616.36–072.7 : 612.396.13.

GALACTOSE TOLERANCE AS A TEST OF LIVER FUNCTION[1]

By N. F. MACLAGAN

(From the Westminster Hospital Medical School)

Introduction

The term 'liver function test' has been applied to such a large number of procedures, some having no very certain relationship to the liver, that it is desirable to consider briefly the general principles underlying these tests. The most useful classification appears to be the following:

(A) *Tests Depending upon the Excretion of Bile*:
Van den Bergh reaction, icterus index.
Bromsulphalein excretion test.
Serum phosphatase and cholesterol estimations.
Examination of duodenal fluid.
Cholecystography.

(B) *Tests not Depending on the Excretion of Bile*:
Deaminating function (*estimation of blood amino-acids*).
Detoxicating function (hippuric acid and *salicyluric acid tests*).
Glycogenic function (*glucose*, laevulose, and galactose tolerance tests).

Numerous other proposed tests appear to have been abandoned by most workers, and even in this restricted list, those in italics are not usually considered to be of any clinical value for the present purpose. The virtue of this division into two classes becomes obvious when we consider the problem of distinguishing jaundice due to obstruction of the bile passages from jaundice due to intrahepatic disease, e.g. toxic hepatitis or cirrhosis of the liver. The excretion of bile is obviously interfered with in both groups, and it is reasonable that the distinction should be made most easily by testing a function which is independent of excretion. Moreover, in this second group it often happens that the excretory function is affected much less than other functions. In support of this statement, it is only necessary to recall the frequency with which advanced hepatic cirrhosis is associated with slight or absent jaundice. It is thus, particularly in the case of generalized lesions of the liver parenchyma, that liver function tests of type 'B' are indicated. This term is intended to include such conditions as toxic hepatitis, focal hepatic necrosis, acute yellow atrophy, cirrhosis of the liver, and ascending cholangitis. We may note here that some kind of generalized liver damage is now recognized in an increasing range of diseases,

[1] Received October 9, 1939.

Downloaded from by guest on February 8, 2015

some recent additions being hyperthyroidism (Beaver and Pemberton, 1933), pneumonia (Curphey and Solomon, 1938), rheumatoid arthritis (Rawls, Weiss, and Collins, 1937), and following certain surgical operations (Boyce and McFettridge, 1938). For the sake of completeness we may list here the commoner of the better known causes, which are catarrhal jaundice, chemical poisoning, certain spirochaetal diseases, toxaemia of pregnancy, and chronic alcoholism.

The present paper is concerned with the galactose tolerance test, which depends upon the fact that galactose is removed from the blood-stream chiefly by the liver, being converted presumably to glycogen (Mann, 1934). It is also utilized slightly by other tissues (Bollman, Mann, and Power, 1935), but to a much smaller extent than glucose or laevulose. In this connexion Mann's opinion of the relative suitability of galactose and laevulose as test agents is of interest in view of a number of recent papers on the laevulose tolerance test (Stewart, Scarborough, and Davidson, 1938, Herbert and Davison, 1938). Mann wrote in 1934: 'Although the liver does make glycogen from laevulose, the muscles can do this also and laevulose can be utilized by an animal without a liver. Consequently, it is difficult to understand how a laevulose tolerance test could be used to measure hepatic injury. Theoretically, it should be possible to indicate hepatic injury by a galactose tolerance test, as the utilization of this sugar appears to depend chiefly on the liver.' If we add to this the fact that blood-galactose is much easier to estimate than blood-laevulose, the advantage of the former sugar appears to be indisputable. The only minor drawback is the somewhat greater cost of the test dose of galactose, about 2*s*. 8*d*. as opposed to 1*s*. 1*d*.

The galactose test has in the past been used in various ways:

(1) Oral galactose: blood-sugar determined (Beaumont and Dodds, 1931).
(2) Oral galactose; urine sugar (or galactose) determined (Shay and Fieman, 1937).
(3) Intravenous galactose; blood-galactose determined (King, 1938).
(4) Oral galactose; blood-galactose determined (Althausen and Wever, 1937).

Of these possibilities, the first has the obvious disadvantage of failing to allow for variations in blood-glucose. A considerable rise of blood-glucose often occurs after oral galactose in normal persons (Harrison, 1938), and this rise is of course accentuated in diabetes (see Fig. 3). This modification has in consequence been largely discarded, except by Uexkull (1939). Similar considerations apply to the second method, unless the urinary glucose is removed by yeast fermentation. This has been advocated by Shay and Fieman (1937) who gave 40 gm. of galactose by mouth and then collected the urine up to five hours. Not more than 3 gm. of galactose should be excreted in this time, so that yeast fermentation was performed if the total sugar exceeded this amount. These authors found the test valuable if performed early in differentiating toxic from obstructive jaundice. Robertson, Swalm, and Konzelmann (1932), on the other hand, state that it gives too

Downloaded from by guest on February 8, 2015

many negative results. In my experience the urinary galactose excretion has depended too much on the rate of urinary flow to be a reliable guide. For example, investigation of one patient suffering from Graves' disease gave the following results:

Blood galactose at ½, 1, 1½, 2 hrs. in mg. %				Urinary volume in 2 hrs. in c.c.	Urine-galactose in gm.
81	128	78	5	250	4·0
47	149	98	39	28	0·9

It will be noticed that on the second occasion, although the blood-galactose values were higher, the urinary output was less than one quarter of that on the first occasion, a finding which is presumably to be correlated with the smaller urine volume. The third method has been used by King (1938), but his results have not yet been published. The present paper is concerned with the development of the fourth possibility, which appears to be the method of choice. It presents two advantages over the third method. Firstly, greater convenience, for the technique of preparing and injecting 50 c.c. of galactose solution intravenously is somewhat laborious, and unpleasant for the patient. Secondly, the galactose is presented to the liver by the physiological route, the portal vein. It may well be that there is a difference in the power of the liver to deal with galactose arriving by this route rather than from the general circulation, and furthermore in this method the sugar reaches the liver before it reaches the other organs. On the other hand, the question of varying rates of absorption from the alimentary tract requires to be considered, but the results given below show that such variations do not in fact destroy the value of the test, except, of course, when obvious failure of absorption is present, e.g. pyloric stenosis, post-anaesthetic state. Very few observations by this method appear to have been made, which is remarkable when it is realized that the principles of blood-galactose determination were fully established by Raymond and Blanco in 1928. The only clinical paper which I have found is that of Althausen and Wever (1937) describing the determination of the blood-galactose after an oral dose of 40 gm. at intervals of five, fifteen, and thirty minutes. Twenty-one normal persons were tested, and normal curves were also obtained in 14 cases of diabetes mellitus. An impairment of liver function was noted in Graves' disease. No cases of jaundice or hepatic cirrhosis were tested. As will appear later, the blood-galactose may not reach its maximum after this dose until 1 or 1½ hours after administration, so that it is desirable to extend the time of the test well beyond thirty minutes.

Methods

The patient is starved overnight, no breakfast or morning tea being allowed. A dose of 40 gm. of galactose, dissolved in 250 c.c. of water, is given by mouth. It is necessary to use hot water and cool subsequently, to obtain complete solution. Blood is then collected into a fluoride or oxalate tube at ½, 1, 1½, and 2 hours after the solution has been drunk.

Downloaded from by guest on February 8, 2015

Either venous or capillary blood may be used. In the latter case it is convenient to collect 0·3 to 0·4 c.c. from the ear into a small tube $1'' \times \frac{1}{4}''$, the sides of which are coated with a mixture of potassium oxalate and sodium fluoride. The use of the sterile glass pricker described by Harrison (1938) is of great assistance here, making possible in most cases the collection of all the samples from a single ear puncture.

The following blood-galactose method is based on that of Harding, Grant, and Glaister (1933), for the details of which I am indebted to Dr. E. J. King, and also upon the method of Raymond and Blanco (1928). The sugar reagent is a modification of Somogyi's reagent No. 2 (Peters and Van Slyke, 1932). The method depends upon the preliminary removal of glucose from the blood by yeast fermentation, followed by deproteinization and determination of the copper-reducing power. The modifications introduced include the new sugar reagent and the use of a weaker (0·002 N.) thiosulphate solution, which result in increased accuracy.

Solutions. (1) Alkaline-copper-iodine reagent. Dissolve 25 gm. of anhydrous sodium carbonate, 20 gm. of sodium bicarbonate, and 25 gm. of Rochelle salt (sodium potassium tartrate) in 600 c.c. of water. Dissolve 7·5 gm. of copper sulphate ($CuSO_4.5H_2O$) separately in about 100 c.c. of water. Introduce the copper solution into the carbonate-tartrate solution through the funnel, the tip of which rests on the bottom of the beaker, stirring the solution well during the addition to prevent loss of carbon dioxide. Add to the mixture 5 gm. of potassium iodide and 0·175 gm. of potassium iodate (KIO_3). Dilute to 1 litre.

(2) Isotonic sodium sulphate (3 per cent.).

(3) 10 per cent. sodium tungstate.

(4) 7 per cent. copper sulphate.

(5) N/1 sulphuric acid.

(6) 0·002 N. sodium thiosulphate. This must be freshly prepared each day by accurately diluting N/10 sodium thiosulphate 50 times.

(7) 1 per cent. starch solution in saturated sodium chloride.

Yeast tubes. Place 1 c.c. of a 1 in 3 suspension in water of fresh brewers' or bakers' yeast into a 15 c.c. round-bottomed centrifuge tube, $4\frac{3}{4}'' \times \frac{5}{8}''$, add 10 c.c. of distilled water, mix thoroughly with a glass rod, and centrifuge for about five minutes at 3,000 revolutions per minute. Decant the supernatant liquid and repeat the washing twice with 10 c.c. of water. At the end of the last washing, drain the tube for a few minutes on a filter paper, and wipe the inside thoroughly with strips of filter paper. Finally, add 2·2 c.c. of isotonic sodium sulphate.

Determination. Place 0·2 c.c. of blood into a yeast tube; mix thoroughly with a glass-rod and allow to stand for fifteen minutes at room temperature. A blank should be put up at the same time, using 0·2 c.c. of blood containing no galactose. This blood may be any sample, preferably fairly normal in character, undergoing routine analysis. This blank tube controls the completeness of removal of glucose, and should give a titration almost identical

Downloaded from by guest on February 8, 2015

with the reagent blank (2 c.c. of water plus 2 c.c. of sugar reagent) which is done occasionally as a check on the thiosulphate solution. It is also desirable to include one further tube containing 2·0 c.c. of isotonic sodium sulphate, 0·2 c.c. of galactose-free blood, and 0·2 c.c. of 0·1 per cent. galactose solution. The occasional samples of yeast which attack galactose are detected by this tube. In my experience only two such yeasts were found out of about one

TABLE I

Blood galactose mg. per 100 c.c.	c.c. of 0·02 N thiosulphate (blank minus unknown).
0	0
20	0·13
60	0·89
130	2·14
180	3·08
240	4·42

hundred tested.[2] At the end of fifteen minutes add 0·3 c.c. of 10 per cent. sodium tungstate, mix thoroughly by shaking, then add 0·3 c.c. of 7 per cent. copper sulphate and mix again. It is essential to mix before adding the copper sulphate solution, otherwise incomplete protein precipitation results. Centrifuge for about five minutes, and decant the supernatant fluid into a pointed centrifuge tube. Pipette 2 c.c. of the centrifugate into a 5″ × ¾″ test tube, followed by 2 c.c. of the alkaline copper iodine reagent, which must be added by means of an accurate, Grade A, grease-free pipette, which should be kept in dichromate-sulphuric acid cleansing mixture when not in use; traces of grease render it impossible to measure exactly 2 c.c. of this reagent. Mix by shaking, and cover the top of the tube with a large glass marble, or else plug loosely with cotton wool. Place the tubes in a briskly boiling water bath for *exactly* ten minutes, cool in running water for two minutes, and immediately add 2 c.c. of normal sulphuric acid and shake once. Keep the tube covered and titrate as soon as possible with 0·002 N. sodium thiosulphate, using a 5 c.c. microburette and adding finally 1 drop of starch solution as indicator. The blank requires 4·8 to 4·9 c.c. of thiosulphate. The difference between the blank and the unknown titre is the figure used in calculating the blood-galactose. It is necessary to arrange that the heating, cooling, and titration are all done consecutively and without delay, although the tubes may be left if necessary for some hours before heating. This is because either re-oxidation of cuprous oxide or evaporation of iodine will otherwise cause errors. The former error is more serious than the latter, hence the direction to add the sulphuric acid immediately after cooling. The iodine liberated then oxidizes all the cuprous oxide.

Calculation. Since the relationship between the thiosulphate titre and the blood-galactose is not quite capable of representation by a straight line it is necessary to prepare a calibration curve. This is made by putting up a series of yeast tubes containing 2·0 c.c. of isotonic sodium sulphate and 0·2 c.c. of galactose-free blood (preferable from a normal or nearly normal

[2] A yeast which has been proved suitable may be stored for at least one month in a stoppered vessel in the refrigerator.

Downloaded from by guest on February 8, 2015

person). Samples of 0·2 c.c. of galactose solutions of known strengths are then added to the tubes, each strength being represented in duplicate, and the estimation completed as above. The figures in Table I were obtained in this way and may be used to construct a curve, but it is preferable for each laboratory to have its own calibration data.

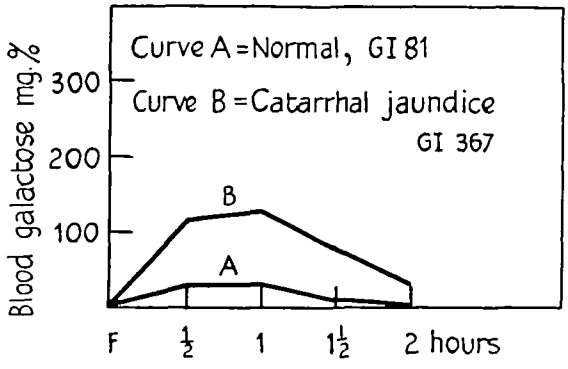

FIG. 1.

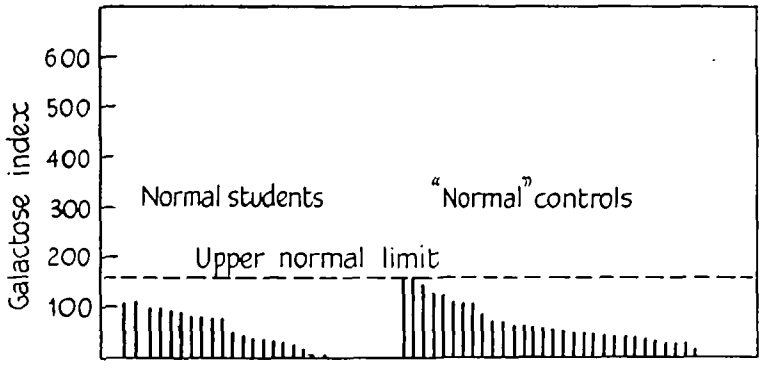

FIG. 2.

Results

Fig. 1 shows a typical normal and a typical abnormal curve. The maximum blood-galactose may occur at ½, 1, or 1½ hours (usually 1 hour), and the sum of these four values, for which the term 'galactose index' (G.I.) is suggested, appears to be the best criterion to take for purposes of comparison, and tends to be about double the highest value. Fig. 2 and Appendix I give the results of the test on 50 normal persons, of whom 20 were healthy male medical students, and 30 were patients from the out-patient department suffering from various diseases unconnected with the liver, thyroid, or gastro-intestinal tract. There is usually a fairly close correlation between the galactose index and the highest value, and it is evident that a peak value of 80 mg. of galactose per 100 c.c. or a G.I. of about 160 may be taken as the upper normal limit. The average normal G.I. is 68. It is noticeable that the students gave a slightly lower reading than the 'normal' controls, who provide eight cases with a G.I. between 100 and 160 as opposed to

Downloaded from by guest on February 8, 2015

only two students in this range. However, the difference is hardly great enough to be of clinical importance.

Fig. 3 gives the results obtained in diabetes mellitus (six cases), toxic jaundice (10 cases), obstructive jaundice (six cases), and Graves' disease (12 cases). The normal figures in diabetes mellitus are in confirmation of

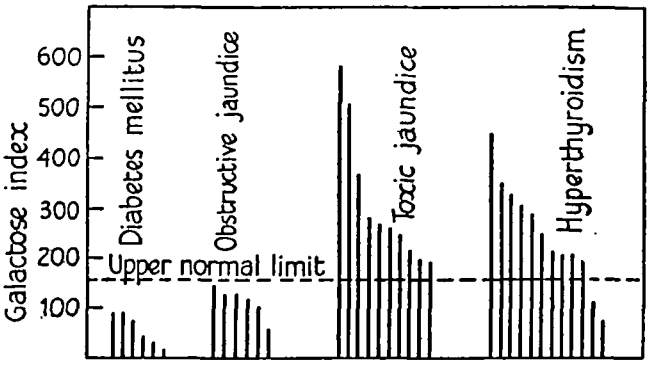

FIG. 3.

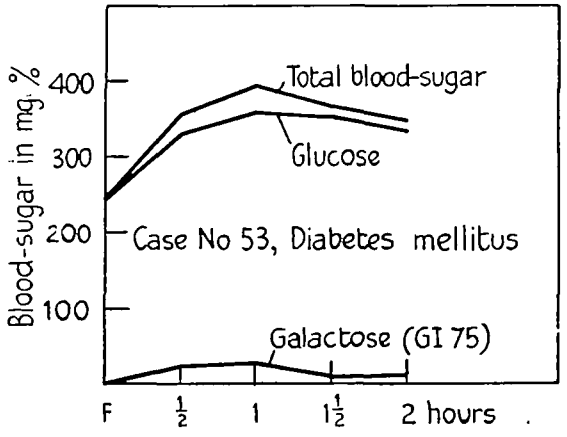

FIG. 4.

those which Althausen and Wever (1937) obtained with the half-hour galactose test. The dissociation between the blood-glucose and blood-galactose in diabetes is well shown in Fig. 4. It will be seen that the 16 cases of jaundice were satisfactorily differentiated, for all the toxic and none of the obstructive cases showed impairment of liver function. This suggests that the test should be of some value in the differential diagnosis of jaundice. In 10 out of 12 cases of Graves' disease definite impairment of function was seen, in some cases of extreme degree. These were clinically severe cases, with basal metabolic rates ranging from +20 to +80 per cent. (average +55 per cent.). This finding is in agreement with the results of Boyce and McFettridge (1938), who used the hippuric acid test. There seems little doubt that this liver damage is a part of the pathology of hyperthyroidism, although it has not yet received general recognition. Support for this view from the morbid

Downloaded from by guest on February 8, 2015

anatomist's standpoint will be found in a paper by Beaver and Pemberton (1933). This subject has been pursued in collaboration with Mr. Frank Rundle, and a paper is in course of preparation.

Discussion

The value of any liver function test must depend upon three things; firstly its sensitivity, secondly the nature of the function tested, and thirdly on the intelligent clinical use of what is, in effect, simply an additional physical sign. With regard to sensitivity, the data presented suggest that the test is sufficiently sensitive to be of clinical value. In this connexion an argument frequently used as a condemnation of all liver function tests needs to be refuted. It is based on hepatectomy experiments, and concludes from the fact that a 70 per cent. hepatectomy produces few symptoms (Mann and Power, 1935) that the reserve power of the liver is too great to allow the demonstration of hepatic dysfunction, except as a terminal phenomenon. This proposition ignores the great difference between a partial surgical removal and the action of poisons which may simultaneously attack all the liver cells. The fact that toxic jaundice can be a chronic condition, lasting for many years, is sufficient to dispose of this argument.

The nature of the function tested is important because it is desirable for many purposes to choose one which is independent of the excretion of bile. The excretory function is, of course, the easiest of all functions to test, and gross impairment is at once revealed by the presence of jaundice. Latent jaundice may be detected by the icterus index or Van den Bergh reaction, and the bromsulphalein excretion test is an even more sensitive index than these. Nevertheless these procedures suffer from the obvious limitation that they are all testing the same function, which may be impaired either by toxins or by biliary obstruction, and it is now generally agreed that the Van den Bergh (1918) reaction cannot be relied upon to distinguish the two types. The only hope of doing this at present is to test some other function, such as the galactose utilization function, which has no connexion with the secretion of bile. Moreover, there are many poisons which affect the glycogenic function much more than the excretory one; the cases of Graves' disease reported above form an excellent example of this, for none of them was jaundiced. Many cases of cirrhosis of the liver also fall into this category. This point is further emphasized by Appendix II, which gives the serum-bilirubin concentration in the 16 cases of jaundice. It will be noted that the obstructive cases (with no impairment of galactose function) average 12·9 mg. of bilirubin per 100 c.c., while the toxic cases (all with impaired galactose function) have an average serum bilirubin of only 5·4 mg. per 100 c.c. The dissociation between the two tests is well marked.

The clinical value of the test, therefore, depends upon its power of testing one function of the liver which is independent of the excretion of bile. It would appear that this information may be useful for the following purposes:

Downloaded from by guest on February 8, 2015

(1) The demonstration of hepatic damage in diseases in which its presence is uncertain or unconfirmed, e.g. hyperthyroidism (see above), pneumonia (Curphey and Solomon, 1938), after surgical operations (Boyce and McFettridge, 1938), and rheumatoid arthritis (Rawls, Weiss, and Collins, 1937).

(2) The detection or confirmation of hepatic cirrhosis of all types. A few examples of this condition are included in this paper among those of toxic jaundice. The test is of particular value when jaundice is slight or absent.

(3) The differential diagnosis of toxic from obstructive jaundice. As noted above, the pigmentary tests are, in general, unreliable for this purpose, but as there is no obvious reason why galactose utilization should be impaired by biliary obstruction, at least in the early stages, the test should be of real value here. The cases of jaundice in this series are too few to reveal the limitations of the test in this respect, but they have at least failed to show any disagreement with the results expected, since all the toxic and none of the obstructive cases showed impaired function. The time factor is no doubt important in obstructive jaundice, and more data are required on this point, but case No. 62 provides an example of obstructive jaundice with normal liver function after eight weeks obstruction due to carcinoma of the pancreas.

Downloaded from by guest on February 8, 2015

Summary

(1) The principles involved in the clinical use of liver function tests are discussed, with special reference to the differential diagnosis of jaundice.

(2) Reasons are given why galactose is to be preferred to laevulose as an indicator of the glycogenic function of the liver.

(3) A modification of the galactose tolerance test is described in which the blood-galactose is estimated at intervals after an oral dose of 40 gm.

The term 'galactose index' (G.I.) is suggested for the sum of the four blood-galactose values, at ½, 1, 1½, and 2 hours, expressed in mg. per 100 c.c.

(4) Results are given for 50 normal persons, six cases of diabetes mellitus, six cases of obstructive jaundice, 10 cases of toxic jaundice, and 12 cases of hyperthyroidism. In normal persons the blood-galactose never exceeded 80 mg. per 100 c.c. and the G.I. did not exceed 160. The average normal G.I. was 68. Normal figures were recorded in diabetes and in obstructive jaundice, and impairment of function was demonstrated in toxic jaundice and in hyperthyroidism.

It is a pleasure to express my thanks to the honorary physicians and surgeons of the Westminster Hospital for permission to investigate cases under their care, and also to the John Burford Carlill trustees for financial assistance. Owing to war-time conditions the paper was written without the aid of a reference library, and it is feared that the bibliography may be incomplete. Apologies are offered to any writers whose papers may have been omitted from the discussion for this reason.

Appendix I

Case.	Age.	Sex.	Blood-galactose in mg. %				G. I.	Diagnosis.
			½ hr.	1 hr.	1½ hrs.	2 hrs.		
1	21	M	19	45	29	18	111	Normal student
2	21	M	24	63	23	0	110	,, ,,
3	22	M	27	47	18	8	100	,, ,,
4	22	M	39	32	16	12	99	,, ,,
5	21	M	29	16	37	15	97	,, ,,
6	22	M	30	41	10	8	89	,, ,,
7	25	M	37	31	10	3	81	,, ,,
8	22	M	32	39	8	2	81	,, ,,
9	22	M	31	28	13	7	79	,, ,,
10	21	M	24	53	0	0	77	,, ,,
11	23	M	4	29	7	7	47	,, ,,
12	20	M	19	19	5	3	46	,, ,,
13	21	M	8	15	15	0	38	,, ,,
14	22	M	18	10	3	3	34	,, ,,
15	22	M	7	10	9	7	33	,, ,,
16	22	M	5	10	7	7	29	,, ,,
17	26	M	10	11	2	0	23	,, ,,
18	21	M	5	13	0	0	18	,, ,,
19	22	M	0	2	2	0	4	,, ,,
20	23	M	0	3	0	0	3	,, ,,
								Controls.
21	23	F	16	47	78	22	163	Haemorrhoids
22	32	F	65	81	9	5	160	Bacilluria
23	45	F	73	44	21	12	150	Angioma of lip
24	77	M	43	68	21	0	132	Arteriosclerosis
25	24	F	45	60	12	9	126	Bacilluria
26	40	F	22	66	16	11	115	Varicose veins
27	56	F	28	43	21	19	111	Mastectomy
28	36	F	28	38	9	33	108	Abdominal pain
29	37	F	72	9	5	0	86	Neurosis
30	28	F	35	25	15	3	78	Abdominal pain
31	47	F	23	26	12	10	71	Old cholecystectomy
32	33	F	40	13	10	5	68	Haemorrhoids
33	37	F	20	34	7	7	68	Haemorrhoids
34	31	F	22	15	18	12	67	Neurosis
35	28	F	19	18	12	13	62	Foot strain
36	27	F	9	12	23	17	61	Bacilluria
37	21	M	26	19	7	4	56	Abdominal pain
38	38	F	19	25	5	5	54	Abdominal pain
39	49	F	25	20	6	0	51	Menopause
40	51	F	19	28	3	0	50	Muscular strain
41	50	F	19	9	9	12	49	Neurosis
42	52	F	10	15	12	9	46	Menopause
43	60	F	0	17	19	10	46	Old cholecystectomy
44	52	F	9	24	12	0	45	Neurosis
45	51	F	18	18	4	2	42	Haemorrhoids
46	60	F	14	10	6	6	36	Asthma
47	53	F	22	10	2	0	34	Asthma
48	33	M	6	11	8	8	33	Neurosis
49	49	F	0	25	4	2	31	Varicose veins
50	26	F	12	3	3	0	18	Rectal abcess

Average for all normal subjects—68

Downloaded from by guest on February 8, 2015

Appendix II

Case.	Age.	Sex.	Blood-galactose in mg. % ½ hr.	1 hr.	1½ hrs.	2 hrs.	G. I.		Diagnosis.
51	52	F	26	49	21	0	96		Diabetes mellitus
52	66	F	35	24	18	14	91		,, ,,
53	67	F	23	31	8	13	75		,, ,,
54	63	M	13	26	3	0	42		,, ,,
55	—	M	8	18	15	0	41		,, ,,
56	56	F	16	6	0	0	22		,, ,,
57	50	F	21	58	37	28	144	6·8 mg. % bilirubin	Obstructive jaundice, gall-stones
58	71	M	44	43	22	11	120	—	Obstructive jaundice, gall-stones
59	71	M	26	32	34	37	129	15·7 mg. % bilirubin	Obstructive jaundice, carcinoma of pancreas
60	59	F	32	28	41	19	120	14·1 ,, ,,	Obstructive jaundice, carcinoma of pancreas
61	58	M	20	19	36	26	101	10·9 ,, ,,	Obstructive jaundice, glands in portal fissure
62	45	F	11	13	10	15	49	17·0 ,, ,,	Obstructive jaundice, carcinoma of pancreas
						Average		12·9 ,, ,,	
63	54	F	84	175	189	136	584	4·0 mg. % bilirubin	Toxic jaundice, hepatic cirrhosis
64	54	F	63	147	152	145	507	5·3 ,, ,,	Toxic jaundice, hepatic cirrhosis
65	59	M	120	132	78	37	367	11·6 ,, ,,	Toxic jaundice, catarrhal jaundice
66	50	F	19	72	103	93	287	12·2 ,, ,,	Toxic jaundice following atophan
67	66	F	60	86	83	39	268	2·2 ,, ,,	Toxic jaundice, catarrhal jaundice
68	47	M	49	107	74	32	262	3·0 ,, ,,	Toxic jaundice, hepatic cirrhosis
69	27	M	159	58	19	13	249	5·6 ,, ,,	Toxic jaundice, catarrhal jaundice
70	31	M	75	87	38	13	213	2·4 ,, ,,	Toxic jaundice following gold therapy
71	56	F	19	102	57	21	199	—	Toxic jaundice, hepatic cirrhosis
72	60	F	49	—	88	60	197	2·3 mg. % bilirubin	Toxic jaundice, hepatic cirrhosis
						Average		5·4 ,, ,,	
73	44	F	100	173	110	65	448	B.M.R. +75 %	Hyperthyroidism
74	46	M	126	147	60	19	352	,, +78 ,,	,,
75	42	F	129	119	75	5	328	,, +53 ,,	,,
76	18	F	44	97	105	66	312	,, +52 ,,	,,
77	42	F	81	128	78	5	292	,, +58 ,,	,,
78	25	F	110	73	66	0	249	,, +53 ,,	,,
79	24	F	60	96	44	13	213	,, +73 ,,	,,
80	42	F	44	68	81	18	211	,, +20 ,,	,,
81	34	F	69	91	40	11	211	,, +62 ,,	,,
82	41	M	149	36	9	5	199	,, +37 ,,	,,
83	17	F	49	58	5	0	112	,, +39 ,,	,,
84	13	F	22	13	16	25	76	,, +56 ,,	,,

Downloaded from by guest on February 8, 2015

REFERENCES

Althausen, T. L., and Wever, G. K., *Journ. Clin. Invest.*, N. York, 1937, xvi. 257.
Beaumont, G. E., and Dodds, E. C., *Recent Advances in Medicine*, Lond., 1931.
Beaver, D. C., and Pemberton J. de J., *Ann. Int. Med.*, Lancaster, Pa., 1933, vii. 687.
Bollman, J. L., Mann, F. C., and Power, M. H., *Amer. Journ. Physiol.*, Balt., 1935, cxi. 483.
Boyce, F. F., and McFetridge, E. M., *Arch. Surg.*, Chicago, 1938, xxxvii. 401.
Curphey, T. J., and Solomon, S., *Amer. Journ. Med. Sci.*, Philad., 1938, cxcvi, 348.
Harding, V. J., Grant, G. A., and Glaister, D., *Canadian Chemistry and Metallurgy*, Toronto, 1933, xvii. 7, cited by King (1938).
Harrison, G. A., *Chemical Methods in Clinical Medicine*, Lond., 1937.
Herbert, F. K., and Davison, G., *Quart. Journ. Med.*, Oxford., 1938, N.S. vii. 355.
King, E. J. (1938), Private communication.
Mann, F. C., *Ann. Int. Med.*, Lancaster, Pa., 1934, viii. 432.
Peters, J. P., and Van Slyke, D. D., *Quantitative Clinical Chemistry*, Lond., 1932.
Rawls, W. B., Weiss, S., and Collins, V. L., *Ann. Int. Med.*, Lancaster, Pa., 1937, x. 1021.
Raymond, A. A., and Blanco, J. G., *Journ. Biol. Chem.*, Balt., 1928, lxxix. 649.
Robertson, W. E., Swalm, W. A., and Konzelmann, F. W., *Journ. Amer. Med. Assoc.*, Chicago, 1932, xcix. 2071.
Shay, H., and Fieman, P., *Ant. Int. Med.*, Lancaster, Pa., 1937, x. 1297.
Stewart, C. P., Scarborough, H., and Davidson, J. N., *Quart. Journ. Med.*, Oxford, 1938, N.S. vii. 229.
Uexkull, T. von, *Deutsche med. Wchnschr.*, Leipz., 1939, lxv. 415.
Van den Bergh, A. A. H., *Presse méd.*, Paris, 1921, xxix. 441.

Downloaded from by guest on February 8, 2015