HDV DIAGNOSIS IN 2022

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INSERM U955 TEAM 18 – CRETEIL, FRANCE
DISCLOSURES

- **speakers on a time-time basis for:**
  - BMS, Gilead, Qiagen, Siemens

- **invitation to scientific congress:**
  - BMS, Gilead, Qiagen, Eurobio

- **consulting & scientific assistance:**
  - Bioactiva diagnostics GmbH
  - Eurobio
  - Gilead
HDV Infection occurs only in patients infected with HBV.
VIRAL PARTICLES

42 NM
HEPATITIS B VIRUS

19 - 22 NM
EMPTY PARTICLES
Viral Particles

HDV Satellite of HBV

42 nm Hepatitis B Virus

19 - 22 nm Empty Particles

35 - 37 nm Hepatitis Delta Virus
DELTA VIRAL HEPATITIS: A WORLDWIDE HEALTHCARE PROBLEM?

- 2 BILLION INDIVIDUALS HAVE BEEN INFECTED WITH HBV
  - Among them: 250 MILLIONS CHRONICALLY INFECTED
  - Risk of developing cirrhosis and HCC X 100
  - 1 MILLION DEATHS PER YEAR

→ ≈10 TO 20 MILLIONS CHRONIC CARRIERS OF HDV

ALEXANDER J. STOCKDALE ET AL., J. HEPATOL. 2020 VOL. 73 J 523–532
HDV INFECTION

HDV infection usually results in:
Inhibition of HBV replication

The most severe liver disease

Williams V. et al., J Viral Hepat 2009;90: 2759–2767
Fattovich G et al., J Infect Dis 1987;155:931-935.
Yurdaydin C. et al., J Viral Hepat 2010;17:749-56.
Niro GA et al., J Hepatol 2010;53:834-40.
DELTAVIR : A RETROSPECTIVE FRENCH NATIONWIDE STUDY OVER 1112 PATIENTS

ROULLET D, BRICHLER S., ET AL., HEPATOLOGY 2020
### Evolution and Severity of the Liver Disease

**Median of follow-up (FU): 3.0 years [0.8 - 7.2]**

<table>
<thead>
<tr>
<th>Clinical Status</th>
<th>At Referral</th>
<th>At End of FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>28.3%</td>
<td>48.8%</td>
</tr>
<tr>
<td>Liver Decompensation</td>
<td>14.8%</td>
<td>24.2%</td>
</tr>
<tr>
<td>HCC</td>
<td>2.7%</td>
<td>9.2%</td>
</tr>
<tr>
<td>Death or Liver Transplantation</td>
<td>-</td>
<td>19.1%</td>
</tr>
</tbody>
</table>

**At the end of follow-up:**
- 584 were treated with IFN or Peg-IFN-α
- 33% of whom being HDV-RNA negative

→ 67% HDV-RNA Positive

*Roulot D, Brichler S., et al., Hepatology 2020*
### Liver Events: Incidence at 10 Years

<table>
<thead>
<tr>
<th>Event</th>
<th>Cirrhosis</th>
<th>Hepatic Decompensation</th>
<th>HCC</th>
<th>Death or Liver Transplantation</th>
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<tbody>
<tr>
<td>Incidence at 10 yrs [95% IC]</td>
<td>57.3 % [53.2 - 61.4]</td>
<td>31.0 % [27.3 - 35.2]</td>
<td>15.3 % [12.1 - 19.3]</td>
<td>25.1 % [21.6 - 28.9]</td>
</tr>
</tbody>
</table>

*Roulot D, Brichler S., et al., Hepatology 2020*
HDV INFECTION

- HDV infection usually results in: Inhibition of HBV Replication
- The most severe liver disease

- MUST BE SYSTEMATICALLY SCREENED IN ALL HBV-INFECTED PATIENTS
HDV INFECTION DIAGNOSIS

- **Total anti-HDV Abs**: Key marker+++  
  - **IgM anti-HDV Abs**  
    - Persist in chronic infection +++  
    - But can lack in African patients *  
    - They are not useful in clinical practice +++

- **Delta Ag**  
  - Between 1996 et 2004: 7 / 2524 positive = 0.28% (FNRC)

- **Delta ARN +++**  
  - Qualitative RT-PCR (~ 50 IU/mL) **  
  - Quantitative Real-time RT-PCR +++ (2 to 8 log IU/ML) ***

* Lunel F, Mansour W et al., J Infect. 2013  
** Radjef N. et al., J. Virol. 2004  
ANTI-HDV-AB SCREENING

ANTI-HDV ABS

ELISA ASSAYS
EIAGEN (ADALTIS);
DIA.PRO (INGEN, BIOEVOLUTION)
LIAISON® XL (DIASORIN)
GB HDV AB (GENERAL BIOLOGICAL CORPORATION) **

Rapid Diagnostic Test ***

Control - Anti-HDV -

NEG

ANTI-HDV POSITIVE

ELISA ASSAY

<table>
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<tr>
<th></th>
<th>Pos.</th>
<th>Neg.</th>
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</thead>
<tbody>
<tr>
<td>RDT Pos.</td>
<td>314</td>
<td>0</td>
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<tr>
<td>RDT Neg.</td>
<td>18</td>
<td>142</td>
</tr>
</tbody>
</table>

Sensitivity: 94.6%
Specificity: 100%

* LIN ET AL. VIROLOGY JOURNAL (2020) 17:76
** LEMPP F ET AL., 2021
ANTI-HDV-AB SCREENING (2)

HDV QUANTITATIVE MICROARRAY ANTIBODY CAPTURE ASSAY (Q-MAC)

Chen X. et al., Hepatology, 2017 Dec;66(6):1739-1749
MAJOR CLINICAL INTERESTS OF HDV VIRAL LOAD QUANTIFICATION

- **Identification of patients with a replicative HDV infection as viral replication is associated with a poor outcome of the hepatic disease**

- **Decision to treat**

- **Evaluation of treatment efficiency and virological response under treatment**

- **Decision to stop the treatment**

- **Evaluation of new anti-HDV compounds**
HDV GENETIC VARIABILITY AND RNA-VL QUANTIFICATION
HDV GENETIC VARIABILITY

NADJIA RADJEF : D (2001), (P. DÉNY ET E. GORDIEN)
MATHIEU TAMBY : M1 (2001) (E. GORDIEN)
FRÉDÉRIC LE GAL : D (2007) (P. DÉNY)

⇒ FROM 3 TO 8 GENOTYPES !
... AND WITH SEVERAL SUBGENOTYPES

IVANIUSHINA ET AL., J Gen Virol, 2001
RADJEF N. ET AL, JOURNAL OF VIROLOGY 2004
Le Gal F. et al, Emerging Infectious Diseases 2006
DÉNY P., CURR TOP MICROBIOL IMMUNOL. 2006
GORDIEN E., ISTANBUL, EASL, 2010
Le Gal et al., Hepatology, 2017
## Geographical Origin of the 2205 Patients Living and Diagnosed in France

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<th>Region</th>
<th>Patients (n)</th>
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<tr>
<td>Eastern Europe</td>
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<tr>
<td>Turkey</td>
<td>51</td>
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<tr>
<td>Near and Middle East</td>
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<tr>
<td>Africa</td>
<td>1,087</td>
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<tr>
<td>Asia</td>
<td>173</td>
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<tr>
<td>Other</td>
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<tr>
<td>Central African Republic</td>
<td>115</td>
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<tr>
<td>Republic Democratic of Congo</td>
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<td>France</td>
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<td>Switzerland</td>
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<td>Portugal</td>
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<td>Greece</td>
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<td>Belgium</td>
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<td>Luxembourg</td>
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<td>Burkina Faso</td>
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<td>Cameroon</td>
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<td>Cap Vert</td>
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<td>Cote d’Ivoire</td>
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<td>Senegal</td>
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<td>Togo</td>
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<td>Tunisia</td>
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<td>Libya</td>
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<td>Rwanda</td>
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<tr>
<td>Equatorial Guinea</td>
<td>2</td>
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<tr>
<td>Unknown</td>
<td>110</td>
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### Regions
- **Unknown**: 5%
- **Central African Republic**: 115
- **Republic Democratic of Congo**: 15
- **Senegal**: 54
- **Sierra Leone**: 9
- **Chad**: 19
- **Togo**: 10
- **Tunisia**: 15
- **Libya**: 1
- **Rwanda**: 1
- **Equatorial Guinea**: 2

### Countries
- **France**: 296
- **Spain**: 13
- **Italy**: 32
- **Portugal**: 16
- **Switzerland**: 3
- **Greece**: 7
- **Belgium**: 1
- **Luxembourg**: 1
- **South Africa**: 3
- **Algeria**: 14
- **Angola**: 4
- **Benin**: 10
- **Burkina Faso**: 11
- **Cameroon**: 280
- **Cote d’Ivoire**: 148
- **Egypt**: 21
- **Gabon**: 34
- **Gambia**: 1
- **Ghana**: 6
- **Guinea Bissau**: 60
- **Liberia**: 3
- **Mali**: 130
- **Morocco**: 17
- **Mauritania**: 67
- **Sudan**: 1
- **Niger**: 4
- **Nigeria**: 3
- **Central African Republic**: 115
- **Republic Democratic of Congo**: 15
- **Senegal**: 54
- **Sierra Leone**: 9
- **Chad**: 19
- **Togo**: 10
- **Tunisia**: 15
- **Libya**: 1
- **Rwanda**: 1
- **Equatorial Guinea**: 2

### Other Regions
- **Other**: 16
- **India Ocean**: 23
- **Mauritius**: 1
- **Comoros**: 3
- **Madagascar**: 12
- **Mayotte**: 5
- **Reunion**: 2

### Countries (continued)
- **Afghanistan**: 3
- **Dagestan**: 3
- **Iran**: 2
- **Kuwait**: 1
- **Lebanon**: 1
- **Oman**: 2
- **Pakistan**: 1
- **Uzbekistan**: 1
- **Azerbaijan**: 1
- **Albania**: 4
- **Bulgaria**: 41
- **Georgia**: 41
- **Armenia**: 10
- **Kosovo**: 2
- **Moldavia**: 29
- **Romania**: 161
- **Russia**: 35
- **Serbia**: 4
- **Georgia**: 2
- **Leetonia**: 2
- **Estonia**: 1
- **Poland**: 1
- **Tchetchenia**: 3
- **Ukraine**: 7
- **Byelorussia**: 1
- **Mongolia**: 115
- **Vietnam**: 14
- **China**: 43
- **Antilles**: 7
- **Colombia**: 1
- **Australia**: 1
- **Bolivia**: 1
- **Brazil**: 1
- **Cayenne**: 1
- **Alaska**: 1
- **Alaska**: 3
- **Guyana**: 3

**FNRL HDV Data**
Genetic Diversity and Worldwide Distribution of the \textit{Deltavirus} Genus: A Study of 2,152 Clinical Strains

Frédéric Le Gal,\textsuperscript{1,2} Ségolène Brichler,\textsuperscript{1,3} Tudor Drugan,\textsuperscript{4} Chakib Alloui,\textsuperscript{1,2} Dominique Roulot,\textsuperscript{2,5} Jean-Michel Pawlotsky,\textsuperscript{3,6} Paul Dény,\textsuperscript{1,7} and Emmanuel Gordien\textsuperscript{1,3}

Hepatitis delta virus (HDV) is responsible for the most severe form of acute and chronic viral hepatitis. We previously proposed that the \textit{Deltavirus} genus is composed of eight major clades. However, no sequences were available to confirm this classification. Moreover, little is known about the structural and functional consequences of HDV variability. One practical consequence is the failure of most quantification assays to properly quantify plasmatic HDV RNA. Between 2001 and 2014, 2,152 HDV strains were prospectively collected and stored in our reference laboratory by means of nucleotide sequencing and extensive phylogenetic analyses of the \textit{R0} region of the genome from nucleotides 889 to 1289 encompassing the 3′ end of the delta protein 2. In addition, the full-length genome sequence was generated for 116 strains selected from the different genotypes for in-depth characterization of the HDV genotypes and subgenotypes. This study confirms that the \textit{Deltavirus} genus is composed of eight genotypes (HDV-1 to HDV-8) defined by an intergenotype similarity >85% or >80% for partial or full-length genome sequence, respectively. Furthermore, genotypes can be segregated in subgenotypes, characterized by an intersubgenotype similarity >90% (>84% for HDV-1) over the whole genome. The systematic analysis of genome and protein sequences revealed highly conserved functional nucleotide and amino acid motifs and positions across all (sub)genotypes, indicating strong conservative constraints on the structure and function of the genome and the protein. \textit{Conclusion:} This study provides insight into the genetic diversity of HDV and a clear view of its geographical localization and allows speculation as to the worldwide spread of the virus, very likely from an initial African origin. (\textit{Hepatology} 2017;66:1826-1841).
HDV Genotypes and Subgenotypes

1. According to the Partial R0 Region (3’end of HDAg ORF):
   - Inter Genotypic Divergence: >15%

2. According to the Complete Genomic Sequence:
   - Inter Genotypic Divergence: >20%

*Le Gal et al., Hepatology, 2017*
HDV Genotypes and Subgenotypes

1. According to the Partial R0 Region (3' end of HDAg ORF):
   - Inter genotypic divergence: >15%

2. According to the Complete Genomic Sequence:
   - Inter genotypic divergence: >20%
   - Inter subgenotypic divergence:
     * For HDV-1 >14% (1A, B, C & D)
     * For HDV-2 to -8 > 10%

Le Gal et al., Hepatology, 2017
HDV Genotypes in France

FNRL Data

VHD-1Eu/As
VHD-1Afr
VHD-2
VHD-3
VHD-5
VHD-6
VHD-7
VHD-8
MOLECULAR TOOLS FOR HDV ARN VL QUANTIFICATION
1st International Quality Control for HDV RNA Viral Load Quantification
## 28 Labs Participated in this Study

<table>
<thead>
<tr>
<th>Contacts</th>
<th>Institution / Addresses</th>
<th>Pays</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dr Jackson Kathy</strong></td>
<td>Head Research and Molecular Development</td>
<td>Australia</td>
</tr>
<tr>
<td><strong>Dr Elizaveta Padalko</strong></td>
<td>Clinical Biology, Virology; University H Polyclinic 8,</td>
<td>Belgium</td>
</tr>
<tr>
<td><strong>Dr Henrik B. Krarup</strong></td>
<td>Section of Molecular Diagnostics Department of Clinical Biochemistry Aalborg University Hospital</td>
<td>Denmark</td>
</tr>
<tr>
<td><strong>Dr Maria Buti Ferret/ Dr M. Homs / F. Rodriguez-Frias</strong></td>
<td>Hospital Universitario Valle Hberon Barcelona</td>
<td>España</td>
</tr>
<tr>
<td><strong>Dr Vincent Thibaut</strong></td>
<td>Laboratoire de Virologie, Hôpital La Pitié Salpetrière, Paris</td>
<td>France</td>
</tr>
<tr>
<td><strong>Pr Sophie Alain</strong></td>
<td>Service de Bactériologie Virologie Hygiène, Limoges</td>
<td>France</td>
</tr>
<tr>
<td><strong>Dr Emmanuel Gordien</strong></td>
<td>CNR Associé Delta</td>
<td>France</td>
</tr>
<tr>
<td><strong>Pr Marianne Coste-Burel</strong></td>
<td>Laboratoire de Virologie CHU de Nantes</td>
<td>France</td>
</tr>
<tr>
<td><strong>Pr Patrice Hervé / Dr Scholtès Caroline</strong></td>
<td>Laboratoire de Virologie Centre de Biologie Nord, CHU Lyon Sud</td>
<td>France</td>
</tr>
<tr>
<td><strong>Dr Jean Dominique Poveda</strong></td>
<td>Laboratoire CERBA</td>
<td>France</td>
</tr>
<tr>
<td><strong>Pr Wedemeyer / Dr Birgit Bremer</strong></td>
<td>Departement of Gastroenterology, Hepatology and Endocrinology Hannover Medical School</td>
<td>Germany</td>
</tr>
<tr>
<td><strong>Dr Bernhard Miller</strong></td>
<td>MVZ Labor Prof. Seelig GbR Brauer</td>
<td>Germany</td>
</tr>
<tr>
<td><strong>Dr Michael Chudy</strong></td>
<td>Moleculare Virologie / Molecular Virology / Paul-Ehrlich-Institut</td>
<td>Germany</td>
</tr>
<tr>
<td><strong>Dr Stephan Urban</strong></td>
<td>University Hospital Heidelberg, Molecular Biology</td>
<td>Germany</td>
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<tr>
<td><strong>Dr Thomas Köhler</strong></td>
<td>LIPSDIAG GmbH, Leipzig</td>
<td>Germany</td>
</tr>
<tr>
<td><strong>Dr Nikolaos Gatselis</strong></td>
<td>Department of Medicine and Research Laboratory of Internal Medicine Medical School, University of Thessaly, Larissa</td>
<td>Greece</td>
</tr>
<tr>
<td><strong>Dr Ada Katsoulidou</strong></td>
<td>Department of Hygiene and Epidemiology Athens University Medical School</td>
<td>Greece</td>
</tr>
<tr>
<td><strong>Dr Antonella Olivero</strong></td>
<td>Laboratorio di Fisiopatologia Epatica e Digestiva;</td>
<td>Italy</td>
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<tr>
<td><strong>Dr Teresa Pollincino</strong></td>
<td>Laboratorio di Biologia Molecolare</td>
<td>Italy</td>
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<td><strong>Dr Garbuglia Anna Rosa</strong></td>
<td>Laboratory of Virology. INMI L Spallanzani</td>
<td>Italy</td>
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<tr>
<td><strong>Dr Bill Carmam</strong></td>
<td>Fast Track Diagnostic</td>
<td>Luxembourg</td>
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<td><strong>Dr Haye El Bouh</strong></td>
<td>Laboratoire Biomedical-24</td>
<td>Mauritania</td>
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<tr>
<td><strong>Dr Chulanov Vladimir</strong></td>
<td>Central Research Institute of Epidemiology</td>
<td>Russia</td>
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<tr>
<td><strong>Dr Rory N Gunson</strong></td>
<td>West of Scotland Specialist Virology Centre</td>
<td>Scotland</td>
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<tr>
<td><strong>Dr Sahli Roland</strong></td>
<td>Institut de Microbiologie, CHUV Bugnon</td>
<td>Switzerland</td>
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<tr>
<td><strong>Dr Liang Kung-Hao</strong></td>
<td>Liver Research Center - Chang Gung Memorial Hospital, Taiwan</td>
<td>Taiwan</td>
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<tr>
<td><strong>Dr A. Mithat Bozdayi</strong></td>
<td>Department of Gastroenterology Hepatology Institute School of Medicine, Ankara University</td>
<td>Turkey</td>
</tr>
<tr>
<td><strong>Dr Jeremy Garson/ Dr RB Ferns</strong></td>
<td>Clinical Microbiology and Virology UCLH NHS Foundation Trust</td>
<td>United Kingdom</td>
</tr>
<tr>
<td><strong>Dr Tonya Mixson-Hayden/ Dr M. Kodani</strong></td>
<td>Associate Service Fellow Division of Viral Hepatitis Assay Development and Reference Laboratory</td>
<td>USA</td>
</tr>
</tbody>
</table>
20 Samples of Various Genotypes and Viral Loads

1. HDV-IQC Panel

- **20 Samples**
  - Including 2 Negative Controls
- **Viral Loads:**
  - 3.5 to 7.5 Log (IU/ML)
- **Genotypes:**
  - HDV-1Afr (N=4)
  - HDV-1Eu/As (N=4)
  - HDV-2 (N=1)
  - HDV-5 (N=3)
  - HDV-6 (N=2)
  - HDV-7 (N=2)
  - HDV-8 (N=2)

2. HDV-WHO Standard Panel

- **Dilutions:** 1:10 and 1:100 (× 3)
- + 2 Negative Controls
"In House" Assays


COMMERCIAL ASSAYS

- **Roche® Lightmix HDV kit (Germany)**
- **AJ-Roboscreen® (Germany)**
- **DiaPro® HV-RNA Quantification kit (Italy)**
- **Lipsgene® HDV Kit (Germany)**
- **HDV Real-TM Quant Sacace® (Italy)**
- **Liferiver™ HDV-Real Time RT-PCR Kit (China)**
- **Amplisens® HDV-Monitor-FRT PCR Kit (Slovakia)**
- **Fast Track Diagnostics™ (Luxembourg)**
- **Primerdesign™ Ltd United Kingdom**
- **Ecoli® (Russia)**
- **Bosphore HDV Quantification-Detection Kit v1 (Turkey)**
18 samples with HDV VL ranging from 3.5 to 7.5 Log IU/mL

Overall Results

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</tr>
</tbody>
</table>
Labs can be classified into 4 « Clusters »

Factor map

- **DIM 1 (56.44%)**
- **DIM 2 (14.29%)**

- **Cluster 1**
- **Cluster 2**
- **Cluster 3**
- **Cluster 4**

Labs can be classified into 4 « Clusters »

Factor Map

Dim 1 (56.44%)

Dim 2 (14.29%)

12/28 \rightarrow 43%
The main results of this 1st International Quality Control: Most available assays underestimate or fail to quantify HDV RNA VL.
Performance Characteristics of a New Consensus Commercial Kit for Hepatitis D Virus RNA Viral Load Quantification

Frédéric Le Gal, a,b Samira Dziri, a,b Athenaïs Gerber, a,b Chakib Alloui, a,b Zahia Ben Abdesselam, b,c Dominique Roulot, b,c Ségolène Brichler, a,b,d Emmanuel Gordien a,b,d

Laboratoire de Bactériologie, Virologie, Hygiène des Hôpitaux Universitaires de Paris Seine-Saint-Denis, Université Sorbonne Paris Cité, Bobigny, France a; Centre National de Référence des Virus des Hépatites B, C et Delta, Laboratoire Associé pour le Virus de l'Hépatite Delta, Bobigny, France b; Unité d'Hépatologie, Hôpitaux Universitaires de Paris Seine-Saint-Denis, Université Sorbonne Paris Cité, Bobigny, France c; Unité INSERM U955, Université Paris Est, Créteil, France d
A NEW CONSENSUS COMMERCIAL KIT
(EUROBIOPLEX HDV KIT ®)

(LE GAL F. ET AL., J. CLIN. MICROBIOL., 2017)

PERFORMANCE COMPARISONS WITH THE FNRL ASSAY RESULTS (N = 611)

<table>
<thead>
<tr>
<th>HDV FNRL assay result</th>
<th>Eurobioplex HDV kit result</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>389</td>
</tr>
<tr>
<td>Negative</td>
<td>14\textsuperscript{a}</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Sample with a very low HDV viral load (<3 log IU/ml).

\textbf{SENSITIVITY: 98.8%}
\textbf{SPECIFICITY: 100%}
A NEW CONSENSUS COMMERCIAL KIT
(Eurobioplex HDV Kit®)


Performance Comparisons with the FNRL assay results (N = 151)

- 33 HDV-1Afr; 61 HDV-1Eur/As
- 1 HDV-2, -3, -4*
- 22 HDV-5; 7 HDV-6; 10 HDV-7; 3 HDV-8
- 12 negative controls

<table>
<thead>
<tr>
<th>Test type</th>
<th>Median viral load by genotype(s) (log IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Eurobioplex kit</td>
<td>5.05</td>
</tr>
<tr>
<td>HDV FNRL</td>
<td>5.16</td>
</tr>
<tr>
<td>Difference between results</td>
<td>-0.11</td>
</tr>
</tbody>
</table>
A NEW CONSENSUS COMMERCIAL KIT
(EUROBIOPLEX HDV KIT ®)

(LE GAL F. ET AL., J. CLIN. MICROBIOL., 2017)

PERFORMANCE COMPARISONS WITH THE FNRL ASSAY RESULTS (N=36)
A NEW CONSENSUS COMMERCIAL KIT

(LE GAL F. ET AL., J. CLIN. MICROBIOL., 2017)

CNR EUROBIOPLEX®
**HDV Infection Screening**

- Total Anti-HDV Antibodies
  - Negative: No HDV Infection
  - Positive: IgM Anti-HDV *
    - HDV RNA Viral Load **
      - Negative: Repetition & Follow-up
      - Positive: Treatments: Interferon Entry Inhibitors (New Drugs in Development)

**Evaluation of HBV Infection**

- HBsAg (qHBsAg)
- Anti-HBeAb
- HBeAg (qHBeAg)
- Other New HBV Markers (HBcAg, HBV-RNA)

- HBV DNA
  - < 2000UI/mL: Repetition & Follow-up
  - > 2000UI/mL: Nucleos(t)ides Analogues

* Persist during chronic infection and often lack in African patients → No clinical interest
** With a validated Assay
CONCLUSIONS

- **HDV** is a unique and amazing virus which is more and more studied.
- It is responsible for a much more serious liver disease.
- Its diagnosis must be systematic in all HBV positive patients and relies mainly upon:
  - Total HDV Abs
  - Quantitative HDV RNA assays which still need further improvements related to the high genetic diversity of HDV genus.
- Active basic and clinical research is absolutely needed to better understand the fundamental biology of HDV and to provide molecular diagnostic tools and specific treatments.
- Diagnostic algorithms and guidelines for management of patients remain to be better defined.
THANK YOU FOR YOUR ATTENTION!