

# CHRONIC HCV DIAGNOSTIC METHODS IN HUNGARY (1992-2019)

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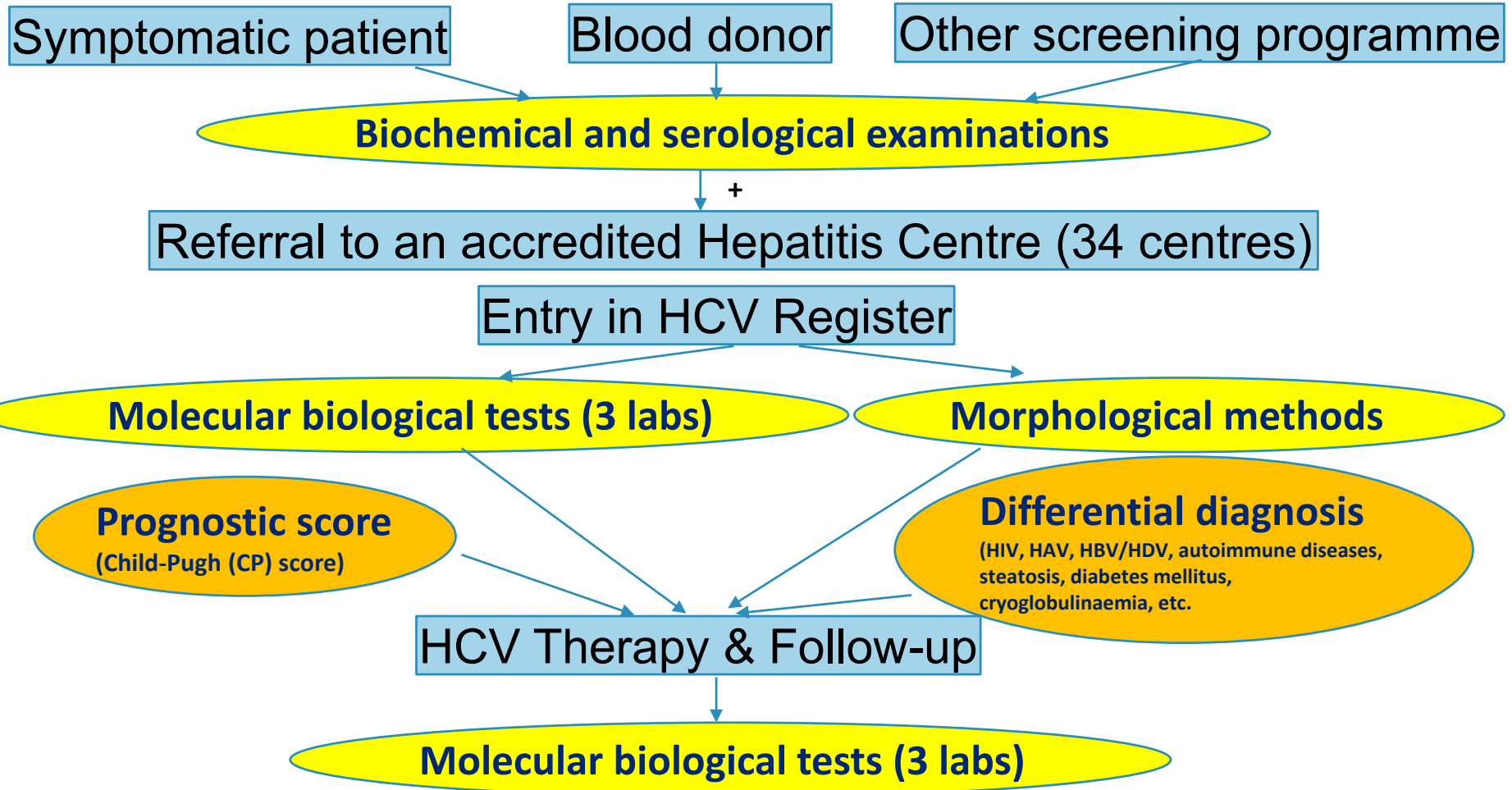
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# Chronic HCV diagnosis in Hungary: ORGANISATION



# Chronic HCV diagnosis in Hungary: DETERMINANTS

- The **screening** of blood donors for HCV infection and further investigation and **treatment** of infected patients started **in 1992 in Hungary**
- It is organised jointly by the national hepatologists and infectologists
- Determinants:
  - International **guidelines**: American Association for the Study of Liver Diseases, European Association for the Study of the Liver
  - National financing landscape: pre-defined **diagnostic and therapeutic budget**
  - **Technological and methodological developments**: most specific and sensitive tests are used
  - Annually reviewed **Hungarian diagnostic and therapeutic protocol**

# SCREENING

- **Biochemical tests** (alanine and aspartate aminotransferase (ALT/AST), alkaline phosphatase (ALP), gamma glutamate dehydrogenase (GGT), lactate dehydrogenase (LDH), creatinine, albumin, total bilirubin, international normalized ratio, haemoglobin, platelet count, glomerular filtration rate)
  - *alanine aminotransferase (ALT) test*:
    - non-specific,
    - first screening test,
    - **normal results in 20%** of all chronic hepatitis patients
- **Serological tests (HCV-antibody)**
  - Done in blood transfusion service centres, public and private labs
  - *anti-HCV*:
    - indirect test, **indicator marker**
    - **sensitive method: 3. gen. CMIA, ELISA, EIA (CE IVD tests)**
    - Problem: tests with different sensitivity exist, therefore, often **false positive** test results!
    - If positive: **HCV-RNA PCR test is necessary!**

# MORPHOLOGICAL METHODS

- Hepatic imaging:
  - **Abdominal** and contrast-enhanced **ultrasonography** (UH, CEUS)
  - Computer Tomography (CT)
  - Magnetic Resonance Imaging (MRI)
- Liver fibrosis:
  - Invasive assessment: liver biopsy (Knodell, METAVIR, Ishak score)
  - **Non-invasive assessment: elastography** (F0-F4 fibrosis),  
FibroTests



# MOLECULAR BIOLOGICAL TESTS

- **Basic method:** *reverse transcription polymerase chain reaction (RT-PCR)*
- Done centrally in **3 NEAK designated laboratories:**
  - **1992-** →Székesfehérvár, Molecular Diagnostic Laboratory
  - **2008-** →Budapest „Szent László Hospital”/Central Hospital of Southern Pest
  - **2013-** →Semmelweis University, Transplantation and Surgical Clinic
- All 3 labs work with **equipments** of the **same sensitivity**
- Diagnostic **tests** have the **same sensitivity and specificity** (CE IVD)
- All 3 labs are available **for all 34 accredited Hepatology Centres**

# MOLECULAR BIOLOGICAL TESTS

## 1. HCV-RNA detection

- Qualitative method: 1994-1995; Cobas Amplicor HCV 1; 2. gen;  
*LLOD<sup>1</sup> < 50 IU/ml*
- **Quantitative (HCV RNA level) methods:**
  - A) endpoint PCR: 1995-2004; Amplicor HCV Monitor test (1995-2001);  
Cobas Amplicor HCV 2 (2001-2004)
  - B) real-time PCR: 2004-: CobasAmpliPrep/TaqMan; Cobas 4800 (Roche);  
m2000 (Abbott);  
*LLOD<sup>1</sup> < 12-15 IU/ml*
- **Measurement time points:**
  - PegIFN th.: baseline, W4, W12, EOT (end of treatment), EOT+W24
  - DAA th: baseline, (EOT), EOT+W12/24

*<sup>1</sup>Lower limit of detection (LLOD)*



# MOLECULAR BIOLOGICAL TESTS

## 2. HCV type/subtype methods

- Serotype (G1-6): 1996-1999; plate enzym-immunoassay
- **Genotype (G1-6(7) + a-c subtype):**
  - A) RT-PCR + reverse *hybridisation*: 2000-2015; INNO-LIPA HCV II.;  
VERSANT HCV Genotype 2.0
  - B) real-time PCR: 2016-; Cobas 4800 (Roche);  
Abbott HCV Genotype II.





## HCV genotype/subtype distribution by different methods in Hungary (n= 5917) (2000-2017)

GENOTYPES	n = 5917 (2000-2017) total	n = 4844 (2000-2015) hibridization method	n= 1073 (2016-2017) real-time PCR	COMMENT
<b>1a</b>	5,6%	6,1%	<b>3,5%</b>	
<b>1b</b>	84,6%	<b>83,1%</b>	<b>91,0%</b>	
<b>1a+1b</b>	5,1%	5,9%	<b>1,7%</b>	
<b>2</b>	0,1%	-	<b>0,2%</b>	
<b>3</b>	1,8%	1,6%	<b>*2,8%</b>	*2 patients: inj. drug use: 3+1b
<b>4</b>	*0,1%	*-	<b>0,8%</b>	* G4 + 1a; 1b
<b>mixed</b>	*1,6%	*1,9%	-	*1a; 1b; 2; 4; mixed
<b>1</b>	*1,1%	*1,4%	<b>&lt; 0,01%</b>	undifferentiated subtype
<b>5</b>		<b>3 patients</b>	-	

## CONCLUSION

- **Since 1992, the most specific and sensitive molecular biological tests** have been used for the screening and antiviral therapy of HCV infected patients
- **Molecular biological tests of all patients** from the 34 accredited Hepatitis Centres **are done in 3 designated central labs**
- Blood samples are transported cooled with specific speed carrier services
- **The 3 labs use the same methods and same sensitivity and specificity tests**  
Current recommended HCV-antibody test: *3. gen. ELISA, CE-IVD*  
Currently used HCV molecular biological tests are ***real-time methods***
- The **dominant HCV type** in Hungary is **GT1/b (92%)**, but the prevalence of **GT3 has increased** in recent years
- **Diagnostic tests** defined in the national protocol **are available for all infected patient without waiting list** thanks to a joint effort of providers, social insurance and the industry

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