2020 13th PARIS HEPATOLOGY CONFERENCE

PHC 2020
January 13 & 14 - 2020
PARIS - Palais des Congrès

LUNCH WORKSHOP

13th January from 12:30 to 14:30

Hepatitis B : practical management

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Hospices Civils de Lyon

Lyon 1

Inserm
Institut national de la santé et de la recherche médicale

CRCL CANCER RESEARCH CENTER OF LYON

CASE REPORT 1

43 years old, caucasian
No medical history
3.2015 : diagnosis of **chronic HBV infection** (GP)

Family history
Father, aged 69, alive, with « liver problems »
Mother, alive, diabetic, hypertension

Virology :
- HBsAg : + HBs Ab : - HBc Ab : +
- HBe Ag : - HBe Ab : +
- HBV-DNA: 8535 IU/mL
- HDV Ab : - HCV Ab : -

Biochemistry:
- ALT : 39 IU/ml (ULN 37)
- gGT : 64 IU/ml (ULN 55)
- Albumine : 38 g/L
- PT : 97%
- FBC : normal (PLQ 235.000)

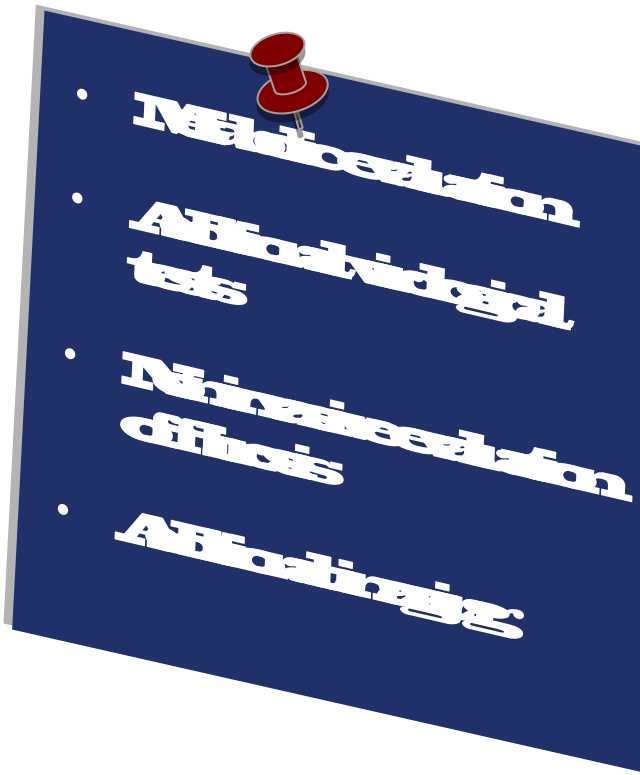
Disease Evaluation
- Ultrasound: no alterations in liver architecture, no focal lesions

What would you do?

Additional tests?

What would you do?

Additional tests?



What we did ...

- BMI : 29
- Fasting glucose : 5.9 mmol/l
- Fasting insulin : 26 IU/ml
- OGTT : T120 insulin 95 IU/ml
- No dislipidemia

- qHBs : 1855 UI
- HBcrAg : 4.2 log
- HBV genotype : D

- Stiffness : 6,3 kPa (Fibroscan)
- Fibrotest : 0.28
- Actitest : 0.37

- Confirmation of borderline LFT (ALAT)

Natural history of HBV

PHASE	1	2	3	4
New terminology	HBeAg positive Chronic *infection*	HBeAg positive Chronic hepatitis	HBeAg negative Chronic *infection*	HBeAg negative Chronic hepatitis
Old terminology	*Immune tolerant*	*HBeAg-positive CHB*	*Inactive carrier*	*HBeAg-negative CHB*
HBsAg	High	High/Intermediate	Low	Intermediate
HBeAg	Positive	Positive	Negative	Negative
HBV DNA	>10E7 IU/mL	10E4-10E7 IU/mL	<2,000 IU/mL*	>2,000 IU/mL
ALT	Normal	Elevated	Normal	Elevated**
Liver disease	None/minimal	Moderate/severe	None	Moderate/severe

* HBV-DNA levels can be between 2,000 and 20,000 IU/mL in some patients without signs of chronic hepatitis

EASL CPG HBV, J Hepatol 2017

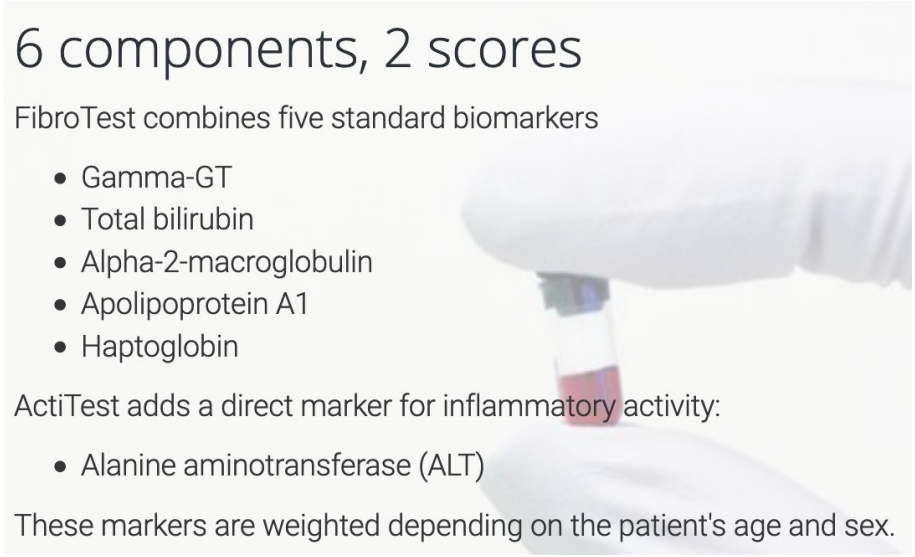
Transient elastography discriminates inactive carriers vs HBeAg negative disease

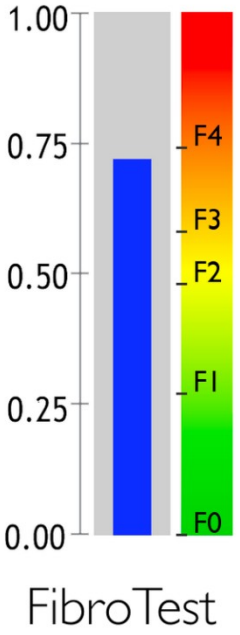
Patients (N=220)	Group 1 (n=125)	Group 2 (n=95)	P
SEX			
Male / Female	48/77	51/44	0.025
AGE			
Mean ± SD	44.58 ± 11.84	46 ±12.54	
STIFFNESS (kPa)			
Mean ± SD	4.83 ± 1.2	8.53 ± 6	<0.001
HBV DNA (copies/ml)			
Mean ± SD	6251 ± 16,293	2,700,889 ± 7,741,960	<0.001
ALT ratio (IU/L)			
Mean ± SD	0.56 ± 0.17	1.56 ± 1.7	<0.001
AST ratio (IU/L)			
Mean ± SD	0.61 ± 0.15	1.27 ± 1.27	<0.001
PLATELETS			
Mean ± SD	240,424 ± 64,309	206,242 ± 62,452	<0.001

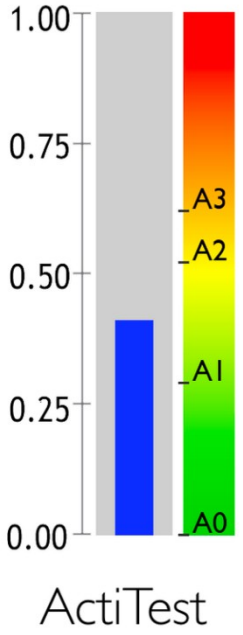
Maimone S, et al. J Viral Hepat 2009;16:769-74

Bio-Predictive Fibrotest and Actitest

(available once a year for all liver patients in Lyon)







cccDNA clearance vs cccDNA silencing

Implications for clinical endpoins and diagnostic tools

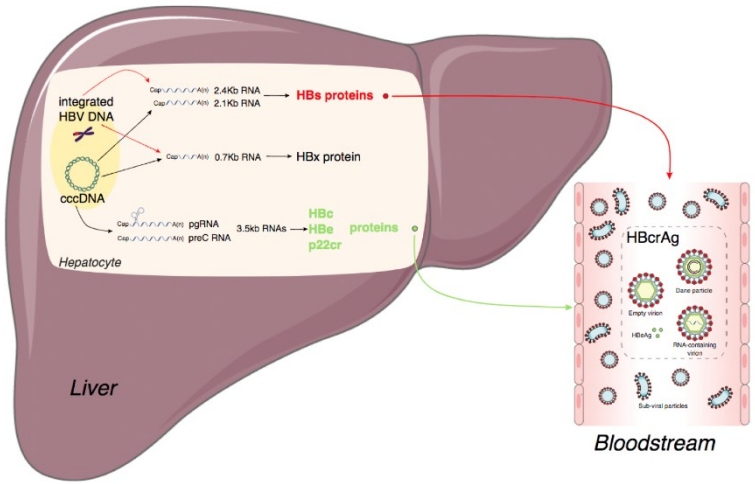
Possible dissociation between cccDNA levels and cccDNA transcriptional activity !

HBV *functional* cure
cccDNA clearance

HBV cure
cccDNA clearance

Measure cccDNA in liver

Estimate residual cccDNA and its status



Measure cccDNA transcriptional activity in liver (pgRNA/cccDNA ratio)

SERUM BIOMARKERS OF cccDNA ACTIVITY

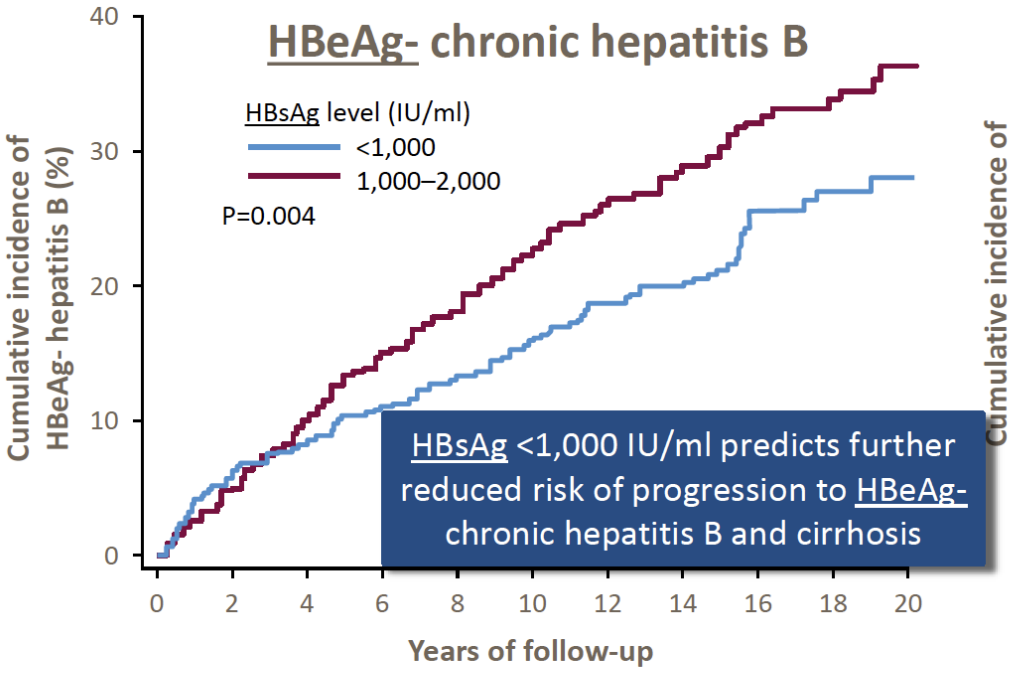
- **qHBsAg poorly reflects cccDNA transcriptional activity**
- **HBcrAg reflects cccDNA transcriptional activity**
  clinical utility limited by:
  - the sensitivity of the assay
  - HBeAg as a confounding

  Testoni et al, J Hepatol 2019
- **cirHBV RNAs may better reflect the cccDNA transcriptional activity** in untreated and treated (depending on the mode of action of the drug) patients

SERUM BIOMARKERSassociated with an inactive carrier state

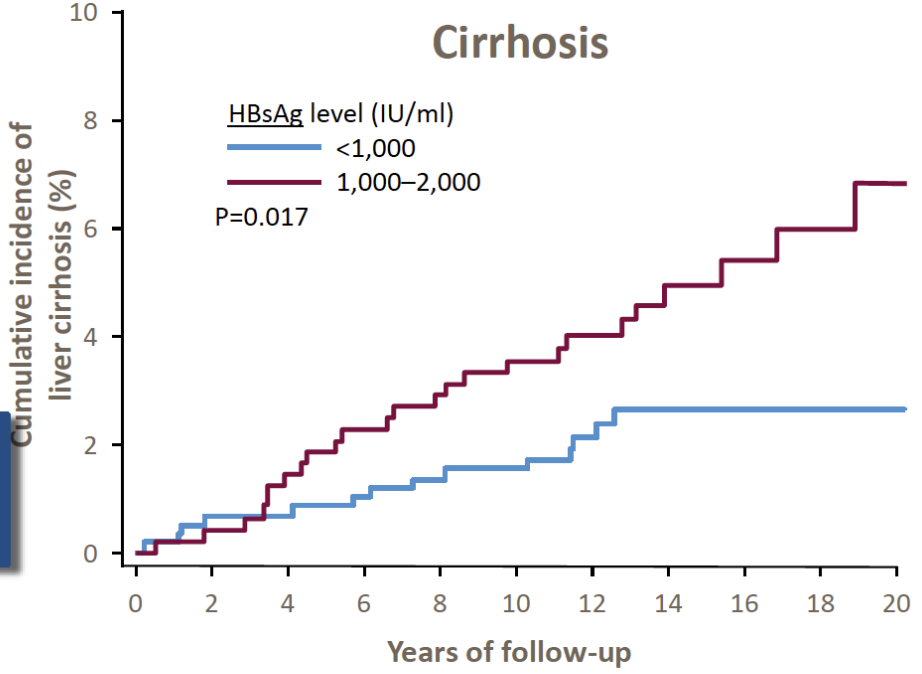
- **The combination of HBsAg <1 000 IU/mL and HBV DNA ≤ 2000 IU/mL** allows identification of inactive carriers with 90% accuracy, 88% PPV
- **A single HBcrAg measurement < 3 logU/mL plus HBV DNA < 2000 IU/mL** was highly accurate for identifying inactive carriers, regardless of their HBVgenotype**.**

HBsAg levels and disease progression in HBeAg patients with HBV DNA <2,000 IU/ml



Number at risk:

<1,000	585	551	536	521	503	454	357	265	146	90	58
≥1,000	483	460	435	410	394	350	288	210	132	100	57



Number at risk:

<1,000	585	581	581	578	573	532	432	315	182	111	71
≥1,000	483	481	476	471	466	436	373	276	182	131	81

Tseng TC, et al. Hepatology 2013;57:441-50

Clinical Microbiology and Infection 23 (2017) 860–867

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Original article

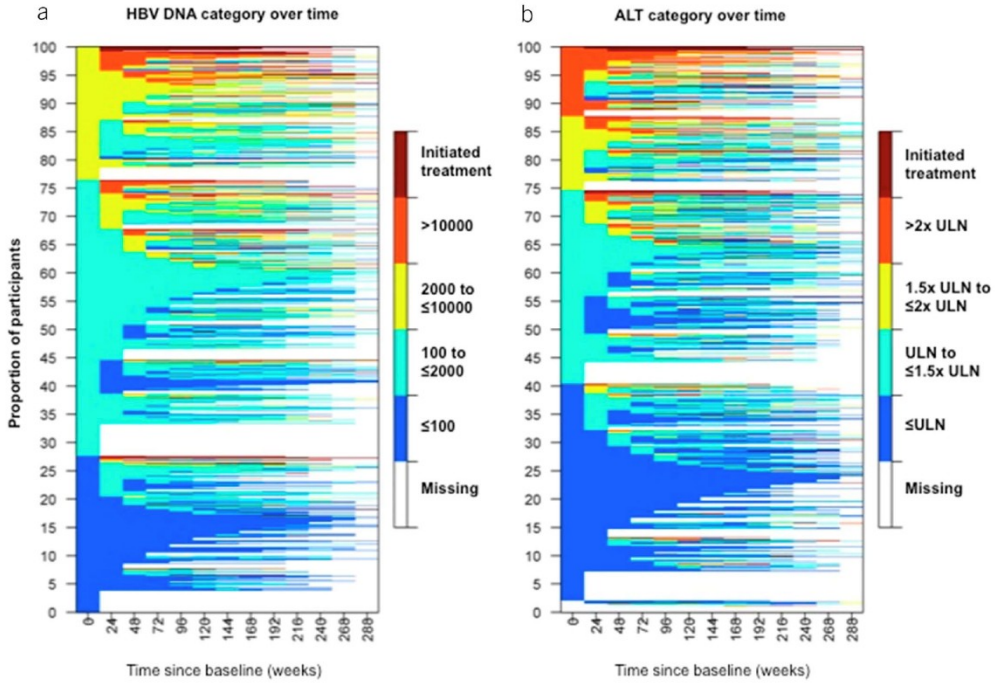
Serum hepatitis B core-related antigen is more accurate than hepatitis B surface antigen to identify inactive carriers, regardless of hepatitis B virus genotype

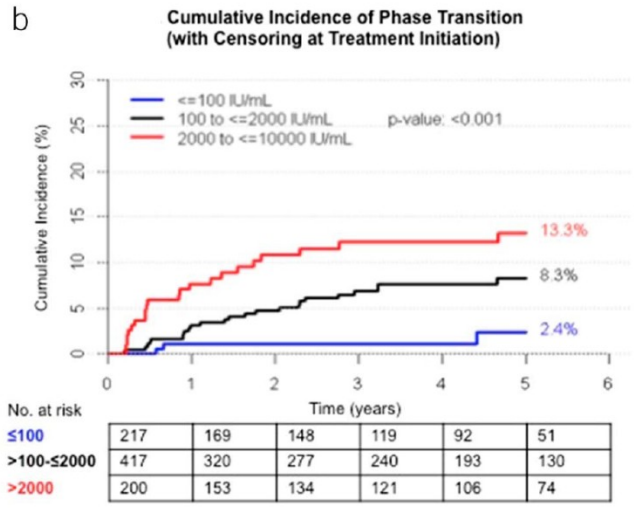
M. Riveiro-Barciela [1, 2, *], M. Bes [2, 3], F. Rodríguez-Frías [2, 4], D. Tabernero [2, 4], A. Ruiz [2, 4], R. Casillas [5], J. Vidal-González [1], M. Homs [2, 4], L. Nieto [4], S. Sauleda [2, 3], R. Esteban [1, 2], M. Buti [1, 2]

The American Journal of GASTROENTEROLOGY 2019

Phase Transition Is Infrequent Among North American Adults With e-Antigen-Negative Chronic Hepatitis B and Low-Level Viremia

Kali Zhou, MD, MAS[1], Abdus S. Wahed, PhD[2], Stewart Cooper, MD[3], Adrian M. Di Bisceglie, MD[4], Robert J. Fontana, MD[5], Marc G. Ghany, MD, MHSc[6], Mandana Khalili, MD[1], Anna S. Lok, MD[5], Robert Perrillo, MD[7], William M. Lee, MD[8], Daryl T.Y. Lau, MD, MSc, MPH[9], Richard Sterling, MD, MSc[10], Harry L.A. Janssen, MD, PhD[11] and Norah A. Terrault, MD[12]





Phase transition or initiated treatment over a median follow-up of 4 years: 9% of those with baseline HBV DNA £ 100 IU/mL, 14% with HBV DNA 101 to 2,000 IU/mL, and 24% with HBV DNA 2,001 to 10,000 IU/mL (P < 0.001) and ios more probable if quantitative hepatitis B surface antigen > 1,000 IU.

Treatment indications according to guidelines

NIM: non invasive methods

Terrault NA et al. Hepatology 2018 67; 1560-1599
Sarin SK et al. Hepatol Int 2016; 10: 1-98
Lampertico P et al. J Hepatol 2017; 67: 370-398

CASE REPORT 2

Follow up (6.2016 ; 3.2017)

No changes in LFTs
Gain of weight (4 kg)
US : no changes
HBV-DNA: 4581 IU/mL

Follow up (11.2017 ; 3.2018)

ALT 1.3x, no other changes in LFTs
Stable weight (+4 kg)
US : no changes
HBV-DNA: 2434 IU/mL

CASE REPORT 3

Follow up (5.2019)

ALT 1.8X ; gGT 1.6x
Gain of weight (+10 kg)
US : evidence of steatosis
HBV-DNA: 9581 IU/mL

Additional tests?

CASE REPORT 3

Follow up (5.2019)

ALT 1.8X ; gGT 1.6x
Gain of weight (+10 kg)
US : evidence of steatosis
HBV-DNA: 9581 IU/mL

Stiffness : 7.8 KPa (Fibroscan)
CAP : 289 dB/m

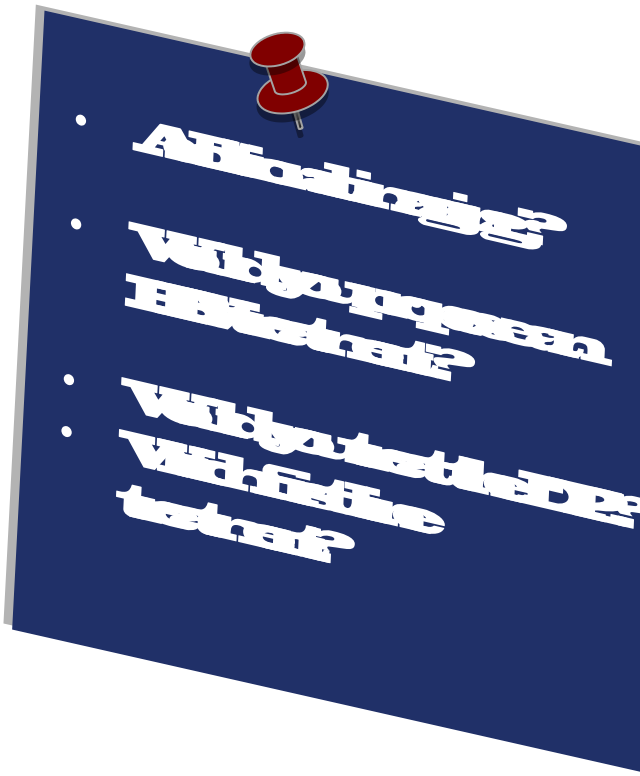
DT2 and fasting hyperinsulinemia

Re assessment of alcohol compsuntion : 10 to 15 doses / week

Indication to liver biopsy (refused by the patient)

What would you do?

What would you do?



What we did ...

- Enrolled in a NAFLD weight control program
  (intensive nutritionist support)

- Started Metformin

- Started Tenofovir

Follow up (12.2019)

ALT 1.4 x; gGT 1.5x
HBA1c 7.1 %
Loss of weight (+8 kg)
HBV-DNA: neg