Havens’ haemagglutination test in infective hepatitis

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In an attempt to find a diagnostic serological test in hepatitis, Havens in 1958 reported the results of his studies using red cells from day-old chicks. He showed that positive haemagglutination tests were found in the sera from 70% of patients in the early stages of viral hepatitis (Havens, 1959, 1960). The exact mechanism of this reaction is not known. Turner, Jha, Crowley, and Sherlock (1962), using the same test, found positive titres in 60% of sera from patients within two weeks of the onset of symptoms of hepatitis. We have used this procedure while investigating an epidemic of infective hepatitis in Bristol; the epidemiological details of this outbreak have been reported elsewhere (Bothwell, Martin, Macara, Skone, and Wofinden, 1963). We report the results obtained during the early phase of the disease and subsequently over a five-year follow-up period.

RESULTS

INITIAL HAEMAGGLUTINATIONS The positive and negative titres which were obtained are shown in Table I. Of the 533 sera tested, 143 (26·8%) were positive. These positive results were obtained in 49·3% of sera from patients who were within the first four weeks of the attack; in 25·6% of those from two to six months after the onset; and in 17·2% of sera obtained during the next six months. Positive results were also found in 25% of the sera which were obtained from one to two years after the onset.

In Table II the results of the tests which were repeated in 203 sera are shown. Of these, positive titres were seen in 59 (29%), 10 of which were still positive three to five years after infective hepatitis. Of 17 sera in which negative results were obtained initially, there was an alteration to definite positive titres later on during the patients’ convalescence. On the other hand, 41 initially positive became negative, and 103 sera showed consistently negative results.

There was no relationship between a positive test and a raised ESR (>20 mm in 1 hr, Westergren). High ESRs occurred in 63% of patients tested.
The mechanism of the haemagglutination is unknown; any evidence of a direct relationship with circulating virus still awaits confirmation. The factor responsible for a persistently positive haemagglutination reaction is also not known. There is no obvious relationship with serum protein abnormalities, although a large number of our patients had abnormal serum proteins for several months, some up to five years, after the attack. This is of interest and may be of practical importance, because abnormal serum proteins and a raised ESR may be mistakenly attributed to continuing liver disease. A gamma globulin has been suggested as the cause of the positive haemagglutination by Havens (1962). A raised gamma globulin level in our series was not related to a continuing positive test, but immuno-electrophoresis may possibly have been more discriminating. Although a positive haemagglutination reaction could indicate a continuing hepatic disorder, our nine liver biopsies have shown no persisting damage.

There was no apparent connexion with the clinical severity of the attack of infective hepatitis. Havens (1962) suggests that the appearance of haemagglutinins is intimately related to the hepatitis and consequently their diminution or disappearance from the blood is usually associated with early recovery. However, persistent positive haemagglutinations were seen in our series in patients who had all apparently recovered completely.

Iber found that this test was completely non-specific; he suggested that it was of no value in determining the cause of liver disease. He obtained positive results in cirrhosis, alcoholic liver disease, nephrosis, and heart failure (Iber, 1964). Our study shows that the test may remain positive without any apparent persistent liver disease. The test is time consuming and does not differentiate infective hepatitis from other types of liver cell jaundice. The cause of its persistence is of interest but further detracts from its usefulness.

**SUMMARY**

Havens’ haemagglutination test was performed on 533 sera from patients during an epidemic of infective hepatitis in Bristol, and was repeated in 203 of these cases. Positive tests were found in 49% of the patients within the first four weeks of the attack, and in a few as long as five years later.

Persistent abnormal levels of serum protein were also found; however, the positive haemagglutination tests were not related to these abnormalities.

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