very tersely and truthfully asserts, "any significant increase of undigested muscle fibres in the stools would be expected only when there was extreme diminution of pancreatic juice in the bowel, gastric digestion was relatively normal, the diet contained no excess of meat, and there was no diarrhoea."

In certain cases fat has been given in excessive quantity in the food to determine the activity of the pancreatic juice. Similarly it would be desirable to recognize in the first place the normal digestive power of an individual for proteids, and then to administer meat in excess in order to see the results thereby recognizable in the faeces. Meat, however, undergoes certain changes in the stomach, and, if possible, it would be desirable to introduce a proteid into the duodenum without having undergone any digestion in the stomach. Sahli suggested, that "glutoid" capsules containing iodoform or salol might be administered by the mouth with food. The coating of the capsules is so hardened by treatment with formalin, that it remains unaffected by the action of the gastric juice for several hours. As soon, however, as the capsule is passed onwards into the intestine, it is rapidly digested by the pancreatic juice, and its contents are liberated. Nencki has shown that salol is split up by the pancreatic juice into salicylic acid and phenol, and that the former is rapidly eliminated in the urine. If iodoform be used, the iodine reaction can be elicited from the saliva as soon as intestinal digestion is begun. In order that the test with the glutoid capsules should be accurate, there must be a normal activity of the gastric juice, a normal or nearly normal gastric motility, and a normal intestinal absorption. Failing any, but especially the two latter, the test loses much of its value. Sahli has related a series of cases in which the test showed absence of the reaction, or its delay for periods over twenty-four hours, and in which malignant disease of the pancreas was found. This test has since then been generally known as the "signe de Sahli." There has been so little purposeful investigation of this method that its value, though probably not small, has never yet been even approximately determined.

4. Fat Necrosis.

This condition was first described by Balser in 1882. In five cases opaque white areas, which microscopically proved to be composed of necrotic fat cells, were found in the fat around, and in the immediate neighbourhood of, the pancreas. In two cases the fat at some distance from the gland was affected also. Since these observations of Balser abundant confirmation of their accuracy has been made. The cause of the fat necrosis was discovered by Fitz. It was he who first suggested that a lesion of the pancreas was the determining and causative factor, and he drew attention to a series of cases in which the two conditions—pancreatic disease and fat necrosis—occurred together. The complete dependence of the fat necrosis upon disease of the pancreas is now universally admitted. The appearances caused by necrosis of the fat are quite typical.

Smaller or larger opaque, white unraised areas are seen studded irregularly in the fat; their colour contrasts in the most striking manner with the bright yellow colour of the fat. Near the pancreas the spots are larger, even a quarter or a third of an inch in diameter, and several of them may be confluent, so that a white streak results. The white areas are generally marked off abruptly from the surrounding tissues, but at times a bright red haemorrhagic zone may surround them. As a rule, the further the patches of necrosis are from the pancreas the smaller and the fewer are they. It is rare to find the fat outside the abdominal cavity affected, though the subcutaneous fat of the abdominal wall, and the pericardial fat, may be affected also. The nature of the fat necrosis was first shown by Langerhans. It consists in the splitting of the fat into fatty acid and glycerin; the fatty acids, deposited at first as acicular crystals in the cell, combine with the calcium salts to form a soap, while the glycerin is absorbed.

The immediate cause of the fat necrosis, whether localized or disseminated, has been shown to be the pancreatic secretion. The juice escaping from the gland diffuses more or less widely, and is in part, perhaps, taken up by the lymphatics. A fat-splitting ferment, probably that of the pancreatic juice, has been found by Flexner in foci distant from the gland, and Opie has possibly discovered its presence in the urine of a patient suffering from acute pancreatitis. Fat necrosis may, therefore, be said to consist in the action upon normal fat of the fat-splitting ferment of the pancreatic juice, which has

escaped from the duct as the result of some serious lesion of the pancreas. It is most commonly found in association with acute pancreatitis, of the haemorrhagic or gangrenous forms, but may also be found in association with chronic interstitial (interlobular) pancreatitis. The significance of fat necrosis is therefore considerable. If in any operation for some acute, but indeterminate, condition within the abdomen, a sharply-defined white, opaque, or ivory-like patch be seen in the omentum, or in any part of the intra-abdominal fat, the operation from being exploratory, becomes at once purposeful, and the pancreas is sought forthwith.

In one remarkable case related by Hansemann, bright red spots seen upon the skin were found to be due to underlying foci of necrosis in the fat of the abdominal wall.

The view that fat necrosis is wholly dependent upon lesions of the pancreas has been verified beyond dispute by the experimental work of Flexner and Opie.

5. Jaundice.

Jaundice is not uncommonly associated with diseases of the pancreas. Its existence is due to the anatomical relationship between the head of the pancreas and the common bile duct, and to the mode of termination of this duct and of the canal of Wirsung in the ampulla of Vater. In chronic pancreatitis or in malignant disease of the head of the pancreas, the enlargement of the gland causes pressure upon the duct from the outside, and, the calibre of the duct being narrowed, the free escape of bile is prevented and jaundice results. In calculus of the pancreas jaundice may be caused by the obstruction of the stone into the ampulla of Vater. Inflammation of the canal of Wirsung, of the mucous membrane of the ampulla, and of the common duct ensue, and the cholangitis is attended by jaundice. In acute haemorrhagic pancreatitis a slight tinge of jaundice has been occasionally observed. In many of these cases, as Opie has shown, the pancreatitis depends upon the retrojection of bile into the canal of Wirsung, as a result of the impaction of a biliary calculus in the papilla of Vater. A cholangitis exists in these cases also.

In cancer of the head of the pancreas the jaundice appears insidiously, deepens gradually, never varies in depth of tinge from day to day, becoming paler and deeper alternately, but progressively and without intermission becomes more and more pronounced. In many cases the gall bladder can be felt to be greatly distended. So constant is the rule that persisting jaundice associated with distension of the gall bladder depends upon cancer of the head of the pancreas, that it is now formulated as "Courvoisier's law," in deference to the distinguished clinician who first called attention to it.

SCIENTIFIC GRANTS COMMITTEE

OF THE

British Medical Association.

REPORT XC.

THE LYMPH-FLOW FROM THE PANCREAS.

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INTRODUCTION.

THE discovery of secretin by Bayliss and Starling has made it possible to obtain pancreatic juice at will; and in 1902 I showed that the injection of secretin caused, concomitantly with the secretion of pancreatic juice, an increased flow of lymph from the thoracic duct. This increase still occurred, though in smaller degree, after ligation of the portal lymphatics, and the lymph was therefore derived from either the pancreas or the intestines, presumably the former.

Recently, Falloise has carefully investigated the action of secretin on the lymph-flow. He found that secretin increased the lymph-flow from the thoracic duct, but that after ligation of the portal lymphatics the increase no longer occurred; ileum extract also caused an increased flow from the thoracic duct, notwithstanding that no pancreatic juice was secreted. On the other hand, secretin solutions, when freed from albumoses and depressor substance, caused a flow of pan-

creatic juice, but no increased flow of lymph; and a similar result was obtained by injecting hydrochloric acid into the duodenum. Falloise therefore concluded: First, that the increased lymph-flow was derived entirely from the liver, and that it was not due to secretin itself, but was produced by the albumoses or bile salts usually present in secretin solutions; and, secondly, that secretory activity of the pancreas (or liver) did not increase the formation of lymph.

The experiments here described were made to ascertain how far the pancreas falls into line with the liver and salivary glands as regards the effects of its metabolism upon lymph formation.

METHODS.

All the experiments were carried out on dogs anaesthetized with the A.C.E. mixture after a preliminary dose of morphine ($\frac{1}{2}$ to 1 gr.). In every case the lymph was collected from the thoracic duct. The abdomen was opened, a cannula was placed in the main pancreatic duct, and the abdomen was closed by means of clips or sutures. A cannula was also placed in the jugular vein for the injection of secretin or ileum extract. The blood pressure in the femoral artery was always recorded. The animals were kept without food for the twenty-four hours preceding the experiment; the pancreas was then in a resting condition, and the lymph was clear and free from fat. The secretin (or ileum extract) was injected from a burette at the rate of from 1 to 2 c.cm. per minute; by making the injections slowly, the fall of blood pressure was comparatively slight, the animals remained perfectly quiet, and rapid physical changes in the circulation were avoided. The injection period generally lasted for twenty minutes. The pancreatic juice and lymph were collected in graduated cylinders, and the amount recorded every five or ten minutes.

RESULTS.

1. The Injection of Secretin and Ileum Extracts.

If secretin be injected rapidly, as was done by Falloise, it gives rise to generalized muscular contractions, intense dyspnoea of short duration, a rapid fall of blood pressure, and an increased flow of lymph commencing immediately after the injection. This increased lymph-flow might well be the result of the dyspnoea and muscular movement, independently of any more specific cause. On the other hand, if secretin be injected slowly the animal remains perfectly quiet, the respirations are not appreciably altered in depth or frequency, the fall of blood pressure is slight, and there is no immediate increase in the flow of lymph. An increase in the lymph-flow does occur, however, after a time; it begins from ten to twenty minutes after the commencement of the injection of secretin, reaches its maximum about twenty minutes later, when the blood pressure has returned to its normal level, and lasts altogether for about an hour. The flow of lymph after the injection is two or three times as large as that previous to the injection.

The slow injection of ileum extract also increases the lymph-flow from the thoracic duct, but its effects are less marked than those of secretin.

It appears, therefore, that an important distinction must be drawn between the effects of a rapid and those of a slow injection of secretin (or ileum extract). In the former case the increase in the lymph flow can be accounted for by the changes in blood pressure and by muscular movements; in the latter case no such factors are at work, and the increased lymph-flow must be brought about by some other means.

Experiment 1.

Dog anaesthetized with morphine and A.C.E. mixture. Cannulae in thoracic and pancreatic ducts, femoral artery and femoral vein. The dog showed no dyspnoea or muscular twitchings throughout the experiment.

Time.	Lymph-flow.	Remarks.
	c.cm.	
3.55 to 4.5	3.5	Lymph-flow clear; good steady flow. Injected 80 c.cm. ileum extract 4.15 to 4.35.
4.5 to 4.15	3.1	
4.15 to 4.25	2.5	
4.25 to 4.35	2.5	
4.35 to 4.45	4.7	Injected 75 c.cm. secretin 5.15 to 5.35.
4.45 to 4.55	6.1	
4.55 to 5.5	5.9	
5.5 to 5.15	4.4	
5.15 to 5.25	3.9	
5.25 to 5.35	4.7	
5.35 to 5.45	5.7	
5.45 to 5.55	9.2	
5.5 to 6.5	9.7	
6.5 to 6.15	9.0	

Experiment 2.

Dog anaesthetized with morphine and A.C.E. mixture. Cannula in thoracic duct, blood pressure taken in femoral artery. The dog remained quiet throughout the experiment.

Time.	Lymph in c.cm.	Blood pressure in mm. Hg.	Remarks.
4.4 to 4.14	1.4	—	Thoracic duct cannula slipped 4.25, and was replaced: 4.53 to 5.8 injected 35 c.cm. secretin (bile free).
4.14 to 4.24	1.4	—	
4.40 to 4.50	1.3	4.50 94	
4.50 to 5.0	2.0	4.55 84	
5.0 to 5.10	2.8	5.00 84	
5.10 to 5.20	5.1	5.10 86	

The first of these experiments illustrates the difference between secretin and ileum extract with respect to the magnitude of their effect upon the flow of lymph from the thoracic duct. The second experiment shows the comparatively small depression of the arterial blood pressure produced by a slow injection of secretin; such a fall of blood pressure is insufficient to account for the increased flow of lymph actually observed.

2. Ligature of the Portal Lymphatics.

After ligature of the portal lymphatics secretin solutions still cause an increased flow of lymph, whereas ileum extract has practically no effect. The increased lymph-flow caused by the secretin solutions is less marked, however, when the portal lymphatics are tied than when they are intact. Now, both ileum extract and secretin solutions contain albumoses, and usually small quantities of bile-salts, both of which increase the formation of lymph by the liver. It seems probable, therefore, that the increased lymph-flow caused by ileum extract is derived solely from the liver, and is due to the depressor substances and bile salts which it contains. And no doubt the depressor substance (and bile salt) present in secretin solutions partly accounts for the increased lymph-flow caused by such solutions; but they are not the only factors, as is shown by the fact that, after ligature of the portal lymphatics, secretin solutions still increase the flow of lymph. Since secretin solutions differ from ileum extract only in the fact that the former contain the specific substance secretin, and since, after ligature of the portal lymphatics, secretin increases the flow of lymph from the thoracic duct whereas ileum extract does not, one must conclude that this increased flow of lymph is due to secretin itself, not to the depressor substances, which are present in both ileum extracts and secretin solutions. Further, this lymph must be formed either by the intestines or by the pancreas.

Experiment 3.

Dog anaesthetized with morphine and A.C.E. mixture. Ligature of the portal lymphatics. Cannulae in thoracic duct and pancreatic duct. No dyspnoea or muscular twitchings throughout the experiments.

Lymph in c.cm. Time per 10 min.	Pancreatic juice in c.cm. per 10 min.	Remarks.
1	—	Injected 35 c.cm. secretin in 25 min.
0.8	—	
0.7	—	
2.2	6.2	
2.2	—	
2.7	2.0	
3.1	2.2	
2.4	1.6	
1.8	0.5	Injected ileum extract 62 c.cm. in 21 min.
1.5	0.1	
1.3	—	
0.9	—	
0.8	—	Injected secretin rather rapidly, 30 c.cm. in 13 min.
0.5	2.5	
1.5	2.9	
2.4	3.0	

3. Relation between Lymph and Pancreatic Juice.

When secretin is injected, and the lymph and pancreatic juice are collected simultaneously, it is found that the variations in the rate of flow are very similar for the two fluids. The secretion of pancreatic juice reaches its maximum, and falls again to zero earlier than does the lymph-flow; otherwise, graphic records of the flow of lymph and pancreatic juice closely resemble each other, except that the increased lymph-flow is of longer duration than the secretion of juice. This point is illustrated by Experiment 3, where the contrast between the action of secretin and of ileum extract is well

marked. The depressor substance can be removed from secretin solutions by means of alcohol, as described by Bayliss and Starling; such preparations cause little or no fall of blood pressure, but give a good secretion of pancreatic juice, and an increased flow of lymph, as is shown in Experiment 4.

Experiment 4.

Dog anaesthetized with morphine and A.C.E. mixture. Cannulae in thoracic duct and pancreatic duct. Dog quiet throughout the experiment.

Time.	Lymph.	Pancreatic Juice.	Remarks.
	c.cm.	c.cm.	
3.40 to 3.50	1.0	—	
3.50 to 4.0	0.9	—	
4.0 to 4.10	2.0	0.5	
4.10 to 4.20	2.3	1.7	
4.20 to 4.30	2.7	1.4	
4.30 to 4.40	2.7	1.0	

4.0 to 4.8 injected 50 c.cm. secretin free from depressor substance; very slight fall in blood pressure.

It seems clear that the lymphagogue action of secretin solutions (after tying the portal lymphatics) is due, not to the depressor substance which they contain, but to secretin itself. And since secretin has a specific action on the secretion of the pancreatic juice, but has, so far as is known, no action on the intestines, it is natural to suppose that the increased lymph-flow produced by secretin also has its origin in the pancreas. This view is supported by the close relation already described as existing between the secretion of pancreatic juice and the flow of lymph. This relation between the lymph-flow and the secretion of pancreatic juice is, moreover, strictly analogous to that shown to exist between the flow of bile and the formation of lymph. I conclude, therefore, that the increased flow of lymph from the thoracic duct consequent on the injection of secretin (after ligation of the portal lymphatics) is derived entirely from the pancreas.

This lymph might be formed by the pancreas in one of two ways. On the one hand, May has shown that secretin causes vaso-dilatation of the pancreas, lasting as long as juice is being secreted; it is possible, therefore, that the lymph might be the result of increased filtration, although I have shown that this does not occur in the submaxillary gland under similar conditions. On the other hand, it is possible that the lymph is formed as a result of metabolic changes in the pancreas accompanying the secretion of the pancreatic juice; if so, the pancreas resembles the liver and salivary glands in that its secretory activity invariably causes an increased formation of lymph, due to the rapid formation of metabolic products, and their entrance into the lymph spaces. On the whole, the evidence is in favour of the second explanation.

SUMMARY AND CONCLUSIONS.

1. The injection of secretin or ileum extract causes an increased flow of lymph from the thoracic duct. This has been previously shown by Falloise and by myself.
2. After ligation of the portal lymphatics secretin still causes an increased flow of lymph, whereas ileum extract has no effect.
3. The increased lymph-flow produced by secretin is not caused by the depressor substance, but by secretin itself.
4. There is a close relation between the secretion of pancreatic juice and the increased flow of lymph. The lymph is derived entirely from the pancreas, and is probably formed as a result of metabolic changes occurring in the pancreas during the secretion of juice.

I wish to express my thanks to Professor Starling for his kindness in allowing me to work in his laboratory.

It is my duty to state that this research formed part of my work as scholar of the British Medical Association; the expenses of the research were defrayed by a grant from the Royal Society.

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MEDICAL STUDENTS IN PORTUGAL.—The total number of medical students in Portugal is 584, distributed as follows in the three medical schools of that country: Lisbon Medico-Chirurgical School, 246; Oporto Medico-Chirurgical School, 209; University of Coimbra, 129.

A PRELIMINARY NOTE ON THE BACTERIOLOGICAL FINDINGS IN SEVEN CASES OF ENLARGED PROSTATE.

BY

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NEARLY all observers are decided that the initial change in enlargement of the prostate gland lies in the glandular tissue. There is not, however, the same unanimity concerning the cause and mode of production of the increase.

Three main opinions are held:

1. That the growth is really a neoplasm.
2. That the increase is due to a fibrosis constricting the ducts near the urethra, and causing a retention of the gland products. The fibrosis is suggested to be the result of a chronic inflammatory process, possibly gonorrhoeal in origin.
3. That the increase is due to an inflammation of the gland tissue, which produces blocking of the ducts by a desquamation of the cells. This inflammation is said to be brought about by an extension of septic organisms from the bladder.

In consequence of these divergent views, it is thought that the following brief investigation will be of general interest.

TECHNIQUE.

Microscopy.—Microscopical examination has been made of each prostate gland. The sections have been stained with haemalum and eosin, and also with van Gieson's picro-fuchsin stain, so as to definitely determine the amount of fibrous tissue present. Lastly, sections were stained by Gram's method so as to demonstrate whether micro-organisms were present in the specimens which were examined.

BACTERIOLOGY.

Urine.—The urine was drawn off into a modified Erlenmeyer flask, with special bacteriological precautions, about thirty-six hours before the prostatectomy was performed. Ten cubic centimetres of the urine were then incubated for twenty-four hours in a large flask of broth. A complete bacteriological investigation was then made from this flask.

PROSTATE GLANDS.

As soon as the tumours were removed the surface of each furthest removed from the urethra was burnt with a red hot flat knife. Sections were then made into the interior of the gland with bacteriologically sterile instruments. In every case we were most careful to avoid the tissue in the immediate neighbourhood of the urethra.

Blood agar and agar plates were inoculated either with small pieces of the gland rubbed over the surface of the media, or platinum loops of the fluid, which is present in the prostates, were used in a similar manner. A complete bacteriological investigation was then carried out in those cases in which colonies appeared on the surface of the agar.

We wish to draw attention to the fact that although we used a medium of blood agar in each case for the examination of the prostatic tumours, we failed to isolate gonococci.

CASE I.

S. J. S., aged 65. Frequent micturition for seven months; catheter passed for similar period; 6 oz. of residual urine; history of gonorrhoea doubtful. Urine: 1007, neutral. Parts removed: Small adenoma. Microscopy: Cystic myo-adenomatous tissue; extensive round-celled infiltration present; no micro-organisms seen. Bacteriology of tumour: Pure cultures of the staphylococcus albus; gelatine media were liquefied on the third day.

CASE II.

F. W. F., aged 66. Catheter passed four years ago for an attack of retention; frequent micturition at present time; 3 oz. of residual urine. Urine: Acid and clear. Parts removed: Weight, 34 grams; twin tumour type, with the urethra enclosed; "capsule" well marked. Microscopy: Fibro-adenomatous tissue; extensive round-celled infiltration present; no micro-organisms seen. Bacteriology:—Urine: Two strains of bacillus coli isolated. Prostate: One strain of bacillus coli isolated. Serum test: Patient's serum was found to cause marked agglutination of the strain of bacillus coli isolated from the prostate gland in the dilutions of 1 in 10 and 1 in 20, but no reaction with dilution of 1 in 50.