

*Dr. Joslin (closing).—*Dr. Hamman's statement about the desirability of saving the urine following the evening meal I think is most valuable.

Emphasis has been rightly laid upon the importance of treating patients in their homes. One can treat patients in their homes perfectly well if one will only give the time to it. It takes more time. In the hospital one can talk to a group. In their homes one must talk to each patient individually. However, one can do it perfectly well, and it is really with that in mind that I have used these cards recently of test diets and maintenance diets, so that these patients may know from day to day what to do when I do not see them.

The favorable results of hospital treatment may be in part due to the entrance of milder cases. Of course, the statement is often made to me that only mild cases come to me, and that is why only 2 per cent die. During the year 1920 the Massachusetts General Hospital, a representative institution, with which I have no connection, treated 98 cases of diabetes, and of this number 2 died. In one other hospital in which I do not think the treatment was as good, the mortality was much higher. Yet there was no reason to believe that the other hospital had any severer type of cases.

Furthermore, in hospitals of today, one treats complications in diabetes which are so serious that one would not have thought of treating them years ago. For instance, Dr. Arthur Chute has taken the prostate out of seven diabetic patients successfully. He has operated upon three for cancer of the bladder or prostate, and one patient had this done last year when possibly some of you may have been in Boston. Dr. Robert C. Cochrane recently had eight surgical diabetics at the Deaconess Hospital under treatment at one time. Formerly, I do not think that there were that number of cases coming for treatment of surgical affections. Now, as we know, one can perform practically any kind of operation upon a diabetic, but one must be very cautious about it. When it is necessary to operate, one should operate without ether or chloroform anesthesia, but with local anesthesia, or gas and oxygen, and everything should be done to prevent unnecessary trauma and to conserve the patient's strength. One likes to have a patient sugar- and acid-free, but if a man's leg, according to the opinion of the surgeon, should come off, I think it ought to come off that same day.

The point is not to try to get the patient sugar-free too suddenly. Under-nutrition at this juncture is useful, and if a patient only gets one-half or even one-third as much to eat as he ordinarily would, he will probably become sugar-free after the operation in the course of a few days or two or three weeks, even though sugar, and acid poisoning as well, should be present at the start.

Most of all, it is important for us all to consider that every doctor can help in the treatment of diabetes. Each can make an attempt to discover a case early and to treat the mild case energetically. If you treat one patient well, all profit thereby.

THE DUODENAL TUBE IN THE STUDY OF LIVER AND PANCREATIC PATHOLOGY*

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The time comes when every new diagnostic or therapeutic procedure is engulfed in a wave of enthusiasm. It is accepted by many, probably by a majority, and is used to the exclusion of all other time-honored methods.

After many honest, although prejudiced and undependable reports find their way into the literature, a certain percentage of physicians, some of a scientific and others of an inquisitive nature, approach the subject with open minds, work out scientifically the problems that are presented, and finally the procedure takes its place among other medical solutions, or is discarded as worthless.

The question of gall bladder, liver and pancreatic pathology and function seems to us to have reached that stage of enthusiasm and faddism, and it now becomes necessary to determine as nearly as possible just what position it must occupy among the other diagnostic and therapeutic procedures, relative to these organs whose value, time, chiefly, has established.

A rather comprehensive review of the literature for the past two years leaves one with the feeling that "Here is something really worth while; its value is proven and we must make use of it." On the other hand we have personally inquired of several well known clinicians and written to others and while few have expressed themselves as having no confidence in the diagnostic value of these procedures, most of them have said that more work and more time was necessary to prove their worth. Fairly representative is the following from a letter recently received from a well known internist:

"We have used the Lyons method for the bacteriology of the bile and have obtained little results from it. I feel that the method has certain

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advantages which should be worked out by careful critical persons who are not misled by their enthusiasm.

We desire to have it understood therefore that we occupy the middle position, neither as special pleaders, intent only on establishing the worth of these several methods, nor as skeptics seeking to discredit them. We furthermore desire to have our data looked upon merely as a preliminary report, since the number of cases studied is not large. We believe that more will be accomplished by an intensive study of the individual case than by the indiscriminate reporting of large numbers of simple drainages. While the simple procedure of drainage has been carried out more than 300 times the data here presented is based on a rather intensive study of 100 individuals, in whom various other diagnostic methods have also been applied. In the study of these 100 individuals we have asked ourselves a number of incisive questions and attempted to find the answers in a tabulated series of results. Among these questions have been:

(1.) Do the various diagnostic procedures check favorably with careful histories and examinations?

(2.) Does the microscopic, macroscopic and cultural study of the biliary contents offer a clue to liver and pancreatic pathology, or may the same findings be encountered in healthy individuals, or in other conditions where the liver is probably spared?

(3.) Is there any reliable method by which liver function may be tested?

(4.) What is the value of other signs and symptoms, usually employed in the study of these conditions?

We do not feel that our findings answer many, if indeed any of these questions conclusively. We present the data accumulated, to be taken at its face value and to throw its small weight in whichever direction it may. We quite appreciate the fact that the final valuation of these methods both therapeutically and diagnostically must be based on a wider experience; but, we believe, along much the same lines. Our investigations in addition to the usual careful history and examination have embraced the following procedures:

(1.) A careful study of the biliary secretion microscopically, macroscopically

and culturally with very strict adherence to the methods outlined by Lyons.

(2.) An estimation of the pancreatic ferments, amylase, protease and lipase in the duodenal contents.

(3.) The function of the liver through:

(a) A colorimetric study of phenoltetrachlorophthalein, recovered in the bile obtained by means of the duodenal tube. (b) The hemoclastic crisis of Widal and co-workers. (c) Urobilin in the urine.

(4.) Gastric analysis, fecal analysis, urinalysis and fluoroscopic and radiographic study of the gastro-intestinal tract, as well as routine Wassermanns.

(5.) In many cases special investigations including blood chemistry methods and basal metabolism.

The theory and technic of the Meltzer-Lyons method of duodenal drainage has been described so often that a repetition is scarcely necessary.

In chart No. 1 we have attempted to show graphically a comparison of our findings in cases clinically gall bladder disease, with cases of other known pathology. It will be noted that of 44 cases which were clinically gall bladder disease 54% were positive as to the macroscopic appearance of the bile recovered, 59% were positive microscopically, and 41% positive culturally. It is interesting to note the percentage of positives in other cases, particularly those of osteo-arthritis. While the number is extremely small and we realize that before any definite conclusion can be obtained, more work is necessary, the fact, however, that in 80% of these cases the bile was positive macroscopically, was positive microscopically 100%, and practically the same percentage were positive culturally as found in clinical gall bladder cases, gives food for thought, particularly since in these five cases no other foci of infection were demonstrable.

The blood chemistry was negative as far as uric acid was concerned, and all were improved by therapeutic use of the tube. The question naturally arises whether foci of infection may not frequently exist in the gall bladder in such cases. The same might be said of cardio-renal disease in which there is a fairly large number of positive findings. The twelve miscellaneous cases show practically the same

figures macroscopically and microscopically as those found in the clinical gall bladder cases, and the question again arises whether these findings necessarily indicate pathology of the biliary tract itself. Certainly in view of the fact that the findings are so similar in the various conditions, doubt arises as to their significance from a diagnostic standpoint. We have considered macroscopically abnormal those biles that have increased viscosity, increased specific gravity, and turbidity. We do not believe it has been definitely proven that any of these conditions necessarily indicate pathology, although usually found where definite path-

tremely rare, and never found in cases that were not easily diagnosed clinically as gall bladder disease. We have found fairly constant a cell varying from the size of a small lymphocyte to a large epithelial cell with a single nucleus in the smaller cells, to four or five nuclei in the larger cells which with Wright's stain take a rather deep blue for the nuclei and a paler blue for the protoplasm. These are not the large irregular polyhedral cells which are recovered from the liver, nor are they to be associated with the columnar epithelia that come from the smaller bile ducts that are strengthened by fibrous connective tissue. We have felt that in all probability this character of cell came from the duodenum.

There is still another cell that has caused us much annoyance and which for a considerable time was thought to be leucocyte. It is about the size of a polynuclear leucocyte, does not vary in size, and in many respects resembles the nuclei of larger cells found in the same specimen. These cells, however, have been watched for a period of twelve hours under the microscope and no degeneration of the protoplasm, leaving the nuclei free, has been demonstrated. It has occurred to us that this difficulty has been encountered by other investigators and we have naturally wondered whether or not many of the reports of pus cells found in the bile were not really these peculiar cells, which by various staining methods, are epithelial. Whether or not this is true, the fact remains that we have not been able to demonstrate pus with anything like the frequency of other observers.

Our bacteriological studies have been carried out under the strictest precautions. The free end of the tube has been thoroughly sterilized and the bile from the different fractions has been allowed to drop immediately into the culture media, which are then immediately placed in the incubator. Several media were used in the beginning of our work, but since invariably the growths appeared on blood agar plates or glucose bouillon, all other media were discarded and the material from the duodenum and the three biliary fractions was planted on these two media and left in the incubator for 48 hours. It is possible that

PANCREATIC FUNCTION TESTS MADE IN 53 CASES: RESULTS

	Good	Per Cent	Moderate	Per Cent	Poor	Per Cent	None	Per Cent
Protense	39	74	8	15	3	6	3	6
Amylase	13	27	11	22	17	31	13	27

LIPASE TEST MADE IN 34 CASES

	Over 5	Per Cent	Less Than 5	Per Cent	None	Per Cent	Paradoxical	Per Cent
Lipase	8	22	18	55	4	11	4	11

Paradoxical results being those in which control showed greater digestion than active specimen.

X-RAY EXAMINATION OF G. I. T. AND GALL BLADDER MADE IN 55 CASES: RESULTS

Negative throughout	36	65%
15% to 25% 4½ hr. residue	17	42%
Gall - stones	13	32%
Marked ptosis	13	32%
Adhesions, duodenum to gall tract	8	20%
Persistent cap deformity	1	2%
Enlarged gall-bladder	1	2%
Diverticulosis - colon	1	2%

ology can be demonstrated. For microscopical abnormality we have considered the presence of many crystals, red and white blood cells, and bile stained epithelia. We believe that any considerable quantity of pus is distinctly abnormal, but we are not yet satisfied that many crystals or even bile stained epithelia, unless in large quantities and of a particular type, are necessarily abnormal. At this point we refer particularly to numerous reports of pus cells being found in the various bile fractions. In our experience this has been ex-

a very small percentage of growths might be obtained on other media by leaving in for a longer period of time.

We are far from being convinced as to the value of positive cultures. It would seem fair to assume that in those cases returning negative cultures from the duodenum itself and positive cultures from the B or C fractions, possibly some significance could be attached. In those cases, however, in which positive cultures are obtained from the duodenum much doubt must attend where a growth is obtained from material which must pass over this infected area. The question then arises

physiological affair and must be under control of stimuli produced by the acid chyme leaving the stomach. This variable factor of digestion dependent upon various food stuffs would appear to us to influence to a marked degree the functioning of this law. The normal stomach is known to vary to a very large extent in the degree of acidity, and even under normal conditions there are times when there is probably no free acid. We would assume under such conditions that there is not the relaxation of Oddi's muscle nor the contraction of the gall bladder that would be found under the opposite conditions. Therefore,

CHART No. 1—DETAILED FINDINGS IN DIFFERENT CLASSES OF CASES STUDIED

Clinical Diagnosis	Macroscopic			Microscopic			Culture			Gastric Analysis				Amylase			Pancreatic Ferments			Lipase			
	No.	Pos.	Per Ct.	No.	Pos.	Per Ct.	No.	Pos.	Per Ct.	No.	-20	Per Ct.	+10	Per Ct.	No.	Neg.	Per Ct.	No.	Neg.		Per Ct.	No.	Neg.
Gall-bladder.....	44	24	54.5	44	26	59	44	18	41	13	12	37.5	7	21.8	27	7	25	27	1	4	13	2	14
Cardio-renal-vascular..	10	1	10	10	4	40	10	3	30						8	2	25	8	0	0	6	2	33
Osteo-arthritis.....	5	4	80	5	5	100	5	2	40						3	1	33	3	0	0	3	1	33
Duodenal ulcer.....	4	2	50	4	2	50	4	1	25	2	0	0	2	50	2	0	0	2	0	0	2	0	0
Endocrine 1.....																							
Epilepsy 1.....																							
Hyperthyroid 1.....	12	6	50	12	6	50	12	2	16.7	5	5	41.5	2	16.6	12	2	16	12	1	8	12	3	25
Enteropneosis 3.....																							
Neuro-syphilis 3.....																							
Pulmonary T. B. 2.....																							
Anemia (second) 1.....																							

whether such organisms as the colon bacillus may not frequently exist in the upper alimentary tract without producing any actual pathology. While the duodenum normally is supposed to be sterile we believe there are many conditions in which it is not sterile. We have on several occasions obtained positive cultural results from the duodenum before sterilization with silver solution, and in the material obtained shortly after, our results were negative. Whether or not we were able to sterilize this portion of the tract must remain questionable.

The quantity of bile recovered, its viscosity and specific gravity are points that we feel must still remain in doubt since there are so many factors, such as the rate of blood flow through the liver, that regulate these things. If Meltzer's law is correct (and while this seems to have been proven there are many who still question it), it would seem that many things, particularly with reference to digestion in the stomach, would influence it. If the law of contrary innervation is true, then it is a

any change of viscosity or specific gravity we feel may be due, temporarily at least, to many physiological phenomena, or at least phenomena not indicating pathology.

PANCREATIC FERMENTS

Since the return from the duodenal tube was bound to contain a certain admixture of pancreatic juice an effort to determine the activity of the pancreatic ferments in the cases studied naturally suggested itself. The method followed was substantially that outlined by Whipple and recently reported in the *Annals of Surgery*. In 27 cases which were clinically gall bladder or liver disease, 25% showed an entire absence of amylase, 4% an entire absence of protease, and 14% an entire absence of lipase. The remainder, and as will be seen by the chart the greater majority of this group, show the presence of all three ferments in varying degrees. In 25 cases in which there was nothing to suggest any gall bladder or liver impairment whatever, five showed an absence of amylase, one showed absence of protease, and six

showed absence of lipase. These results vary so widely and with so little regard for any demonstrable underlying pathology that we have felt that the method as herein outlined was practically without value. It is quite impossible in connection with the gall bladder drainage procedure as here outlined to administer the various pancreatic meals which have been recommended and which promise far greater and more reliable information as to pancreatic function. Our conclusion

been evolved in the intervening years may be classified broadly in accordance with that phase of liver function which they have attempted to estimate. The liver activities may be defined primarily as the exocrinous or combined secretory and excretory functions, and the group of endocrinous functions under which are comprised ureagenesis, glycogenesis, sanguinopoiesis, the fixation of toxins, cytopexis, and the lipasic function.

Earlier attempts concerned themselves

CHART No. 2--PHENOLTETRACHLORPHTHALEIN TEST IN 22 CASES

Case	Phenoltetrachlorphthalein			Bile					Diagnosis
	Return	fax.	cc. H ₂ O	Feces	Urine	Stool	Micro.	Culture	
A	7	25	47.0	0	0	0	0	0	Normal
B	25	Trace	Trace	0	0	0	0	Stren.	Gouto-arthritis
C	17	29	40.00	0	0	0	0	Unknown	Cholecystitis
D	11	39	70.0	0	0	0	0	0	Cholecystitis
E	89	Trace	Trace	0	0	0	0	Colon	Cholecystitis
F	15	45	10.8	0	+	+	+	Colon	Osteo-arthritis
G	37	40	9.2	0	+	+	0	B. Pyne.	Cholecystitis
H	39	Trace	Trace	0	+	+	+	Colon	Hypertension
I	31		5.7	0	+	+	+	Colon	Hypertension
J	30	40	8.5	0	+	+	0	0	Neuro-syphilis
K	20	90	10.5	0	0	0	0	0	Secondary anemia
L	15	90	33.5	0	+	+	0	0	Cholecystitis
M	19	90	38.4	0	+	+	0	Colon	Cholecystitis
N	47		7.2	0	0	0	0	0	Pernicious anemia
O	60		1.8	0	0	+	+	Colon	Hypertension
P	30		7.6	0	0	+	0	0	Normal
Q	24		6.5	0	0	0	0	0	Hypertension
R	47	90	20.0	0	+	+	+	0	Tachycardia
S	90		6.5	0	+	+	+	0	Hypertension
T	20	90	12.5	0	+	+	+	0	Normal
U	0		0	0	0	0	0	0	Chronic appendicitis
V	0		0	0	0	0	0	0	Normal
W	0		0	0	0	0	0	0	Normal

Note that in two of the normals there was no appearance of the drug whatever either in bile, stool or urine; also, that in several definite cholecystitis cases there was a comparatively high percentage returned with a short appearance time.

then is that where the pancreas comes under considerable suspicion, an independent effort, aside from the gall bladder drainage procedure, should be made by the use of pancreatic meals to determine more accurately the activity of the pancreatic ferments.

HEPATIC FUNCTION

Efforts to arrive at a satisfactory clinical method of establishing the function of the liver date back almost to the time of the discovery by Claude Bernard of the glycogenetic function of that organ. The considerable number of tests which have

largely with the estimation of sugar tolerance as evidenced by the appearance or non-appearance in the urine of glucose after the ingestion of measured amounts of various sugars. These were all found so unreliable, owing to the numerous factors other than hepatic function which were capable of influencing them, that they have only historical interest. Attempts to utilize the ureagenetic function of the liver as an index to liver capacity were made by estimating nitrogenous products in the blood, and more particularly in the urine. The

fact that the results obtained in these estimations were so largely dependent upon the integrity of the kidney, has invalidated them as tests of liver function and relegated them to another field. Several tests based on an effort to determine the antitoxic power of the liver cells have been taken up and subsequently, for the most part, discarded. Of these may be mentioned the Chauffard methylene blue test which was dependent upon supposed variations in the urinary excretion of subcutaneous injections of methylene blue solutions in cases of impaired hepatic efficiency; Roche's modification of this pro-

Of more current interest are the attempts to estimate the biliary functions of the liver, most prominent among which are the urobilinogen and urobilin tests, and the phenoltetrachlorophthalein method. The only bile pigment present in fresh liver bile is bilirubin. It is only with the oxidation of bilirubin in the gall bladder or in the intestines that biliverdin, the darker pigment, is formed, it being the oxidation product of the former. The bilirubin is of course formed in the liver from the disintegrated hemoglobin of the red blood cells which is carried to and fixed by the liver, where it is converted into the

CHART NO. 3.—CONTRASTING THE HEMOCLASTIC CRISIS TEST IN 7 CASES OF GALL BLADDER DISEASE WITH 10 CASES WITH NO GALL-BLADDER PATHOLOGY

Diagnosis	Hemoclasis					Duodenal Drainage		
	Start	15 Min.	30 Min.	45 Min.	60 Min.	Macro.	Micro.	Cultures
Hypertension.....	9800	9600	6000	7400	10000	+	+	Colon
Anemia—Ca. ?.....	8000	6500	6400	5000	5500	0	0	0
Hypertension.....	7800	9000	9400	12000	7600	0	+	Colon
G. B. adhesions—P. O.....	6900	7100	7200	8300	6800	+	+	0
Gastric ulcer.....	8600	6800	6600	6400	7400	+	+	?
Cholecystitis.....	9200	7800	7000	7500	8500	+	0	?
Normal.....	12000	12100	13000	12900	13100	0	0	0
Normal.....	10300	10500	11000	10400	10900	0	0	0
Arthritis.....	11300	11200	10300	11000	10000	+	+	0
Hypertension.....	8300	8500	9000	8500	8000	+	+	Colon
Cholecystitis.....	7500	10300	10000	10600	8000	+	+	0
Normal.....	9000	10100	10000	9400	9300	+	+	0
Cholecystitis.....	6800	8000	7000	7100	6800	+	+	0
Cholecystitis.....	9200	8600	8900	8600	8400	+	+	0
Cholecystitis.....	14300	15600	15700	15500	15000	+	+	0
Cholecystitis.....	6800	8000	7700	7400	6800	+	+	0
Neuro-syphilis.....	12000	16600	8600	12300	12200	+	+	0
Average 7 G. B.	8670	9200	9350	9340	8750			
Average 7 other.....	9100	9050	8420	9210	9100			

cedure; indicanuria both spontaneous and that provoked by the ingestion of indol; and the provocative sulphoconjugation test of Foster and Kahn. The intimate connection of the liver with the elaboration of certain constituents of the blood, particularly fibrinogen, has led to a number of tests to estimate the sanguinopoietic function of the liver cells. Of these the estimation of blood coagulation time with the assumption that decreased coagulation time indicated impaired hepatic function, the fibrinolysis tests of Goodpasture; Whipple's estimation of blood lipase, and the estimation of proteolytic ferments by the Abderhalden method should be mentioned. These tests all concern themselves with the endocrinous functions of the liver.

iron-free pigment bilirubin. Under normal conditions bilirubin does not appear in the feces but there does appear there the related product urobilin, which is the reduction product formed in the intestines by the action of the hydrogen on bilirubin. A portion of the urobilin thus formed escapes in the stools. Another portion undergoes reabsorption in the form of urobilinogen which again is partly eliminated in the stool, while the remainder returns to the liver and is reconverted into bilirubin.

It is with the last step in this process that the bilirubin test for hepatic function concerns itself, since it is assumed that in the presence of marked impairment of the liver cells the final fixation and reversion of the urobilinogen will not occur, thus permitting the excretion

of that substance in the urine where it very shortly spontaneously changes into urobilin by oxidation. The two substances, so far as urinary determinations are concerned, may then be regarded as practically identical, being the same substance in different forms.

Urobilinuria may be caused by a large variety of conditions, among them malaria, pneumonia, lead poisoning, decompensated heart disease, severe anemias, and hemorrhage, in addition to liver conditions. The mechanism of its occurrence in connection with hepatic conditions may

action was the most widely used of these tests and had a considerable vogue. In recent years it has fallen into disrepute owing to the large list of conditions other than primary hepatic impairment which give positive findings. However, a test for urobilinuria, the results of which shall not be deemed in any way definite and which shall be considered in conjunction with and in relation to a number of methods calculated to throw light on the status of hepatic function, no doubt has a place, in view of its simplicity and its confirmatory value.

CHART No. 4—TABULATED FINDINGS IN 10 CASES OF POSITIVE CULTURAL FINDINGS

Case	Age	Amount in Bile	Culture			Macro.	Pancreatic Ferments			Gastric		Tetrachlor- phthalein	
			"A"	"B"	"C"		Amylase	Protease	Lipase	History Typhoid	Free Acid	Total Acid	Return
A. 47	100		Pure			Neg.	Nor.	+	0	No			
B. 53	140	P	P			Neg.	Nor.	+	0	Yes	39	73	0
C. 50	40	P	P			Mucus	Floc.	+	0	No		31	5.7
D. 43	158	P	O			Neg.	Stat.	+	0	.3	Yes	66	90
E. 45	82	P	P			W.B.C. Mucin	Stat. Floc.	+	+	6.6	Yes	0	20
F. 46	0	P	O			W.B.C.R.B.C.	Floc.	0	+	3.3	Yes	80	106
G. 57	60	P	P			Mucin	Floc.	+	+	0	No		13
H. 40	50	P	P			W.B.C.	Floc.	0	+	5.4	Yes		39
I. 75	130	P	P			Mucin Cryst.	Stat. Floc.	0	+	.3	No	0	68
J. 46	156	P	B. Coli and Staph.			Mucin	Nor.	+	+	.2	No	6	24

Note.—"P" indicates that a pure culture of some organism was obtained from the particular biliary fraction designated.

be either partial or incomplete interference with the biliary flow in the ducts, or insufficiency of the liver cells themselves. Obviously, in complete obstruction of the ducts no bile would be thrown into the intestines and hence no urobilin formed. Urobilinuria may therefore be either relative or absolute; relative in cases in which the greatly increased destruction of red blood cells overwhelms the normal capacity of the liver to care for the liberated pigment; and absolute when the liver parenchyma is unable to fix and reconvert normal amounts of urobilin. It is only in the latter case that urobilinuria becomes an index to hepatic function. In hepatic disorders which are ultimately characterized by jaundice there is ordinarily a period of urobilinuria preceding the icterus. The well known Ehrlich's urobilinogen test based on the benzaldehyde re-

THE PHENOLTETRACHLORPHTHALEIN TEST

In an effort to find a dye which would provide a test of liver function similar to the 'phthalein test for kidney function, Abell and Rountree, in 1909 began a pharmacological study of phenoltetrachlorphthalein. A considerable amount of experimental work established the fact that under normal circumstances in normal individuals a suitable quantity of this drug injected intravenously escaped from the body exclusively in the bile. While some reabsorption by the bowel was found to occur, it was thought that this could be very largely prevented by hurrying the progress of the fecal stream with purgatives. Work on dogs done by Whipple, Mason, Peightel, and Clark further established the fact that in dogs in which experimental injury had been done to the liver parenchyma the rate of excretion of

to prevent precipitation during sterilization of the ampoules. Our later tests were made with this preparation and the results we obtained varied quite widely from those obtained with the first preparation. Although the quantity used was the same, the red color was more marked in the returned fluid and was apparently very much less altered in its passage through the body as it could be easily read against the standard without any previous addition of bile to the standard. The earliest return of color with experimental subjects of apparently normal liver function was 15 minutes, and the largest total return 38% as contrasted with 70% in the first series. Our first test was done on a perfectly normal subject. The drug appeared in 7 minutes with the maximum return in 25 minutes, and a total of 47% in two hours, and the total disappearance of the drug from the bile in three hours. The feces were saved for 48 hours and no trace of the drug could be found here nor in the urine.

With this single experiment we were very hopeful that the test would prove of great value in determining liver function since it seemed that it would be possible to establish a normal appearance time and a normal two-hour return if all of the drug was recovered in the bile, and the feces did not have to be considered. We attempted to explain the absence of the dye in the feces on some physical basis, believing that possibly through syphonage the entire amount of bile was diverted to the tube. The problem, with diagrams, was presented to a physicist who explained that this could not be a constant finding and there was no physical basis to make it even probable.

With further work we were, however, doomed to disappointment since frequently small quantities were found in the feces, occasionally small amounts in the urine, and the time of return and the quantity recovered in two hours was so variable and so entirely out of keeping with what was to be expected that we, at this writing have serious doubts as to its value from a diagnostic standpoint. Five cases in which there was no ground in the final analysis for a suspicion of any hepatic impairment gave a total return in the two hour interval of less than 10% of the drug, and in

one instance less than 5%. Two perfectly normal individuals that were used merely for experimental purposes showed absolutely no trace of the drug in two hours time although there was a steady return of bile. In four cases of hypertension with a moderate amount of kidney involvement the appearance time of the drug varied from 30 minutes to 60 minutes, and the total two-hour quantity was less than 10%. On the other hand two cases of quite typical cholecystitis gave appearance times of 15 minutes and 19 minutes respectively with a total return of 33% and 38%. Our largest total return of 70% was obtained in a patient with quite definite history of gall tract trouble whose symptoms were being markedly relieved by repeated therapeutic drainages. In other words, so far as our small series of cases enable us to draw any conclusions in regard to the value of the phenoltetrachlorophthalein test as used in connection with the gall bladder drainage there seems to be no uniformity of relationship between either the appearance time or the total return, and the clinical diagnosis, x-ray, cultural, or physical findings. Furthermore we are unable to see how the obvious sources of error such as the destruction of the dye by the liver itself, the amount of reabsorption from the intestines, and the amount excreted by the kidney can be corrected.

HEMOCLASIS

The digestive hemolysis test for insufficiency of the liver was originated by Widal, Abrami and Lancovisco and presented in the *Presse Medicale* in the early part of the present year. The value of the test was based upon their claims that some of the proteins in the food which escaped disintegration pass through the wall of the intestines and penetrate into the portal vein. The liver holds back some of these disintegrated proteins when the blood passes through it. They call this the proteopexic function of the liver. When the liver is incapable of thus retaining these incompletely disintegrated proteins they pass into the general circulation where they exert a destructive action on the blood corpuscles, the digestive hemoclastic crisis, as they call it.

They did not find this in a large number of healthy persons examined, nor in other than liver conditions. In various forms of liver disease, however, this hemoclastic crisis was pronounced, the leucocytes dropping to one-half or one-third of the predigestive figure. The test consists simply of counting the leucocytes before and at intervals for an hour after taking a glass of milk on the fasting stomach. They claim that in normal subjects the leucocyte count is about the same, but with derangement of liver function there is a pronounced destruction of leucocytes during the first hour or two of digestion. Working on this principal a comparatively small number of cases were studied without in the slightest degree having our figures agree with the work done by these investigators. The chart is a tabulation of 17 cases, seven of which were clinically liver or gall bladder disease and ten other pathology. On the same chart will be noted the macroscopical, microscopical and cultural study of the bile obtained by the Lyon method. It will be seen that the average counts in the seven gall bladder cases and the ten remaining cases are practically identical, neither showing any reduction in the number of leucocytes. As a matter of fact, in the one case showing more than the others this so-called hemoclastic crisis, the bile was perfectly normal in every respect. In only one case of cholecystitis was this reduction in leucocytes noted, and then to a moderate degree only. From our own experience, therefore, we are quite convinced that the determination of the hemoclastic crisis has little or no place in the diagnosis of liver pathology unless it may indicate damage done to the liver by arsphenanim treatment or chloroform. Indeed it seems that a large number of patients investigated by these workers were under some form of arsenic treatment and it is quite possible that this may account for their results.

THE INDUCED GLYCURONURIA TEST

This test was proposed by Chiray and Caille who make rather extravagant claims for it. We have had no experience and simply mention it as a test for liver function that is being given some attention. It consists of taking two capsules

each containing .5 grams of natural camphor on the fasting stomach. The urine is collected at once and again six hours later. The liver function is estimated through determining the glycuronic acid in the urine by lead colorimetric method. In the normal individual glycuronuria follows, the figure running from .01 or .04 up to .08 grams in four hours, and it remains high for six or eight hours. The test is merely given for what interest it may arouse.

X-RAY STUDIES

Considerably over half of the cases reported have had a complete x-ray examination of the gastro-intestinal tract including films of the gall bladder region. Of 55 cases studied up to the present time 36, or 65%, were negative throughout, and 8 or 17% show as their only x-ray abnormality a $4\frac{1}{2}$ hour barium residue in the stomach varying from 15 to 25%. In four cases there was evidence through misplacement or deformity of the duodenum of adhesions involving the duodenum and the gall bladder. In three cases there was only marked general enteroptosis. In three cases there was a characteristic duodenal cap deformity persisting at repeated examinations, of the sort accepted as characteristic of ulcer. In one case an enlarged dense gall bladder was demonstrated on the x-ray films. In one case there was a diverticulum of the transverse colon and in two cases definite shadow evidence of gall-stones.

Of the cases showing a $4\frac{1}{2}$ hour barium residue, five were clinically gall bladder disease, the remaining three having no symptoms pointing toward the gall tract. The two cases showing gall stones were clinically characteristic of cholecystitis, although neither had had colic. None of the enteroptotic cases had any evidence of associated gall bladder disturbance. The cases showing duodenal cap deformity were typically duodenal ulcer both as to history and clinical findings, no evidence pointing to associated gall bladder disturbance. We found it necessary in only a very few instances to verify the position of the tip of the Lyons tube in the duodenum fluoroscopically. In these instances where it had been impossible to

obtain a satisfactory alkaline bile stained return from the tube the tip was found to be invariably outside the duodenum. The results are noted in chart No. 5.

OTHER INVESTIGATIONS

History of Typhoid.—It is rather interesting to note that 27% of the cases that were clinically gall bladder disease gave a history of typhoid fever. This would seem to be of some significance when compared with 13% of all other cases that gave a typhoid history.

Blood Counts.—A complete count of the red and white blood cells as well as a differentiation of the latter was done routinely, but the results were not sufficiently instructive or interesting even to present here.

Gastric Analysis.—If the theory of Meltzer's law is correct it would appear that in all probability any condition which would bring about an acidity of the gastric contents would in turn interfere with the normal functioning of the phenomena of gall bladder contraction and sphincter relaxation and thus bring about stasis and eventually infection and possibly gall stone formation. Therefore, it would seem that in a majority of cases at least where cholecystitis or gall bladder disease was present we could expect subnormal figures at least for gastric acidities. It will be noted in chart No. 1 that in 37.5% of the cases with clinical findings positive free acid was under 20, and that in only 21.8% were the acidities above 40. The theory of the functioning of the law of contrary innervation is probably correct. Where hyperacidities exist in connection with gall bladder disease, in all probability the disease was primary and the hyperacidity was a reflex affair much as we get in disease of the appendix or other portions of the alimentary tract. When we pass on down the chart and find that of the 12 miscellaneous cases in which the gall bladder was not even suspected 41.5% had free acids below 20 and only 16% free acids above 40, the question naturally arises, just how far can we apply such findings to the biliary tract.

Some rather interesting points have developed in connection with our gastric analysis that would suggest the advisabil-

ity of the fractional method of analysis in most cases. We have in several cases obtained markedly subnormal figures after the usual Ewald test meal and the following day when the gastric residuum was removed before starting the usual drainage we found extremely high figures for free acid. The reverse of this has even more frequently been demonstrated.

We should like to call attention to the chart showing ten cases in which pure cultures were obtained from the biliary tract and the comparison of the other findings in the same individual. This does not represent the total number of positive cultures and is produced merely to show the comparison between this and other findings. For instance in case A with pure cultures of *B coli* from "A", "B", and "C" fractions the bile was negative macroscopically and microscopically. The same was true of case B in which there was practically a normal gastric analysis, but a total absence of phenoltetrachlorphthalein in two hours. Case F, a post-operative case with dense adhesions surrounding the gall bladder, upon a recurrence of symptoms, showed a pure culture in the "A" and "C" fractions (no "B" bile being obtained) with positive microscopical and macroscopical findings, an intense gastric hyperacidity, with a total tetrachlorphthalein output of 38.4%, a wholly inconsistent finding. The high acidity is in keeping with the theory that the gall bladder infection was primary and not dependent upon previous disturbance of the gastric secretion. Pure cultures of the colon bacillus have been recovered in a far greater percentage than other organisms. In only one instance have we obtained a pure culture of typhoid, and quite strange to relate, no history of typhoid infection could be obtained. One pure culture of bacillus pyocyaneus was obtained at three different drainages. Various streptococci were of less frequent occurrence than colon bacilli.

What then are we to conclude from a study of our figures obtained in this rather small series? Frankly, we do not know. It is our intention to carry the work still further hoping to arrive in time at some conclusion that will be of real value. Un-

til that time the questions that present themselves are as follows: shall we let negative results from our various laboratory methods of studying the biliary contents influence our judgment where a careful and painstaking history and examination indicate the presence of liver or gall bladder disease? On the other hand, shall we be influenced by positive macroscopic, microscopic, or cultural findings of the biliary contents where from history and examination we are unable to find evidence of such pathology? We still have unbounded faith in the results obtained from a properly recorded history and a thorough and painstaking physical examination. We feel furthermore that any laboratory procedure to be of greatest value must corroborate to some extent at least the impressions obtained from these time-honored methods. This is true of practically every laboratory procedure that has been accepted in the medical practice of today.

The various methods herein outlined give great promise for the future. Much time and much hard scientific work, however, will be necessary before their value can be established. We shall continue to hope to see more light in the future, but at the present time when such procedures do not conform to a greater extent with impressions obtained from the two leading diagnostic methods, viz., a careful anamnesis and a thorough physical examination, their diagnostic value must be more or less questioned.

TECHNIC OF DIAGNOSTIC GALL BLADDER DRAINAGE AS USED IN THE CASES HEREIN REPORTED

The patient presents himself with fasting stomach at 9 a. m. The teeth are well brushed and the mouth cleansed with potassium permanganate and zinc chloride solution. A sterile Lyons tube is introduced into the stomach; residuum removed and preserved for analysis; stomach rinsed with sterile water until the return is perfectly clear. The stomach is then doused with diluted zinc chloride solution, followed by sterile water, 1-5000 silvol solution and again by sterile water. These solutions are warmed and as complete a return as possible is obtained before the succeeding solution is introduced. The patient then lies on the right side and takes twenty minutes to swallow the next 20 cm. of the tube. After the tube has entered the duodenum sufficient material for pancreatic ferment tests is first set aside and the duodenal cultures are taken. The duodenum is then doused with 100 c. c. of 1-5000 silvol solution,

following the recovery of which 50 to 75 c. c. of 33 per cent magnesium sulphate solution is introduced. The "A" or duct, "B" or gall bladder, and "C" or liver bile are obtained in order. The amount of each, specific gravity, macroscopic and microscopic characteristics are recorded, and cultures made from each type of return by allowing the fluid to flow directly from the end of the alcohol cleansed tube into glucose bouillon, which is immediately placed in the incubator. A sterile centrifuge tube is also filled with each type of return, centrifuged and the sediment planted on blood agar immediately.

We wish at this point to express our gratitude for the careful and painstaking work of Miss Beatrice Fuge in supervising the laboratory aspects of this investigation.

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DISCUSSION

Dr. J. E. Paullin, Atlanta, Ga.—The paper of Drs. Dowden and Enfield brings to our attention very interesting observations which have particular reference to duodenal drainage as a diagnostic procedure. For some time we have made a study of the drainage obtained from the duodenum, both microscopically and bacteriologically as they have outlined. From the studies which we made in perhaps 100 cases or more we feel that the information obtained from this particular procedure, as being of great benefit in the diagnosis of gall bladder disease, was practically worthless. In other words, we obtained results which at times were so at variance with the clinical condition of the patient that as a diagnostic procedure it was practically valueless. It was virtually impossible to obtain cultures from the duodenal contents in normal individuals with sterile bile. As Dr. Dowden has well said, when a culture made from the washings of the duodenum showed a growth of either the colon bacillus, the staphylococcus, or some of the other organisms, we felt sure that cultures obtained from drainage with the bile would naturally show the same infection. In at least 15 cases we

attempted to check the bacteriology between the findings obtained from the duodenal drainage and the findings at operation; we were not able in the majority of instances to corroborate at operations the bacteriological findings obtained from duodenal drainage. In other words, in any gall bladder infections cultures made at the time of operation frequently did not show the organisms which we thought were obtained from the bile from the duodenal drainage, so this has caused us to lose confidence in the method as a diagnostic procedure.

As to the value of duodenal drainage in the relief of symptoms, that is entirely a different story and is not here for discussion.

Dr. J. Rowan Morrison, Louisville, Ky.—From my observations of the work of Dr. Dowden, checked up by the work of others, I can not say that we have very much of diagnostic value from duodenal drainage. I think it is very appropriate that men like Dr. Dowden should take up this subject and have it discussed from all angles to determine the value of this method of procedure. As the previous speaker has said, I am convinced that this method offers something as a method of treatment.

Dr. George M. Niles, Atlanta, Ga.—I have listened just as attentively as I could and with great interest to the paper of Dr. Dowden. I have endeavored to follow every word of it, and I realize that what he has read in a few minutes represents an immense amount of labor and thought, and still he says this work is preliminary. I think you will admit that as a result of his researches he strikes an uncertain note.

As to the diagnostic worth of this method it is very much *sub judice* as yet, but I believe on the whole the trend of his argument is somewhat against its value.

I received a letter from Dr. Lyon less than two weeks ago in which he stood for everything that he has heretofore claimed, and he does not "back water" in anything. Of course, we have to allow for enthusiasm, but Dr. Lyon is not a weak man by any means, and I feel sure he would not make a positive statement unless he felt reasonably certain of his ground.

I have had some clinical experience with this method. I have up to date made 614 of these duodenal taps on 141 cases. I have a certain amount of bacteriologic, microscopic and macroscopic data on hand which I am not ready to present as yet, and I am in a maze of uncertainty as far as these findings are concerned. I would be glad if Dr. Dowden would depart a little from the title of his paper and restrict the interpretation of his closing remarks so as to give us a few of his clinical results. We do not want in any way to get back to the old German trend of therapeutic nihilism where they used to say diagnosis was everything and therapeutics was nothing. I am anxious to get Dr. Dowden's viewpoint, if he will give it to us, as to the clinical potentialities of that which is at least worth while at present, and in the meantime I am sure he and other competent investigators will continue along these lines until they either come to a positive or a negative conclusion.

Dr. Dowden (closing).—The analysis of Dr. Niles' remarks would seem to indicate that we are in fair agreement concerning this procedure. He has spoken with particular reference to the method as a therapeutic procedure while my remarks have dealt with its diagnostic value. The point I want to make is simply this: that in many apparently normal cases as far as clinical symptoms were concerned we were able to demonstrate bacteriologically and microscopically similar findings to those obtained in other conditions that were clinically gall bladder or liver disease. I quite agree with Dr. Niles that where gall bladder disease or liver disease is diagnosed clinically that the procedure is warranted, and furthermore I believe will frequently give most satisfactory results. Certainly it is worth a trial and if satisfactory results are not obtained no harm has been done so far as we have been able to determine. As stated in my opening remarks, our results are presented for what they are worth and we are claiming nothing nor attempting to discredit anything. We shall continue with the work, but more in the future I am sure as a therapeutic aid than as a diagnostic procedure. It is possible that with further experience there will not be such a conflict between our laboratory findings and suggestions obtained from the history and careful physical examination. As long as this continues to occur, however, we feel that it is well to question such findings.

THE NEWLY-BORN SERVICE*

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Of all the periods of life, that of the newly-born is probably the one which receives the least scientific attention, though it be the one scientifically most fruitful. This period is neglected because the infant is frequently overlooked in the interest shown the mother during the puerperium by her attendant who may be adept in the care of the mother but who has not devoted sufficient time, energy and study to the care of the newly-born. Were these newly-borns placed in charge of those whose life work is devoted to the early years and days of life it would be far better for all concerned. Because of the special study required of the normal newly-born infant and the diseases to which he is subject only those especially interested and trained in this period of life should be entrusted with his care. It is reasonable,

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