# Detection of the hepatitis B surface antigen (HBsAg) in patients with occult hepatitis B using a sensitive HBsAg assay

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## Introduction

Patients with occult hepatitis B infection (OBI) have undetectable hepatitis B surface antigen (HBsAg) by conventional assays, but detectable hepatitis B virus (HBV) DNA in the blood and/or liver. Conventional HBsAg assays generally have a limit of detection (LLOD) of 0.02 – 0.05 IU/mL. Sensitive assays for HBsAg detection have been developed, one of which is the ARCHITECT HBsAg Next Qualitative Assay (Abbott Laboratories; referred as HBsAg NEXT), with an enhanced analytical sensitivity of 0.0052 IU/mL.1.

## Aim

To evaluate the performance of HBsAg NEXT with respect to HBsAg detection in patients with OBI.

## Materials & Methods

HBsAg was measured by HBsAg NEXT in archived samples collected from 4 groups of patients/subjects with undetectable HBsAg by conventional assays but with serological/clinical evidence of OBI:
Group 1: 200 HBsAg-negative, HBV DNA-positive blood donors.
Group 2: 38 HBsAg-negative patients receiving immuno-suppressive therapy.
Group 3: 800 chronic hepatitis B (CHB) patients with spontaneous HBsAg seroclearance.
Group 4: 100 HBsAg-negative subjects recruited from a community project.

HBsAg was measured by HBsAg NEXT on an ARCHITECT i2000SR analyzer (Abbott Laboratories). Results were expressed as signal over cut off (S/CO). A S/CO of ≥1 was considered initial reactive. Initial reactive samples were retested in duplicate and confirmed with the NEXT Confirmatory test.

## Results

Group 1: HBsAg-negative, HBV DNA-positive blood donors, 200 blood donors:

- Undetectable HBsAg by the PRISM HBsAg Assay [Abbott].
- Detectable HBV DNA results by NAT (determined by Procleix [Grifols Diagnostic]; LLOD 3.4 IU/mL), followed by confirmation by an in-house PCR assay[2].
- Referred from the Hong Kong Red Cross Blood Transfusion Service to the Queen Mary Hospital, Hong Kong for clinical follow up during 2009 – 2020.
- 10/200 (5%) were confirmed positive by HBsAg NEXT. (mean S/CO 3.78 ± 1.17) An increment of 5% detection rate if HBsAg NEXT was used instead of PRISM HBsAg Assay.

Group 2: HBsAg-negative patients receiving immuno-suppressive therapy:

- 38 HBsAg-negative (determined by either ARCHITECT HBsAg Qual II or Elecsys HBsAg II [Roche]), anti-HBc-positive patients with haematological malignancies were followed up for 2 years after receiving either rituximab-containing therapy or allogeneic hematopoietic stem cell transplantation[3].
- 20 patients had HBV reactivation whereas the remaining 18 did not experience reactivation.
- 1/20 (5%) patients with reactivation had reactive HBsAg NEXT result at 4 weeks before reactivation.

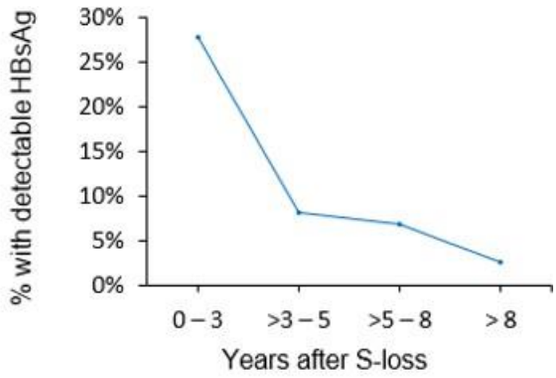
Table 1: The use of HBsAg NEXT could depict HBV reactivation prior to the emergence of HBV DNA

| | Patients with detectable HBsAg by NEXT (%) | | |
|---|---|---|---|
| | Baseline | Before reactivation | End of 2-year follow-up |
| 18 patients without HBV reactivation | 0 | N/A | 0 |
| 20 patients with HBV reactivation | 0 | 1 (5%)* | N/A |

* Sample at 4 weeks before HBV reactivation.

Group 3: Patients with HBsAg seroclearance:

- 800 patients with HBsAg seroclearance determined by either ARCHITECT HBsAg Qual II [Abbott] or LIAISON XL MUREX HBsAg Assay [DiaSorin]). Samples collected 0.5 – 29.7 years (median 7.8 years) after HBsAg seroclearance.
- 59 (7.3%) had detectable HBsAg by HBsAg NEXT.
- Distribution of detectable HBsAg (by HBsAg NEXT) with sample collection time is as follows:




| | | | | |
|---|---|---|---|---|
| Total number of samples | 90 | 146 | 174 | 390 |
| No. of samples with detectable HBsAg by NEXT (%) | 25 (27.8%) | 12 (8.2%) | 12 (6.9%) | 10 (2.6%) |

Fig 1: HBsAg NEXT detected HBsAg in 7.3% patients with HBsAg seroclearance determined by conventional assays.

Group 4: HBsAg-negative individuals from a community project:

- 100 HBsAg-negative apparently healthy subjects (determined by Elecsys HBsAg II) from a territory-wide community study[4], out of which 29 (29%) were anti-HBc positive.
- 7 (7%) had HBsAg detectable by HBsAg NEXT.
- All 7 samples with detectable HBsAg were also anti-HBc positive:

Table 2: HBsAg NEXT could detect OBI in apparently healthy HBsAg negative and anti-HBcpositive subjects in the community.

| | HBsAg NEXT-positive (n = 7) | HBsAg NEXT-negative (n= 93) | P value |
|---|---|---|---|
| Anti-HBc-positive (%) | 7/7 | 22/93 (23.7%) | <0.0001 |
| Median anti-HBs, IU/L | 2.0 | 39.8 | 0.013 |

## Conclusion

Overall, HBsAg NEXT conferred an increment of 5 – 7.3% detection rate when comparing with conventional HBsAg assays:

Table 3: HBsAg NEXT can improve the prevention of HBV transmission and HBV reactivation and allow a better policy implementation regarding the prevention of HBV-related complications.

| Patient cohort | Number of samples tested | Increment detection by NEXT |
|---|---|---|
| Group 1: HBsAg-negative, HBV DNA-positive blood donors | 200 | 10 (5%) |
| Group 2: HBsAg-negative patients with HBV reactivation | 20 | 1 (5%) |
| Group 3: CHB patients with HBsAg seroclearance | 800 | 59 (7.3%) |
| Group 4: HBsAg-negative individuals from a community project | 100 | 7 (7%) |

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## Disclosures

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