definite basement membrane. There were no Paget cells in the dermis. Sections of lymph glands showed no metastases. *Diagnosis.*—Chronic cystic disease with desquamative epithelial hyperplasia; papillary cystadenocarcinoma of the breast.

CASE 5

Mrs. A.G. (No. W.D.—730-33), aged 19 was admitted to the Western Division of the Montreal General Hospital complaining of discomfort in the left breast and was seen by me in consultation with Dr. Albert Ross on June 2, 1933.

Personal history.—Married at 16. One full term pregnancy; one miscarriage.

Present illness.—The patient stated that for five years she had had a swelling in the left breast, which varied in size but had recently become larger. She had nursed her child (two years old) for several months.

Examination.—The breasts were large and symmetrical; the nipples, normal. There had been no bleeding. In the left breast there was an irregular mass, about 1.5 by 1 cm. in diameter, in the upper and inner quadrant, at the margin of the areola, just above the equator. The striking feature was the dimpling of the overlying skin. The mass was fixed in the surrounding breast tissue and quite firm; the surface was smooth.

Operation.—With the patient prepared for radical operation resection of the tumour was first performed. The frozen sections showed it to be carcinoma, and a radical operation was then carried out.

Microscopical examination showed a circumscribed, non-encapsulated tumour, composed of small, closely-packed acini, lined with cuboidal cells. Throughout the nodule there was a diffuse fibrous tissue stroma. In places the epithelium was arranged in small cords without alveolar formation, these cords extending irregularly into the surrounding fat. *Histological diagnosis.*—Carcinoma of the breast. No axillary lymph-node metastases.

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PHOSPHATASE IN OBSTRUCTIVE JAUNDICE*

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PHOSPHATASE is the name given to an enzyme shown to be present in bone and ossifying cartilage by Robison[4] at the Lister Institute. He has demonstrated that this enzyme is intimately related with the process of bone formation. In conditions of generalized bone disease the phosphatase appears to leak out of the bone into the blood in large amounts. Its quantitative determination in the plasma or serum in cases of rickets, Paget's disease, osteitis fibrosa cystica, and in any cases of generalized bone disease is of some diagnostic value.

Phosphatase has recently created considerable interest among the medical profession because of its alleged usefulness as a means of differentiating obstructive from other types of jaundice. Last spring (1933) we made estimations on several specimens of blood obtained from the Toronto General Hospital, some of which were from obstructive jaundice cases, and in these the phosphatase content was found to be higher than normal. Our attention was then drawn to an article by Roberts[3] from the Sheffield Royal Infirmary. Roberts published his study of 50 consecutive cases of jaundice, reaching the conclusion that "The obstructive nature of jaundice can be recognized by the increased phosphatase activity of blood, which occurs strikingly in this type alone." In view of the fact that such a test would be of great value to the clinician, it was decided to attempt to confirm these findings and, further, to place the work on an experimental basis by the production of jaundice of various types in dogs. The present communication is an account of observations on both clinical cases and experimentally-produced obstructive jaundice; and in addition there are presented for contrast the protocols of the experiments on hæmolytic jaundice, although this phase of the study has just been commenced. The phosphatase was determined by the method to be described in a later issue of this *Journal*, (King and Armstrong[2]); the bilirubin determinations were made by the Thannhauser and Andersen modification[5] of the van den Bergh method.

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PART I: EXPERIMENTAL OBSTRUCTIVE JAUNDICE IN DOGS

Obstruction to the common bile duct has been produced in 19 dogs, and the serum phosphatase activity and bilirubin have been determined each day following the operation. All the animals sooner or later became definitely ill, exhibiting a typical series of signs. These were lassitude, loss of appetite passing on to complete refusal of food, vomiting, constipation, biliuria and, terminally, marked dehydration. The only therapeutic measure adopted was the giving of intravenous glucose and saline when dehydration became apparent. Only in a few cases was an icteric tint of the skin or scleræ observed. This fact is explained by the great ease with which the kidney excretes bilirubin in this animal.

Relief of the obstruction was attempted in several ways, with only partial success, except in the case of two animals. The reason for this is twofold. Firstly, the common bile duct becomes necrotic and ruptures at the point at which it has been tied off, unless fibrous adhesions grow around it sufficiently rapidly. This can be aided by securing in place a small piece of omentum. Secondly, the animal is in very poor physical condition by the time the second operation is performed, since the liver is badly damaged by the back pressure. Infection takes place very rapidly, and in addition to those dogs dying from peritonitis a few have died from bronchopneumonia.

In order to conserve space a composite chart of the phosphatase activity in the serum of ten dogs following complete obstruction to the common bile duct has been compiled, and a general description of these animals will be given. More in detail, however, the results of three other experiments will be described. In two of these after a period of some days the obstruction to the flow of bile was removed, and the animals recovered completely. The remaining case, although the dog finally died, is instructive, since it combines the effect produced on relief of obstruction, first, when the phosphatase is at a medium height, and later, when the value is exceedingly high.

1. *Obstruction of the common bile duct.*—The common bile duct was dissected out under ether anæsthesia in ten dogs. The duct was then either cut and ligatures applied to the cut ends, or it was tightly tied in two or more places and left uncut. The animals were then placed in metabolism cages and observed for from 4 to 6 days. They were supplied with food and water each day, but no therapeutic measures were applied. Blood was withdrawn from the femoral vein prior to the operation and on each succeeding day for estimation of phosphatase and bilirubin. In Chart I units of phosphatase in

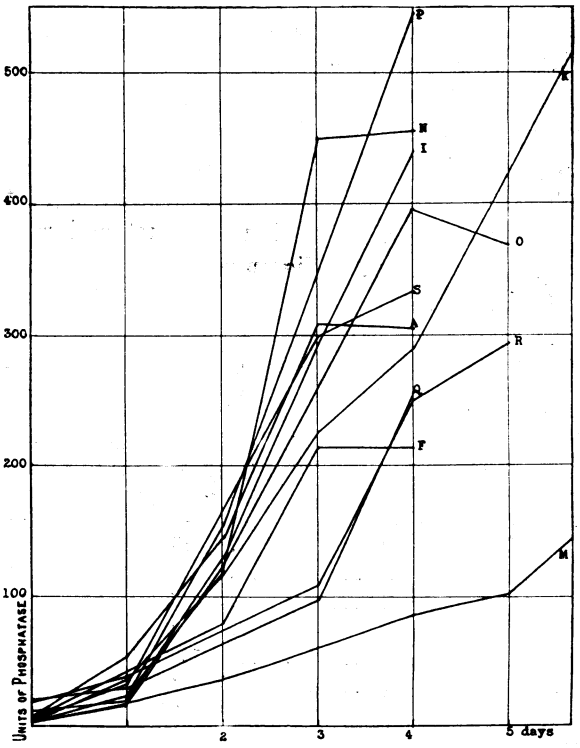

CHART I.—Units of serum phosphatase in dogs after obstruction of the common bile duct.

the serum have been plotted at daily intervals for each experiment. On the day following operation the majority of the dogs had recovered satisfactorily and were taking food. In a few cases bilirubin was present in the urine. In all cases there was a definite increase in serum phosphatase (10 to 50 units). The van den Bergh reaction was negative. On the second day they all appeared to be quite well. The urine, however, invariably showed the presence of bilirubin and continued to do so on succeeding days. Bilirubin could now be detected in the serum and was always present from then on. The serum phosphatase had increased very markedly (a further 20 to 85 units). By the third day most of the dogs were refusing some of their food. A further marked increase in serum phosphatase was present, the value being in the majority of cases over 200 units. On the fourth day the animals were drowsy and fre-

quently appeared acutely ill. An icteric tint was visible in the scleræ and mucous membranes. In only one case was the phosphatase value below 200, while one animal reached the height of 545 units. Only three dogs were observed in the obstructed state until the sixth day, and in these the clinical picture became more pronounced, while the phosphatase continued to rise. The remaining dogs died of bile peritonitis either before or after an attempt was made to relieve the obstruction.

It will be noticed on reference to Chart I that four of the curves fall off slightly, or fail to rise higher after the third and fourth days. This fact was associated with the finding at autopsy or laparotomy that the duct had ruptured at the point of ligature.

Gall-bladder bile was obtained at autopsy on a number of these animals and the phosphatase activity per 100 c.c. was estimated. The following values were obtained:

Dog	*Units of phosphatase per 100 c.c. bile*
F	819
I	138
K	227
M	410
O	750
Q	394
R	1710

The autopsy findings were in general the same for all dogs. The bile ducts and the gall bladder were markedly dilated; except where rupture had occurred they contained a large amount of bile under tension.

2. *Obstruction of the common bile duct followed by relief of obstruction.—*

Experiment 1.—A large mongrel police dog.

Under morphine and ether anæsthesia the common bile duct was dissected out for a distance of 2 cm. from the intestinal end. A small wire paper clip, bent so as not to be too tight, was slipped into place. This produced obstruction not only by pressure but also by virtue of its bending the duct on itself. Pressure was now made on the gall bladder and it was seen that the duct became dilated above the clip, and that apparently none of the bile could pass beyond this point. A silk thread was then tied to the clip. The wound was closed leaving the other end of the thread beneath the muscle layer.

The serum phosphatase and van den Bergh reaction are shown graphically in Chart II(a). The latter value has been multiplied by 10 before plotting, in order to give it greater significance on the same scale as phosphatase.

The initial phosphatase was 4.5 units. After the operation the rise was slow, but definite. On the third day the animal was still apparently quite well. The phosphatase value lay at 106 units, while the van den Bergh reaction could just be read (0.4 units). The urine was bile-stained. Under morphia and ether anæsthesia the wound was now re-opened. The abdomen was free from peritonitis. Adhesions in the region of the gall bladder were carefully broken down and the clip exposed. By steady traction it was removed. No leakage of bile was observed. The abdomen was closed again. On the following day a marked drop in phosphatase had occurred; the van den Bergh reaction was negative, but bilirubin was present in the urine. In the course of 20

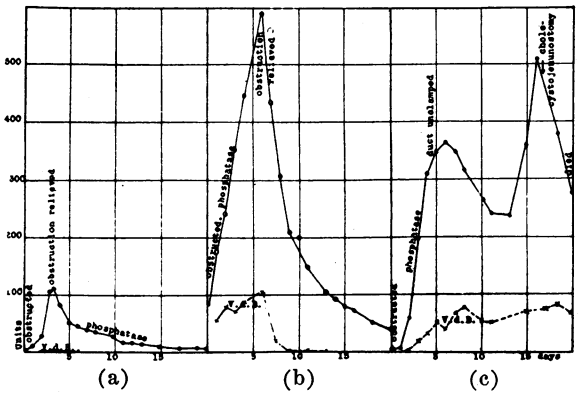

CHART II.—Units of serum phosphatase and bilirubin (van den Bergh x 10) after obstruction to the common bile duct in dogs.

days the phosphatase fell continuously and reached finally the initial level. The urine became negative for bilirubin on the eleventh day. During the early stages of recovery the animal suffered from mild diarrhœa.

Experiment 2.—A large pack hound.

Obstruction of the common bile duct was produced in a second dog in the same manner as before. When the duct was exposed an unusual condition was encountered, namely, the duct was seen to be dilated and contained bile under slight pressure. It did not occur to us at the time that this represented other than the physiological emptying of the gall bladder at that moment. However, when the initial phosphatase determination was made it was found to be very high (88 units). Unfortunately, the van den Bergh reaction was not carried out on this first blood sample, but on the next day it had reached 6 units. (This is much higher than can be obtained by a single day's obstruction).

Chart II(b) shows the phosphatase and van den Bergh units graphically from day to day. The response to the experimental obstruction was very marked as regards phosphatase, the activity of the serum by the sixth day being 592 units. The van den Bergh reaction reached 10.5 units by this day, and an icteric tint to the scleræ was evident as early as the fourth day. The urine was not observed until the second day, when it was found to contain a large amount of bilirubin.

On the sixth day it was decided to remove the clip in view of the fact that the dog was refusing food and appeared acutely ill. A slight discharge was present in the nose. For this reason the abdominal wound was opened under morphia and a local anæsthetic (novocaine). There was no evidence of any peritonitis and the clip was removed without difficulty. Recovery was good, clinically, and the nasal discharge rapidly disappeared. By the fifteenth day the icteric tint was scarcely visible in the scleræ. The phosphatase had fallen to 21 units on the thirtieth day, and the van den Bergh reaction had been normal for some time. During the early recovery stage the stools were loose and deeply pigmented.

Experiment 3.—A large police dog.

The obstruction in this animal was produced in such a way that it could be relieved by unclamping a pair of forceps which kept tight a rubber band around the duct. The handles of the forceps were left in the wound under the skin. After four days the signs of obstruction were well marked, and the serum phosphatase had reached a high level (315 units). The forceps were now unclamped. After a lag of two days clinical improvement was noted, and this corresponded to a fall in serum phosphatase to 235 units. On the sixteenth day, however, the animal was again becoming very ill, and, as can be seen by reference to the chart, the serum phosphatase was at this time rising rapidly and reached 515 units. Cholecysto-jejunostomy was performed on the twentieth day, following which a marked fall in phosphatase content occurred (to 280 units). Unfortunately, the animal died two days later. Autopsy revealed a very marked dilatation of all the bile ducts and an intense peritonitis. The point at which obstruction had been produced was stenosed by fibrous adhesions. Gall-bladder bile obtained at autopsy contained 962 units of phosphatase in 100 c.c. of bile.

3. *Experimental hæmolytic jaundice.*—Owing to the rapidity of excretion of bilirubin by the kidney in dogs we have so far been unable to produce clinical jaundice by the hæmolytic agents employed; nor have we been able definitely to obtain a positive van den Bergh reaction in the serum, although it is quite easy to cause bilirubin to appear in the urine in large amounts. When such amounts of bilirubin are thus excreted, it is probable that had the same degree of hæmolysis occurred in a human being, clinical jaundice would have occurred. On the other hand, the experiments are inconclusive, since it might be argued that failure of the serum phosphatase to rise appreciably under such conditions is directly related to the absence of bilirubinæmia. The experiments are therefore presented only as preliminary observations.

Hæmolysis has been produced in two ways: (1) 100 to 200 c.c. of blood were removed from the animal, laked in water, strained through a sterile towel, and re-injected into a vein; (2) 1 per cent sodium oleate solution was injected intravenously on successive days.

DISCUSSION

In all of the nineteen animals examined following obstruction there was a rapid and pronounced rise in serum phosphatase. The rapidity of the rise and the height reached varied from one individual to another. After five or six days the value was at least thirty times the normal, and in some cases as much as one hundred times. The rapidity of the rise is no doubt governed in some degree by the elasticity of the gall bladder and by the amount of bile in it when the obstruction is produced.

In the cases in which we have been able to relieve the obstruction without losing the animal, two types of response have been noted: one an immediate and marked fall in the phosphatase activity (100 units or more in a day); the other a slowing up of the rise, then a plateau, and finally a slow fall towards normal. This latter response we have reason to believe is associated with cases in which there is marked damage to the liver cells.

Protocols of 3 such experiments are as follows.

Experiment 1. A fox terrier, weighing 7 kilos.

Day	*Treatment*	*Plasma Phosphatase*	*Hunter's test for Bilirubin in Urine*	*Clinical Condition*
0	Anæsthetized with ether. 100 c.c. blood removed, laked in 100 c.c. water, 0.9 g. NaCl added, strained through towel, the whole re-injected.	3.5	Negative	Healthy.
1	–	6.9	Positive	Anorexia.
2	–	12.7	Negative	Refused all food.
5	–	9.5	Negative	Refused all food.
6	–	7.8	Negative	Refused all food.
8	–	7.2	Negative	Return of appetite.
16	–	4.4	Negative	Quite well.

The van den Bergh reaction (indirect) was just noticeable one day after the injection, while the urine contained a large amount of reddish purple pigment. The hæmoglobin on the same day had fallen 12 per cent, but returned to normal on the following day.

Experiment 2. A small Boston bull, weighing 10 kilos.

Day	*Treatment*	*Plasma Phosphatase*	*Hunter's test for Bilirubin in Urine*	*Clinical Condition*
0	100 c.c. blood removed, laked in 200 c.c. water, filtered through towel, re-injected.	9.2	Negative	Sudden collapse, vomiting, and voiding of urine & fæces, with rapid recovery during injection.
1	–	11.8	Positive	Quite well.
2	–	12.4	Positive	" "
4	–	10.8	Negative	" "
7	–	10.0	Negative	" "
15	–	8.4	Negative	" "

The van den Bergh reaction was negative throughout the experiment. A slight fall in hæmoglobin was encountered one day after the injection, followed by a rapid return to normal. On the same day a reddish purple pigment was present in large amounts in the urine.

Experiment 3. A fox terrier, weighing 10 kilos.

Day	*Treatment*	*Plasma Phosphatase*	*Hunter's test for Bilirubin in Urine*	*Clinical Condition*
0	50 c.c. 1% sodium oleate intravenously	8.2	Negative	Quite well.
1	"	8.5	Strongly positive	" "
2	"	10.6	Positive	" "
3	"	12.6	Positive	" "
5	"	10.7		" "
6	"	11.3		Left fore-limb swollen at site of injection.
7	"	12.2		Left fore-limb swollen at site of injection.
9	Injection stopped	9.4	Positive	Refusing all but a little food.
10		8.7	Positive	Nasal discharge.
12		7.8		" "

From the 1st to the 14th day the hæmoglogin slowly fell from 92 to 56 per cent. Bilirubin was present in the urine whenever examined. The van den Bergh reaction of the serum remained negative throughout.

Other investigators have been aware that bile contains some phosphatase. However, the amounts were considered to be small. Difficulties were encountered by these other workers in applying their methods to the estimation of bile phosphatase, whereas the method used by us is remarkably suitable for work with bile. Bile taken from animals, either at operation, at autopsy, or from a biliary fistula, was examined. The results for bile given above indicate that gall-bladder bile contains large amounts of phosphatase after obstruction to the common bile duct (av. 635 units). It was at first thought, therefore, that small amounts of phosphatase were excreted daily by the liver and that during obstruction the enzyme became concentrated in the bile. However, using bile-fistula animals with no obstruction, we found that as much as 5,000 units per 100 c.c. were being excreted daily for several days, the total amount of bile varying from about 50 to 125 c.c. Thus the present indication is that large amounts of phosphatase are excreted daily into the bile and that the excretion diminishes or ceases when obstruction to the bile ducts is produced, and, since the producing mechanism has presumably not been damaged, the amount of enzyme in the serum rises.

In view of the enormous amount of phosphatase excreted in bile it seemed advisable to examine the fæces. In normal dog fæces even much greater amounts of enzyme were found present than in bile. After obstruction to the common bile duct, no marked change in the phosphatase content of the stools was observed. The fæces of only two animals have been tested during obstruction to the flow of bile, and thus we are not prepared to make further comment on this finding at the present time. It may be pointed out that a high content of phosphatase exists in and is presumably elaborated by the intestinal mucosa, and that various bacteria manufacture the enzyme. The fæces phosphatase may come in part from both these sources. The urines of obstructed animals were tested for phosphatase, but we were unsuccessful in demonstrating its presence.

The increased production and excretion of bilirubin caused by experimental hæmolysis is unaccompanied by any change in serum phosphatase activity comparable to that found in the obstructed cases. There is, it is true, in each of the three cases evidence of a slight increase in the value, but we do not look upon this as significant without further corroboration. Such a change might represent mild liver damage brought about concomitantly with the hæmolysis, especially in experiment 3 when sodium oleate was administered. In a future paper it will be shown that toxic damage to the liver cells gives rise to definite increases in serum phosphatase.

PART II: CLINICAL OBSTRUCTIVE JAUNDICE

The opportunity to follow several proven cases of obstructive jaundice in the wards of the Toronto General Hospital has been utilized to determine the value of serum phosphatase before, during, and after the occurrence of obstruction of the common bile duct. Brief abstracts of their clinical histories follow.

CASE 1

W.A., aged 60, was admitted to the surgical wards on January 29, 1934, complaining of loss of weight (50 pounds), loss of strength, pain in the left side, diarrhœa, jaundice of three months' duration and slowly increasing intensity. The stools were clay-coloured. Examination showed intense jaundice (van den Bergh 30 units); liver enlarged to umbilicus, but not tender; numerous ecchymoses; no masses were felt in the abdomen. A pre-operative diagnosis of carcinoma of the head of the pancreas was confirmed at operation on January 30, 1934. The gall bladder was anastomosed to the stomach. This was followed by rapid subsidence of the jaundice and hæmorrhages. The first phosphatase estimation was made when he was transferred to the surgical wards January 29, 1934, and gave the high value of 162 units. Following operative relief of the obstruction the serum phosphatase fell rapidly. Its fall was paralleled by a similar fall in the intensity of the van den Bergh reaction and coincided with the subsidence of the jaundice (see Chart III).

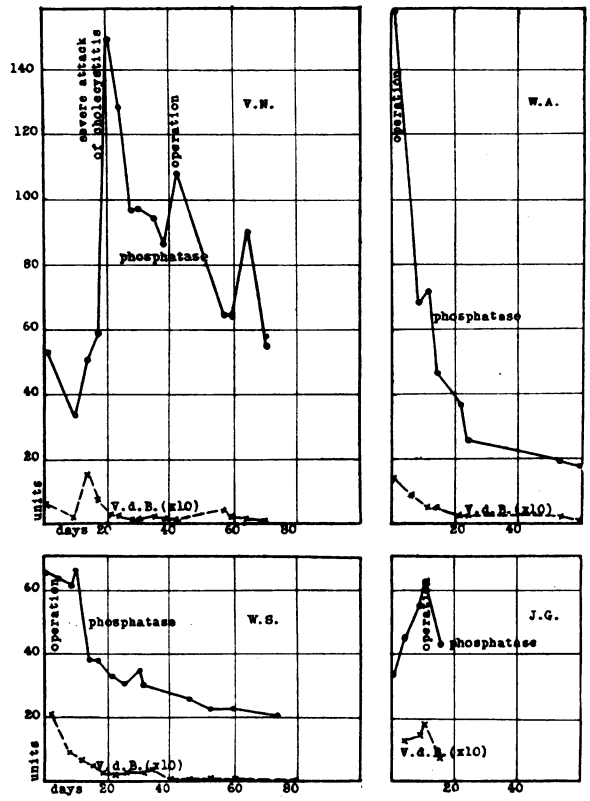

CHART III.

CASE 2

W.S., aged 46 years, was admitted on January 25, 1934, with the following history: upper abdominal pain (one brief but severe attack three months before admission); jaundice of three months' duration increasing in intensity; intense itching of the skin, clay-coloured stools, and loss of 45 pounds in weight. Examination revealed intense jaundice (van den Bergh 30 units), great enlargement of the liver (below umbilicus), marked pruritus. Operation on January 30, 1934, revealed a small hard mass in the head of the pancreas, great dilatation of the biliary tract and of the gall bladder. No stones were felt. It was not possible to determine whether the pancreatic mass was carcinoma or chronic pancreatitis; a cholecystogastrostomy was performed. The intense itching disappeared in twenty-four hours. The jaundice diminished slowly but steadily. By March 30th he was greatly improved; jaundice had almost completely disappeared; he had gained 25 pounds in weight, and the liver had diminished in size. The first serum phosphatase estimation was made on January 26, 1934—65 units. Following operation the figure fell slowly for a week and then more rapidly. There was a coincident, but more rapid, fall in the van den Bergh reaction. During the same period the jaundice faded (see Chart III).

CASE 3

V.N., aged 44 years, was admitted on February 23, 1934, with a history of recurring attacks of biliary colic. An attack in September, 1933, was accompanied by jaundice. Her present attack was of five days' duration, and jaundice had been present for three days. Examination showed moderate jaundice (van den Bergh 5.8 units); no fever; the liver, enlarged but not tender; the gall bladder, enlarged and tender. The spleen was considerably enlarged. Though the history and physical findings were those of recurring attacks of cholecystitis and common duct obstruction, the enlarged spleen introduced the possibility of Banti's syndrome. She had been born in the Balkans and presumably exposed to malaria. Her condition was carefully investigated during a period of six weeks. In this time she had a severe attack of cholecystitis with great enlargement of the gall bladder, fever and leucocytosis. Operation on April 10, 1934, revealed a large gall bladder surrounded by recent adhesions, filled with stones, and stones in the common duct. The gall bladder was removed and the common duct drained with a T tube. The serum phosphatase on admission was 54 units. It fluctuated about this level until her severe attack of cholecystitis during the period of observation, and then rose sharply to 148 units. At the time of operation it was 108, and by May 7th it had fallen to 55.

CASE 4

J.G., aged 59 years, was admitted on February 14, 1934, with a large carcinoma of the stomach and nodules in the liver. On February 19, he became jaundiced and this condition rapidly deepened. Operation performed on March 1, 1934, revealed a large carcinomatous mass in the head of the pancreas obstructing the common bile duct. There were numerous secondary nodules in the liver. The gall bladder was drained. He died on March 5, 1934. Serum phosphatase on the day jaundice was first noted was 36.7 units and this rose to 61 units as the jaundice deepened. It fell after operation to 43 units (see Chart III).

CASE 5

J.C., aged 54 years, was admitted on March 8, 1934, for recurring attacks of pain in region of gall bladder; a severe attack in October, 1933, since which time there had been more or less grumbling pain. Two weeks prior to admission the pain had become more severe, and on March 5th she developed intense pain, with vomiting. Examination on admission revealed slight jaundice; temperature 101.4° F.; white blood cells 12,800; the abdomen was distended, tender and rigid in the region of the gall bladder; liver three fingers' breadth below the costal margin; gall bladder palpable and tender. The diagnosis was made of acute cholecystitis with stones, and partial obstruction of common duct, either by stone or œdema. She was treated conservatively with some improvement. Her condition fluctuated from time to time without ever completely clearing up. Fever was constantly present. April 11th her condition was worse and operation was undertaken. This revealed an inflamed gall bladder which had perforated. Stones were present in the gall bladder cystic duct, and several were impacted in the common duct. Bile peritonitis was present. She died on April 15, 1934, and autopsy revealed, in addition to the operative findings, an extensive suppurative cholangitis with an abscess in the left lobe of the liver. During the course of her obstructive jaundice the phosphatase and van den Bergh reaction were constantly high (serum phosphatase 60 to 182 units; van den Bergh 9 to 28 units) (see protocol).

PROTOCOL—CASE OF J.C.

Date	*Day*	*Serum phosphatase*	*van den Bergh*
March 9	0	17	9
" 14	5	59	21
" 19	10	81	9
" 21	12	182	21
" 26	17	101	21
April 5	27	87	25
" 12	34	106	28

These five patients are proved examples of obstruction to the common bile duct in which the serum phosphatase was followed by numerous estimations either during the development

of the jaundice (as in the case of J.G.) or during the subsidence of the jaundice (as in the other four cases). In all the obstructive jaundice was accompanied by a great rise in the serum phosphatase, which roughly paralleled the intensity of the jaundice. To date, these represent all of the cases of obstructive jaundice we have been able to follow continuously, and at the same time demonstrate the nature of the jaundice. A number of isolated observations on proved jaundice cases confirm the belief that obstructive jaundice is accompanied by a marked rise in the serum phosphatase.

No cases of frank hæmolytic jaundice were available in the Toronto hospitals at the time this part of the study was undertaken. We were fortunate, however, in obtaining blood from two cases of latent hæmolytic jaundice. A single estimation on the blood of each of these cases yielded the following values.

Name	*Age*	*Serum phosphatase per 100 c.c.*	*van den Bergh*
B. (M.)	27	7.2 units	2 units (indirect)
L.		7.8 units	1.7 units (indirect)

The normal phosphatase value for adults by the method employed lies within the range 3 to 13 units, so that no appreciable rise has occurred in these two cases. This fact is in agreement with the observations reported on dogs.

SUMMARY

1. Obstruction to the common bile duct has been produced in 19 dogs and the serum phosphatase activity and bilirubin content determined daily.

2. The serum phosphatase in every case rose to progressively higher values each day following the obstruction, reaching thirty to one hundred times the initial amount after six days.

3. In two cases the obstruction was later relieved and the animals allowed to recover. The recovery period was accompanied by a fall in the serum phosphatase until the initial value had been reached.

4. Gall bladder bile contains large amounts of phosphatase, while bile from a fistula has been noted to contain even greater amounts.

5. Fæces from the dogs before and after obstruction possessed very great phosphatase activity.

6. Five hospital cases of proved obstructive jaundice were followed daily in regard to the serum phosphatase activity. During the development of jaundice the serum phosphatase increased from day to day, while during the subsidence of the jaundice the value diminished, although somewhat more irregularly. When the patient recovered it reached very nearly the range given by normal individuals.

7. The height to which the phosphatase activity rose in the human cases was considerably less than that attained in dogs.

8. Three cases of experimentally produced latent hæmolytic jaundice in dogs and two cases of latent hæmolytic jaundice in humans were investigated. No appreciable rise was observed in serum phosphatase.

We wish to express our thanks to Dr. F. G. Banting for his advice and constructive criticism while this work was being carried out.

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ALLERGIC REACTION TO DINITROPHENOL.—Gerald M. Frumess stresses the fact that alpha-dinitrophenol produces skin eruptions in a large percentage (at least 7 per cent) of those to whom the drug is administered. These eruptions occur when non-toxic amounts of the drug are used. Some of these eruptions are definitely allergic, specific antibodies being produced in some individuals by the ingestion of the drug. In at least one case, these antibodies were demonstrable by the Prausnitz-Küstner passive transfer test. It is theoretically dangerous to resume the use of the drug after a skin reaction from its ingestion has subsided.—*J. Am. M. Ass.*, 1934, **102**: 1219.

Man is a dupeable animal. Quacks in medicine, quacks in religion, quacks in politics, know this and act upon this knowledge. The credulity of man is unfortunately too strong to resist the impudent assertions of the quack. Credulity has been justly defined as belief without reason. It diffuses itself through the minds of all classes, by which the rank and dignity of science are degraded, and its valuable labours confounded with the vain pretensions of empiricism.—Southey.