Neither was cholesterol with albumen in the patients in the group of obstructive jaundice as is present in the cases with hepatic diseases.

DR. JOHN G. MATHEER (Detroit, Mich.) (closing the discussion): We agree fully with Dr. Mann's emphasis upon the dissociation of different liver function tests. Because of limited time, we were unable to show our lantern slide tables of the results of the four newer liver function tests in individual cases. These tables of individual cases show in a striking manner the dissociation of the results of the different tests. A survey of these tables reveals the need, therefore, of performing at least several tests in each case, rather than conducting only the single test which yields the highest per cent of positive results in a group of cases.

Dr. White's inquiry about the different statistical results obtained by different workers with the cephalin test is a very reasonable question. In this study we have made no attempt to use this test to differentiate obstructive and hepatogenous jaundice. We have used the test simply as an index of impairment of hepatic function, regardless of whether the patient was jaundiced or not. As a matter of fact, no obstructive jaundice cases were included in this clinical material. Hanger, in his second paper, and Pohle and Stewart in their recent communication attempted to evaluate the cephalin test as a method to differentiate the two common types of jaundice. The difference in their experience, we believe, was due, at least in part, to the fact that Hanger's jaundiced patients, as a group, were studied at a somewhat earlier stage in the course of the jaundice. So much depends upon the duration of the jaundice when the test is performed, that no liver function test should be expected to serve as a final differential criterion between hepatogenous and obstructive jaundice. The earlier any liver function test can be conducted in the course of jaundice, the more reliable will be its differential aid.

We agree with Dr. Rosenberg's explanation of the apparent differences between his experience and ours with the cephalin test. Evidently he has been using unripened cephalin. We have used unripened cephalin, following Hanger's published technique. Hanger's more recent suggestion to use ripened cephalin represents an improvement in the method. The need is thus eliminated for excluding the 25 per cent of faintly positive one + results from the total positive results obtained with unripened cephalin. According to Hanger, false faintly positive reactions upon normal subjects do not occur with ripened cephalin.

As to the optimum dose of bromsulphthalein for evaluation of liver function, Macdonald's recent experiments would suggest that the 5 mg. dose per kilo provides a more sensitive test than the 2 mg. dose. However, regardless of which dose may be selected, the employment of the serial method will increase the sensitivity of the test.

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A New Galactose Test for Differentiation of Obstructive from Parenchymatous Jaundice*

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SINCE Claude Bernard first demonstrated the participation of the liver in carbohydrate metabolism, investigators of hepatic physiology have stressed the importance of the liver in an increasing number of physiologic processes. Metabolism of carbohydrates, fats and proteins, erythropoiesis, detoxification, production of prothrombin, and water balance are but a few of the many vital processes with which the liver is concerned. Pathologic lesions rarely impair all functions of the liver equally; one or more functions are disturbed in various degrees while others may to all appearances be spared. Therefore the expression, “impaired liver function” is ambiguous unless the function is specifically defined. Precise evaluation of hepatic disease requires the application of various tests each of which is designed to test a specific function. In some instances the status of a particular function may be extremely valuable in distinguishing between two different hepatic disorders which stimulate each other. Only in this limited sense can one speak of a “best” liver function test. We offer the intravenous galactose clearance test as a relatively accurate measure of the glycogenic function of the liver and as a test which in our experience, in addition to being generally useful, has proved superior to other liver function tests in the differentiation of obstructive from parenchymatous jaundice.

Bauer (1) in 1906 suggested the use of galactose as an agent for testing the glycogenic function of the liver. Subsequent investigation has confirmed the wisdom of this choice. It has been proved in several species of mammals, including man, that only the liver can utilize galactose in significant amounts (2, 3, 4, 5), that this utilization is independent of insulin (6), and that there is no renal threshold for galactose (7). The quantitative determination of galactose in the blood is simple and accurate (8). Galactose thus fulfills the requirements for a testing agent of the glycogenic function of the liver.

The original galactose test, which involves oral administration of the sugar and measurement of its urinary excretion, has proved inadequate. Most workers consider it unreliable in the differentiation between obstructive and parenchymatous jaundice; in chronic liver disease, notably cirrhosis, it is of even less value. However, certain features of this test suggest that the technic of application rather than the choice of testing agent is responsible for its

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limited usefulness. Particularly intestinal absorption and renal excretion of galactose may vary sufficiently to mask the functional capacity of the liver, and quantitative determinations of urinary galactose are inaccurate in the presence of bile. These deficiencies of the conventional galactose tolerance test were recognized by several earlier workers. In 1933 Roe and Schwartzman (9) described a modification of the test in which 1 gm. of galactose per kilogram of body weight was given orally and the function of the liver was measured by the resulting blood galactose curve. Although this method was an improvement, it failed to differentiate between variations in intestinal absorption of sugars, which are by no means rare (10), and utilization of galactose by the liver. In 1937 Jankelson, Segal and Aisner (11) proposed a galactose liver function test in which a standard dose of 25 gm. of galactose was injected intravenously and determinations of galactose in the blood were made at intervals. This galactose test was better than the original oral test, as shown by the fact that in 64 per cent of the patients with cirrhosis of the liver so tested the outcome was positive. On the other hand, the amount of galactose was below the optimum and the use of a standard dose failed to take into account the essential difference between oral and intravenous administration of galactose. In the former case the maximal absorptive capacity of the intestine automatically controls the amount of galactose which enters the blood stream according to the size of the patient. In the latter case the task imposed on the liver is identical in all patients regardless of size. Recently Maclagan (12) reported work with a test similar to that of Roe and Schwartzman except that he used a standard oral dose of galactose (40 gm.).

After publication of our preliminary paper (13) on the intravenous galactose test, King and Aitken (14), who consider that there is no advantage in graded doses of galactose, reported their results with the technic of Jankelson, Segal and Aisner. Their conclusions regarding the differential value of the intravenous galactose test in obstructive and parenchymatous jaundice agree with ours although their absolute values for galactose levels differ, probably because they used different brands of galactose and yeast and different chemical methods. The objections to the use of a standard dose of galactose have already been stated. The favorable results obtained by these workers may have been due to an accidental lack of variation in body weight in a small series of cases (10 patients with obstructive jaundice and 15 patients with acute hepatitis).

In devising our intravenous galactose clearance test, we attempted to eliminate all variables except the glycogenic function of the liver. We found that the rate of clearance of galactose injected intravenously depended upon the size of the dose in terms of body weight as well as upon the functional state of the liver. Therefore the dose was graded according to the patient's ideal weight. An amount was sought which would be large enough to detect slight impairment of function and yet small enough to permit rapid intravenous injection with a luer syringe of available size. One-half gram of galactose per kilogram of body weight best fulfilled these requirements. Originally the blood galactose level was determined every 15 minutes for two hours following the injection. Subsequently the critical period was established at 75 minutes and the 60-minute specimen was used as a check.

**TECHNIC OF THE TEST**

After an oxalated blood sample has been obtained, a dose consisting of 1 cc. of a 50 per cent solution of galactose per kilogram of body weight, is injected intravenously over a period of four to five minutes. Oxalated blood samples are again secured 60 to 75 minutes after the injection. Glucose is removed from the blood samples by fermentation with yeast according to Raymond and Blanco's (8) modification of Somogyi's method. The filtrates are analyzed for the nonfermentable reducing substance by the Hagedorn-Jensen method. In order to obtain the galactose content of the blood, the figure for reducing substances in the fasting blood is subtracted from the corresponding figure in the 60 and 75 minute specimens. A correction of 24 per cent must be added if conversion tables for glucose are used. The details of the procedure and its adaptation to the Folin-Wu method have been described elsewhere (15).

The test is usually performed on the fasting patient, but in our experience such foods as toast and coffee has produced no rise in the galactose level of the blood. The injection is made with a 100 cc. syringe with eccentric tip, fitted with a short 19-gauge needle. Contamination of the samples of blood by galactose may be avoided by using opposite arms or separate veins of the same arm for injection and collection. The galactose solution used in our studies was prepared by dissolving chemically pure galactose (Pfanstiehl) in triple distilled water. The solution should be prepared fresh each morning because on cooling small crystals of galactose form which may escape notice on reheating. Over 200 tests have been performed in this manner without the occurrence of systemic reactions. Occasionally small amounts of the solution have been injected extraveneously, but aside from a transitory burning pain no local reactions have resulted.

**RESULTS**

*Normal State.* Fifteen adults who had no evidence clinically or by other function tests of impaired liver function, served as normal controls. In all these the blood had been cleared of galactose 75 minutes after the injection. No galactose remained in the blood of most of the young adults (under 30 years of age) 60 minutes after the injection. Further study may show that complete clearance of galactose in 60 minutes is normal for this group. For the present, however, the more conservative 75-minute limit will be used in all cases. We have not determined the normal value for children. The 15 controls are represented on Chart 1. All values given in this paper refer to milligram per cent of galactose in the 75-minute specimen of blood.

*Acute Jaundice*—(Hepatitis and Extra-Hepatic Obstruction). The intravenous galactose clearance test was performed on 71 patients with acute jaundice (Table I). In the 51 patients with parenchymatous jaundice the mean galactose blood level was 48 mg. per cent (σ = 2.85). In the 33 patients with obstructive jaundice of less than six months' duration, the mean galactose blood level was 13.5 mg. per cent (σ = 1.71); however, in the seven patients with obstructive jaundice of longer than six months' duration