THE OXYGEN EXCHANGE OF THE PANCREAS.

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The interest of the investigations, about to be recounted, on the oxygen metabolism of the pancreas centres about two facts; firstly the stimulus used is a chemical stimulus—secretin, secondly "there is no direct relationship between the rate of secretion of pancreatic juice and the extent of the blood supply[1]." The observed vascular changes are probably due to the experimental conditions under which our researches were conducted (the presence of depressor substance in our secretin extracts[2], etc.).

We must not be understood to contend that a decreased blood supply ever normally goes hand in hand with pancreatic secretion, or to quarrel with the deduction of O. May[3] who contends that the dilation of the gland which he observes on plethysmographic tracings is due to dilation of the vessels.

Our point is that in experimental conditions local effects may be overruled by general effects. In muscle, Ludwig and Sczelkow[4] and later Chauveau and Kaufmann and Hill and Nabarro dealt with tissues which were at once in a state of excitation and active hyperæmia. In the salivary glands one of us, and later Moussu and Tissot[5], worked under similar conditions. There has therefore been always a doubt as to the relative parts played by activity and hyperæmia in the increased metabolism observed. This doubt has been combated with regard to muscle by Ludwig and Schmidt, who perfused their muscles with results which cannot be regarded as wholly beyond criticism[6], and in the

[1] O. May. This *Journal*, xxx. p. 413. 1904.
[2] Bayliss and Starling. This *Journal*, xxviii. p. 325.
[3] This *Journal*, xxx. p. 413.
[4] *Schäfer's Text Book*, i. p. 764.
[5] *Comptes rend. Acad. d. sc.*, Paris, 1904.
[6] Gamgee. *Text Book*, i. p. 376.

case of the submaxillary by comparing the phenomena of the active with those of the atropinised gland. In the experiments, which we shall recount below, we have found that on injection of secretin into the general circulation the blood-flow through the active pancreas is sometimes faster and sometimes slower than through the resting organ, and on occasions its rate is not appreciably altered.

An experiment which we performed on February 5, 1903 may serve as a sample of the whole series. The dog was anæsthetised with morphia and subsequently with A.C.E. mixture. Tracheotomy was performed and the abdomen was opened.

The vein leading from the tail of the pancreas (which amounts to about one-sixth of the whole organ) was dissected out and ligatures were so placed that a cannula might be rapidly inserted into the vein at a later stage of the operation. A cannula was put into the pancreatic duct and the abdomen was closed up. The blood-pressure was taken from the carotid artery. Cannulæ were placed in the femoral artery and jugular vein: the former for the abstraction of samples of arterial blood, the latter in order to return whipped blood into the dog.

It is necessary at this point to render the dog's blood non-coagulable. In a few of our earlier experiments we used leech extract for this purpose, but we soon adopted the method of defibrinating the animal. Before the beginning of the defibrination the dog was placed in a bath of warm salt solution where it remained for the rest of the experiment. When the blood was sufficiently free from fibrin the cannula was placed in the vein leading from the pancreas. The blood which flowed from this cannula, other than that which was used for analysis, was collected and injected into the jugular vein.

The gases in this experiment were determined by the chemical method described by Barcroft and Haldane[1]. For the collection of the blood an ordinary 1 c.c. pipette graduated in $\frac{1}{100}$'s of a cubic centimetre was used as described in their paper[2].

Before the period of observation commenced as many blood-gas bottles were prepared as we expected to require—a fresh bottle for each sample. These bottles were of known volume and their identity was recognised by numbers engraved on them (*B* 1, *B* 2, etc.). Into each was put 1·5 c.c. of ammonia solution and the bottles were kept closed to prevent the ammonia absorbing CO_2 from the air.

Three samples of blood referred to as *A*, *B*, and *C* in the following

[1] This *Journal*, XXVIII. p. 232. [2] *Ibid.* p. 234.

table were taken in rapid succession, *A* and *C* from the pancreas vein, *B* from the femoral artery. These were put at once into their respective bottles. The injection of secretin was then made and when the flow of pancreatic juice was well established and the blood-pressure restored, three more samples of blood *D*, *E* and *F* were taken in rapid succession, *D* and *F* from the pancreatic vein and *E* from the femoral artery. The rate of flow of pancreatic juice was also noted. It was not sufficient to appreciably alter the concentration of the blood as is the case when the submaxillary glands are actively secreting.

The following table gives the observations which were made on these samples:

Sample	Bottle	Volume of bottle for O_2	Pressure of O_2 in mm. of H_2O	Time of collection of 1 c.c. of blood	Absorption of O_2 per minute
A	B_3	323 c.c.	83 mm.	15″	·12 c.c.
B	B_6	310	97	—	—
C	B_7	337	80	15	·12
D	B_8	345	82	9	·34
E	B_{10}	320	103	—	—
F	B_{12}	322	81	11	·34

Correction for temperature, pressure and aqueous vapour = × ·934.

The method of calculating the "oxygen output per minute," taking the first venous and arterial samples given above (*A* and *B*) as examples, is as follows:

The volume of oxygen in 1 c.c. of blood in *A* is determined from the following data:

(i) "The volume of the bottle for oxygen." (This is the volume of the bottle and attached tubing, less the volume of the fluids it contains) = 32·3 c.c.

(ii) The pressure of the oxygen liberated = 83 mm. of water.

(iii) The atmospheric pressure in millimetres of water = 10340.

(iv) The volume of blood taken = 1 c.c.

(v) The correction factor for temperature, pressure and aqueous vapour = ·934.

The oxygen in 1 c.c. of blood *A* is

$$\frac{32{\cdot}3 \times 83}{10340 \times 1} \times {\cdot}934 = {\cdot}24 \text{ c.c.}$$

The volume of oxygen in 1 c.c. of blood, *B*, is ·273 c.c.

The time which elapsed during the collection of blood *A*, was 15 seconds.

The output of the gland, per minute, is therefore

$$({\cdot}273 - {\cdot}243)\ \tfrac{60}{15} = {\cdot}12 \text{ c.c.}$$

To the results of the above experiment (that of Feb. 5), we add the results of three others, in all of which there was a good flow of pancreatic juice on the injection of secretin.

Date	Oxygen absorbed per minute		Time for collection of 1 c.c.		Response to Injection of Secretin
	Resting Pancreas	Active Pancreas	Resting Pancreas	Active Pancreas	
Jan. 8	·49 c.c.	1·71 c.c.	7 secs.	8 secs.	good
	·60	3·50	6	4	
Jan. 21	·25	·51	17	20	good
	—	·34	—	34	
Feb. 5	·12	·28	15	9	2·1 c.c. in 8′
	·11	·34	15	11	
March 18	·08	·33	27	17	·9 c.c. in 5′
	·06	·29	31	23	
Total	1·71	7·36	118	126	

The oxygen absorption per minute is in every case very much greater in the active than in the resting gland, while the rate of blood-flow is sometimes greater and sometimes less.

It will be noticed that no allowance has been made for the concentration of the blood passing through the secreting gland. No such correction is necessary in the pancreas. For supposing, as in the case of the submaxillary gland, the concentration is approximately equal to the volume of the secretion, the correction for it would work out as follows in the experiment of Feb. 5. One cubic centimetre of blood flowed through the tail of the gland (about $\frac{1}{6}$ of the whole) in nine seconds. The approximate blood flow from the gland is therefore 20 c.c. per minute. But the gland secreted 2·1 c.c. in 8 minutes and therefore ·26 c.c. per minute. In other words 20·26 c.c. of blood was concentrated to 20 c.c.—a change of about 1 %.

A second series of experiments was performed with the mercurial pump.

The blood was collected directly from the vessels of the defibrinated dog into tubes of known volume, of the form already described by one of us for the estimation of the carbonic acid in saliva[1]. The receivers and tubes were larger in size than those figured, the latter being about 10 c.c. in capacity, the former 250 c.c. Care was taken that the calibre of the tubes and their taps was sufficient to avoid venous congestion in the pancreas.

These experiments were performed at University College and the tubes were sent down to Cambridge by train for analysis. Two hours or more elapsed therefore from the time when the samples were withdrawn from the dog till the analyses were made.

[1] This *Journal*, XXVII. p. 36. 1901–2.

We have therefore investigated the effect of time upon the oxygen in the blood and we find that both the arterial, and the venous defibrinated blood from the pancreas, contain as much oxygen after standing some hours at the temperature of the laboratory as they do while still warm.

Feb. 27. Blood drawn under oil (1) from the femoral artery, (2) from the pancreatic vein (the anastomoses with the intestine were tied). The dog was defibrinated. The analyses were made with the pump.

	(*a*) at 11.30 a.m.	(*b*) at 4.30 p.m.
Arterial	19·3	19·5
Venous	10·3	10·9

Volumes of O_2 for every hundred of blood.

The results of the series of experiments performed with the pump may be stated as follows:

(1) Oct. 12. Morphia, A.C.E., Dog defibrinated.

11.55 a.m.	Samples I (arterial) and II (venous) were collected.
12.0.	5 c.c. secretin injected.
12.8.	5 c.c. secretin, 1 c.c. of juice.
12.15.	Samples III (arterial) and IV (venous active) were collected.

Analyses of samples:

	I	II	III	IV
Oxygen	2·60 c.c.	1·25 c.c.	2·85 c.c.	1·65 c.c.
Volume of blood	11·1	9·76	10·6	10·45
Time of collection	—	155″	—	130″

The absorption of oxygen per minute by the resting gland is

$$\left(2{\cdot}60 \times \frac{9{\cdot}76}{11{\cdot}1} - 1{\cdot}25\right) \times \frac{60}{155} = {\cdot}40 \text{ c.c.}$$

The absorption of oxygen per minute by the active gland is

$$\left(2{\cdot}85 \times \frac{10{\cdot}45}{10{\cdot}6} - 1{\cdot}65\right) \times \frac{60}{130} = {\cdot}53 \text{ c.c.}$$

This again shews an increased oxidation accompanying secretion.

A similar experiment performed on December 21 gave a similar result, namely an absorption of ·23 c.c. per minute in the resting gland and ·31 c.c. per minute in the active gland. In this case, however, the blood flow was markedly slower in the active than in the resting gland.

We have obtained one experiment in which the oxygen consumption was approximately the same in rest and in activity. In this case the blood flow was very much reduced indeed. The times of collection were, for 9·9 c.c. of venous blood from the resting gland 100 seconds, and for 10·8 from the active gland 160 seconds. The oxygen absorptions were ·29 and ·32 c.c. per minute respectively.

There remains one point of interest, viz.:—to compare the oxidation taking place in the resting pancreas with that of other organs. The mean of eight determinations by the chemical method gives ·25 c.c. per minute for one-sixth of the gland. The three experiments with the pump cited above give ·40, ·21, ·29 c.c. per minute respectively, giving an average of ·30 c.c. per minute. The mean of all the experiments would then be ·26 c.c. for one-sixth of the pancreas, or in round numbers 1·5 c.c. of oxygen per minute for the whole organ, the weight of which in our experiments may be taken as 30 grammes. These figures give the oxidation per gramme per minute as ·05 c.c. The oxidation in the resting pancreas is therefore about the same as in the submaxillary gland.

Conclusions.

1. Pancreatic secretion is accompanied by an increased oxygen absorption from the blood by the pancreas. This is shown both by the chemical method and the pump.

2. This increased oxidation takes place irrespective of increased blood flow through the organ.

3 The normal oxidation of the pancreas is much greater than that of the body generally and about the same as that of the submaxillary gland.