LIVER FUNCTION AS INFLUENCED BY THE DUCTLESS GLANDS.*

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In recent publications1,2 we have shown that valuable information concerning liver function and liver disease can be obtained by the intravenous injection of a solution of phenoltetrachlorphthalein. The drug is excreted through the bile by the activity of the hepatic epithelium and may be extracted from the feces and estimated with considerable accuracy. The phthalein excretion of normal dogs is quite constant, as is shown by the tables given below. The normal base line curve of phthalein excretion for an individual dog under uniform conditions is still more constant.

We have reported elsewhere3 experiments that indicate that injury of the liver by means of specific poisons such as chloroform, phosphorus, and hydrazin causes a fall in the phthalein excreted in the feces. The fall in the phthalein curve is proportional to the amount of liver injury and in acute fatal poisoning may reach zero. Given a definite liver injury it is found that a definite amount of the phenoltetrachlorphthalein will appear in the urine, which is free from the drug under normal conditions. Moreover, injury of the liver by actual cautery will cause a definite drop in the phthalein curve, depending upon the amount of injury and inflammatory reaction.

Under various conditions in which the functional capacity of the liver cell is interfered with, the output of phthalein falls below

* Received for publication, June 23, 1914.
3 Whipple, Peightal, and Clark, loc. cit.
normal, depending upon the extent of the derangement. For example, in passive congestion of the liver, either experimental or clinical, there will be periods of decreased phthalein output corresponding to the intensity of the stasis or breaks in cardiac activity. The Eck fistula (dog 12-2) provides evidence in the same direction. When the portal blood is shunted around the liver by this means we may not at first get a decrease in liver function, but with the development of liver atrophy and fatty degeneration, a distinct and sometimes a marked depression in the excretion curve will be noted.

It is clear that injury or any definite functional derangement of the liver is associated with a definite change in its excretion of phenoltetrachlorphthalein. Passive congestion and Eck fistula are of especial importance in connection with the experiments given below for they show that a change in nourishment of the liver cell leading to atrophy and perhaps fatty degeneration can be recognized by this functional test.

It is important to recall that shortly after repair of an injury by chloroform or phosphorus the liver may give evidence of hyperactivity and excrete more phthalein than under normal conditions. The same may occur after a small dose of a liver poison, which we may assume acts as an irritant to the liver cells. Young dogs and pups will, as a rule, show a slightly higher excretion than adult or old dogs.

All the evidence suggests strongly that a decrease in functional capacity of the liver is paralleled by a lowered phthalein output. May we not assume that a decrease in the phthalein output means a decrease in the functional capacity of the liver? We have studied the liver function in the pathological states brought about by removal of the various ductless glands. The liver function, as indicated by the phthalein excretion is definitely impaired when the body is suffering from pancreatic or adrenal insufficiency. The liver may show no histological evidence of this change in function, but a constant fall in the phthalein curve occurs which may return to normal if, in the case of partial adrenal extirpation, the remaining fragment undergoes an hypertrophy sufficient for the needs of the body.

After complete pancreatic extirpation there is a steady fall in
phthalein excretion which may fall as low as one third or one fifth normal. This fact speaks strongly for the idea that pancreatic activity is essential to proper liver function, which is the case with the adrenals; and it contradicts the idea that the pancreas tends to inhibit liver activity, while suggesting that the pancreas may be looked upon as having an accelerating influence on the liver. This may have some relation to recently proposed theories of diabetes.

Hypophysis extirpation may cause fluctuations in the excretion curve, — an initial fall and secondary rise. A definite fall occurs shortly before death and is noted before the appearance of subnormal temperatures which may supervene a day or so before death.

Thyroid extirpation causes no change in the excretion curve unless the parathyroids are interfered with. Perhaps in experiments of longer duration we may be able to demonstrate some change in liver function.

Parathyroid extirpation and tetany cause no fall in the phthalein excretion curve, but rather a slight rise above normal. In the last day of fatal tetany the liver function will be normal or slightly above normal, which is remarkable considering the prostration that is present at this time. Also given a falling curve due to pancreas extirpation one can produce a rise in output by parathyroidectomy and tetany, a fact which speaks in favor of the supposition that the parathyroid glands exert directly or indirectly inhibitory action upon the liver.

When we recall the amount of injury that must be done to the liver to cause a definite fall in the phthalein excretion curve, it is obvious what marked influence the adrenals and especially the pancreas must exert upon the liver. It is more than possible that this derangement in liver function may be an important factor in the symptom complex of ductless gland insufficiency.

METHOD.

The method employed has been described in detail in an earlier publication,4 but some points will be reviewed here. The tetrachlorphthalein solution used for the injections was made up in 100 to 200 c.c. lots in 2.5 per cent. strength, as it was found that such a solution does not precipitate within a couple of weeks if kept in a dark place. The method of preparation has been previously

4 Whipple, Peightal, and Clark, loc. cit.
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described. This solution for injection was standardized with great care against a known solution containing 10 mg. of tetrachlorphthalein to the liter. This insures the injection of 100 or 200 mg. at each injection and makes for constant excretion. The experiments were done in groups using from three to six dogs of which one normal animal served as a control. The solution was injected using a glass syringe and needle in the jugular vein. Injections were usually made about noon and on the following morning a purge of magnesium sulphate insured complete evacuation of the phthalein-containing feces. A second collection must be made to insure complete evacuation of the drug, but will usually be found to contain only a faint trace, provided the purgation has been satisfactory. It is important to clean the feces from the metabolism cages with great care, using a wash bottle and spatula. It is essential to add about 5 c.c. of alkali to the liter wash bottle, as this shows at once any traces of phthalein which otherwise might be overlooked and helps in the solution of the drug.

The method of extracting the phthalein from the feces may be outlined briefly as follows: The collected feces are diluted to one or two liters including 10 c.c. of strong sodium hydroxide (40 per cent.) and shaken in a machine until a uniform fluid is obtained. One tenth of this mixture is diluted to 500 c.c. with water and 4 to 5 c.c. of strong sodium hydroxide. Of this 500 c.c. solution, 100 c.c. are taken for precipitation with the calcium solution,—calcium chloride 20 per cent. To this 100 c.c. are added 5 to 10 c.c. of the calcium solution, followed by 5 c.c. of strong sodium hydrate and water up to 200 c.c. This effects a final dilution of one tenth of the feces to one liter, including the alkali and calcium solutions. This solution may be filtered at once and read against a standard phthalein solution containing 10 mg. per liter. The readings will be directly in per cent. if 100 mg. have been injected.

It will be noted that the phthalein excretion in normal dogs is constantly higher than in our last report. This is due to a more accurate method for standardizing the injection solution which in these experiments contained 100 mg. in each 5 c.c. In our earlier experiments the solutions were of constant strength, but the amount of phthalein was overestimated giving a lower excretion in the feces. All these dogs have been injected with the correctly standardized phthalein so that no fluctuations in the curve are attributable to this factor except some of the earlier observations in the first experiment (Eck fistula, dog 12-2) which were made during the year 1912-1913.

EXPERIMENTAL OBSERVATIONS.

In all operations the dogs were given morphia before operation and ether anesthesia during the operation, which in no instance lasted more than one hour. The usual aseptic surgical technique was employed and great care exercised in the postoperative treatment to insure a rapid return to normal if possible.

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ECK FISTULA OF EIGHTEEN MONTHS' DURATION.

Dog 12-2.—Black and tan mongrel, female.

Feb. 1, 1913. Ether anesthesia. Eck fistula produced as usual with ligature of portal vein at hilum of liver.

Feb. 3. Dog in good condition; weight 13½ pounds. The dog presented the usual picture seen in successful Eck fistula experiments, having occasional digestive upsets, but in general maintaining normal weight with gradual increase in strength and general activity. Phthalein excretion is shown in the accompanying table, and in part has been recorded elsewhere in an earlier report. The condition has been practically unchanged during the year succeeding the last observation. There were slight fluctuations in the weight curve, but the condition during this time has been uniformly excellent.

June 10, 1914, 12 M. Dog in excellent condition. Weight 16 pounds. Phthalein 0.1 gm. intravenously.

June 11. Urine contains a good deal of phthalein as usual. No feces.

June 12. Abundant fluid feces. Phthalein excretion 45 per cent. 4 P.M. Ether anesthesia and bleeding from femoral. Weight 15½ pounds.

Autopsy.—Performed at once. Thorax, heart, lungs, and spleen are all quite normal. Pancreas, kidneys, adrenals, thyroid, and parathyroid all normal. Stomach and intestinal tract normal. Eck fistula shows clean margins and an opening about 3 by 4 mm. The portal vein is completely obliterated at the site of the ligature, and there are no collaterals above this ligature. There are large collaterals in the neighborhood of the kidney, forming easy collateral circulation between the portal and lumbar veins. Liver after bleeding and removal of gall bladder weighs 189 gm. This is to be compared with the normal dog 13-45, weight 15½ pounds, killed at the same time under the same conditions. Normal liver without gall bladder weighed 232 gm. The Eck fistula liver shows regular lobulation and definite evidence of fatty change. The bile passages are everywhere normal.

Microscopical Examination.—Liver shows a remarkable grade of fatty degeneration involving about all of the central two thirds of each lobule. The

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm</th>
<th>Phthalein excreted, per cent.</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
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<tbody>
<tr>
<td>March 1913</td>
<td></td>
<td></td>
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<td>0.10</td>
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<tr>
<td>Apr. 8</td>
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<tr>
<td>May 26</td>
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<td>0.10</td>
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<td>July 10</td>
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<td>0.10</td>
<td>0.10</td>
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<tr>
<td>Oct. 27</td>
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<td>0.10</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>June 10</td>
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<td>0.10</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>June 12</td>
<td>0.10</td>
<td>0.10</td>
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</table>
Liver Function as Influenced by Ductless Glands.

Liver cells contain large droplets of neutral fat and the nuclei stain sharply. There are no phagocytes nor any evidence of cell necrosis. The marginal third of each lobule is normal. Bile passages and canaliculi are normal. Other organs negative.

The preceding experiment (dog 12–2, Eck fistula) shows several points of interest. A dog can live in health for a year and a half with an Eck fistula. This dog had a liver smaller than a healthy normal dog of the same weight, and the Eck fistula liver was supplied by about one third the normal amount of blood, yet excreted about two thirds the normal amount of phthalein. This is a simple example of atrophy and slight fatty degeneration due to decreased or changed blood supply. The dog showed no clinical evidence of liver insufficiency and appeared to be in perfect health, yet this physiological test shows a uniformly subnormal output of phthalein. It must be kept in mind that the mere presence of an Eck fistula does not effect a drop in the phthalein curve which may remain normal for some time after the operation, but the drop in the curve follows when the liver atrophy develops. This comes out in experiments previously reported. Another point of interest in this dog and others of similar type is that pregnancy will not develop. The dogs appear normal in all respects and may go in heat frequently and take the male repeatedly, but no pregnancy follows.

After the first few weeks when the animals are given plenty of bones and milk with no meat, these animals may be kept indefinitely on the usual mixed diet of cooked meat and bread cakes. They do not stand confinement in cages as well as normal animals, and exercise is needful. These observations bear on the question of operation in liver disease in man, and it seems that a suitable technique for the operation is all that is required before applying the Eck fistula operation successfully to human cases of cirrhosis in which the symptoms of portal obstruction are the dominant ones.

ADRENAL EXTIRPATION.

Dog 13-56.—Young male pup; weight 14 pounds.
Jan. 23, 1 p.m. Phthalein 0.1 gm. intravenously.
Jan. 27, 11 A.M. Ether anesthesia. Right adrenal removed completely. Left

*Whipple, Peightal, and Clark, loc. cit.
adrenal cut across, and the lower pole including about one third of the gland parenchyma left in situ. The upper two thirds were removed.

Jan. 28. Dog is quite weak, pulse fair, wound dry; weight 12½ pounds. Phthalein 0.1 gm. intravenously.

Jan. 29. Diarrhea marked. Phthalein excretion 44 per cent.

Feb. 3 and 4. Dog improving and quite lively.

Feb. 7. 3 P.M. Dog appears normal; weight 13½ pounds. Phthalein 0.1 gm. intravenously.

Feb. 8. Dog has diarrhea without any purgation. Phthalein excretion 52 per cent.

Feb. 10. Diarrhea continues.

Feb. 21, 12 M. Dog in good condition. Weight 13½ pounds. Phthalein 0.1 gm. intravenously.


Feb. 25. Soft feces and fluid stools persisted.

Apr. 8, 1 P.M. Dog in good condition; weight 16 pounds. Phthalein 0.1 gm. intravenously.

Apr. 10. Formed feces. Phthalein excretion 70 per cent.

May 1, 3 P.M. Dog is normal. Operation under ether anesthesia. Left adrenal shows very definite hypertrophy. The fragment is more than double its former size. Fragment cut transversely, the lower half removed and the upper half left intact.

Pancreas.—Both upper and lower arm of gland extirpated, but the parenchyma adherent to the duodenum was left undisturbed. Probably three fifths of pancreatic parenchyma were removed and the blood supply to the remainder left undisturbed.

May 2. Dog in good condition.

May 3, 12 M. Dog appears normal. Wound is dry. Weight 16 pounds. Phthalein 0.1 gm. intravenously.

May 4. No feces. Urine contains no sugar. 3 P.M. Fluid feces. Phthalein excretion 52 per cent.

May 6. Dog vomits occasionally, but has no diarrhea; weight 16½ pounds. Phthalein 0.1 gm. intravenously.

May 7. Abundant fluid feces. Phthalein excretion 51 per cent.

May 17. Dog appears quite sick and suffers from dyspnea. Temperature 35° C.

May 18. Found dead.

Autopsy.—Performed at once. The striking thing is the general anasarca. There is marked subcutaneous edema and accumulation of clear yellow fluid, about 300 c.c. in the peritoneal cavity, and almost the same amount in the thorax. The pericardial cavity is clear. Heart contains no clots. It shows dilatation and hypertrophy of the right side. Lungs show emphysema and small pulmonary thrombi. Spleen, kidneys, and intestinal tract normal. Liver is rather large, and lobules are conspicuous, due to edema. Pancreatic remnant looks normal. There are adhesions about the sites of operation. Adrenal fragment has increased in size to almost that found at the second operation. Cortex shows very marked hypertrophy. The cause of the general anasarca is quite obscure.
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Microscopical Examination.—Adrenal gland removed at second operation shows the hypertrophy and increase in fat described by Crowe\(^7\) in a recent publication. The adrenal fragment examined at autopsy shows the same picture together with a certain amount of necrosis, probably dependent upon interference with the blood supply. The parenchyma cells in places look much degenerated. There was undoubtedly a good deal of interference with the adrenal parenchyma and probably a marked insufficiency. The lungs show small patches of organizing pneumonia and induration. Pancreas and kidney are normal. Liver shows central congestion with slight atrophy and fatty degeneration. Some sections show definite central necrosis with thrombosis of adjacent capillaries.

\[\text{Text-FIG. I. Dog 13-56. Adrenal extirpation.}\]

The preceding experiment (dog 13-56, text-figure 1) shows clearly the depression of liver function depending upon adrenal insufficiency. With hypertrophy of the remaining adrenal fragment

the liver function returns to normal, as would be expected. The second operation in which one half of the remaining adrenal fragment was removed was followed by a similar drop in phthalein excretion. At this second operation a portion of the pancreas was removed, but this procedure by itself would have no effect upon liver function. The cause of the anasarca is obscure, but may have been due in part to the changes in the pulmonary circulation causing hypertrophy of the right heart and more or less venous stasis.

The following experiment (dog 13-94) shows that a small adrenal fragment is more efficient in maintaining normal liver function when it is in connection with the sympathetic system by means of its nerves. Furthermore, a simple section of the large nerves going to this upper pole and no interference with the blood supply caused a depression in the phthalein curve when the first operation and removal of three fourths of the gland parenchyma had given no evidence of insufficiency.

ADRENAL EXTERNAL. NERVE SECTION.

Dog 13-94.—Small fox-terrier, male; weight 13 pounds.
Mar. 20, 12 M. Phthalein 0.1 gm. intravenously.
Mar. 28, 11 A.M. Operation under ether anesthesia. Right adrenal removed completely. Left adrenal cut across leaving the upper two fifths of the gland intact, the lower three fifths being removed.
Mar. 29, 11 A.M. Dog in fair condition. Phthalein 0.1 gm. intravenously.
Mar. 30 and 31. Abundant feces. Total phthalein excretion 71 per cent.
Apr. 8. Dog very active; weight 13 pounds. Phthalein 0.1 gm. intravenously.
Apr. 9. Abundant feces. Phthalein excretion 74 per cent.
Apr. 25, 12 M. Operation under ether anesthesia. Left adrenal exposed with very little bleeding and no interference with the blood supply. The large nerve bundle to the upper pole was isolated and cut. The adrenal was handled very little and only this large nerve disturbed. Duration of operation about thirty minutes, which was about half the time required for the first operation, and there was much less handling of viscera during this second operation.
Apr. 26, 11 A.M. Dog is lively and appears normal in all respects. Weight 13½ pounds. Phthalein 0.1 gm. intravenously.
Apr. 27 and 28. Abundant feces. Total phthalein excretion 59 per cent.
May 3, 12 M. Phthalein 0.1 gm. intravenously. Weight 13½ pounds.
May 4. Abundant feces. Phthalein excretion 72 per cent.
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Autopsy.—Performed at once. Thorax, heart, and lungs are normal. Thymus is large, milky, and soft. Testicles are of adult type. Lymph glands are not particularly enlarged, nor are the lymph follicles conspicuous in the intestine and spleen. The liver is quite normal. Pancreas, kidney, thyroid, and parathyroid are normal. Adrenal fragment has increased considerably in size. On section the cortex and medulla appear to be both involved in this hypertrophy.

Microscopical Examination.—Liver is normal. Thymus and lymphatic tissue show considerable hyperplasia. Adrenal shows the usual hyperplasia, especially of the cortex. Other organs normal.

DOG 13-94.

Adrenal Extirpation (Partial).

<table>
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<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion in per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
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<td>Mar. 28</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Good recovery.</td>
</tr>
<tr>
<td>Mar. 29</td>
<td>0.10</td>
<td>71</td>
<td>13</td>
<td>Sympathetic to adrenal fragment cut.</td>
</tr>
<tr>
<td>Apr. 8</td>
<td>0.10</td>
<td>74</td>
<td>13</td>
<td>Good recovery.</td>
</tr>
<tr>
<td>Apr. 25</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Autopsy.</td>
</tr>
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<td>Apr. 26</td>
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<td>59</td>
<td>13.3</td>
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<tr>
<td>May 3</td>
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<td>72</td>
<td>13.5</td>
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<td>June 11</td>
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ADRENAL EXTRIPATION.

Dog A-5.—Black mongrel pup, female.
Dec. 8, 1913. Ether anesthesia and operation. Right adrenal removed completely. Left adrenal in large part removed leaving small fragment, estimated at about one fifth of the gland.
Dec. 9, 12 M. Dog in fair condition; weight 10 pounds. Phthalein 0.09 gm. intravenously.
Dec. 10. Soft feces. Phthalein excretion 17 per cent.
Dec. 16, 1 P.M. Dog greatly improved and quite active, in spite of some loss of weight (9 pounds). Phthalein 0.1 gm. intravenously.

Autopsy.—Gastritis, which may have been associated with purgation. Other organs normal. Adrenal fragment had undergone the usual hypertrophy. Liver and bile passages are quite normal.

ADRENAL EXTRIPATION.

Dog 13-107.—Strong mongrel pup, female; weight 19½ pounds.
Apr. 8, 1 P.M. Phthalein 0.2 gm. intravenously.
Apr. 9. Abundant feces. Phthalein excretion 74 per cent.
Apr. 20. Ether anesthesia and operation. Right adrenal extirpated with the

*This operation was performed by Dr. S. J. Crowe.
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exception of a tiny bit of parenchyma at the upper pole, less than one tenth of
the substance of the gland. Blood supply much interfered with. Left adrenal
exirpation leaving the lower one fourth in situ. The blood supply to this frag-
ment was also somewhat interfered with. A good deal of bleeding and handling
of viscera.

Apr. 21. Dog looks well, but pulse is weak and rapid. Diarrhea present.
Temperature 37.5° C.

Apr. 22, 12 M. Dog in fair condition; weight 18 pounds. Temperature
38.2° C. Phthalein 0.2 gm. intravenously.

Apr. 23. Fluid feces. Phthalein excretion 28 per cent. Dog refuses food
and given milk by stomach tube. 3 P.M. Death.

Autopsy.—Performed at once. The peritoneal cavity shows a little peri-
tonitis at the site of operation, consisting mostly of fibrin, and there is no free
fluid. Adrenal fragments show considerable edema and obvious necrosis, but
some parenchyma seems normal. Liver and bile passages are normal. In this
animal the adrenal insufficiency was close to the lowest possible limit.

The two preceding experiments (dogs A-5 and 13-107) show
the remarkable depression of liver function that may be present in
dogs that have almost the minimum necessary adrenal parenchyma.
Both these dogs were close to this line of minimum adrenal tissue
and the last dog might well have survived but for the peritonitis,
which was too much for the animal in this condition of grave ad-
renal insufficiency. Such a drop in liver function to one third nor-
mal is found only in severe hepatic injury by poisons which, like
chloroform, may destroy one half or more of the liver epithelium.
This brings out the paralyzing effect of this adrenal insufficiency
upon the liver cells which are quite normal histologically.

PANCREAS EXTRIPATION.

Dog 13-20.—Mongrel pup, male; weight 11½ pounds.
Apr. 19, 11 A.M. Phthalein 0.1 gm. intravenously.
Apr. 20. Phthalein excretion 59 per cent.
Apr. 23, 12 M. Ether anesthesia and operation. Pancreas completely ex-
tirpated, with clean dissection along the duodenum.
Apr. 24. Pup is active and lively. Weight 10⅔ pounds. Phthalein 0.1 gm.
intravenously.
Apr. 25. Abundant feces. Phthalein excretion 45 per cent.
Apr. 26, 11 A.M. Dog in good condition; weight 10⅓ pounds. Phthalein
0.1 gm. intravenously. This caused no appearance of phthalein in the urine.
Apr. 27. Abundant, soft feces. Phthalein excretion 24 per cent.
Apr. 28. Dog rather drowsy and eats but little.
Apr. 29. Urine contains a large amount of sugar. Dog is losing weight
steadily (9 pounds). 11 A.M. Phthalein 0.1 gm. intravenously. 4 P.M. Urine
contains phthalein 3.5 per cent.
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Apr. 30. Much feces with diarrhea. Phthalein excretion 15 per cent. 3 P.M. Ether anesthesia for twenty minutes. Thyroid and parathyroid glands removed completely.

May 1. Dog refused food and given milk by stomach tube. Feces are fluid and slightly blood tinged. There is definite evidence of tetany, muscular twitchings being in evidence in the neck. 11 A.M. Phthalein 0.1 gm. intravenously.

May 2. Dog is dull and drowsy. Small amount of feces. Phthalein content 22 per cent.

Text-Fig. 2. Dog 13-20. Pancreas extirpation.

May 4, 9 A.M. Dog in poor condition. Temperature 39.5° C. Phthalein 0.1 gm. intravenously.

May 5, 9 A.M. Dog found dead. Some fluid feces in cage containing 17 per cent. phthalein. Urine contained no phthalein but some bile pigment.

Autopsy.—Performed at once. Intestinal contents as well as gall bladder analyzed for phthalein. 4 per cent. found, making a total phthalein output in about twenty hours of 21 per cent., which is about equal to or slightly more than
that of May 2. Lungs show a little bronchopneumonia in lower lobe. Adrenals show a slight atrophy of the cortex. Spleen is rather small, because of interference with the vascular supply at the time of operation on the pancreas. The liver is very fatty, suggesting the picture of phosphorus poisoning.

**Microscopical Examination.**—Liver cells about the portal spaces for a distance of one or two rows appear normal. Those in the center of the lobule contain great numbers of small fat droplets, but the nuclei are well preserved. No cell necrosis and no wandering cells in the capillaries. Adrenal cells contain a great amount of fat, but appear normal (text-figure 2).

**PANCREAS EXTIRPATION.**

*Dog 13-98.*—Yellow adult, male; weight 13½ pounds.

Mar. 19. Ether anesthesia and operation, with complete removal of pancreas, except a few small lobules close to the duodenum.

Mar. 20. Dog appears well. 12 M. Phthalein 0.1 gm. intravenously.

Mar. 21. Urine contains sugar, but no phthalein.

Mar. 22. Abundant feces, phthalein excretion 58 per cent. 12 M. Dog in good condition; weight 12½ pounds. Phthalein 0.1 gm. intravenously.

Mar. 23. Catheterized urine contains no phthalein but considerable sugar.

Mar. 24. Much feces. Total phthalein excretion 50 per cent. 4 P.M. Phthalein 0.1 gm. intravenously.


Mar. 26. Condition unchanged; weight 13 pounds. 3 P.M. Phthalein 0.1 gm. intravenously.

Mar. 27. Abundant feces. Phthalein excretion 46 per cent.

Apr. 15. Dog in poor condition and much emaciated; weight 8½ pounds. 11 A.M. Phthalein 0.1 gm. intravenously. 4 P.M. Urine contains phthalein 1.2 per cent.

Apr. 17. Abundant feces. Phthalein excretion 44 per cent.

Apr. 18. 12 M. Ether anesthesia and operation with complete removal of thyroid and parathyroid glands. Anesthesia twenty minutes.

Apr. 19. 11 A.M. Dog shows signs of tetany; weight 9 pounds. Phthalein 0.1 gm. intravenously.

Apr. 20. Abundant feces. Phthalein output 50 per cent. Typical signs of tetany present.

Apr. 21. 12 M. Condition remains the same; weight 9 pounds. Temperature 37.2° C. Phthalein 0.1 gm. intravenously. 4 P.M. Urine contains phthalein 1.9 per cent.

Apr. 22. Dog in violent tetany. Abundant soapy feces. Phthalein excretion 55 per cent. 4 P.M. Death.

**Autopsy.**—Performed at once. Thorax, heart, and lungs negative. Total absence of subcutaneous and visceral fat. Kidneys normal. Adrenals are rather small, with atrophy of the cortex. Pancreas: there are a few tiny beads of parenchyma close to the duodenum and pylorus. The liver shows no evidence of fat. It looks rather atrophic. The lobules are regular and normal in color.

**Microscopical Examination.**—The adrenal glomerular zone is narrow. Fat
Liver Function as Influenced by Ductless Glands.

is inconspicuous in the cells. The liver shows slight central congestion. The liver cells show distinct atrophy, somewhat similar to that seen with the Eck fistula. Fatty change is not conspicuous. Phagocytic endothelial cells containing pigment are present in the capillaries.

DOG 13-98.

Pancreas Extirpation.

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion in per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mar. 19</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Pancreas extirpation.</td>
</tr>
<tr>
<td>Mar. 20</td>
<td>0.10</td>
<td>58</td>
<td>13.5</td>
<td>Sugar in urine.</td>
</tr>
<tr>
<td>Mar. 22</td>
<td>0.10</td>
<td>56</td>
<td>12.5</td>
<td></td>
</tr>
<tr>
<td>Mar. 23</td>
<td>0.10</td>
<td>65</td>
<td>23.5</td>
<td></td>
</tr>
<tr>
<td>Mar. 24</td>
<td>0.10</td>
<td>46</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Apr. 15</td>
<td>0.10</td>
<td>44</td>
<td>8.5</td>
<td>Dog emaciated and weak.</td>
</tr>
<tr>
<td>Apr. 18</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Thyroid, parathyroid extirpation.</td>
</tr>
<tr>
<td>Apr. 19</td>
<td>0.10</td>
<td>50</td>
<td>9.0</td>
<td>Tetany present.</td>
</tr>
<tr>
<td>Apr. 21</td>
<td>0.10</td>
<td>55</td>
<td>9.0</td>
<td>Tetany marked.</td>
</tr>
<tr>
<td>Apr. 22</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Death.</td>
</tr>
</tbody>
</table>

The two preceding experiments (dogs 13–20 and 13–98) show the same drop in phthalein output after pancreatic extirpation. The fall in the phthalein curve is much more marked when the pancreas removal is complete. Given this fall in phthalein curve due to pancreatic insufficiency, the onset of parathyroid tetany will cause a distinct rise in phthalein excretion. This experiment gives better evidence for the acceleration of liver function during parathyroid tetany than can be gotten in simple cases of tetany which will be discussed later.

Pancreas Extirpation.

Dog 13–104.—Mongrel black and tan, male.
Mar. 25, 4 P.M. Ether anesthesia and operation. Pancreas removed almost completely. A few tiny bits remain close to the duodenum.
Mar. 27. Dog doing well. Urine contains much sugar. Weight 14½ pounds.
Mar. 28. Sugar abundant in urine. Weight 13 pounds. 3 P.M. Phthalein 0.1 gm. intravenously.
Apr. 2. Phthalein 0.1 gm. intravenously.
Apr. 3. Abundant feces. Phthalein output 56 per cent.
Apr. 8, 1 P.M. Dog is weak and emaciated. Weight 9½ pounds. 12 M. Phthalein 0.1 gm. intravenously. 6 P.M. Urine contains phthalein 2 per cent.
Apr. 9. Abundant feces, phthalein excretion 32 per cent.
Apr. 10, 2 P.M. Dog in poor condition and very weak. Ether anesthesia and bleeding.

_Autopsy._—Performed at once. Thorax, heart, and lungs normal. Fat has completely disappeared. All viscera are normal except the pancreas and liver. One tiny nodule of the pancreas close to the duodenum remains. Dimensions 3 by 5 by 1 mm. Liver shows some focal yellow areas and the centers of all lobules are fatty. Elsewhere the parenchyma is brownish and translucent.

_Microscopical Examination._—Liver resembles closely that of dog 13-98. The cells show a little atrophy and slight fatty degeneration. Large pigmented endothelial cells are found in the blood vessels. There are a few polymorphonuclears in the capillaries. No necroses.

**THYROID AND PARATHYROID EXTIRPATION.**

_Dog 13-97._—Mongrel adult, male; weight 15½ pounds.

Jan. 17, 12 M. Ether anesthesia and operation; thyroid and parathyroids removed. At the end of the operation intravenous injection of phthalein 0.1 gm.

Jan. 18. Good recovery.

Jan. 19. Muscular tremors definite. Abundant feces. Phthalein output 35 per cent. 12 M. Muscular tremors are more marked; weight 16¼ pounds. Phthalein 0.1 gm. intravenously. 5 P.M. Convulsive seizures.

Jan. 20 and 21. Tremors present but less violent with milk diet. Total phthalein output 50 per cent.

Jan. 21, 6 P.M. Phthalein 0.1 gm. intravenously.

Jan. 23, 4 P.M. Total phthalein output 45 per cent. Delay in purgation, which was incomplete until Jan. 24, may explain this in part.

Jan. 24, 6 P.M. Phthalein 0.1 gm. intravenously. Weight 15½ pounds. Dog on milk diet.


Jan. 27. Much diarrhea. Total phthalein output 57 per cent. Dog in violent tetany and the slightest touch causes a violent spasmodic reaction. 5 P.M. Death.

_Autopsy._—Performed at once. The autopsy showed nothing abnormal except venous engorgement of organs.

_Microscopical Examination._—Liver normal.

**THYROID AND PARATHYROID EXTIRPATION.**

_Dog 13-13._—Fox-terrier, male; weight 15¾ pounds.

Nov. 13, 12 M. Phthalein 0.08 gm. intravenously.

Nov. 15. Abundant feces. Phthalein output 45 per cent.

Dec. 23, 12 M. Dog in good condition. Ether anesthesia, and operation. Thyroid and parathyroids removed.

Dec. 24. Muscular tremors are present; weight 10½ pounds. 1 P.M. Phthalein 0.1 gm. intravenously.


Dec. 26. Phthalein 0.1 gm. intravenously.

Dec. 27. Muscular tremors very marked. Dog refuses food; weight 11½ pounds. Abundant feces. Phthalein output 68 per cent.
Liver Function as Influenced by Ductless Glands.


Autopsy.—Normal organs throughout.

The two preceding experiments give definite evidence that there is no decrease in liver functional capacity even during the extreme prostration of fatal tetany. The last of the series (dog 13-13) suggests a definite rise above the normal base line. It must be recalled that the feces excretion of phenoltetrachlorphthalein may be very nearly the same whether the drug is injected intravenously or given by stomach tube. This shows how completely the drug is excreted by the normal liver and how little is lost in the transfer from the blood to the bile. One experiment may be cited as illustrative of this point.

Dog 13-125.—Young female pup; weight 14½ pounds.
May 6, 4 p.m. Phthalein 0.1 gm. intravenously.
May 8 and 9. Total phthalein excretion 57 per cent.
May 8, 12 m. Phthalein 0.1 gm. given with milk by stomach tube.
May 9, 12 m. Phthalein excretion 60 per cent.

This experiment shows how narrow the margin may be between the normal phthalein excretion and presumably total excretion into the alimentary tract. Other experiments may show a much greater difference.

One of the experiments given below (dog 13-36) gives evidence of a slight rise in phthalein excretion above normal in periods of mild tetany, as it is clear that this dog suffered at times from parathyroid insufficiency and died in tetany. Better and more convincing evidence that tetany causes an increase in phthalein liver excretion is found in the preceding experiments under pancreatic extirpation (dog 13-20 (text-figure 2) and dog 13-98). With a falling phthalein curve due to pancreatic insufficiency we see a definite rise caused by parathyroid tetany. This rise is noted, although the general condition of the dog is much less favorable than before the removal of the thyroid and parathyroid glands.

From all this data it seems safe to conclude that during tetany there is a tendency towards an increase in phthalein excretion by the liver, indicating an overstimulus and hyperactivity of the liver epithelium.
THYROID EXTRIPATION.

Dog 13-26.—Active adult, male; weight 20½ pounds.
Jan. 26, 3 P.M. Phthalein 0.2 gm. intravenously.
Jan. 27. Abundant feces. Phthalein output 65 per cent.
Mar. 21, 11 A.M. Operation with ether anesthesia. Extrication of both thyroid lobes, one large parathyroid being left at the lower pole on the left side.
Mar. 22. Dog is well; weight 19 pounds. 12 M. Phthalein 0.2 gm. intravenously.
Mar. 23. Dog is normal. No feaces.
Mar. 25. No muscular tremors. Weight 19½ pounds. Appetite good. 12 M. Phthalein 0.2 gm. intravenously.
Apr. 16, 11 A.M. Dog in normal condition; weight 18½ pounds. Phthalein 0.2 gm. intravenously.
Apr. 17. Abundant feces. Phthalein output 66 per cent.
June 8. Dog has been in good condition over the entire period since the operation. Weight 20½ pounds. 12 M. Phthalein 0.2 gm. intravenously.
June 11. Ether anesthesia and bleeding.
Autopsy.—Performed at once. All the organs are perfectly normal. Neck shows no definite thyroid tissue. One large parathyroid is found and appears to be normal. Liver and bile passages normal.
Microscopical Examination.—Liver normal. Two tiny bits of thyroid tissue found in section. The acini contain little colloid and show a cubical type of epithelium. Parathyroid large and normal. Other organs normal.

DOG 13-26.

Thyroid Extirpation.

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan. 26</td>
<td>0.20</td>
<td>65</td>
<td>—</td>
<td>Thyroid extirpation.</td>
</tr>
<tr>
<td>Mar. 21</td>
<td>0.20</td>
<td>63</td>
<td>19.0</td>
<td>No tetany.</td>
</tr>
<tr>
<td>Mar. 22</td>
<td>0.20</td>
<td>63</td>
<td>19.3</td>
<td>No tetany.</td>
</tr>
<tr>
<td>Mar. 25</td>
<td>0.20</td>
<td>66</td>
<td>18.7</td>
<td>No tetany.</td>
</tr>
<tr>
<td>Apr. 16</td>
<td>0.20</td>
<td>67</td>
<td>20.5</td>
<td>Good condition.</td>
</tr>
<tr>
<td>June 8</td>
<td>0.20</td>
<td>—</td>
<td>—</td>
<td>Autopsy</td>
</tr>
</tbody>
</table>

THYROID EXTRIPATION.

Dog 13-36.—Active young female; weight 21 pounds.
Jan. 19, 12 M. Phthalein 0.15 gm. intravenously.
Jan. 23. Chloroform 15 c.c. by stomach tube, causing slight intoxication.
Jan. 24. Dog will eat little food; weight 20½ pounds. 6 P.M. Phthalein 0.2 gm. intravenously.
Liver Function as Influenced by Ductless Glands.

Jan. 28. Condition appears to be normal.
Feb. 7. 11 A.M. Ether anesthesia with removal of thyroid lobes. One parathyroid at left upper pole was left undisturbed.
Feb. 8. Dog appears well, except for slight muscular tremors. 10 A.M. Phthalein 0.2 gm. intravenously.
Feb. 9. Abundant feces. Total phthalein output 70 per cent.
Feb. 15. Dog in good condition; weight 22 pounds. 11 A.M. Phthalein 0.2 gm. intravenously.
Feb. 16. 12 M. Abundant feces. Phthalein excretion 66 per cent.
Mar. 18. Dog in good condition, except for a little mange. Weight 21½ pounds. 4 P.M. Phthalein 0.2 gm. intravenously.
Mar. 19. Abundant feces. Phthalein output 52 per cent.
Apr. 16. 11 A.M. Dog in good condition. Weight 19½ pounds. Phthalein 0.2 gm. intravenously.
May 6, 4 P.M. Dog in good condition. Weight 21½ pounds. Phthalein 0.2 gm. intravenously.
May 7. No feces.
June 1. Dog has developed violent tetany which resists all treatment.
June 2. Death.

Autopsy.—Organs showed advanced postmortem change.

DOG 13-36.

Thyroid and Partial Parathyroid Extirpation.

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan. 20</td>
<td>0.15</td>
<td>57</td>
<td>21.0</td>
<td>Chloroform by stomach (15 c.c.)</td>
</tr>
<tr>
<td>Jan. 23</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Jan. 24</td>
<td>0.20</td>
<td>19</td>
<td>20.7</td>
<td>Thyroid and 3 parathyroids ex-</td>
</tr>
<tr>
<td>Feb. 7</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>_</td>
</tr>
<tr>
<td>Feb. 8</td>
<td>0.20</td>
<td>70</td>
<td>18.5</td>
<td>Slight tetany.</td>
</tr>
<tr>
<td>Feb. 15</td>
<td>0.20</td>
<td>67</td>
<td>22.0</td>
<td>Good condition.</td>
</tr>
<tr>
<td>Mar. 18</td>
<td>0.20</td>
<td>53</td>
<td>21.5</td>
<td></td>
</tr>
<tr>
<td>Apr. 16</td>
<td>0.20</td>
<td>62</td>
<td>19.7</td>
<td>Good condition. No tetany.</td>
</tr>
<tr>
<td>May 6</td>
<td>0.20</td>
<td>53</td>
<td>21.5</td>
<td>Violent tetany. Death.</td>
</tr>
</tbody>
</table>

The two preceding experiments (dogs 13–26 and 13–36) show that thyroid insufficiency has no effect upon the curve of phthalein liver excretion. During periods of tetany due to removal of too much parathyroid tissue the excretion curve may fluctuate. It is possible that longer periods of observation may bring out a change
in hepatic function with complete thyroid removal. Observations on human cases of exophthalmic goitre would be of interest in this connection.

**HYPOPHYSIS EXTRIPATION.**

*Dog 13-79.*—Active male pup; weight 15 pounds.

Feb. 18, 11 A.M. Phthalein 0.1 gm. intravenously.

Feb. 19. Abundant feces. Phthalein excretion 70 per cent.

Mar. 20, 12 M. Dog has practically recovered from distemper; weight 12½ pounds. Phthalein 0.1 gm. intravenously.

Mar. 22. Delay in purgation. Phthalein output 63 per cent.

Apr. 20. Ether anesthesia and operation.* Removal of hypophysis.


Apr. 22. No feces.

Apr. 23. Soft feces. Phthalein output 52 per cent. Edema of head wound is marked. Temperature 39.2° C.

---

**DOG 13-79.**

**Hypophysis Extirpation.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb. 18</td>
<td>0.10</td>
<td>70</td>
<td>15.0</td>
<td>Young pup.</td>
</tr>
<tr>
<td>Mar. 20</td>
<td>0.10</td>
<td>63</td>
<td>12.5</td>
<td>Recovering from distemper.</td>
</tr>
<tr>
<td>Apr. 20</td>
<td>—</td>
<td>—</td>
<td>12.5</td>
<td>Hypophysis extirpation (incomplete).</td>
</tr>
<tr>
<td>Apr. 21</td>
<td>0.10</td>
<td>52</td>
<td>15.5</td>
<td>Slight fever.</td>
</tr>
<tr>
<td>Apr. 24</td>
<td>0.10</td>
<td>57</td>
<td>15.0</td>
<td>Improving.</td>
</tr>
<tr>
<td>Apr. 27</td>
<td>0.10</td>
<td>67</td>
<td>14.7</td>
<td>Good condition.</td>
</tr>
<tr>
<td>Apr. 29</td>
<td>0.10</td>
<td>76</td>
<td>15.0</td>
<td>Good condition.</td>
</tr>
<tr>
<td>May 3</td>
<td>0.11</td>
<td>57</td>
<td>15.0</td>
<td></td>
</tr>
<tr>
<td>May 8</td>
<td>0.10</td>
<td>52</td>
<td>16.5</td>
<td>Good condition.</td>
</tr>
<tr>
<td>June 8</td>
<td>0.10</td>
<td>61</td>
<td>16.5</td>
<td>Autopsy. Remnant of anterior lobe.</td>
</tr>
</tbody>
</table>

Apr. 24, 12 M. Dog appears normal; weight 15 pounds. Phthalein 0.1 gm. intravenously.

Apr. 25. Abundant feces. Phthalein output 57 per cent.

Apr. 27, 12 M. Condition unchanged; weight 14¾ pounds. Phthalein 0.1 gm. intravenously.

Apr. 28. Abundant feces. Phthalein output 67 per cent.

Apr. 29. Condition normal. 11 A.M. Phthalein 0.1 gm. intravenously.

Apr. 30. Abundant feces. Phthalein output 76 per cent.

May 3. Condition the same; weight 15 pounds. 12 M. Phthalein 0.11 gm.

May 4. Abundant feces. Phthalein output 57 per cent.

May 8. Good condition; weight 16½ pounds. 12 M. Phthalein 0.1 gm. intravenously.

*This operation was performed by Dr. A. P. Jones.
Liver Function as Influenced by Ductless Glands.

May 9. Abundant feces. Phthalein output 52 per cent.
June 8, 12 M. Good condition; weight 16½ pounds. Phthalein 0.1 gm. intravenously.
June 11. Ether anesthesia and bleeding.

Autopsy.—Performed at once. Hypophysis absent except a small fragment of anterior lobe at the base of the sella turcica. All other organs appear normal in all respects. The subcutaneous fat is well preserved. Liver and bile passages are normal.

Microscopic Examination.—Liver is normal. Other organs are negative.

Hypophysis Extirpation.

Dog 13-74.—Active young male; weight 18½ pounds.
Feb. 10, 10 A.M. Phthalein 0.1 gm. intravenously.
Feb. 11. Abundant feces. Phthalein output 66 per cent.
Feb. 18. Condition good. 11 A.M. Phthalein 0.1 gm. intravenously.
Feb. 21. Dog improving; weight 20½ pounds. 12 M. Phthalein 0.1 gm. intravenously.
Feb. 25, 11 A.M. Dog in good condition; weight 18½ pounds. Phthalein 0.1 gm. intravenously.
Feb. 28. Convulsions and coma, with almost complete absence of pulse, giving the appearance of death.
Mar. 1, 10 A.M. Dog is quite toxic. Temperature 36.8° C. Weight 17 pounds. Phthalein 0.1 gm. intravenously.
Mar. 2. Dog in semistupor. Temperature 36.7° C. No feces.
Mar. 3, 9,30 A.M. Pulse slow. Temperature 31.3° C. Weight 16 pounds. Thin, blood stained feces. Phthalein excretion 50 per cent. 2 P.M. Death.

DOG 13-74.

Hypophysis Extirpation.

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feb. 10</td>
<td>0.10</td>
<td>66</td>
<td>18.5</td>
<td>Hypophysis extirpated.</td>
</tr>
<tr>
<td>Feb. 17</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Dog improving.</td>
</tr>
<tr>
<td>Feb. 18</td>
<td>0.10</td>
<td>55</td>
<td>18.7</td>
<td>Good condition.</td>
</tr>
<tr>
<td>Feb. 21</td>
<td>0.10</td>
<td>65</td>
<td>20.3</td>
<td>Convulsions and coma.</td>
</tr>
<tr>
<td>Feb. 25</td>
<td>0.10</td>
<td>69</td>
<td>18.5</td>
<td>Subnormal temperature.</td>
</tr>
<tr>
<td>Mar. 1</td>
<td>0.10</td>
<td>50</td>
<td>17.0</td>
<td>Death. Temperature 31.3° C.</td>
</tr>
<tr>
<td>Mar. 3</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

10 This operation was performed by Dr. S. J. Crowe.
Autopsy.—Performed at once. All organs are normal. Liver and bile passages are normal.

Microscopical Examination.—Spleen and lymph glands show slight hyperplasia of lymph follicles. Liver shows acute engorgement of centers of lobules.

HYPOPHYSIS EXTRIPATION.

Dog H-3.—Mongrel female; weight 17 pounds.
Jan. 28. Dog in good condition; weight 17¼ pounds. Phthalein 0.1 gm. intravenously.
Feb. 4. Abundant feces. Total phthalein output 57 per cent.
Feb. 7. Dog is drowsy. Temperature 39.8° C. Phthalein 0.1 gm. intravenously. Weight 17½ pounds.
Feb. 10. Dog developed definite signs of distemper.
Feb. 12. Dog is drowsy; weight 15½ pounds. Phthalein 0.1 gm. intravenously.

DOG H-3.

<table>
<thead>
<tr>
<th>Date</th>
<th>Phthalein in gm.</th>
<th>Phthalein excretion per cent. in feces</th>
<th>Weight in pounds</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan. 26</td>
<td>0.10</td>
<td>41</td>
<td>17.3</td>
<td>Hypophysis removal.</td>
</tr>
<tr>
<td>Jan. 28</td>
<td>0.10</td>
<td>62</td>
<td>16.5</td>
<td>Temperature 39.4° C.</td>
</tr>
<tr>
<td>Jan. 31</td>
<td>0.10</td>
<td>57</td>
<td>16.0</td>
<td>Temperature 39.6° C.</td>
</tr>
<tr>
<td>Feb. 3</td>
<td>0.10</td>
<td>47</td>
<td>17.3</td>
<td>Dog very drowsy.</td>
</tr>
<tr>
<td>Feb. 7</td>
<td>0.10</td>
<td>46</td>
<td>15.5</td>
<td>Distemper mild.</td>
</tr>
<tr>
<td>Feb. 12</td>
<td>0.10</td>
<td>40</td>
<td>14.9</td>
<td>Convulsions.</td>
</tr>
<tr>
<td>Feb. 16</td>
<td>0.10</td>
<td>—</td>
<td>—</td>
<td>Death.</td>
</tr>
<tr>
<td>Feb. 17</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

Feb. 16. Dog in convulsions. Temperature 40.9° C. Weight 14 pounds. 3.30 P.M. Phthalein 0.1 gm. intravenously.
Feb. 17. Dog in stupor; pulse weak. 10.30 A.M. Death. Phthalein in cage and from intestinal contents combined, 40 per cent.

Autopsy.—Performed at once. Lungs show ecchymoses and some small patches of bronchopneumonia. Pancreas shows fat necroses with hemorrhage,

This operation was performed by Dr. A. P. Jones.
Liver Function as Influenced by Ductless Glands.

an example of spontaneous hemorrhagic pancreatitis. Kidneys show small gray nodules in the cortex. Intestinal tract negative. Liver is rather pale and fatty.

Microscopical Examination.—Pancreatitis is of considerable age, showing a good deal of scar tissue throughout the gland, although there are some relatively fresh necroses of pancreas parenchyma and fat. The lungs show atelectasis and some bronchopneumonia. The kidneys show accumulations of mononuclear wandering cells in some parts of the cortex. Parenchyma is normal. There is slight atrophy of the liver cells in the center of the lobule. Otherwise normal.

The three preceding experiments are uniform in all respects. Complete removal of the hypophysis will cause little change in the liver function, as indicated by phthalein excretion. There is an initial drop in the phthalein excretion following the operation, and this cannot be attributed to the anesthetic. Possibly the cerebral edema and trauma may account for it. This is followed by a recovery to normal or even a little above normal. Just before the fall in body temperature, which usually precedes death in these dogs, there is a definite impairment of liver function. In the experiment (dog 13-79) in which a bit of the anterior lobe remained, one sees minor fluctuations in the phthalein curve, which may be dependent in part on the hypophysis insufficiency which was undoubtedly present.

SUMMARY.

When phenoltetrachlorphthalein is injected intravenously, it is eliminated from the body in the bile through the activity of the hepatic epithelium. The feces may be collected after purgation and the phthalein extracted and estimated against a standard solution. The estimation of phthalein can be done with accuracy in a suitable colorimeter and the elimination in normal dogs is quite constant.

Given a definite liver injury by means of poisons (chloroform, phosphorus), the amount of phthalein excreted will be diminished and the fall in output will be proportional to the amount of injury. With an acute fatal poisoning the curve may fall to zero.

Under certain conditions of vascular interference the liver phthalein may show a decreased output; in passive congestion of the liver and with the Eck fistula the liver output may fall considerably below normal.

Known disturbances of the liver function due to parenchymatous
injury or vascular disturbances are indicated by a fall in the phthalein excretion curve. Conversely it may be claimed that a drop in phthalein excretion may indicate a decrease in the functional capacity of the liver even if there be no detectable histological changes.

Adrenal insufficiency produced by extirpation of three fourths or more of the gland tissue will be associated with a drop in liver phthalein excretion. With hypertrophy of the adrenal fragment the excretion comes back to normal, but may fall again when more adrenal tissue is removed (text-figure 1).

Pancreatic insufficiency causes a progressive fall in the phthalein excretion indicating a grave lowering of the functional capacity of the liver (text-figure 2). This fact has a direct bearing on the question of diabetes.

Parathyroid insufficiency with tetany causes no decrease in phthalein output, but at times a rise above normal. This comes out best when the phthalein curve is low following pancreas extirpation. Parathyroid tetany may cause hyperactivity on the part of the liver cells.

Thyroid insufficiency produces no change in the uniform curve of phthalein excretion.

Hypophysis insufficiency shows an initial fall in the curve, followed by a return to normal and a final drop in the last few days before death.

These experiments supply evidence to the effect that the liver is very much concerned in the derangement that follows the removal of the ductless glands. Hence it seems probable that this disturbance of the liver function may be an important factor in the general symptom complex of ductless gland insufficiency.

In conclusion we wish to express our appreciation to Dr. S. J. Crowe and Dr. A. P. Jones for assistance rendered in performing some of the operations for gland removal.