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Performance evaluation of the ADVIA Centaur® anti-HBe and HBeAg assays

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ABSTRACT

Background: Detection of HBeAg and anti-HBe is valuable for the evaluation and therapeutic management of hepatitis B infection.
Objectives: To determine the clinical performance of the newly CE-approved[a] HBeAg and anti-HBe assays on the fully automated, random access ADVIA Centaur® immunoassay system.
Study design: Patient samples collected at two sites were used to compare the ADVIA Centaur assays to Abbott AxSYM™ assays. Consensus of discordant results was reached using Roche Elecsys® assays. Additionally, two well-characterized seroconversion panels were evaluated.
Results: The ADVIA Centaur HBeAg assay sensitivity was 100% and specificity was 99.5%. The ADVIA Centaur anti-HBe assay sensitivity was 100% and the resolved specificity was 98.2%. Fewer samples required retesting with the ADVIA Centaur assays than with the AxSYM. In two well-characterized seroconversion panels, the ADVIA Centaur anti-HBe assay detected anti-HBe 20–25 days earlier than the AxSYM assay; the ADVIA Centaur and AxSYM HBeAg assays detected HBe reactivity on the same day.
Conclusions: The ADVIA Centaur HBeAg and anti-HBe assays demonstrated good sensitivity and specificity, and thus are suitable for clinical use. Their novel algorithms require reduced retesting, suggesting these assays may be more cost effective.

1. Introduction

An estimated 360 million people are chronically infected with hepatitis B virus (HBV) worldwide.[1] Infection is associated with the development of cirrhosis and hepatocellular carcinoma. Several routine serologic tests, including HBe antigen (HBeAg) and antibodies to HBeAg (anti-HBe), are used to distinguish recovered or recovering patients from those with chronic infection. Chronic HBV infections are typically characterized by prolonged elevated HBeAg associated with severely delayed and attenuated anti-HBe response (i.e., poor seroconversion).

Recent data suggest that HBeAg may modulate host response through induction of the interleukin-1 pathway, thereby promoting T-helper2—like responses that lead to suppression of the host immune response. This suppression facilitates viral persistence and inhibits viral clearance,[2] which is characteristic of the chronic patient.

HBeAg in patient sera indicates ongoing HBV replication and liver disease; anti-HBe is associated with lower levels of viremia and remission of liver disease. Additionally, HBeAg-positive patients are at increased risk for progression to chronic active (replicative) hepatitis and cirrhosis, and are at highest risk for hepatocellular carcinoma (HCC): studies comparing men negative for both HBsAg and HBeAg to men positive for either HBsAg alone or in addition to HBeAg showed that the relative risks for developing HCC were 9.6, and 60.2, respectively.[3,4]

Abbreviations: HBV, hepatitis B virus; HBeAg, HBe antigen; anti-HBe, antibodies to HBeAg; mAb, anti-HBe monoclonal antibody; RLUs, relative light units; CTS, common technical specifications.

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Table 1
The study populations

Patient type	Anti-HBe study $n=625$		HBeAg study $n=621$	
	Anti-HBe (+) ($n=216$)	Anti-HBe (−) ($n=409$)	HBeAg (+) ($n=218$)	HBeAg (−) ($n=403$)
Chronic infection	216	0	196	0
Acute infection	0	1	22	1[a]
Hospitalized/clinic patient	0	201	0	202
Blood donor	0	207	0	201

HBV infection and HBeAg/anti-HBe status as originally determined using the Roche ElecSys anti-HBe and HBeAg assays.

[a] This sample was not included in the specificity study because it was not drawn from a patient known to be infected with HBV. In accordance with CTS guidelines, specificity is determined using samples from low-risk populations presumed to be HBV-negative.

Table 2
Reactivity criteria

	ADVIA anti-HBe	AxSYM anti-HBe	ADVIA HBeAg[a]	AxSYM HBeAg
Reactive	≥1.2 index	≤1.0 S/CO ratio	≥1.0 index	≥1.0 S/CO ratio
Nonreactive	<0.80 index	>1.0 S/CO ratio	<1.0 index	<1.0 S/CO ratio
Equivocal	≥0.80 index/<1.2 index	–	–	–

[a] ADVIA HBeAg initial results that are ≥0.80 index and <10.0 index are retested in duplicate and HBeAg status determined by two of three results using reactivity criteria above.

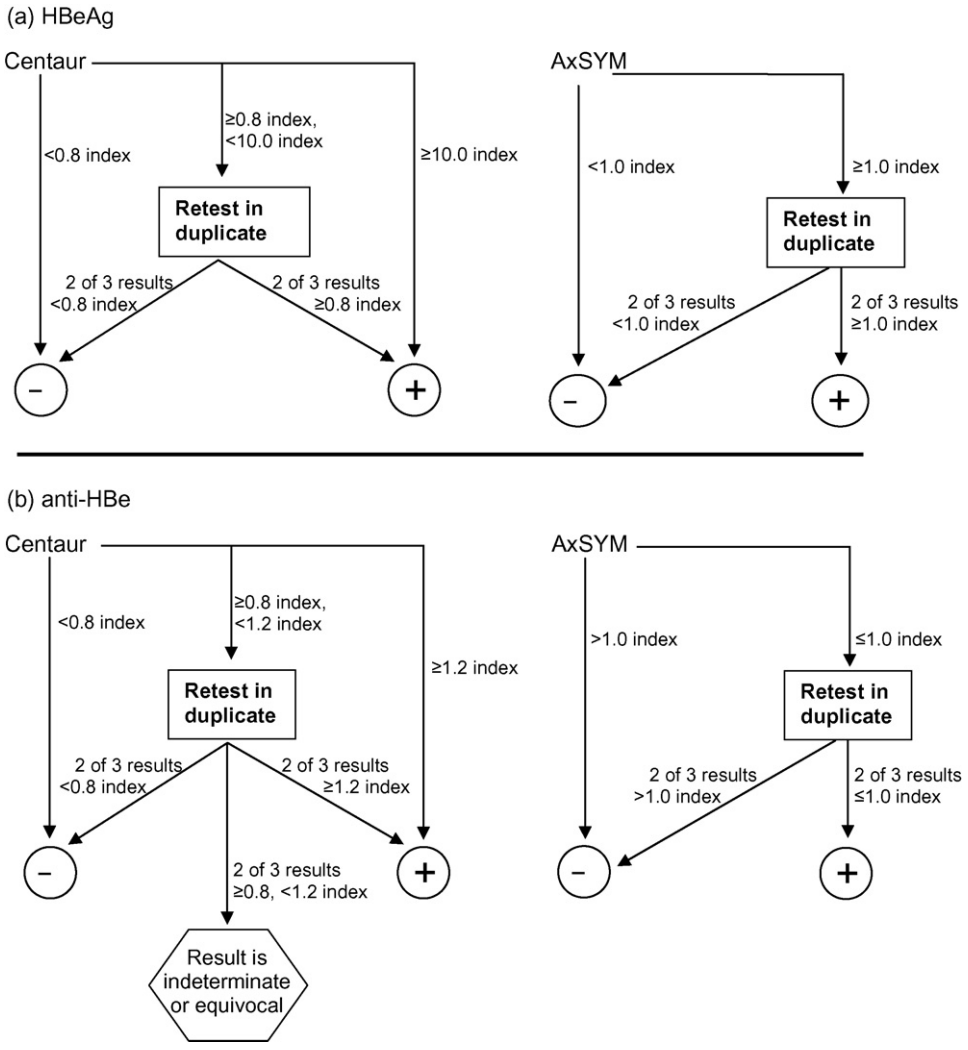

Fig. 1. Testing algorithms for the method comparison studies.