

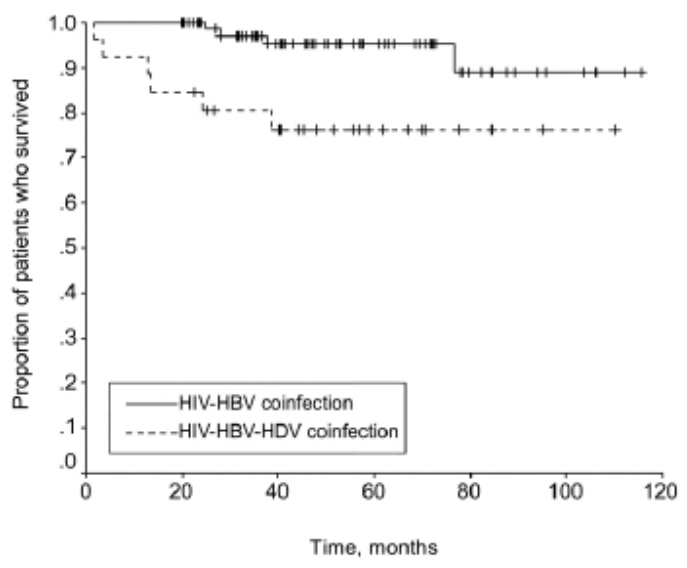


Figure 2. Kaplan-Meier survival estimates of mortality for patients with HIV, hepatitis B virus (HBV), and hepatitis D virus (HDV) coinfection and patients with HIV-HBV coinfection. $P = .02$, by log-rank test.

conclusion co-infection

- **impact sur le diagnostic**
  - fluctuation ADN HB, ARN VHC et ARN Delta
    (Schaper et al: une seule mesure $\Rightarrow$ sous-estimation de la co-infection B-D dans 20% des cas)
  - anti-HBc isolés
  - hépatites B occultes

conclusion

- impact sur le diagnostic
- impact clinique et pronostique
- impact thérapeutique et vaccinal
  - réponse vaccination HBV ↘ qd HIV et/ou HCV
  - attention rebond virologique virus non traité

conflits d'intérêt

subventions, honoraires et participation aux frais de formation continue /congrès:

laboratoires pharmaceutiques:

Bristol-Myers Squibb Gilead Sciences
Janssen-Cilag ViiV Healthcare MSD Roche

ANRS