LATEX FIXATION TESTS IN LIVER DISEASES

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Rheumatoid factor is a macroglobulin which has been found to be present in the sera of most patients with rheumatoid arthritis. One of the techniques used to demonstrate the presence of this macroglobulin which agglutinates with gamma globulin is by the use of latex fixation test. Though Singer (1961) reported the incidence of positive tests in rheumatoid arthritis to be about 64%—76%, it has been found by a number of investigators that this test is non-specific and is present in various other conditions *viz.* sarcoidosis, leprosy, active pulmonary tuberculosis, subacute bacterial endocarditis, hepatic, haemopoietic and collagen diseases and also on a very small percentage of normal people. Since this factor has been found to be present in liver disease by other investigators, the objects of this paper are:

1. to determine the incidence of positive latex fixation tests in various types of liver disease seen in this country;
2. to determine whether this test could be of value in the diagnosis of various types of liver diseases.

METHODS

The test was carried out on all the patients with evidence of jaundice and/or liver disease. The method used was the HYLAND RA TEST,—a rapid slide screening test—prepared by Hyland Laboratories and it is briefly as follows:—

1. An approximately 1:20 dilution of the serum under test was prepared by adding one drop (about 0·05 ml.) of serum to 1 ml. of buffer diluent.
2. One drop of diluted serum specimen was placed in a rectangle of the divided slide.
3. One drop of reagent was added and this was mixed with an applicator, and spread over an area of approximately 20 × 25 mm.
4. Positive and negative controls were prepared by mixing one drop of appropriate RA-TEST Control Serum (without further dilution) with one drop of Reagent. Separate applicators were used for each mixture.
5. The slide was tilted from side to side for one minute and macroscopic clumping was looked for.

The results were interpreted as follows:

1. Smooth suspension with no visible flocculation as shown by negative control was considered as negative. The result was also considered as negative even if there was partial clumping or visible flocculation with small aggregates.
2. A positive reaction was one in which there were visible aggregates and complete clumping as shown by positive control. This visible flocculation usually occurred in a few seconds.

Hepatic Amoebiasis

All the 11 cases were negative to the latex fixation tests. Of these 11, 4 were abscesses while the rest were hepatitis, the diagnosis of which was based on clinical evidence and the therapeutic response to either emetine or chloroquin. A liver biopsy was done on one of these seven cases and the histological section revealed the presence of the parasite.

Primary Carcinoma of the Liver

All these cases were confirmed by either liver biopsy or at post-mortem (3 cases by necropsy). Six out of ten cases of primary carcinoma of the liver had positive latex fixation tests.

Cirrhosis

The term cirrhosis used here embraces both types of cirrhosis—Laennec's and the postnecrotic, because there is no complete agreement on pathological features which distinguish portal from the postnecrotic type. Further-

RESULTS

Diseases	No. of patients	Positive	Percentage
Hepatic amoebiasis	11	0	0
Primary carcinoma of the liver	10	6	60
Cirrhosis of the liver	39	17	43
Infective hepatitis	24	8	33
Obstructive jaundice	10	0	0
Cholelithiasis 2		0	0
Carcinoma of the head of pancreas 7		0	0
Fibrosis of the head of pancreas 1		0	0
Miscellaneous			
Steven-Johnson	2	0	0
Haemochromatosis	1	0	0
Leptospirosis	1	0	0
Glucose-6-phosphate dehydrogenase	2	0	0
	100		

Figure 1

more, a single liver may show some features of both types. When Popper et al (1960) tried to eliminate differences in terminology by defining the two types on the basis of the main features described in the literature, they found that postnecrotic cirrhosis occurred quite commonly in alcoholics and portal cirrhosis in non-alcoholics. Thirty-nine cases were tested and seventeen were positive while the rest were negative. These cases were either confirmed by liver biopsy and/or other biochemical and radiographical investigations. One case had concomitant deficiency of glucose-6-phosphate dehydrogenase, and was one of the negative cases.

Infective Hepatitis

Eight cases out of twenty-four gave a positive reaction to latex fixation tests. The diagnosis of this condition was based on the clinical presentations and the ancillary investigations. No liver biopsy was done on any of the patients.

Obstructive Jaundice

All the ten cases of obstructive jaundice of varying causes gave negative results. Of these ten, two were cholelithiasis, one was due to fibrosis of the head of the pancreas and the rest were due to the carcinoma of the head of pancreas. All these cases were confirmed at operating table and by histological sections.

Miscellaneous

Two cases of Steven-Jonhson Syndrome (probably due to drugs), two cases of glucose-6-phosphate dehydrogenase deficiency, one case each of leptospirosis and haemochromatosis were all negative to this test.

DISCUSSION

According to Barfeld (1960) the incidence of positive latex fixation test in the normal people is 1% and when the sick people are used as controls the incidence rises to 5%. In this investigation, the positive tests in infec-

tive hepatitis, cirrhosis and the primary carcinoma of the liver are more frequent than one would expect in the population of healthy individuals. The results of this test in cirrhosis of the liver and in infective hepatitis seem to be in keeping with some of the investigators. While Caplan (1963) and Atwater and Jacox (1963) have a higher incidence of positive tests in viral hepatitis and cirrhosis, the figures obtained by Trombly and Dresner (1959) are fairly close to the figures obtained in this investigation (see Figure 2). As for the obstructive jaundice of the extra-hepatic type, the present figure is the same as that of Caplan (1963). No figures are available for comparison for hepatic amoebiasis and primary carcinoma of the liver.

Investigators	Infective Hepatitis	Cirrhosis
Atwater & Jacox	42%	60%
Caplan	100%	79%
Trombly & Dresner	37%	25%
Chew & Yeo	33%	43%

Figure 2

The active factor that gives the positive latex fixation test in cirrhosis has been found by Bonomo et al (1963) by the method of cellulose chromatography and ultracentrifugation to be 19S protein. Whether this same protein is the active factor in the case of primary carcinoma of the liver is difficult to say as no study has been made on this type of condition. Howell et al (1960) put forth a suggestion that the agglutinating factors in liver diseases might be antibodies, which might be stimulated by:

1. a viral agent or other foreign organism,
2. an interaction product of invading organisms and host tissues,
3. normal or altered host tissues not previously exposed to antibody producing cells until the time of the disease according to Burnet's theory of 'self'. They also mentioned that Vaughan also put forward the arguments in support of the theory that these factors are antibodies.

The reason why only some cases of cirrhosis, infective hepatitis and primary carcinoma of the liver gave positive latex fixation tests is difficult to explain as the factors that are responsible for this reaction are not completely known, though as mentioned above they are being thought to be antibodies by some of the investigators. Dresner et al (1959) and Atwater et al (1963) considered that the positive tests reflect the activity of the hepato-cellular damage, because they observed that some of the positive reactions in infective hepatitis cases became negative following clinical recovery and that in cirrhotics the disease progressed more rapidly downhill in those with positive results. In this study, no attempt was made to correlate the severity of the disease with the incidence of the test. Although this observation might be correct, it is difficult to explain the negative tests in some of the cases of primary carcinoma of the liver. It cannot be said that this negative reaction was due to the fact that there was no active or insufficient active hepato-cellular damage taking place in these cases because the enzyme studies of this condition revealed that the activity is invariably increased (Chew & Lee—to be published).

As to whether this test is of value in the diagnosis of various types of liver diseases, the results indicate that in only two of the conditions studied *viz.* hepatic amoebiasis and obstructive jaundice this test is going to be of help. In these two conditions, the test was negative in all the cases. In the case of hepatic amoebiasis if the clinical diagnosis is in doubt, it would appear that the negative latex fixation test will support the clinical impression. It has been a well recognized fact that it is very difficult to distinguish medical jaundice from surgical jaundice (by which is meant extra-hepatic obstructive jaundice) even with the help of the biochemical tests. The biochemical test that are at present available are noted to be unreliable. Quite often patients have to be subjected to laparotomies whenever there is doubt as to whether the jaundice is surgical or not. Therefore if there is any test that can help the clinician to determine whether a patient is suffering from extra-hepatic jaundice or not preoperatively then it can be considered to be a breakthrough in one of the most difficult clinical problems. The results of this investigation reveal that all the cases of extra-hepatic obstructive jaundice have negative latex fixa-

tion tests and this is in keeping with that obtained by Caplan (1963). It can therefore be said that a severely jaundiced patient with some evidence of obstruction as shown by other biochemical tests is likely to be extra-hepatic if the latex fixation test is negative. To illustrate this point two examples shall be quoted. A fairly elderly Chinese male was admitted with very severe jaundice (serum bilirubin was 29 mg%). The biochemical results suggested that it was likely to be an extra-hepatic obstructive jaundice, but the latex fixation was positive. He was then submitted to surgery and at operation he was found to be suffering from cirrhosis of the liver. On the other hand a Chinese female patient was admitted for investigations for the complaints of generalised itchiness, yellowness of the eyes and the body and passing clay coloured stool. The biochemical tests done did not suggest any evidence of obstruction but the latex fixation test was negative. As the clinical impression was that she was probably suffering from surgical jaundice, she was operated on and was found to be suffering from carcinoma of the head of pancreas. These two illustrative cases were included in this series. Since the number of cases of the extra-hepatic obstructive jaundice tested was small, a firm conclusion as to the value of this test in the differential diagnosis of jaundice cannot be made. Nonetheless it can be said that it serves as an eye opener to the clinicians as to the possible value of this test in these conditions.

Since this test can give either a positive or negative reading in infective hepatitis, cirrhosis of the liver and primary carcinoma of the liver, it can be concluded that as an aid to the diagnosis of these conditions this test is of doubtful value. No conclusion can be made for the miscellaneous conditions that are included in this trial.

SUMMARY

1. The use of latex fixation test in different types of liver diseases commonly seen in this country is described.
2. Of 100 cases with various types of liver disease tested, there were 11 cases of hepatic amoebiasis, 10 primary carcinoma of the liver, 10 extra-hepatic obstructive jaundice, 39 cirrhosis of the liver, 24 infective hepatitis and 8 other miscellaneous cases.
3. All the cases of hepatic amoebiasis and the extra-hepatic obstructive jaundice were negative to the latex fixation test. 17 out of 39 cirrhosis of the liver, 6 out of 10 primary carcinoma of the liver and 8 out of 24 infective hepatitis gave positive reactions.
4. A brief discussion on the factors responsible for this test and the value of this test as an aid to the diagnosis of the liver diseases is made.

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