

## GALACTOSE RETENTION: AN ALTERNATIVE TO THE BROMSULPHTHALEIN TEST

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### SYNOPSIS

**A simple galactose retention test is described for clinical use. It appears to be useful as an aid in distinguishing between parenchymatous and obstructive liver disease. It correlates well with the B.S.P. test when such an alternative is required.**

Bromsulphthalein excretion, a delicate test of liver function, is based upon the capacity of the liver cells to remove the dye from the bloodstream and then excrete it into the bile. The test has the disadvantage that, although the liver is the organ principally concerned in the removal of bromsulphthalein, extra-hepatic tissues also play a part in its disposal (Caesar *et al*, 1961). Moreover the test is of little use in jaundiced patients despite corrections made to overcome the effects of hyperbilirubinaemia (Metzler *et al*, 1956). Fatal hypersensitivity reactions have also very occasionally been reported (Venger 1961). Hence a clinical test of comparable sensitivity to the bromsulphthalein test which can be used to assess liver function in the presence of jaundice would be of value.

Tygstrup and Winkler (1954) demonstrated that galactose is almost exclusively metabolised by the liver; only a small part is excreted by the kidneys and this is directly related to the blood concentration (Harding and Grant 1932-33; Nissen 1937; Gammeltoft and Kjerulf-Jensen 1943 cited by Tengstrom 1966). Urinary excretion accounts for approximately seven per cent of the galactose cleared and this amount remains constant whether the total elimination rate is high or low. Although very little is known about the extra-hepatic metabolism of galactose, it is generally regarded as being negligible under normal conditions.

Tengstrom (1966) used the galactose half-time as an empirical measure of hepatic function and found a certain correlation between it and the bromsulphthalein half-time value. He also found that the galactose test was normal in biliary obstruction even with a high bilirubin value,

making this a useful test in the differentiation of obstructive and hepato-cellular jaundice.

Despite their great potential value, galactose and bromsulphthalein half-time determinations are too complicated for general use and it was felt that simpler methods should be investigated. The present study was therefore undertaken to determine whether the galactose and bromsulphthalein retention tests give equivalent information.

### MATERIAL AND METHODS

Twelve control subjects and 38 patients were studied. They comprised:

1. twelve healthy students, doctors and nurses. The average age of the group was 25.3 years and ranged between 21-35 years.
2. eight patients who were hospitalised with obstructive jaundice caused by stones in the common bile duct in two cases, carcinoma of the pancreas in two cases and single cases due to drugs, primary biliary cirrhosis, congenital hyperbilirubinaemia and duodenal diverticulum. The mean age of the patients was 60.8 years and the range 22-90 years.
3. five patients with cancer metastases in the liver. The mean age was 64.8 years and the range 47-75 years.
4. eight patients with infective hepatitis. The mean age of the patients was 31.4 years and the range 19-56 years.
5. seventeen patients with cirrhosis. The mean age of the patients was 55.6 years and the range 43-71 years.

All control subjects and patients had been on a normal diet and had then fasted for 8-12 hours prior to testing. The galactose test was carried out with the subject in the recumbent position. 350 mg. of galactose per Kg. body weight was administered intravenously as a sterile 25 per cent

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solution over a period not exceeding three minutes. A stop watch was started when half the volume had been given and 30 minutes later, 0.1 ml. of capillary blood was taken from a finger tip for galactose determination.

In 15 of the 17 patients with cirrhosis, a 45 minute bromsulphthalein (B.S.P.) retention test was carried out immediately after the galactose test using 5 mg. bromsulphthalein per Kg. body weight.

Galactose determinations were carried out using a slight modification of the method described by Varley (1962). Bromsulphthalein retention was assessed by the colorimetric method described by Varley (1962).

RESULTS

The results of the galactose retention tests are shown in the histogram (Fig. 1). The mean galactose retention was  $26.4 \pm 19.8$  mg. per 100 ml., standard deviation (S.D.) and range (mean  $\pm 2$  S.D.) 0-66 mg. per 100 ml. in the group of healthy controls.

Abnormal galactose retention was noted in one of the eight cases of obstructive jaundice and in four of the five cases of cancer metastases in the liver. The mean galactose retention in the group of patients with obstructive jaundice was  $31.6 \pm 21.0$  mg. per 100 ml. S.D. and range 0-73.6 mg. per

100 ml., while the mean galactose retention in the group of patients with metastases in the liver was  $84.0 \pm 45.2$  mg. per 100 ml.

The mean galactose retention in the group of patients with hepatitis was found to be  $48.2 \pm 39.2$  mg. per 100 ml. S.D. and range 0-126.7 mg. per 100 ml. In patients with cirrhosis, the mean galactose retention was  $88.8 \pm 30.9$  mg. per 100 ml. S.D. and range 27.1-150.6 mg. per 100 ml. and abnormal values were found in 12 of the 17 patients studied.

Comparison was made between the results of the galactose and B.S.P. retention tests in 15 patients with cirrhosis (Fig. 2). Statistical analysis showed a good correlation between the per cent B.S.P. retention and galactose retention in mg. per 100 ml. The correlation coefficient  $r = 0.67$  and at 13 degrees of freedom,  $0.01 > P > 0.001$ . It was found possible to express the relation between the galactose retention and B.S.P. retention by the formula  $Y = 1.8, X + 43.9$  where Y is the galactose retention in mg. per 100 ml. at 30 minutes and X the per cent B.S.P. retention at 45 minutes. There is thus a highly significant correlation between the galactose retention and B.S.P. retention tests.

DISCUSSION

The galactose retention test is a satisfactory empirical measure of the galactose elimination rate and thus of liver function. It is sometimes useful in distinguishing between parenchymatous and non-parenchymatous liver disease. The galactose retention was found to be normal in 87.5 per cent of patients with biliary obstruction and in four single cases of mucocoele of the gall bladder, the Budd-Chiari syndrome, duodenal ulceration and polycythaemia respectively.

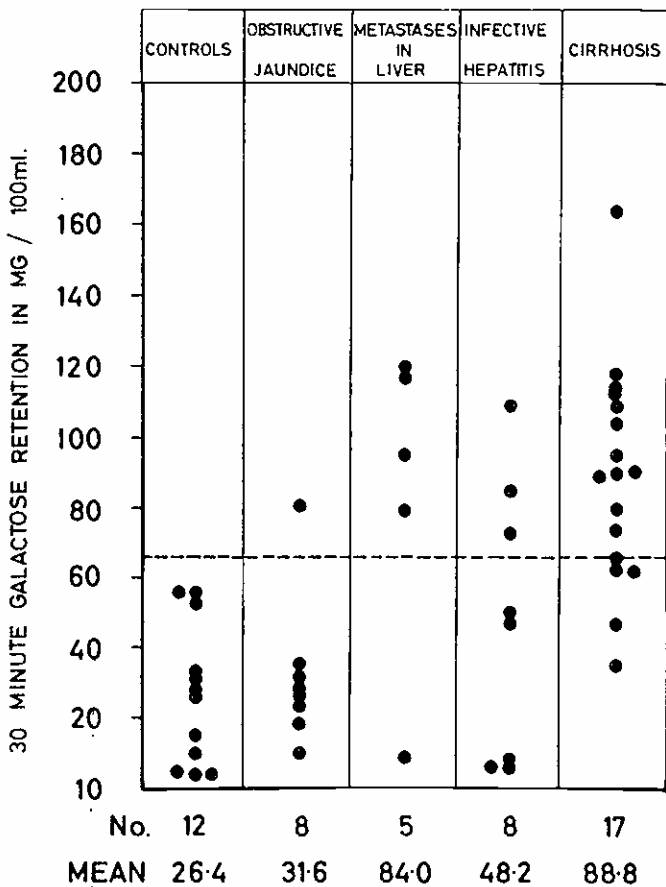


Fig. 1. Results of Galactose Retention Tests.

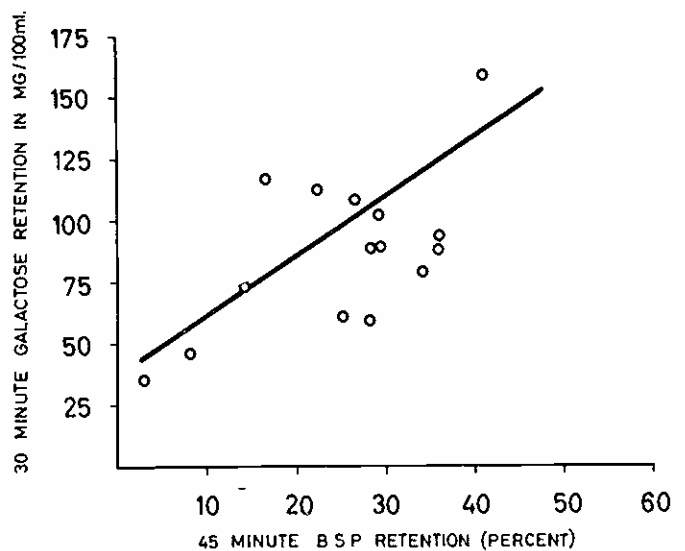


Fig. 2. Correlation between Results of Galactose and Bromsulphthalein Retention Tests.

Tengstrom (1966) pointed out that although galactose elimination is not affected by a purely obstructive jaundice even when pronounced, very prolonged obstruction can probably damage the liver parenchyma sufficiently for the galactose test to show abnormal results. The only patient with obstructive jaundice who was found to have an elevated galactose retention was an 82 years old female who attended hospital with a history of colicky pain in the right hypochondrium for one week, followed subsequently by the onset of jaundice. Radiological investigations revealed the presence of calculi in the common bile duct. The serum bilirubin was 2.4 mg. per 100 ml., alkaline phosphatase 26 K.A. units, pseudocholinesterase 35 units, S.G.O.T. 560 units, S.G.P.T. 620 units and S.L.D.H. 779 units. These associated results indicate parenchymal damage. Because of the patient's advanced age, liver biopsy was not undertaken and operative treatment was declined.

Although the number of cases investigated is small it was considered that galactose elimination is not affected by a purely obstructive jaundice. A comparison of galactose retention between patients with obstructive jaundice on the one hand and those with hepatitis or cirrhosis on the other shows that the galactose test distinguishes only incompletely between the two groups of patients. This is because the retention of galactose was found to be normal in some patients with hepatitis or cirrhosis. This is not surprising in view of the fact that damage to hepatic parenchyma may not always be sufficiently marked to cause a reduction of the galactose elimination rate in every case of hepatitis or cirrhosis.

The results of the galactose retention test were found to correlate well with the B.S.P. test. In patients with cirrhosis abnormal galactose retention was found in 66.6 per cent of cases compared with 93.3 per cent abnormal B.S.P. retention (normal B.S.P. range = 0.5 per cent).

The galactose and the B.S.P. retention tests behave differently in jaundice. Since B.S.P. is excreted by the same paths as bilirubin, the B.S.P. test does not give proper information about liver function in patients with jaundice whereas the galactose retention test is usually normal in biliary obstruction even in the presence of a high serum bilirubin level, the result not being affected by jaundice per se. (Tengstrom 1966).

It is believed that the galactose test does have a place in the group of liver function tests at present available in that it can be used as an aid in

differentiating between parenchymatous and obstructive jaundice and also as a substitute for the B.S.P. test in the presence of jaundice or where there is a history of allergy to B.S.P. Broadly speaking, it would be possible to make an approximate estimation of the B.S.P. retention in a patient with jaundice from the formula given above, provided the value for galactose retention in that patient is known.

Tengstrom (1966) found normal galactose half-times in all patients with obstructive jaundice, in 36 per cent of patients with cancer metastases in the liver, in 51 per cent of patients with infective hepatitis and in 11 per cent of patients with cirrhosis. This appears to correspond approximately with the results obtained with our galactose retention tests where it was found that 87.5 per cent of patients with obstructive jaundice, 20 per cent of patients with cancer metastases in the liver, 62.5 per cent of patients with infective hepatitis and 29.4 per cent of patients with cirrhosis had normal galactose retention. These findings suggest that the simpler galactose retention test may furnish equivalent information to that obtained by the more complicated galactose half-time investigation.

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