Acute hepatitis: significance of antibody to hepatitis B core antigen

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SUMMARY The value of testing for core antibody (anti HBc) in acute hepatitis was assessed in 503 patients. All hepatitis B surface antigen (HBsAg) positive patients tested were also anti HBc positive. Of the 110 HBsAg negative, anti HBc positive patients, 32 were found to have surface antibody, indicating previous infection with hepatitis B virus (HBV). Of the remaining 78 patients in whom anti HBc alone was detectable, follow-up specimens were received from 28 and, of these, 21 were then found to be anti HBc negative. Thus in acute hepatitis non-specific transient reactions to core antigen may appear, and the presence of anti HBc alone cannot be considered adequate evidence for a diagnosis of HBV infection.

In acute hepatitis due to hepatitis B virus (HBV) the surface antigen (HBsAg) is first detected in the serum during the incubation period. Core antibody (anti HBc) is also produced during the incubation period and appears in the serum at a variable time interval after the surface antigen. By the time symptoms occur both are readily detectable. As the acute illness resolves the HBsAg disappears but anti HBc persists and in most cases surface antibody (anti HBs) is then produced. In the HBsAg carrier the presence of surface antigen is also associated with core antibody. Only in the immunosuppressed carrier and in the very earliest phase of infection is HBsAg found in the absence of anti HBc. The presence of core antibody in the absence of surface antigen has usually been presumed to indicate infection, either current or past, with HBV. However, in a recent paper (Cohen and Cossart, 1977), it has been suggested that some of these reactions may be nonspecific, particularly in liver disease. Similar reactions were demonstrated using both a more highly purified core antigen and a comparable extract prepared from a normal liver.

This paper describes and assesses the results of tests for core antibody on sera from cases of acute hepatitis received in the laboratory over a seven-month period.

Material and methods

Altogether 503 serum samples were tested from

patients with a provisional differential diagnosis of acute hepatitis.

Tests for HBsAg were performed by conventional methods—counter-immunoelectrophoresis (CIEP), reverse passive haemagglutination (RPHA) (Hepanosticon), and RIA (Ausria II). RIA (Ausab) was used to detect anti HBs.

Core antibody was detected by CIEP using an antigen prepared from the liver obtained post mortem from an immunosuppressed human carrier (Cohen and Cossart, 1977). Selected sera were further tested for anti HBc by RIA (Corab).

Specimens were routinely tested for HBsAg by CIEP and RPHA, and those found to be HBsAg negative were tested by CIEP for anti HBc. The anti HBc positive specimens were then further tested for HBsAg and anti HBs by RIA.

Results

A flow diagram of the tests carried out and the results obtained is presented (Figure).

Of the 503 specimens tested, 133 were HBsAg positive by routine methods (CIEP, RPHA). A sample of 59 of these were tested for anti HBc, and all were positive. All 133 were presumed to be from cases of acute hepatitis B infection; in a country where the carrier rate of HBsAg is very low the incidence of non-B hepatitis occurring in the HBsAg carrier must also be low.

All of the remaining 370 specimens HBsAg negative by routine tests were tested for anti HBc; 118 were positive. Table 1 shows the age and sex

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Figure Flow diagram of tests performed on specimens from 'acute hepatitis'

Table 1 Anti HBc results in 'acute hepatitis'—HBsAg negative by routine tests (CIEP, RPHA)

Age	Male (193)		Female (170)	
	anti HBc +	anti HBc -	anti HBc +	anti HBc -
< 5	1	4	0	3
6-9	1	3	0	4
10-14	3	1	4	6
15-24	**27	18	*13	25
25-39	27	24	8	20
40-59	10	33	*4	30
> 60	5	23	3	32
NK	8	5	3	15
Total	82	111	35	135

Sex not stated for seven patients (one anti HBc +)

NK = not known

* 1 patient HBsAg + (RIA)

**6 patients HBsAg + (RIA)

distribution of the patients providing these specimens; the incidence of core antibody was highest in males aged between 15 and 39.

No further tests were done on the specimens that were anti HBc negative as previous studies in this laboratory (Vandervelde, 1975) had shown that the use of the much more expensive RIA test was unlikely to reveal any more antigen positive specimens.

Of the 118 core antibody positive specimens that were HBsAg negative by routine tests, eight were found to be HBsAg positive when tested by RIA. Three of these were taken more than one month after the onset of jaundice. Seven of these eight patients were aged between 17 and 22; six were male. Further specimens were tested from five of these eight

patients: three had detectable surface antibody when tested respectively two, three, and six months later, one was still HBsAg positive three weeks later but the radioactive count had fallen to a level just above the cut-off point, and one was HBsAg negative but had not developed detectable surface antibody two months later. Unfortunately, no further specimens were received from these last two patients. All five patients remained anti HBc positive.

Of the 110 core antibody positive specimens that were HBsAg negative by all tests, 32 had detectable surface antibody—20 males aged 21-71, 12 females aged 17-65—indicating previous infection with HBV.

Of the remaining 78 patients in whom anti HBc was the only marker suggesting HBV infection, further specimens were obtained from 28. Twenty-one of these, mostly tested after an interval of three to four weeks, no longer had detectable core antibody. Of these 21 patients, sera from 11 were tested for anti HBc by RIA; nine had no detectable antibody. Seven remained anti HBc positive, two were retested within two weeks, four one month later, and one six weeks later. All 28 follow-up specimens were HBsAg and anti HBs negative when tested by RIA.

Core antibody titres were determined to see if the titre was of any significance in specimens that were HBsAg negative by routine tests (Table 2). Seven of the sera that were HBsAg positive by RIA only had titres of at least 1 in 10, whereas six out of 14 with surface antibody had titres of less than 1 in 10, as did eight out of 14 with transient core antibody.

Table 2 Titration of anti HBc positive sera (all HBsAg negative by CIEP and RPHA)

RIA results	Number tested	Anti HBc titre			
		N	10 ⁻¹	10 ⁻²	10 ⁻³
HBsAg+ anti HBs-	7		3	4	
HBsAg- anti HBs+	14	6	4	3	1
HBsAg- anti HBs- (anti HBc transient)	14	8	5	1	

Discussion

The CIEP test for anti HBc is easy to perform and does not require very expensive equipment; most laboratories will already have the necessary apparatus. The preparation of the antigen is relatively easy, the main problem being the source as livers from most antigen carriers do not yield sufficient core antigen because of the presence of core antibody; when it can be obtained the best source is the post-mortem liver from an immunosuppressed carrier.

Many specimens referred to this laboratory for further evaluation of positive or equivocal results obtained with RPHA tests were found to be HBsAg negative when tested by RIA. Only about 15% of

these HBsAg negative specimens had detectable core antibody. Jaundiced sera often interfere with the sedimentation of the cells in the RPHA test systems; in such cases failure to detect core antibody excludes HBV infection.

The presence of core antibody as the only marker of HBV infection should be interpreted with caution. In some cases it denotes a previous infection and may be associated with surface antibody; in others, particularly in acute hepatitis, the reaction may be non-specific and transient.

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References

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