Intravenous Galactose Liver Function Test*

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IN a previous communication by one of us (1) the intravenous and oral galactose liver function tests were discussed. In the oral method there are at least two possible sources of error, which materially influence the sensitiveness of the test. The first is the intestinal rate of absorption. The second is a renal factor; the excretion of galactose may be influenced by a possible renal threshold value (2) or by renal disease. Both of these factors are eliminated in the intravenous test. On the other hand, the complicated chemical procedures and the multiple venipunctures constitute disadvantages and limitations to the practical applicability of the intravenous galactose liver function test. These, however, are of a degree comparable with other accepted tests like the glucose tolerance test and can be conducted by any well equipped clinical laboratory.

It is believed that galactose is metabolized by the liver only. Hence, any delay or diminution in the utilization of the galactose can be referred to a diminished liver function. A normal liver can metabolize within one hour, 25 gms. of intravenously injected galactose. Thus, any demonstrable galactose in the venous blood, one hour or longer after the injection of 25 gms. of galactose implies liver pathology. The rate of utilization can be studied by repeated observations at intervals of 15 minutes beginning one hour after the injection. The greater the retention of galactose, the greater the liver damage.

TECHNIQUE

Further observations with this test lead to some modifications of the technique. Instead of a 50 per cent, we are now using a 25 per cent solution of galactose. In this way, the viscosity of the solution is diminished and caramelization after autoclaving prevented. To avoid annoying reactions, characterized by chills and tremors, a buffer is added to the sterilized galactose solution. We have eliminated the analysis 30 minutes after galactose injection as of no practical value. On the other hand, a blood sample 75 minutes after the injection of the galactose solution proved of interest.

The present technique is as follows: A fasting venous blood sample is taken and oxalated in the usual way. Through the same needle 100 c.c. of a properly warmed, sterilized and buffered 25 per cent galactose solution, is injected slowly intravenously. Venous blood samples are taken and oxalated 60, 75 and 90 minutes later. The patient remains throughout this period in a fasting state.

From each of the four blood samples a Folin and Wu tungstic acid filtrate is prepared. The fermentable reducing substance is fermented out by the technique of Somogyi (3). The amount of non-fermentable reducing substance is determined by the method of Folin and Wu. The difference between the non-fermentable reducing substance in the first blood sample and in the blood samples following the injection of galactose, divided by 0.75 for the difference between glucose and galactose reduction, represents the galactose retained within the venous blood.

OBSERVATIONS

We have studied the rate of galactose utilization in five groups of patients: (1) Patients without demonstrable liver or biliary tract disease; (2) Patients with intrahepatic jaundice; (3) Patients with obstructive jaundice; (4) Patients with cirrhosis of the liver; (5) Patients with gall bladder disease.

(1) *The patients without liver or biliary tract disease* have all shown complete utilization within one hour of 25 gms. of intravenously injected galactose. Thus, the standard of normalcy has been established and our previous observations confirmed on a much larger group of cases. Included in this group are people without any demonstrable disease as well as patients with a great variety of pathological changes but without obvious liver pathology.

(2) *In patients with hepatitis,* whether toxic or infectious, retention of intravenously injected galactose one hour or longer is found in all cases except in subsiding catarrhal jaundice, when the galactose test may be negative. In a general way, the highest degree of galactose retention occurs at the height of the disease. The galactose retention drops rapidly as recovery from the liver damage ensues. There is no obvious relationship between the height of jaundice as determined by the icteric index or the Van den-Bergh test, and the degree of galactose retention. The latter diminishes or may become normal before the jaundice clears. The amount of galactose retention depends, on one hand, upon the amount of liver cell degeneration and, on the other hand, upon the amount of cell regeneration. Therefore, it varies from case to case and in the various stages of an individual case.

The curves of galactose retention in these cases vary a great deal. We have observed variations of 2.3 to 13.3 mgs. of galactose per 100 c.c. of blood plasma 60 minutes after the intravenous injection of galactose. Similar variations occur in the 75 and 90 minutes blood samples in which the galactose values varied from 0 to 10.1 and 0 to 2.6 mgs. per 100 c.c. of blood plasma respectively. The mean curve of 10 cases studied is shown on Chart I.

(3) Six *cases of obstructive jaundice* were studied with the intravenous galactose liver function test. Four of these cases had a carcinoma of the head of the pancreas and two a common bile duct stone. Two cases of carcinoma of the head of the pancreas and one case of common duct stone with obstruction gave

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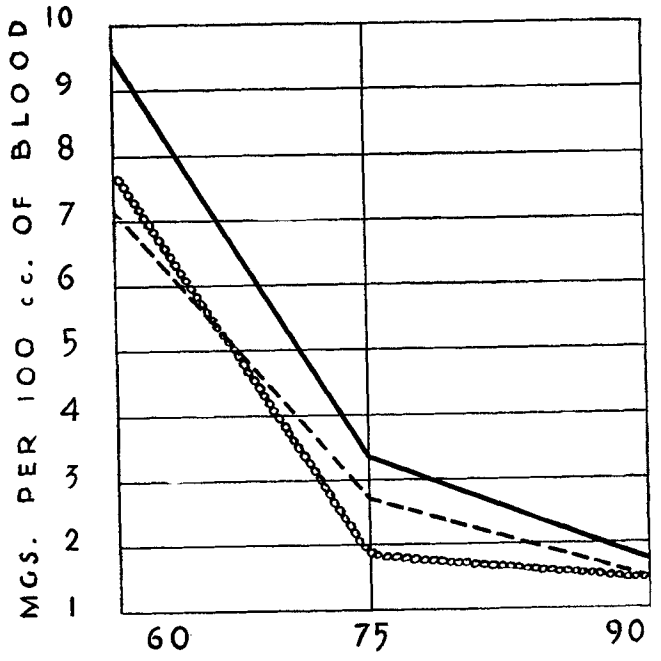

Chart I

Minutes after injection.

——— curve in cirrhosis of liver ..... curve in hepatitis

ooooo curve in obstructive jaundice.

positive galactose tests. Thus, 50 per cent of the obstructive jaundice cases had some galactose retention one hour after an intravenous injection of the standard amount of galactose. The mean curve in the three cases is shown on Chart I. It can be seen from the chart that the greatest variation between the two types of jaundice occurs at 75 minutes. In obstructive jaundice there are only traces (0.70 mgs. per 100 c.c.) while in intra-hepatic jaundice 2.7 mgs. is found in the blood plasma. Both at 60 and 90 minutes the galactose retention in both groups is practically the same. It would appear that the factor, which determines whether galactose is retained or not, is the duration of the obstruction and not the degree of jaundice. In the cases with a positive test the jaundice was distinctly of longer duration than in the negative ones. This should be interpreted as a secondary hepatitis or biliary cirrhosis from a long-standing obstruction.

(4) Twenty-five cases of *portal cirrhosis* were studied with the intravenous galactose liver function test. In this group 16 patients (64 per cent) gave a positive, while 9 (36 per cent) gave a negative test. The mean curve of the 16 positive cases is shown in Chart I. The galactose values were as follows: At the end of one hour (9.42 mgs. per 100 c.c.) at 75 minutes (3.33 mgs. per 100 c.c.) and at 90 minutes (0.96 mgs. per 100 c.c.). The degree of retention is higher than in the two previous groups. In individual cases the amount of galactose in the venous blood varied at 60 minutes from 2.7 to 22.4 mgs., at 75 minutes from 0 to 13.3 mgs. and at 90 minutes from 0 to 10.4 mgs. As these figures show, there is a great deal of variation in these cases. We were, however, unable to correlate the retained galactose with jaundice or size of the liver. In all cases of portal cirrhosis with ascites galactose retention was present.

(5) All cases of *cholecystitis*, with or without stones in the absence of obstruction to the biliary tract, metabolized 25 gms. of intravenously injected galactose within one hour. Several cases had a mild transient jaundice. As has been mentioned before, one of the two cases of cholelithiasis with common duct obstruction gave a positive intravenous galactose liver function test.

DISCUSSION

Positive intravenous galactose tests indicate liver damage. On the other hand, negative tests do not rule out liver disease. At no time did we find galactose retention at the end of an hour in patients without demonstrable liver or bile duct disease. Gall bladder disease without common bile duct obstruction gives a negative intravenous galactose liver function test. Intrahepatic jaundice cases show a definite retention of galactose which is demonstrable in all cases, except in the stage of recovery. In obstructive jaundice, retention of galactose may be absent or present. If present, the amount of galactose retention seems to depend upon the duration of biliary obstruction. Therefore, if this test is to be used in the differential diagnosis between intrahepatic and obstructive jaundice, it must be performed in the early stages of the disease. When so done, a positive test indicates intrahepatic jaundice. When the disease is of long standing, intrahepatic jaundice may give a negative response, while obstructive cases show a tendency to galactose retention. Apparently, the higher the amount of retained galactose the greater the liver damage. With a diminishing amount of galactose within the blood on repeated examinations a conclusion of improved liver function is justified. It will bear reemphasizing that the galactose test does not parallel the degree of jaundice. Very frequently in intrahepatic jaundice the galactose liver function test becomes negative before the jaundice clears. Therein lies its importance from a prognostic point of view. Whereas by the oral method in the absence of jaundice the galactose test is of no value, by the intravenous test indications of liver damage may be obtained.

The highest degrees of galactose retention are encountered in portal cirrhosis of the liver. The test is positive in 64 per cent of cases. In 36 per cent it is negative whether jaundice is present or not. We have not encountered, however, cases of cirrhosis of the liver with ascites which gave a negative intravenous galactose liver function test. Cases of cardiac ascites give persistently a negative galactose test. Therefore, this test can be used in the differential diagnosis of the etiology of ascites.

SUMMARY

The intravenous galactose liver function test, the technique of which is here described, is positive in a high per cent of cases with liver damage. It is negative in all cases where there is no liver damage. A negative test, however, does not rule out liver disease. In the early stages of jaundice it may be used in the differential diagnosis between hepatic and obstructive jaundice. In ascites it is of help in differentiating between a cirrhosis of the liver and cardiac decompensation. The progress of hepatic disease may be followed by repeated intravenous galactose liver function tests.

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