the latter case, by day 4, a yellow, non-water soluble substance was precipitated. The fluorescence spectrum of the incubating solution of the slides and also that of the supernatant of the precipitated albumin-glucose are identical: the excitation maximum was 370 nm, that of emission, 435 nm. The fluorescence parameters of the brown incubating solution diluted with G-6-P were: excitation 410, 470 nm; emission, 525, 540 nm. These values agree with the maxima of fluorescence measured for lipofuscin in situ.

Lipofuscin (and wear pigment) are known to be PAS, protein, performic acid-Schiff and lipid positive, fluorescent pigments chiefly found in tissue rich in glycogen or glucose (muscle, liver, nerve cells). The causes of PAS positivity and the fluorescence of lipofuscin have so far not been conclusively clarified.

The paraffin wax slides of the resin-like fluorescent substance forming from albumin-glucose in vitro are PAS positive, and give the Schmorl and NBT protein reaction. On the basis of our data we believe that besides lipoproteins and glycoproteins the glycosylated proteins are also considerable constituents of the lipofuscin-like pigments.

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Sensitivity of anti-HBc IgM kits and the diagnosis of acute hepatitis B

It was suggested by Morris that the presence of HBeAg and subsequent seroconversion to anti-HBe is a better indication of acute hepatitis B infection than the presence of anti-HBc IgM in cases where the patient is hepatitis B surface antigen (HBsAg) positive. This conclusion is based on data showing that anti-HBc IgM concentrations remain high, even some months later, in HBsAg carriers after HBeAg/anti-HBc conversion.

That anti-HBc IgM can be a useful diagnostic aid in active disease has been shown by other authors, and the detection of increased concentrations of anti-HBc IgM is normally associated with the acute phase of hepatitis B virus infection. One reason for the various opinions on the value of core IgM tests is the different cut-offs recommended by kit manufacturers of the assay methods used. We compared the performance of five commercial kits using a panel of sera with medium and low anti-HBc IgM concentrations and expressed the results in units of the Paul Ehrlich Institute reference preparation (U/ml). The effects of the different cut-offs of these tests can be seen in the results for a panel of 20 samples from chronic carriers (table). It is evident that the antibody titre at the recommended cut-off for these assays varies by a factor of up to 20, and the assays where the cut-off is positioned at a low level give a higher detection rate with sera from chronic carriers. Using a panel of serial samples, we also showed that the mean period of positivity is different after the acute phase of infection varies from about two months for the less sensitive (high cut-off) assays to more than seven months with the most sensitive assay. The assay used by Morris was of high sensitivity and it would account for the finding of positive anti-HBc IgM results after the HBe/anti HBc seroconversion.

Detailed clinical studies have shown that an anti-HBc IgM concentration of >600 U/ml is the best indication of the acute phase of hepatitis B infection. It is therefore important to consider not only the cut-off sensitivity but also the response range of the assay to be used. The assays have a variable upper level range (table) and some have limited or no ability to discriminate medium antibody titre from the more clinically important high (>600 U/ml) titres of antibody. It is these variations in sensitivity and response range that contribute to the divergence of opinions on the value of anti-HBc IgM in the diagnosis of acute hepatitis B. With an appropriate choice of cut-off, anti-HBc IgM concentrations remain positive only in the period of active disease (typically two months), and such a test is a useful vehicle for this application.

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Comparison of sensitivity, range, and detection of chronic cases in five commercial anti-HBc IgM kits

<table>
<thead>
<tr>
<th>Kit name (manufacturer)</th>
<th>Cut-off antibody titre U/ml</th>
<th>Approximate antibody titre at assay response plateau U/ml</th>
<th>No of positive or (retest) results on 20 sera from chronic HBV cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alermite anti-HBc IgM Assay (Amelrite Diagnostics, Amersham)</td>
<td>250</td>
<td>800</td>
<td>0 (2)</td>
</tr>
<tr>
<td>Corezyme-M (Abbot Diagnostics)</td>
<td>290</td>
<td>800</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Wellzyme anti-HBc IgM (Wellcome Diagnostics)</td>
<td>60</td>
<td>350</td>
<td>4 (3)</td>
</tr>
<tr>
<td>Core IgM K EIA (Sorin Biomedica)</td>
<td>30</td>
<td>500</td>
<td>7*</td>
</tr>
<tr>
<td>Hepanostika anti-HBc IgM Micro ELISA (Organon Teknika)</td>
<td>15</td>
<td>510</td>
<td>12*</td>
</tr>
</tbody>
</table>

*Estimated using a panel of 22 samples. The anti-HBc IgM titres of these samples was determined from a calibration of Alermite results and the Paul Ehrlich Institute reference preparation.

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