THE ABSORPTION OF FAT IN PARTIALLY, AND IN COMPLETELY DEPANCREATIZED DOGS

By CHARLES W. McCLURE, M.D., BETH VINCENT, M.D., and JOSEPH H. PRATT, M.D.

(From the Laboratory of Medicine, Harvard Medical School, Boston.)

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For more than 50 years physiologists have studied the relation of the pancreas to the absorption of fat from the intestine, but the problem still remains unsolved. Many studies have been made on animals to determine whether the pancreatic juice is essential to the absorption of fat, or whether fat absorption is regulated by an internal secretion of the pancreas.

In 1856 Claude Bernard (1) presented detailed evidence for his claim that the pancreatic juice was of great importance in the process of digestion and in the absorption of fat by the intestines. In two dogs out of a series of ten, he found, after injecting melted suet or other substances into the main pancreatic duct, that the stools became very fatty. From the 11th to the 15th day one of these dogs passed large amounts of clear fat. In the 3rd week the feces contained less fat, and when the animals were autopsied it was found that the pancreatic juice was again discharging into the intestine.

The importance of the experiments of Claude Bernard was not appreciated for many years. The physiologists of his time, unable to confirm his observations, opposed the view that the pancreatic secretion was essential to the absorption of fat. Bernard replied to his opponents and showed that their experiments were without value, as they failed to exclude all the pancreatic secretion from the intestine. They remained unconvinced, and their conclusion, as expressed by Colin (2), that the pancreatic juice is not necessary for the digestion and absorption of the normal amount of fat, is the one held today by most investigators.

In 1890 Abelmann (3), working under Minkowski, studied fat absorption in dogs after partial and complete depancreatization. All communication between the pancreatic remnant and intestines was destroyed in the partially depancreatized dogs. These animals absorbed from 25 to 65.8 per cent of fats derived from olive oil, horse flesh, or butter. After the complete removal of the pancreas, the dogs were unable to absorb any of these fats, unless raw pancreas was fed, but they did absorb 28 to 90 per cent of the fat of milk.

The unabsorbed fats, however, were found to be split in the intestines. 35 to 85 per cent of the fat in fresh stools consisted of fatty acids and soaps. The fat in the small intestines contained 30 per cent of fatty acids and that in the colon 76 per cent, 12 hours after feeding neutral fat to a completely depancreatized dog.

The observations that fats were split but not absorbed, unless raw pancreas was added to the food, led Abelmann to conclude that: All fats, with the exception of milk fat, unquestionably require pancreatic juice to be absorbed. He explained fat absorption in the partially depancreatized dog by assuming that the agent effecting absorption is carried to the lumen of the intestine in some way as yet unknown.

Sandmeyer (4) reported finding in the stools of a partially depancreatized dog a greater amount of fat than had been fed. The pancreatic remnant in this dog consisted of a portion of the processus lienalis 3 cm. in length. A persistent glycosuria developed 1 month after the operation. Consecutive metabolism experiments were made throughout a period of 5 months. The percentages of fat lost in the dog's stools varied from 9.1 to 102 per cent in twenty-six experiments; from 104.6 to 111.2 per cent in eight; and from 122.08 to 163.5 per cent in four.

Rosenberg (5) separated the pancreas from the duodenum in a dog with the object of shutting out all the pancreatic secretion from the intestine. For a time the absorption of fat remained normal, but within 2 months a slight reduction occurred. In a series of fifteen experiments the absorption of fat averaged about 85 per cent and only once fell as low as 64 per cent.

In 1906 Lombroso (6), working with dogs, found that a large percentage of fat was absorbed, after all direct communication between the pancreas and duodenum was supposed to have been removed. This was also true, if the pancreas was extirpated except for a small portion which discharged its juice through a permanent fistula in the abdominal wall. When complete depancreatization had been effected, there was either slight or no absorption of fat. He concluded from his findings that the absorption of fat from the intestine is governed by an internal secretion of the pancreas.

Niemann (7) observed good absorption after tying the ducts. In five experiments on one dog 91.2 to 98.7 per cent of the fat in the food was absorbed; in three experiments on a second dog, 85.6 to 98.5 per cent.

Burkhardt (8) concluded from experiments on one dog that fat absorption was not regulated by an internal secretion of the pancreas. He extirpated all of the pancreas except the processus uncinatus. This portion was transplanted under the skin and a cutaneous pancreatic fistula was produced.

In the first metabolism experiment the animal was allowed to lick the fistula and in this way obtained pancreatic secretion. 80 per cent, or 47 gm., of the fat ingested was absorbed. In a second experiment in which licking the fistula was prevented, only 13 per cent, or 8 gm., of the fat was taken up by the intestine.

The findings in this pair of experiments were not verified in two succeeding

pairs of experiments. In these, no appreciable difference occurred in the fat absorption whether the dog did or did not lick the fistula.

Fleckseder (9) made a similar study. The splenic portion and the upper part of the body of the pancreas were extirpated. The remainder of the gland was separated from the duodenum and the main duct and surrounding pancreatic tissue transplanted into the abdominal wall, so that the secretion discharged externally. In only one experiment was there poor absorption (20 per cent) of fat, and later the same animal absorbed a much larger percentage (65 per cent), although it was prevented from obtaining any pancreatic juice. In one metabolism experiment a dog was allowed to lick the fistula, and less fat was absorbed than in the experiments when all pancreatic secretion was withheld. He concluded that the power of absorption of fat by the intestinal mucous membrane is chiefly dependent on an internal secretion of the pancreas.

Lombroso (10) in his later investigation repeated Burkhardt's work and obtained contradictory results. Sometimes more fat was absorbed when the dog was free to lick the pancreatic secretion from the permanent fistula and sometimes less. The absorption of fat in the animals with a subcutaneous graft varied from 48.5 to 80.3 per cent.

Pratt, Lamson, and Marks (11) in experiments on a series of five dogs found that when the pancreas was entirely separated from the duodenum, serious disturbance of fat absorption took place. The percentage of fat taken up by the intestine ranged from 4.8 to 76.6.

Jansen (12) partially extirpated the pancreas of a dog and transplanted the remainder under the skin. In three experiments the animal absorbed 74.9 to 76.4 per cent of the fat ingested. After the removal of the pancreatic graft the fat lost in the feces ranged from 15 to 156 per cent.

Visentini (13) devised a method of determining at autopsy whether or not pancreatic juice had been secreted into the intestine. In five dogs in which he had succeeded in permanently excluding all pancreatic secretion after ligature and resection of the ducts, the fat absorbed ranged from 28.7 to 44.0 per cent. In four dogs in which the corpus pancreatis and processus uncinatus were extirpated, the smallest percentage of fat absorbed was 8.7, and the largest was 25.7.

Much of the experimental work summarized above is open to criticism. There are three chief sources of error.

1. Failure to exclude all the pancreatic juice from the intestine. The difficulty of excluding permanently the pancreatic juice was shown clearly by Claude Bernard. Hess (14) thought that this was chiefly due to the presence of accessory ducts which were left untied. He showed that dogs might have three or four pancreatic ducts. This anomaly is probably much less common than Hess believed. Visentini failed to find more than two in a series of twenty dogs.

In 1909, Pratt, Lamson, and Marks showed that after the pancreatic ducts were tied and cut between double ligatures a sinus quickly formed between the main duct and the lumen of the intestine. Visentini in a careful investigation has demonstrated that after tying and resecting the two excretory ducts the flow of pancreatic juice may frequently be reestablished by the formation of a sinus.

2. Absorption experiments of too short duration. Abelmann's experiments lasted only 1 day and Burkhardt's 2 days. Some of Jansen's experiments were of only 1 and 2 days' duration. It is now generally recognized that trustworthy results cannot be obtained in such a short time.

3. No intervening period between experiments. Lombroso in his earlier studies often began a second experiment the same day that the preceding one was finished. We have found that dogs may pass stools containing the residue from a single meal for a period of 2 to 3 days. Therefore, in spite of the use of carmine to demarcate the stools, the possibility of the collection, during the second experiment, of feces which belonged to the first cannot be denied. In the final results this error would produce too high a figure for fat absorption in the first experiment, while the figure for fat absorption in the second experiment would be too low. This source of error can account for the results obtained by Burkhardt in his first two metabolism experiments, an explanation supported by the fact that in the two experiments the percentages of fat in the feces were nearly the same (23.8 and 26.3 per cent), but the amount of dried stool was nearly four times as great in the second as in the first.

In the animals studied by Pratt, Lamson, and Marks, rapid and progressive atrophy of the pancreas occurred. Pratt and Spooner (15) found that the power to assimilate glucose was rapidly reduced after tying the ducts, a fact which indicated damage to the internal function of the pancreas. Hence it might be asserted that the experiments of Pratt, Lamson, and Marks in which they found poor fat absorption after separating the pancreas from the duodenum did not disprove Lombroso's theory that the absorption of fat is largely due to some internal function of the pancreas. It should be pointed out, however, that Pratt and his coworkers found that the disturbance in fat absorption developed as soon as pancreatic secre-

tion was absent from the intestine while it was several weeks before there was a marked drop in the power to assimilate glucose.

Lombroso and Fleckseder published accounts of experiments which showed that the fat was fairly well absorbed when a subcutaneous pancreatic graft was made which was allowed to secrete externally, although the remainder of the gland had been extirpated. If the ducts secrete freely, then the degeneration of the gland tissue from back pressure does not occur. According to the view held by Pratt, Lamson, and Marks, it would make no difference in the absorption of fat whether the gland underwent degeneration or remained intact, provided the pancreatic juice did not enter the intestine.

It is a difficult procedure to remove all the pancreatic tissue from the wall of the duodenum, but to explain Lombroso's and Fleckseder's results by ascribing them to technical errors on their part would be unfair until their experiments had been repeated and refuted.

After complete extirpation of the pancreas it is held that little, if any fat is absorbed, except milk fat. This conclusion is based on the experiments of Abelmann and Lombroso. If true, it furnishes strong support for the theory that the presence of pancreatic tissue in the body, even when not connected with the intestine, aids in some way the absorption of fat. In all the experiments of Pratt, Lamson, and Marks, in which all pancreatic juice was excluded from the intestine, some absorption of fat took place. In only one experiment was as little as 4.8 per cent absorbed. If no absorption of fat occurs when the pancreas is totally removed, then the experiments published from this laboratory would indicate either that an internal pancreatic function regulated fat absorption, or that the presence of pancreatic tissue in the body in some other way affected the power of the intestinal wall to take up the fat. Abelmann, Rosenberg, Pflüger (16), and Burkhardt held that the pancreatic juice, after it is shut out from the duodenum, continues to form, but is taken up by the blood and carried to the other digestive glands and by them secreted into the intestines. Experiments by Lombroso overthrew this theory.

The first part of the present study deals with the absorption of fat in dogs with subcutaneous transplants of the pancreas which discharge their secretion externally. In the second part the results of experiments on completely depancreatized dogs are presented.

Methods.

Partial Pancreatectomy and the Formation of a Cutaneous Pancreatic Fistula.—Ether anesthesia was used in all the operations. Before etherization a subcutaneous injection of morphine was given. The processus lienalis and corpus pancreatis were completely extirpated, and great care was taken to remove from the duodenal wall every bit of adherent pancreatic tissue. The processus uncinatus of the pancreas was then freed from all its attachments except where the blood vessels entered at the lower end. Leaving these vessels intact, the major portion of the processus uncinatus was transplanted under the skin of the abdominal wall. This was accomplished by first incising the parietal peritoneum about 3 cm. to the right of the median abdominal incision. Then by blunt dissection the muscles were penetrated and a space for the pancreatic remnant was made in the subcutaneous tissue. After incising the skin a hemostat was passed through this space into the abdomen. By means of the hemostat the pancreatic remnant was drawn into the subcutaneous space. The distal end of the remnant was drawn through the incision to a little beyond the level of the skin. It was now fastened by a few fine stitches to the edge of the peritoneum and the skin.

This method was modified in Dog 4. The subcutaneous transplant consisted of the processus uncinatus and that portion of the body of the pancreas containing the main duct. The duct was preserved intact by excising that portion of the duodenal wall which contained the opening of the duct. The blood vessels entering this portion of the intestine were preserved. The portion of the pancreatic remnant containing the duct was made the distal end of the subcutaneous transplant.

Extirpation of the Subcutaneous Transplant.—In a second stage of the experiments the pancreatic remnant was completely extirpated. The abdominal portion of the remnant was first removed. This was done through an opening in the abdomen just to the right of the original median incision. Care was taken to close the opening made in the peritoneum. The remainder of the pancreatic transplant was removed through a skin incision.

Food.—The food consisted of a mixture of six parts of finely chopped,

boiled horse flesh, three parts of cracker dust, two parts of butter, and four parts of water. The butter was melted in boiling water and then intimately mixed with the solid ingredients. Fresh food was prepared for each feeding.

Metabolism Experiments on Dogs with a Subcutaneous Pancreatic Graft.—A period of from 5 to 7 days elapsed after operation before the dogs would take food readily. The experiments were then begun. A meal of milk was given 24 hours previous to the beginning of the experiment. This produced a thin, light colored stool quite different in appearance from the more formed deep yellow or gray stools resulting from the solid food of the metabolism experiment. 20 to 30 gm. of powdered charcoal were intimately mixed with the food of the first meal of each experiment. The resulting stools were very dark gray or black and easily separated from feces derived from other food. Feedings were made once daily over a period of 4 or 5 days. No food was given during the 48 hours succeeding the last meal of an experiment. Then bread and milk mixed with 20 to 30 gm. of charcoal were given. This permitted the collection of all feces belonging to the metabolism experiment. Each animal was kept in the same metabolism cage throughout an experiment except at the time of feeding, when it was transferred to a clean cage.

Metabolism Experiments on Completely Depancreatized Dogs.—These dogs received no food for 24 hours prior to the operation for the removal of the subcutaneous pancreatic remnant. Experiments were begun the next day after this operation. With the exception of this preliminary period of starvation the technique of the experiments was the same as described for partially depancreatized dogs. After the completion of one metabolism experiment a period of not less than 3 days elapsed before beginning another experiment.

Preservation of Specimens for Analysis.—One-fifth of the amount of food mixture eaten at each meal was preserved for analysis. It was mixed with 95 per cent alcohol containing 1 to 2 per cent by volume of hydrochloric acid and dried to constant weight on a water bath at 50–55°C. After drying, the food was finely triturated in a mortar and preserved in sealed jars. The same procedure was carried out with the stools, except that the entire amount of feces was preserved.

Analytical Methods.—Nitrogen was determined by the Kjeldahl method. Specimens were analyzed in duplicate. 0.5 to 1 gm. was used in each determination.

Fat was determined by the Folin-Wentworth (17) method. Specimens were analyzed in duplicate. 2 to 3 gm. of sieved material were used for each analysis. Extraction was carried on for a period of 20 hours. This method was not devised for the determination of the fat content of foodstuffs. However, we found that the same results were obtained by drying the fat, extracted by this method from our food mixture and from milk at 95°C., as when dried to constant weight at 55°C.

Interpretation of Findings.—The factors to be considered in comparing the results of absorption experiments are the percentage and weight of the fat absorbed in relation to the amount ingested and the weight of the animal. In the past, workers in this field have drawn their deductions from the percentages of absorption of the fat ingested. This method of expressing results does not tell the whole story regarding the fat absorbed. A relatively high percentage of absorption may represent but a small amount of actual fat, while a lower percentage may represent a great deal more fat. Not only should the percentage of absorption and the actual amount in grams be considered, but also the quantity of fat ingested. Within certain limits the larger the amount fed to an animal, the greater will be the amount absorbed by the animal. Size is an important factor if the number of grams of fat absorbed is to be compared in different dogs. In animals appearing to be about equally nourished the weight offers a simple and fairly reliable means for comparison of the size.

The metabolism in a completely depancreatized dog with the resulting diabetes is greatly disturbed. Animals after total pancreatectomy usually remain in suitable condition for experimentation but a short time. Because of this, it was necessary to work rapidly and without regard for certain factors which interfered somewhat with the accuracy of the results. Experiments were begun the day following the operation without regard to any possible postoperative effect upon absorption. No attempt was made to make the amounts fed uniform. The appetites of the dogs are often capricious.

In order to make certain of as large a food intake as possible during an experiment, the animals were given at a feeding as much food as would be taken.

ILLUSTRATIVE PROTOCOLS.

Dog 1.—Young adult female.

Dec. 21, 1915. Weight 14 kilos.

Dec. 22. Operation. Partial pancreatectomy. Corpus and processus lienalis, 20 cm. in length and weighing 16.5 gm., extirpated. Processus uncinatus, 9.4 cm. long, transplanted under skin of abdomen and a fistula made.

Dec. 25. Graft is noticed for the first time to be discharging. Dog appears well. No sugar in urine. Fed milk and ground pancreas.

Dec. 29. Dog ate ravenously. Some reddening of skin near opening in graft.

Dec. 30. Fistula closed.

Dec. 31. Dog appears ill. Tissues about graft distended; on opening with knife about 15 cc. of thin sanguineous fluid obtained which digests casein.

Jan. 2, 1916. On incising swollen area about graft 60 cc. of thin sanguineous fluid escaped.

Jan. 3. Weight 12.3 kilos. Fistula discharging thin watery fluid. Urine does not reduce Fehling's solution.

Jan. 5. *Metabolism experiment begun.* 559.8 gm. of food eaten, containing 30 gm. of charcoal.

Jan. 6. Weight 11.9 kilos. 647.5 gm. of food eaten. Large fatty stool. A few grams do not contain charcoal, and these are rejected. Weight of stool admixed with charcoal, 529.5 gm. Stools contain numerous muscle fibers, of which about half retain their striations.

Jan. 7. Weight 11.9 kilos. Dog seems well. Ate 948.6 gm. of food. Stools weigh 436 gm.

Jan. 8. Ate 948 gm. of food.

Jan. 9. Weight 11.6 kilos. No food fed. Fistula was discharging throughout experiment. Stools weigh 676 gm.

Jan. 10. Stools weigh 31 gm. Fed milk, bread, and 60 gm. of charcoal.

Jan. 11. Stool black with charcoal.

Jan. 19. Operation. Subcutaneous transplant removed. It measured 6.6 by 3.1 by 1.9 cm. At the first operation the graft was 9 cm. long, but fully 2 cm. of this was left projecting beyond the skin incision and was lost by desiccation and necrosis. Aside from some increase in firmness the pancreatic tissue of the graft appears normal.

Jan. 20. Dog died of peritonitis.

Metabolism Experiment. Jan. 5 to 8 (4 Days).

Food:	Moist weight	3,104 gm.	Dry weight 1,336 gm.
	Nitrogen:	71.5 "	5.35 per cent.
	Fat:	431.1 "	32.3 " "
Feces:	Moist weight	2,052.5 "	Dry weight 699.5 gm.
	Nitrogen:	39.0 "	5.6 per cent.
	Fat:	313.1 "	44.8 " "
Nitrogen absorbed:		45.37 per cent;	lost 54.63 per cent.
Fat "		27.37 " "	" 72.63 " "

Dog 2.—Adult male. Weight 15.1 kilos.

Feb. 11, 1916. Operation. Pancreas extirpated except processus uncinatus. This measured 5.6 cm. in length and was planted into the anterior abdominal wall and a permanent fistula made. The pancreatic tissue removed weighed 22 gm.

Feb. 12. Dog lively. Graft healthy.

Feb. 13. Fed 300 cc. of milk.

Feb. 14. Weight 13.85 kilos.

Feb. 15. Dog appears sick. Fistula not discharging.

Feb. 16. Dog active. Drank 500 cc. of milk. Fistula secretes a thin fluid admixed with blood. No sugar in urine.

Feb. 17. Weight 13.9 kilos. *First metabolism experiment begun.*

Feb. 18. Graft secreting actively.

Feb. 19. Weight 13.7 kilos. Feces partly formed, partly semisolid. They contain flakes resembling butter in appearance and consistency. Microscopic examination reveals many well preserved muscle fibers and fat globules.

Feb. 20. Dog lively. Fistula secreting freely.

Feb. 21. Weight 13.2 kilos. Stools slate-gray, fatty.

Metabolism Experiment 1. Feb. 17 to 21 (5 Days). Subcutaneous Graft. Extirpation of Remainder of Pancreas.

Food:	Moist weight	1,765 gm.	Dry weight 610 gm.
	Nitrogen:	37.9 "	6.22 per cent.
	Fat:	175.7 "	28.8 " "
Feces:	Moist weight	521.5 "	Dry weight 196 gm.
	Nitrogen:	16.9 "	8.6 per cent.
	Fat:	43.6 "	22.2 " "
Nitrogen absorbed:		21.12 "	43.96 " "
Fat "		132.1 "	75.20 " "

Feb. 22. No food given.

Feb. 24. Weight 12.96 kilos. Operation for removal of subcutaneous graft, which was firmly adherent to the surrounding tissues. Considerable blood lost

in cutting the adhesions, showing a large new blood supply to the graft. The excised pancreatic tissue was of normal appearance; the subcutaneous part was of firmer consistency than the intra-abdominal portion.

Feb. 25. Weight 11.8 kilos. Wound clean. *Second metabolism experiment started.* Ate 438.5 gm.

Feb. 26. Weight 11.2 kilos. Stool yellow, semisolid, and fatty, with rancid odor. Ate 9 gm. of food.

Feb. 27. Weight 11.2 kilos. Ate 91 gm. of food. Stool on microscopic examination found to contain many muscle fibers and much fat in the form of globules.

Feb. 28. Dog found dead in cage.

Autopsy.—No cause for death found. No pancreatic remnants in the abdomen or at the site of the pancreatic transplant in the abdominal wall. Stomach and small intestine empty. 58.5 gm. of fecal material were present in the colon and were added to the stools for analysis.

Metabolism Experiment 2. Feb. 25 to 27 (3 Days).

Food: Moist weight	539	gm.	Dry weight	160.0 gm.
Nitrogen:	10.88	"	6.8	per cent.
Fat:	43.60	"	27.3	" "
Feces: Moist weight	232.5	"	Dry weight	96.5 gm.
Nitrogen:	7.68	"	7.9	per cent.
Fat:	23.85	"	24.7	" "
Nitrogen absorbed:	3.20	"	29.41	" "
Fat "	19.75	"	45.3	" "

Dog 3.—Mar. 9, 1916. Weight 16.5 kilos. Operation. Subcutaneous transplant of processus uncinatus which was 10 cm. long. Remainder of pancreas, weighing 27 gm. extirpated.

Mar. 13. Good recovery from operation. Graft began to secrete.

Mar. 14. Weight 15.2 kilos. Dog lively. Fistula discharges a thin colorless fluid. *First metabolism experiment begun.*

Mar. 15. Weight 14.7 kilos.

Mar. 16. Weight 14.9 kilos. Stool semisolid, fatty, and contains a great number of muscle fibers and fat drops. Weight of feces 356 gm.

Mar. 17. Weight 14.9 kilos. Dog lively. Stools light yellow and of rancid odor; weight 411 gm.

Mar. 18. Weight 15.0 kilos. Fistula secreting. No food today. Stools weigh 173 gm.

Mar. 19. Stools 10 gm. Fed milk, bread, and charcoal.

Mar. 20. Weight 14.6 kilos. Stools black with charcoal.

Metabolism Experiment 1. Mar. 14 to 17 (4 Days).

Food:	Moist weight	2,110.5	gm.	Dry weight 765.0 gm.	
	Nitrogen:	45.08	"	5.9	per cent.
	Fat:	215.88	"	28.2	" "
Feces:	Moist weight	1,161.5	"	Dry weight 417.5 gm.	
	Nitrogen:	28.81	"	6.9	per cent.
	Fat:	164.29	"	39.4	" "
Nitrogen absorbed:		16.27	"	36.1	" "
Fat	"	51.6	"	23.9	" "

Mar. 21. Weight 14 kilos. Operation for removal of subcutaneous graft. The pancreatic remnant appeared normal.

Mar. 22. Weight 13.5 kilos. *Second metabolism experiment begun.* Ate 807.5 gm. of food. Dog appears in good condition but lies in cage.

Mar. 23. Dog lies in cage. Ate 77 gm. of food. Urine (480 cc.) reduced Fehling's solution. Stool 245 gm., semisolid, dark with charcoal. 3 gm. of stool not containing charcoal discarded.

Mar. 24. Dog much more lively. Stools weigh 143 gm.; the greater part admixed with charcoal. They are semisolid and microscopically show large numbers of well preserved muscle fibers and fat droplets.

Mar. 25. Dog very active. Stools weigh 284 gm.; diarrheal, light yellow.

Mar. 26. No food today. Stools weigh 113 gm.

Mar. 27. Weight 13.5 kilos. Feces 10 gm. Milk, bread, and charcoal fed. Dog appears well.

Metabolism Experiment 2. Mar. 22 to 25 (4 Days).

Food:	Moist weight	1,786.0	gm.	Dry weight 575.0 gm.	
	Nitrogen:	34.5	"	6.0	per cent.
	Fat:	176.18	"	30.6	" "
Feces:	Moist weight	1,172	"	Dry weight 397.5 gm.	
	Nitrogen:	25.21	"	6.3	per cent.
	Fat:	145.19	"	36.5	" "
Nitrogen absorbed:		9.29	"	26.9	" "
Fat	"	30.99	"	17.6	" "

Mar. 28 to Apr. 8. The dog became progressively weaker and after Apr. 2 was unable to stand. A severe and persistent glycosuria developed within 24 hours after the removal of the pancreatic remnants. Apr. 8. Killed with chloroform. No pancreatic tissue found in the abdominal cavity.

Dog 4.—Adult male dog.

Apr. 13, 1916. Weight 14.4 kilos. Entire pancreas removed except the processus uncinatus and lower part of the corpus pancreatis, which were transplanted with the main duct into the subcutaneous pocket.

Apr. 16. Recovery uneventful. No sugar in urine. Fed milk.

Apr. 17. *First metabolism experiment begun.* Weight 13.2 kilos. Fistula

secretes a clear colorless fluid. Ate 819 gm. of food. It contained 35 gm. of charcoal. Dog lively.

Apr. 18. Dog vomited; experiment stopped.

Apr. 19. Fed milk. Dog appears well.

Apr. 20. *First metabolism experiment recommenced.* Weight 13.4 kilos. Fistula discharges copiously. Ate 745.5 gm. of food.

Apr. 21. Food 375 gm.

Apr. 22. Dog well. Food 748 gm. Stool 163 gm. The skin about the fistula is reddened and excoriated.

Apr. 23. Dog lively. Fistula secreting. Food 799 gm. Stool 202 gm.; light yellow, and semisolid; contains abundance of muscle fibers and fat droplets.

Apr. 24. Weight 13.35 kilos. No food today. Stool 155 gm.

Apr. 25. Stool 25 gm. Food: milk, bread, and charcoal.

Apr. 26. Part of stools contains no charcoal. This portion weighs 116 gm. and was saved for analysis.

Metabolism Experiment 1. Apr. 20 to 23 (4 Days).

Food:	Moist weight	2,668 gm.	Dry weight, 1,052.5 gm.	
	Nitrogen:	46.31 "	4.4 per cent.	
	Fat:	312.80 "	29.7 "	"
Feces:	Moist weight	781.0 "	Dry weight 260.0 gm.	
	Nitrogen:	16.12 "	6.2 per cent.	
	Fat:	80.42 "	30.9 "	"
Nitrogen absorbed:		30.19 "	65.2 "	"
Fat	"	232.38 "	74.3 "	"

Apr. 27. Food: milk.

Apr. 28. Weight 12.3 kilos. *Second metabolism experiment started.* Fistula secreting actively. Throughout the experiment the dog wore a muzzle covered with tin in order to prevent licking of the fistula. The pancreatic transplant secreted freely.

Apr. 30. Stools are semisolid. Microscopically there are many well preserved muscle fibers and fat droplets.

May 2. Weight 12.9 kilos. No food.

May 3. Stool 197 gm. Dog well. Fed milk, bread, and charcoal.

Metabolism Experiment 2. Apr. 28 to May 1 (4 Days).

Food:	Moist weight	3,582 gm.	Dry weight 1,495 gm.	
	Nitrogen:	78.49 "	5.3 per cent.	
	Fat:	488.57 "	32.7 "	"
Feces:	Moist weight	2,018 "	Dry weight 713.5 gm.	
	Nitrogen:	43.74 "	6.1 per cent.	
	Fat:	257.65 "	36.1 "	"
Nitrogen absorbed:		34.75 "	44.3 "	"
Fat	"	230.92 "	47.3 "	"

May 5. Weight 12.00 kilos.

May 7. Fistula secretes 0.5 cc. of fluid per minute. One drop of the fluid digests 5 cc. of 1 per cent casein in 4 hours.

May 8. Weight 11.35 kilos. Dog is growing weaker. He eats ravenously.

May 8 to 19. Dog remains well. He is fed raw pancreas of three pigs, with chopped horse flesh and 500 cc. of milk daily. A gain in weight from 11.35 to 12.5 kilos occurred. The secretion of the fistula has gradually diminished.

May 19. Weight 12.5 kilos. The dog is in good condition but looks thin. Removal of the subcutaneous graft.

May 20. Weight 11.6 kilos. Dog lively and appears well. Urine, 370 cc., contains 18.5 gm. of glucose. *Third metabolism experiment started.*

May 21. Weight 11.15 kilos. Dog apathetic, but does not appear sick. Ate 441 gm. of food. No stools.

May 22. Food 380 gm. Stools have rancid odor and all contain charcoal; weight 131 gm.

May 23. Weight 11.15 kilos. Dog lively. Food 285 gm. Feces weigh 222 gm., 110 gm. of which contain much charcoal. On microscopic examination found to contain many muscle fibers and fat droplets.

May 24. Food 673 gm. Feces 266 gm.; partly formed, partly semisolid.

May 25. Weight 10.65 kilos. No food allowed. Stools 358 gm.

May 26. Fed milk, bread, and 30 gm. of charcoal. Stools 94 gm.

Metabolism Experiment 3. May 20 to 24 (5 Days).

Food:	Moist weight	1,836 gm.	Dry weight 717.5 gm.
	Nitrogen:	37.88 "	5.3 per cent.
	Fat:	213.67 "	29.8 " "
Feces:	Moist weight	1,071 "	Dry weight 413 gm.
	Nitrogen:	28.13 "	6.8 per cent.
	Fat:	155.45 "	37.6 " "
Nitrogen absorbed:		9.76 "	25.8 " "
Fat "		58.22 "	27.2 " "

The dog lost 600 gm. during this experiment. He emaciated rapidly and became progressively weaker.

May 27. Weight 10.6 kilos. All the stools contain much charcoal. Urine, 650 cc., contains 81.25 gm. of glucose. *Fourth metabolism experiment started.* Lard fed instead of butter. Food 1,099 gm.

May 28. Weight 10 kilos. Dog stands steadily and seems well. Food 926 gm. Feces 409 gm.

May 29. Weight 9.9 kilos. Dog appears well. Food 747 gm. Feces 227 gm.; light yellow, semisolid.

May 30. Weight 9.9 kilos. Food 677 gm. Feces 532 gm.

May 31. Weight 9.75 kilos. Dog found lying in cage, but arises when approached; unsteady on his feet. Feces 440 gm.

June 1. Weight 9.2 kilos. No food today. Dog very weak. Stool 70 gm.

Metabolism Experiment 4. May 27 to 31 (5 Days).

Food:	Moist weight	3,449 gm.	Dry weight	1,402.5 gm.
	Nitrogen:	73.35 "	5.2 per cent.	
	Fat:	483.72 "	34.5 " "	
Feces:	Moist weight	1,678 "	Dry weight	664 gm.
	Nitrogen:	37.18 "	5.6 per cent.	
	Fat:	304.31 "	45.8 " "	
Nitrogen absorbed:		36.17 "	49.3 " "	
Fat "		179.41 "	37.1 " "	

June 2. Weight 9.1 kilos. Stands very unsteadily. Lies in cage unless some one approaches him. Etherized. No pancreatic remains found in the abdomen.

Dog 5.—Female pup.

Mar. 16, 1916. Weight 4.8 kilos. Entire pancreas except processus uncinatus removed. The latter was left *in situ*. It measured 5 by 2.5 cm. The pancreatic tissue is separated from the duodenum by mesentery.

Mar. 17. Dog lively. Fehling's solution not reduced by urine.

Mar. 23. Dog drinks milk and eats meat; seems well.

Mar. 26. Weight 3.5 kilos.

Mar. 27 to Apr. 8. Fed raw pancreas ground up with cooked horse flesh and milk.

Apr. 9. Fed only milk.

Apr. 10. Weight 4.8 kilos. *First metabolism experiment begun.* Dog in good condition. Food eaten 209.5 gm., containing 20 gm. of charcoal.

Apr. 11. Food 558 gm. Large part of feces contains charcoal; weight 108 gm. Portion free from charcoal easily separated.

Apr. 12. Food 651.6 gm. Feces 122 gm.; dark gray, formed, and found to contain on microscopic examination large amounts of muscle fibers and fat droplets.

Apr. 13. Food 239 gm. Feces 158 gm.; semisolid, yellow, fatty.

Apr. 14. Food 260 gm. Feces 123 gm.

Apr. 15. Fed 300 cc. of milk with charcoal. Feces 57 gm. Dog lively.

Apr. 16. Feces, 22 gm., unmixed with charcoal.

Apr. 17. Weight 4 kilos. Fed raw pancreas with chopped cooked horse flesh and milk. All the feces contain charcoal.

Metabolism Experiment 1. Apr. 10 to 14 (5 Days).

Food:	Moist weight	1,709 gm.	Dry weight	550 gm.
	Nitrogen:	32.01 "	5.8 per cent.	
	Fat:	150.9 "	27.4 " "	
Feces:	Moist weight	592 "	Dry weight	220 gm.
	Nitrogen:	14.98 "	6.8 per cent.	
	Fat:	72.07 "	32.8 " "	
Nitrogen absorbed:		17.98 "	56.2 " "	
Fat "		77.8 "	51.6 " "	

June 1. Weight 4.8 kilos. Urine contains sugar for the first time. Since Apr. 15 the dog has been given raw pig's pancreas daily.

June 29. Weight 4.1 kilos. Urine reduces Fehling's solution.

July 26. Found dead this morning. Weight 2.9 kilos.

Autopsy.—Dog greatly emaciated. All internal organs seem free from disease. A piece of tissue resembling a lymph node lies near the lower end of the duodenum in the mesentery. It is about 1 cm. in diameter and the thicker portion is surrounded by a zone of thinner tissue making the whole mass measure 3 by 1 cm. On histological examination this was found to be the atrophied and sclerosed pancreatic remnant.

Fat Absorption in Partially Depancreatized Dogs.

Metabolism experiments were done on four partially depancreatized dogs with subcutaneous transplants, which discharged the pancreatic juice externally. The animals were free to lick their fistulas and thus ingest pancreatic juice. How much pancreatic secretion was obtained in this way could not be determined. The amounts and percentages of fat absorbed are given in Table I.

TABLE I.

Fat Absorption in Partially Depancreatized Dogs in Which All Pancreatic Juice Was Excluded from the Intestine.

Dog.	Weight.*	Fat ingested.		Fat absorbed.			Remarks.
		Total amount.	Amount per kilo.	Total amount.		Amount per kilo.	
	kg.	*gm.*	*gm.*	*gm.*	*per cent*	*gm.*	
1	11.9	431.12	36.1	118.0	27.37	9.88	Subcutaneous transplant; remainder of pancreas extirpated.
2	13.5	175.68	13.0	132.1	75.2	9.78	
3	14.9	215.88	14.5	51.6	23.9	3.47	
4	13.4	312.8	23.38	232.38	74.3	17.4	
5	4.4	150.9	34.28	77.8	51.6	17.66	Processus uncinatus left *in situ;* remainder of pancreas extirpated.

*The weights given are the averages of the daily weights of each dog.

Dogs with functionating subcutaneous grafts with the external secretion discharging freely may absorb no more fat than a dog in which the ducts are occluded and the gland undergoing rapid and progressive atrophy. This is seen by comparing the results of the experiments on the first four dogs (Nos. 1, 2, 3, and 4) with those on Dog 5, presented in Table I. In Dog 5 the processus uncinatus

was left in the abdomen and the remainder of the pancreas removed. There was no communication between the pancreatic remnant and the lumen of the duodenum; the dog received neither pancreatic juice nor pancreas in its food, and yet this animal absorbed 51.6 per cent of the fat ingested. The mean average of the percentages absorbed by the other four animals is 50.19 per cent. Dog 5 absorbed 17.66 gm. of fat per kilo of body weight. 17.38 gm. was the maximum per kilo absorbed by any of the other animals, in the tabulated results.

The fact that the fat absorption in the dogs with atrophied pancreas, studied by Pratt, Lamson, and Marks, was less on the average than in our dogs with pancreatic transplants which were discharging pancreatic juice freely, would seem at first sight to support Lombroso's view that absorption varied with the condition of the pancreatic remnant. But in Dog 5 with atrophying pancreas, as we have shown, the absorption was equal to that in the dogs with subcutaneous transplants that were not undergoing rapid atrophy. The same food mixture was given to all the animals in the present investigation. In the earlier study of Pratt, Lamson, and Marks a different food mixture was fed and it may have been less easily absorbed. However, there is no doubt that different animals when deprived of their pancreatic juice vary greatly in their power to absorb fat, and furthermore, that there is a great variation in the same animal on the same diet at different times. This was shown in the experiments of Pratt, Lamson, and Marks.

In the present study Dogs 2 and 4 absorbed the relatively large percentages of 75.2 and 74.3 per cent of the fat ingested, while Dogs 1 and 3 absorbed but 27.37 and 23.9 per cent.

Much more secretion flowed from the cutaneous fistula in Dog 4 than from the fistulas of the other animals. A proteolytic ferment was demonstrated in the secretion. The dog was seen to lick the fistula frequently and it is probable that the animal ingested more secretion than did the other dogs. Nevertheless, the percentage of fat absorbed by Dog 4 was no greater than that absorbed by Dog 2.

The number of grams of fat absorbed per kilo of body weight varied in the different dogs. No relation existed between the number of grams of fat ingested and the amount absorbed.

Burkhardt, Fleckseder, and Lombroso carried out metabolism experiments on dogs with pancreatic cutaneous fistulas. Experiments were made during two periods, one in which the fistulas were licked and one in which the licking was prevented. Conflicting results were obtained.

Fleckseder and Lombroso concluded from their experiments that, since it made little difference in the absorption of fat whether or not the animal obtained the pancreatic secretion from the pancreatic transplant, the absorption must be governed by an internal function of the pancreas. We have repeated the experiments on one dog. The results are given in Table II.

TABLE II.

Fat Absorption in Dog 4 with and without Licking of Pancreatic Juice.

Experiment No.	Date.	Weight.*	Fat ingested.		Fat absorbed.			Remarks.
			Total amount.	Amount per kilo.	Total amount.		Amount per kilo.	
		kg.	*gm.*	*gm.*	*gm.*	*per cent*	*gm.*	
1	Apr. 20 to 23	13.37	312.80	23.38	232.38	74.30	17.38	Fistula licked.
2	" 28 " May 1	12.60	488.57	38.77	230.92	47.3	18.32	Licking prevented; dog muzzled.

* The weights given are the averages of the daily weights during each experiment.

Dog 4 in the first metabolism experiment was permitted to lick the fistula and thus obtain the pancreatic juice. In the second experiment the dog was prevented from licking the fistula by means of a muzzle covered with tin. The fistula in this animal continuously secreted enough fluid to bathe the entire ventral parts of the abdomen and chest. The skin over these areas showed evidences of being digested. The secretion from the fistula contained trypsin.

In the first experiment 74.3 per cent of the ingested material was absorbed. After muzzling the dog the absorption dropped to 47.3 per cent. This increased loss in the feces of 27 per cent of the fat ingested suggests that the pancreatic secretion increased the amount of fat absorbed. This view is supported by the fact that the feces contained 5.2 per cent more fat. The total amount of fat absorbed, however, was nearly the same in the two experiments, and the amount of fat absorbed per kilo was actually greater when the dog was prevented from licking the fistula. As the dog was not muzzled

until the experiment was begun, it is possible that pancreatic secretion ingested previously influenced somewhat the absorption of fat.

It would not be surprising if the pancreatic secretion introduced *per os* had increased somewhat the absorption of fat, because Pratt, Lamson, and Marks observed a greater absorption after the feeding of pancreatic ferments to dogs in which the pancreas had been separated from the duodenum.

Lombroso believed that a definite relation existed between the state of preservation of the pancreatic remnant in his dogs and the amount of fat absorbed. This conclusion was based upon the finding of degenerated pancreatic remnants in dogs showing a poor fat absorption. But his own findings and those of other investigators do not support this view. In the first metabolism experiments following partial pancreatectomy, one of his dogs absorbed 46 per cent (48 gm.), and another dog absorbed none of the fat ingested. 2 weeks later the same animals absorbed 68 per cent (66 gm.) and 16 per cent (13 gm.). There is no reason to assume that the pancreatic remnant was in a better state of preservation 2 weeks after the first metabolism experiments.

Two dogs, reported by Rosenberg, absorbed from 49.06 to 84 per cent of the fat ingested, at a time when the pancreas had undergone almost complete fibroid degeneration. Sandmeyer studied the fat absorption in a partially depancreatized dog in which he believed no communication existed between the pancreas and duodenum. The percentages of fat lost in the stools of this dog varied from 9.1 to 163.5 per cent. The greatest fat losses were not confined to any one period, but occurred from time to time throughout the investigation. Hence, they could not be attributed to degeneration of the pancreatic remnant.

Dogs 1 and 3 absorbed but 27.37 and 23.9 per cent. These low percentages of fat absorption could not be ascribed to degenerative changes in the pancreatic remnants as maintained by Lombroso, because when these were removed at the second operation they were found to be well preserved.

Fat Absorption in Completely Depancreatized Dogs.

At a second operation the pancreatic remnant was removed from Dogs 2, 3, and 4. Fat absorption was then studied in these animals. The results are given in Table III.

TABLE III.

Fat Absorption in Completely Depancreatized Dogs.

Experiment No.	Dog.	Weight.*	Fat ingested.		Fat absorbed.		
			Total amount.	Amount per kilo.	Total amount.		Amount per kilo.
		kg.	*gm.*	*gm.*	*gm.*	*per cent*	*gm.*
2	2	11.4	43.6	3.82	19.75	45.3	1.73
2	3	13.4	176.18	13.11	30.99	17.59	3.05
3	4	11.2	213.67	19.00	58.22	27.24	5.17
4	4	10.1	483.72	48.22	179.41	37.1	17.88

* The weights given are the averages of the daily weights of each dog.

Dog 2 was in poor condition during the metabolism experiment and died before its completion. The animal ingested but 43.6 gm. of fat. Nevertheless, 45.3 per cent of this was absorbed.

Each dog absorbed a considerable amount of fat, although the percentages, the actual amount, and the number of grams per kilo of body weight varied much in the different animals and in the two experiments on the same animal. As the autopsies on these dogs showed that all pancreatic tissue had been extirpated, the experiments prove that fat may be absorbed from the intestine by depancreatized dogs in relatively large amounts, even when the fat fed is not in the form of an emulsion. Dog 4 absorbed 37 per cent of fat fed, chiefly in the form of lard, 9 to 12 days after the removal of all pancreatic tissue. In the other experiments butter was given. Since the publication of Abelmann's studies in 1890, it has been generally held that a depancreatized dog can absorb only the fat of milk.

A comparison of the fat absorbed during the stage of partial depancreatization and after complete pancreatectomy is given in Table IV.

After partial depancreatization Dog 2 absorbed 75.2 per cent of the fat ingested (Metabolism Experiment 1), while 45.3 per cent was absorbed after complete pancreatectomy. Results almost identical to these were obtained in the first and second metabolism experiments on Dog 4, although the transplant was still secreting in the second experiment. The only difference is that the dog obtained no secretion, as it was muzzled. It will be seen that Dog 2 absorbed a larger percentage of fat when completely depancreatized

TABLE IV.

Comparison of Fat Absorption before and after Complete Depancreatization.

Experiment No.	Dog.	Date.	Weight.*	Pancreatectomy.	Fat ingested.		Fat absorbed.			Remarks.
					Total amount.	Amount per kilo.	Total amount.		Amount per kilo.	
			kg.		*gm.*	*gm.*	*gm.*	*per cent*	*gm.*	
1	1	Jan. 5 to 8	11.9	Partial.	431.12	36.10	118.0	27.4	9.88	Fistula licked.
1	2	Feb. 17 to 21	13.5	Partial.	175.68	13.0	132.1	75.2	9.78	Fistula licked.
2		" 25 " 27	11.4	Complete.	43.60	3.82	19.75	45.3	1.73	
1	3	Mar. 14 to 17	14.9	Partial.	215.88	14.5	51.6	23.9	3.47	Fistula licked.
2		" 22 " 25	13.4	Complete.	176.18	13.11	30.99	17.6	3.05	
1	4	Apr. 20 to 23	13.4	Partial.	312.8	23.38	232.38	74.3	17.4	Fistula licked.
2		" 28 " May 1	12.6	"	488.56	38.77	230.92	47.3	18.32	Muzzled.
3		May 20 " 24	11.2	Complete.	213.67	19.00	58.22	27.2	5.17	
4		" 27 " 31	10.0	"	483.72	48.22	179.41	37.1	17.88	

* The weights given are the averages of the daily weights throughout an experiment.

than did Dog 4 which possessed functionating pancreatic tissue. These findings are decidedly against Lombroso's theory that absorption is controlled by an internal secretion of the pancreas. Dogs 3 (Metabolism Experiments 1 and 2) and 4 (Metabolism Experiments 2 and 4) absorbed but 6.3 and 10.2 per cent less fat after complete depancreatization than after partial extirpation of the gland. Greater differences in the percentage absorption of fat in the same animal are reported by Lombroso, and Pratt, Lamson, and Marks, in their studies on partially depancreatized dogs.

The number of grams of fat absorbed per kilo of body weight varies in experiments on the same dog and on different dogs, as is shown in Table IV. Dog 2 absorbed much less fat after complete than after partial depancreatization. But it will be noted that much less fat was ingested. A similar result occurred in the first metabolism experiment following complete depancreatization in Dog 4.

The poorer absorption in these dogs may have been a result of the operation. The experiments were begun the day following. However, under the same experimental conditions Dog 3 did not show an appreciable increase in the fat lost in the feces. In the first experiment Dog 3 absorbed 3.47 gm. of fat per kilo of body weight. At this time the dog was partially depancreatized and was allowed to lick the secretion from the fistula. After complete depancreatization 3.05 gm. of fat per kilo were absorbed. After complete extirpation of the gland, Dog 4 (Metabolism Experiment 4) absorbed but 0.44 gm. less fat per kilo than after partial depancreatization (Metabolism Experiment 2). In the latter experiment the dog possessed a cutaneous pancreatic fistula, but was muzzled so that no pancreatic secretion could be ingested. In Metabolism Experiment 4, 0.5 gm. more fat was absorbed per kilo than in the first metabolism experiment, in which the dog licked the pancreatic fistula. These findings show that it is possible for a completely depancreatized dog to absorb as much fat per kilo of body weight as when the same dog possesses functionating pancreatic tissue which does not secrete into the intestines.

CONCLUSIONS.

It was found that dogs with a subcutaneous transplant secreting and discharging pancreatic juice externally absorbed no more fat than dogs in which the pancreatic remnant was undergoing rapid atrophy and sclerosis. Hence, the condition of the pancreatic tissue remaining in the body does not influence the amount of fat absorbed by the intestine.

The absorption of fat by the intestinal mucous membrane is always markedly disturbed when the pancreatic secretion is excluded from the intestine.

After the complete removal of all pancreatic tissue from an animal, the absorption of considerable amounts of fat can still take place.

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