شبکه تحقیقات بیماری های ویروسی ایران

مرکز تحقیقات ویروس شناسی بالینی
دانشگاه علوم پزشکی تهران

سنجش HBV DNA برای یافتن واجدین شرایط درمان و پایش پاسخ به درمان

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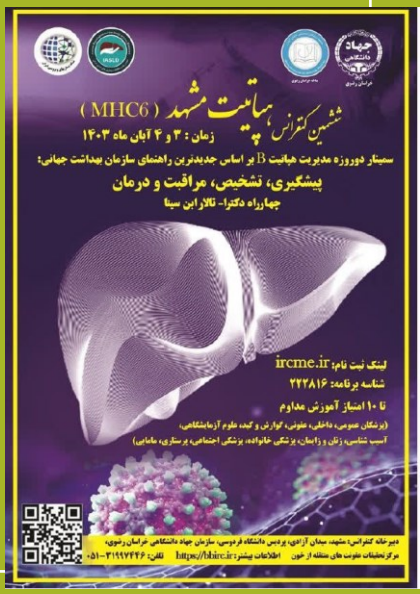
شبکه تحقیقات بیماریهای ویروسی ایران

مرکز تحقیقات ویروس شناسی بالینی

دانشگاه علوم پزشکی تهران

آبان ۱۴۰۳

مشهد



HBV Diagnosis (HBV DNA)

- In acute infection, when HBV DNA reaches a concentration above approximately 2000 copies per ml HBsAg becomes detectable.
- HBV DNA is detected 3 to 5 weeks after infection and up to 6-15 days before the appearance of HBsAg.
- Newer, more sensitive HBsAg assays could close this gap.
- It rises slowly at low levels (10^2 to 10^4 cop/ml) during the early HBsAg seronegative window period.
- It exceeds 10^9 cop/ml often during the prodromal, acute, or chronic phase.

Indications for Molecular Detection of HBV

- Blood donor screening
- Antiviral therapy
- Follow up of chronic infection and evaluation of infectivity
- First time detected isolated anti-HBc
- Unusaul seroconstellations (HBsAg negative but HBeAg positive)
- Hepatitis of unknown etiology (in anti-HBc and anti-HBs positive patients)
- Prodromal symptoms of hepatitis B.
- Indicator of disease activity
- Quantification of antiviral efficacy
- Dynamics on therapy may be predictor of outcome
- Early detection of resistant virus
- Occult HBV

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HBV DNA QUANTITATION

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- WHO has established an international standard for universal standardisation of HBV DNA quantitation units (along with HCV, HIV and CMV).

10. Measuring HBV DNA to guide treatment eligibility and monitor the response, WHO Guidelines, 2024

10.1 Recommendations

Existing and maintained recommendation

Laboratory-based HBV DNA assays[a] *(1,2)*: Directly following a positive HBsAg serological test result, the use of HBV DNA nucleic acid testing (NAT) (quantitative or qualitative) is recommended as the preferred strategy to assess viral load level for treatment eligibility and to monitor treatment response.

(strong recommendation, moderate-certainty evidence)

New recommendation

Point-of-care (POC) HBV DNA assays: POC HBV DNA nucleic acid testing (NAT) assays may be used as an alternative approach to laboratory-based HBV DNA testing to assess HBV DNA level for treatment eligibility and to monitor treatment response.

(conditional recommendation, low-certainty evidence)

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Summary of quality-assured HBV DNA laboratory-based technologies

Product	Manu-facturer	Specimen type	Analyser platform	Regulatory status
Alinity m HBV	Abbott	serum, plasma	Alinity m System	CE-Mark
Real*Time* HBV Viral Load Assay		serum, plasma	m2000 RealTime System	CE-Mark
Artus HBV RG RT-PCR Kit / Artus HBV QS-RGQ Kit	Qiagen	plasma	Rotor-Gene Q or Rotor-Gene Instrument	CE-Mark
AccuPower HBV Quantitative PCR Kit	Bioneer	serum, plasma	ExiStation Universal Molecular Diagnostic System	CE-Mark
Cobas HBV Test	Roche	serum, plasma	CAP/CTM, Cobas 4800/5800/ 6800/8800 systems	CE-Mark and US FDA
Aptima HBV Quant Assay	Hologic	serum, plasma	Panther System	CE-Mark, US FDA

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Cobas HBV Test	Roche	serum, plasma	CAP/CTM, Cobas 4800/5800/ 6800/8800 systems	CE-Mark and US FDA
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WHO Guideline

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- Laboratory-based nucleic acid amplification as the gold standard to quantify HBV DNA.
- However, in many low- and middle-income countries, especially in sub-Saharan Africa, access to HBV DNA assays is limited because of:

1. High costs
2. Requirements for specialized laboratory infrastructure
3. Trained personnel
4. Sample transport system.

WHO Guideline

- This has been a major barrier to more widespread uptake and initiation of hepatitis B treatment.
- There is now high-certainty evidence demonstrating the clinical impact of POC assays for HIV viral load monitoring, early infant diagnosis of HIV, diagnosis of TB and diagnosis of chronic viraemic HCV infection and as a test of cure.

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POCT Benefits

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- Uptake of viral load testing
- Turnaround time,
- Excellent examples of a centralized laboratory- based system being highly effective
- Efficient sample transport
- Rapid electronic delivery of results

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POCT Recommended By WHO

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1. Xpert HBV Viral Load (Cepheid, USA)
2. Truenat HBV (Molbio, India)

- At present, these products do not have WHO prequalification approval for this use.

POCT Recommended By WHO

- Diagnostic accuracy (sensitivity and specificity) of POC HBV DNA assays compared with laboratory-based NAT.
- The pooled sensitivity and specificity for other POC assays also demonstrated high sensitivity and specificity 98% and 99%, respectively.

10.4 Rationale for the recommendations

The Guidelines Development Group recognized the limited access to laboratory-based HBV DNA NAT assays in resource-limited settings because of the high cost and laboratory requirements of these assays and the fact that this represents an important barrier to treatment uptake. The increased availability of these POC platforms for use in HIV and TB care and during the COVID-19 pandemic represents an opportunity for greater access to HBV DNA assays.

The Guidelines Development Group conditionally recommended the use of POC NAT assays as an alternative to laboratory-based NAT assays to measure HBV DNA based on moderate to high certainty of evidence for high diagnostic accuracy (sensitivity (96–98%) and specificity (98–99%)) from a systematic review of 15 studies of POC versus conventional laboratory-based HBV viral load assays

بیمارستان لولاگر

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Molecular POCT

Company : Alere™ q

- **Target:** HIV, HCV, MTB
- **Technology:** real-time based on competitive reporter probe hybridisation on an integrated micro array

Company: Epistem

- **Country:** UK
- **Trade mark:** Genedrive
- **Target:** HCV, HIV, TB
- **Technology:** PCR+ Melting Curve A.

Company : GENSPEED

- **Country:** Austria
- **Trade mark:**
- **Target:** MRSA; Clos Diff; VanABC; Carbapenem
- **Technology:** PCR

Company: HiberGene

- **Country:** Ireland
- **Trade mark:** HG Swift
- **Target:** Meningococcus, GBS, C.Diff, Norovirus
- **Technology:** LAMP

Company : GenePOC

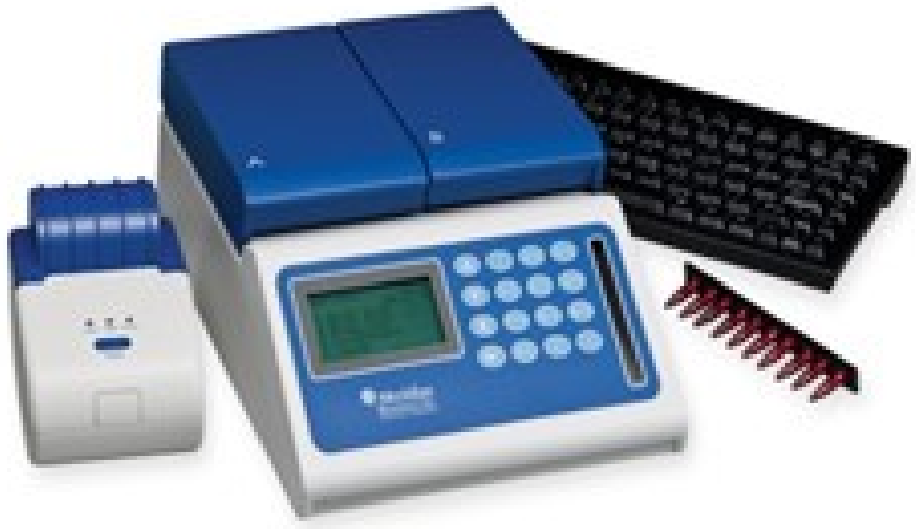
- **Country:** Canada
- **Trade mark:** Revogene
- **Target:** GBS, C. Diff (FDA), STD, Respiratory, HAP, Critical Infections, GI, Neonatal
- **Technology:** Real Time PCR

Company : **Micronics (SONY)**

- **Country:** USA
- **Trade mark:** PanNat
- **Technology:** Real-time PCR & melt curve

Company : **Meridian Bioscience**

- **Country:**USA
- **Trade mark:** Illumigene
- **Target:** Viral, Bacterial, Fungi
- **Technology:** LAMP



Company :Molbio Diagnostics Pvt

- **Trade mark: Truelab(Truenat)**
- **Target:** MTB, HBV, HIV, HCV, dengue fever, Chikungunya, H1N1 and malaria
- **Technology:** Real Time PCR

Company : OptiGene

- **Country:** UK
- **Trade mark:** Eazyplex/ Amplex
- **Target:** C.Diff, VRE, MRSA, CNS (Multiplex), Superbug (Carbapenem)
- **Technology:** LAMP

Company : **Ustar Biotechnologies**

- **Target:** HCV
- **Technology:** Cross Priming Amplification

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HBV POC Challenges

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- POC HBV testing has no notable harm but presents several challenges.

1. POC platforms have more limited test throughput than laboratory-based platforms. This is particularly a challenge when POC platforms are used for multiple diseases.
2. There are still few manufacturers of POC HBV NAT assays and therefore limited competition to drive down costs and options for country selection.
3. There are specific requirements of high-temperature incineration for safe waste disposal of guanidinium thiocyanate, which is contained in some assays, including those for Xpert assays.

Conclusions

- تکنولوژی اصلا وارد کشور نگردیده است.
- بخش آکادمیک کشور با این پدیده به کلی بیگانه است.
- طبیعتا به دلیل عدم آگاهی کادر دانشگاهی و متخصص کشور، وزارت بهداشت در مورد این ورود و توزیع این تکنولوژی فعالیتی انجام نداده است.
- لازم است انجمن مطالعات بیماریهای کبدی و شبکه های تحقیقاتی کشور (هپاتیت و بیماریهای ویروسی) در داین خصوص اطلاع رسانی جامعی را در دستور کار خود قرار دهند.

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