1858

Mexico.

On the Chemistry and Physiology of the Pancreas.

"

"Invenit nostro quoque aevo Pancreas viros in arte"
"celebres, qui abditum illud denique objectum, et ad"
"servile a piscis anatomicis damnatum munus atque"
"officium, in lucem revocârunt ad majorem dignitatem"
"quin maximam extulerunt, ut medicinam nonnisi sub"
"hujus auspiciis adiendam, nonnulli sibi imaginati"
"fuerint". Brunner — Experim.ta nova circa Pancreas — Amst: 1682

"

Two centuries ago, while Physiological science, stimulated by the numerous discoveries in Anatomy which took place at the Commencement of the 17th. Century, had found many diligent enquirers, it appears that the Physiology of the Pancreas had created for itself an interest of no small importance — as these word of Brunner sufficiently testify — Previous to the discovery of the Pancreatic duct by Johan. Georg. Wirsung a Bavarian anatomist at Batavium in 1642, the functions ascribed to the organ were mere crude speculations which it is unnecessary here to recount. Following out and explaining more fully Wirsung's discovery Francis ~~Sylvius~~ de le Boe Sylvius, Principal of the University of Leyden, a few years after, was the first to ascribe to the Pancreas a secreting function — while at the same time he taught

that

⁂ De Succi Pancr. Natura et usu — Exercitatio Anatomico-medica — Lugd. Batav. 1664

that the fluid secreted by it - and which he describes as "subacidum" - "assisted and promoted the fermentation of" the chyle sent into the duodenum by the stomach." De Graaf, ※ being a pupil of De le Boe's, and embracing the doctrine of his Master on this matter, instituted a series of Experiments, for the purpose of collecting the fluid, and so of ascertaining its' properties - and the exact nature of its' action upon the aliments Contained in the bowel. After several failures, he at length succeeded in obtaining from 1/2 oz. to 6 drachms from one dog - And, from another, even 1oz. in 8 hours - He found that this fluid was acid in itself - and that it caused effervescence with Bile - and hence he concluded that there was a constant effervescence going on in the duodenum - due to the Pancreatic fluid - Whereby that "the useful was separated from the useless" part of the aliments previous to this useful being driven into" the lacteals, by the peristaltic motion of the bowel." -

Such was the amount of information - concerning the functions of the Pancreas - possessed by physiologists at the period to which Brunner refers - Further than this, they could not go - The further elucidation of this subject, like many others connected with the physiology of Digestion, required a vast addition to the existing State of Science at the time. Brunner himself indeed, endeavoured, by actual Experiment, to prove that those glands in the Duodenum which bear his

Name

* Vide. Kölliker's Gewebe des Menschen - idem - Dowlen's Physiol. des Menschen. 1ster Th. - Deutsche Übersetzung.

name, are supplementary to the Pancreas - but failed to do so -
Since his time, the Physiology of the Pancreas, had sunk into
comparative Obscurity again - until - within recent years -
the Researches of Continental Physiologists have invested it anew
with so great an interest as to render these words of Brunner,
so far, strikingly applicable to our own times - The important
Results that have been obtained from these researches - both
for Chemical and Physiological Science - & the fact that these
Contributions towards the advancement of Science in this direction
have been made almost exclusively by French & German
Physiologists - will, I hope, sufficiently excuse my making choice
of this subject for a Thesis.

With regard to the Structure of the Pancreas - there is little to remark -
- It is a compound racemose gland exactly analogous in general
Configuration to the Parotid and other Salivary glands - consisting
of a main excretory duct, whose numerous ramifications end
in small follicles - arranged in lobes and lobules, which are
held together by connective tissue - this whole structure resembling
the stem, branches, and leaves of a tree - The proper secret-
ory structure of the gland consists in a single layer of Epithelium
which lines this dendritic framework, and is of the tessellated
or pavement Kind in the terminal follicles, cylindrical in the
ducts. These flattened Epithelial cells have a granular content
and a clear nucleus with 1 or 2 nucleoli - and frequently

in man

★ Programmata Collecta 1831 - p. 188.

⁂ loc. cit.

in man, contain many small fat globules, which mostly lie grouped round the nucleus - This fatty content of the Epithelium cells has the effect of giving a yellow tinge to the whole appearance of the gland, - in which respect it is more like the Submaxillary than the other Salivary glands - The ultimate follicles measure from $\frac{1}{50}$ to $\frac{1}{25}$ of a Line in diameter - but $\frac{2}{3}$ of this space being occupied by the Epithelial lining - the actual Calibre of these is only $\frac{1}{150} - \frac{1}{75}$ of a Line in diameter - While the Ductus Wirsungianus at its mouth has a diameter varying from 1 to 1½ Lines - The fluid Contents of the Epithelia of the ultimate follicles is peculiar - It is rendered somewhat opaque by dilutes Acetic acid - but dissolved by strong Acetic acid and alKalies - In the fluid which escapes on a thin section - Acetic acid causes a fine granular precipitate - The same from the Parotid gives scarcely a similar precipitate - While that from the Submaxillary becomes membraniform. In the walls of the larger Secretory ducts - * Weber some years ago discovered small racemose glands - Whose epithelia were found by Kölliker to contain no fat - and hence he is inclined to consider these glands as simply Mucous and not part of the proper secreting tissue of the Pancreas. — The walls of the Wirsungian duct consist of fibro-elastic tissue - and, - so far as Kölliker could determine, - contains no smooth muscular fibre like the Whartonian duct - The duct of the Pancreas is single

in

* Kölliker could determine, - contains no smooth muscular fibre

† Memoire sur le Pancreas. Paris 1854 -

⊛ loc. cit.

✡ Elemens. Physiologie tom. VI. p. 451.

in the Human subject, and enters the bowel in conjunction with the common Choledoch duct – The observation is not new, however, that in the dog, rabbit and many other animals there are two such ducts – the one corresponding to the Wirsungian duct proper – the other entering the bowel separately about 1½ – 2 inches below this – which latter ⁑ Bernard has wrongly supposed to have been discovered by himself – for I find that ⊕ De Graaf – who accurately understood the position and relations of the Pancreas to surrounding organs – states that he found the chief pancreatic duct, in the dog, entering the bowel not with the common Bile duct but about 2 finger breadths below this – and also that he was able to trace a communication between the two – within the substance of the gland. ✱ Haller, also, was aware of the fact – as he expresses himself in the following words – referring to what was observed in a dog whose common Bile and Pancreatic duct had been previously tied –. "Aut novus nasci visus" "est ductus quem ego credam esse secundum canibus fa-" "miliarem ductum"

With these few remarks on the more important anatomical peculiarities of this organ – I pass on to the more immediate object of this paper – viz. Remarks on the Chemistry & Physiology of the Pancreas – in the course of which I propose to consider 1° The Chemical Constitution of the tissue proper of the Pancreas itself – as necessarily approximate to that

of

of the Fluid secreted by it - 2ly The so-called Pancreatic Juice - its nature and the phenomena of it' Secretion - And 3ly - The relation of this Secretion to the Digestion of the more important alimentary principles. —

I. With regard to the Chemical Composition of the Pancreas - I venture to put forward the following Qualitative Analysis - Which I made in the Chemical Laboratory at Würzburg under the directions of Professor Scherer - to whom I owe the process - And which I give in full -

1. Seven pounds of Ox- pancreas were freed as much as possible from fat and other extraneous matter - Cut down into minute morcels, & then placed in perhaps thrice it' Volume of distilled Water and allowed to stand for 36 hours at a temperature from 40° - 50° Fah. - The fluid from this was then pressed out and on testing - yielded an acid reaction.

2. This was boiled, in order to separate the Albumen - filtered and Evaporated to the half - On testing with $A\bar{c}$, a precipitate was given - but after a further Concentration of the liquid to half its volume - no such Reaction was obtained by the addition of $A\bar{c}$ alone, to the Whole - After adding Acetate of Copper ($Cu\bar{O}, A\bar{c}$), boiling and allowing to stand in the Cold for 24 hours - a precipitate was obtained - which was separated on the filter - washed and set aside for Examination - While the Filtrate with the fluid obtained from the washing - added -

3. Was -

3. Was then treated with Lime water, till no further precipitate was given - boiled and filtered while hot. A copious precipitate remained on the filter - which was carefully washed and set aside for examination - The washings were added to the filtrate and on being tested with hydrosulphuric acid - no precipitate of CuS, was given -

4. This filtrate treated with Neutral Acetate of Lead gave a copious precipitate, which was separated on the filter - washed and set aside like the former -

5. The filtrate from this (with the washings added as before) was treated next with Basic Acetate of Lead - which also gave a plentiful precipitate - This was separated on the filter - well washed with boiling water - and the filtrate (with the washings added)

6. treated with Caustic Ammonia. The precipitate from this was also washed out with boiling water - and the Whole fluid treated with H_2SO_4 as long as a precipitate was given - in order to remove the Lime and Lead which had been added in excess - This being done, the filtered fluid, which by it's green colour betrayed the presence of Copper, having been freed from this by HS - was slowly concentrated, by evaporation in the water-bath, till a mass of solid matter crystallized out - This was separated on the filter - and the filtrate being again still further concentrated - gave a further quantity of the same crystals - which being separated and added to the

the Journes, were set aside for further investigation — The Mother-liquid was evaporated till it became a thick Syrupy Mass — The product of the Crystallization was examined and found to consist of Leucin along with Crystals of CaO, SO_3 (— the latter being a combination of the Reagents used in the process. —.) — The Leucin was separated from these by dissolving it out with Alcohol (of 85—90 per cent.) and then purified from Colouring Matter by Animal Charcoal.

The various precipitates (which we distinguish by the numbers affixed to the several steps in the process from which they were obtained) from 2. — 6. inclusive — except No 3 — (viz. that from CaO,HO) — being suspended in distilled Water — and freed from the Reagents (CuO & PbO,) by means of HS — were evaporated to Dryness in the Water-bath. The Residues thus obtained from each were then treated with a little cold water (about 2 or 3 times their volume) — allowed to stand for an hour in this — filtered — the filtrates poured into small bottles (4 oz. bottles) and treated with Alcohol (of 90 per cent.) as long as a troubling appeared — The undissolved parts of these Residues were set aside for examination — After this treatment with alcohol ~~Acetic acid~~ each was allowed to stand in the cold for 2 or 3 days — and again treated with alcohol as before — this treatment being repeated every 2 or 3 days during a period of a fortnight or three weeks — ——

Analysis —

Analysis of the Precipitates.

(A)- Precipitate No. 3. (from $CaO, HO_,$) was analyzed like a Urine sediment — and gave the following results —

(a) - The whole was soluble in dilute HCl — ∴ no Uric acid — but the solution took place with discengagement of CO_2

(b) - After precipitation with NH_4O the Alkaline reaction established — the filtrate was found to contain - (1.) no H_2SO_4

— — — — — (2.) CaO —

— — — — — (3.) no MgO —

(c) — The precipitate was found to contain (1.) $3\,CaO, PO_5$ — in large quantity

— — — — — — — — (2.) $2MgO, NH_4O, PO_5$ — in small qty

(3.) Fe_2O_3, PO_5 — in considerable qty

(B.) Precipitate No. 2 (from $CuO, A\bar{c}$) after being treated as above (a) notices — was found to be dissolved entirely in a little water.

(b). This watery solution treated (as above noted) with Alcohol gave a precipitate — this precipitate was filtered out and found to be Albuminoid — the inorganic elements of which were found, by heating it to redness — to be

1. Soluble in water — $NaO, (CO_2?)$

2. Soluble with aid of HCl — $3CaO, PO_5$

(The quantity of the original precipitate being so small that Magnesia and Iron — tho' perhaps present could not be tested for —)

(C.) Precipitate No. 4. (from Neutral Acetate of Lead) having been as above treated with a little cold water and filtered —

(a)

(a) – there remained on the filter a residuum which was found to consist entirely of colouring matter – of a reddish brown colour – soluble in water and alkalies – and precipitated from such a solution by acids.

(b.) The filtrate, treated with alcohol – gave a small precipitate, which was found to consist of Hyporanthin and albumen.

(c.) The alcoholic solution, after being treated with Sulphuric Ether and allowed to stand for 2 or 3 days in the cold, was evaporated to dryness – The residuum from this consisted entirely of that peculiar syrupy body – found to exist in many animal tissues – and which is not yet fully investigated – from its occurring in so small quantities –

D. Precipitate N.° 5 (from Basic Acetate of Lead) was treated in exactly the same manner – and contained the following elements.

(a) The residuum insoluble in a little water consisted of an albuminoid matter, – a little Hyporanthin & Crystals of CaO, SO_3

(b) The precipitate with alcohol was albumen, Hyporanthin & colouring matter –

(c.) The alcoholic solution, treated with Ether, and evaporated to dryness in the water-bath contained – besides the unknown syrupy body formerly mentioned, and traces

traces of Leucin, (the latter from the precipitate not having been perfectly washed at first) - Also crystals of KO,SO_3

(E.) Precipitate No. 6. (from Ammonia) treated in the same manner gave the following results.

(a.) The residuum from the Watery solution - When placed under the Microscope - was found to consist of Tyrosin and Hypoxanthin - These were held together by an albuminoid body - and, in order to separate them, the Whole was dissolved in boiling water and allowed to stand in the cold for 24 hours. In this manner the Tyrosin and Hypoxanthin were crystallized out - these being separated together and the Tyrosin dissolved by HCl - the Hypoxanthin was left pure upon the filter - The acid solution of the Tyrosin, being evaporated to dryness - (so as to remove the HCl) - and the residue treated with Caustic Ammonia - which was suffered spontaneously to evaporate - the Tyrosin then crystallizes out pure.

(b.) - The precipitate with Alcohol - consisted of Colouring matter - and an Albuminoid body in small quantity. This Albuminoid body was soluble in cold water and gave the following reactions.

1. With Tincture of Galls - a White flocculent precipitate
2. With $A\bar{c}$ and a drop or two of Ferrocyanide of Potash - at first nothing - but after standing for 24 hours -

a

(2.) a copious White precipitate.

3. With H,NO_6 nothing – even after heating.

4. With Solution of Corrosive Sublimate – a thick flocculent White precipitate.

5. With Concentrated H,SO_4 and a drop or two of Iodine – no change of Colour – but a grayish White precipitate.

(C.) The Alcoholic Solution, treated with Ether and evaporated – contained – besides the Syrupy body (before mentioned) a little Leucin (from impurity of the original precipitate.)

(F.) Finally – the Mother-liquor of the Leucin – being evaporated to a Syrupy Consistence – was found to contain besides a Considerable Quantity of Leucin not removed by the Crystallization – also Lactic acid – KO. – NaO – and some more of the Unknown Syrupy body – and probably NaCl

The Results of this Analysis – Exhibited in a Tabular View – are –

Inorganic Elements.

1. KO,
2. NaO,
3. NH_4O,
4. CaO,
5. MgO,
6. Fe_2O_3
7. CO_2
8. SO_3
9. PO_5
10. HCl.

Organic Elements

Albumen (Common, Similar to blood Albumen)
Albuminoid matter (from B.)
Albuminoid (from E.)
Leucin
Tyrosin
Hypoxanthine
Unknown Syrupy Body
Lactic acid –
Colouring Matter

※ Programm zum Eintritt in den Königlichen Akad. Senat.
der Friedr.-Alex. Universität zu Erlangen 1836.
item. Canstatts Jahresbericht. 1836.

The Inorganic Elements being probably grouped thus :-

CaO, CO_2

$3CaO, PO_5$

$2MgO, NH_4O, PO_5$

Fe_2O_3, PO_5

KO, SO_3

$KO, \overline{L}$

NaO, CO_2

$NaO\ \overline{L}$ -

Of the Organic elements - The Albumen (having the Characters of Blood Albumen) - which was separated at first by boiling - predominated greatly over the rest - Next to this in quantity stood Leucin which was obtained in large quantity - (perhaps from $1\frac{1}{2}$ - 2 Oz.) - And here it may be stated that this substance was nowhere found so plentiful as in the Pancreas - Similar Analyses being made, in Professor Scherer's Laboratory, at the same time as this, of the Liver, Spleen, the Thymus gland - and the Muscular tissue of the Heart; - In the Liver and Spleen it was found in very small quantity - in the Thymus in considerable quantity - though not so plentifully as in the Pancreas - While in the Heart-flesh it was not found -

X. Gorup Besanez, in seeking to determine the occurrence of Leucin in the principal glands, analyzed thus - Beginning in the manner here noted, he evaporates the Filtrate, after precipitation

Witte

with Baryta (or Lime), [redacted] in the water bath to syrup consistence — treated this with alcohol (of 82. per cent) and from the alcoholic filtrate after evaporation to syrup consistence the Leucin was allowed to crystallize out. In this way he got Leucin from the Thymus, Thyroid, - Spleen, - Pancreas and, in small quantity from the Liver :- Which on Quantitative Analysis gave the following data, for finding its formula -

Leucin from

	Thymus	Spleen	Pancreas	Calculated to
Carbon	54.94 to 54.88	54.66	54.32	C_{12} — 54.96
Hydrogen	9.93 to 9.97	10.00	10.99	H_{13} — 9.92
Nitrogen	10.83	- -	10.80	N — 10.68
Oxygen	- -	- -		O_4 — 24.48

Besides this - he found a new body, which, on examination, turned out to be Homologous with Leucin - tho' differing from it in appearance and Chemical properties. It was found, in the Spleen but in still greater quantity in the Pancreas, in the residuum after the first treating with Alcohol - This was boiled with Alcohol (of 82. per cent) - filtered while hot and this substance allowed to crystallize out. It showed itself in the form of well formed Stellar - grouped transparent prisms, when observed with the naked eye on the surface of the alcohol solution - but White and glancing when observed individually - and when dry, not transparent - microscopically - as broad rhombic plates & prisms

the

The following figures were given by two quantitative analyses of the body -

	Found I	Found II		Calculated to
Carbon	51.68	51.44	C_{10}	51.28
Hydrogen	9.44	9.49	H_{11}	9.40
Nitrogen	12.28	11.65	N	11.96
Oxygen	26.60	27.42	O_4	27.36

This body has never been found by Scherer - and even it's discoverer is disposed to think that it does not occur in all circumstances in glandular solutions - but that it may be merely a product of the further decomposition of Leucin - belonging as it evidently does to the same Homologous Series - of which the following are known -

$C_2 H_3 N O_4$ - - ——

$C_4 H_5 N O_4$ - - Glycin

$C_6 H_7 N O_4$ - - Sarcosin & Alanin

$C_8 H_9 N O_4$ - - ——

$C_{10} H_{11} N O_4$ - - - this body from the Pancreas.

$C_{12} H_{13} N O_4$ - - Leucin.

Compared with Leucin - it is recognized thus: —

Leucin	Homologous Body.
1. Shining white chalk-like crystals which under the microscope are fine needles.	1. Crystals - glancing + white - and prismatic recognized by the naked eye.
2. Sublimable without decomposition	2. —— not without partial decomposition.

Leucin	Homologous Body.
3. Inodorous & completely tasteless	3. Inodorous, but distinctly sharp bitter taste.
4. Soluble with difficulty in Alcohol	4. More insoluble than Leucin.
5. Compounds with acids are dissolved in the air	5. Compounds with acids deliquesce in the air.
6. Forms Compounds readily with Bichloride of Platinum.	6. Compounds with Bichloride of Platinum could not be obtained.
7. Salts with HCl when allowed to Crystallize out by Spontaneous Evaporation - forms 4 sided prisms.	7. The salt with HCl - Crystallizes with difficulty in fine needles.
8. The salt with NO_3 Crystallizes in fine elongated prisms	8. The salt with NO_3 - Crystallizes in broad leaves and prisms.

Tyrosin and Hypoxanthin were found in small quantity - the former occurring much more plentifully in the Thymus, from which indeed it was obtained in very considerable quantity -

The history of the occurrence of Leucin and Tyrosin in the Animal body is a subject too wide for discussion here, - but as it is one intimately associated with the Chemistry of the Pancreas and at the same time promises to lead by slow to most important results, I cannot avoid ~~entirely~~ briefly noticing the principal facts regarding it.

Attention was first called by Frerichs (Wiener Med. Wochenschrift July 1854) to the formation of these bodies, as pathological products in the liver - first observed by him in a case of Acute Yellow Atrophy of the liver - and subsequently in Typhus, Variola - and in others

of

of the Exanthemata, while at the same time, in these cases their presence in the blood was demonstrated - In Nov. 1854, Virchow found them in the Portal vein in a case of Common Icterus - and shortly afterwards observed them crystallized out as a Cadaverous phenomenon - in the Pancreas - the Kidney - and Splenic vein, in various diseases. Liebig had indeed previously mentioned that he had found Leucin in the liver of the Calf - And Robin and Verdeil had noticed its occurrence in the dispersed fluid from the lung - but it was not till Virchow had discovered that Leucin is not exclusively a pathological product, but at the same time a constant element of the normal Pancreas, that Professor Scherer identified it with what he had just discovered in the Spleen and had described under the name of Lienin -

Besides the crystalline appearance of Leucin already mentioned by which it may be readily recognized - the following is its characteristic reaction -: When treated with H,NO_6 on a Platinum plate and warmed Leucin dissolves without colour, leaving a residue of a glancing aspect -; if NaO,HO or KO,HO be applied to this and evaporated gently over the flame, still no colour ensues, but the substance draws itself into the form of Oil-drops, which is the proper reaction.

Tyrosin, which shows itself under the Microscope in the form of fine needles, gives when treated with NO_6,H in the same manner and evaporated, a greenish yellow spot - on addition of NaO,HO the colour

※ Verhandlungen der Phys.-med. Gesellschaft zu Würzburg - 1855.

the colour becomes reddish yellow and when heated passes into a dark brown -

Hypoxanthin gives with NO_3H a sulphur yellow colour when evaporated, which is smooth, (but not glancing like that of Leucin) - add NaO, HO, and a beautiful red appears, which on heating assumes somewhat of a violet hue -

Such are the chief points connected with the History and nature of these Extractive matters considered per se -: they are generally looked upon as products of the decomposition of Proteine or Albuminoid substances - but as to their specific origin and probable relation to the Change of matter within the Organism we are still of course completely uninformed -

Taking for granted that Leucin and Tyrosin (for of them chiefly we speak) are constant elements of those of the normal Animal fluids, as has been rendered all but certain with regard to the Pancreatic fluid, by the researches of Kölliker and H. Müller, the question may arise - Are they present as secretions or as excretions? Are they poured out temporarily into the cavity of the intestine for the purpose of aiding in the process of digestion, or finally, to be extruded with the faeces? or again - if not (active agents) (immediately in this respect - are they incidentally present in virtue of a function exercised previously in the formation of the Pancreatic fluid, as Heinrich and Haeckel supposed them to minister to the formation of the Bile? Answers at all desirable -

Factory

※ Loc. cit.

✡ Loc. cit.

⊕ Physiol.-Chem. Untersuch. über die Verdauungssäfte u. den Stoffwechs

∧ Untersuch. über die secr. des Bauchspeich. Inaug. Dissert.

† De Lacte puae. Dorpati 1834.

Satisfactory to these Speculative Questions cannot be even broached in the present State of our Knowledge of these Subjects -

II - Of the Pancreatic Juice - : — While the results of recent investigations as to the Role which the Pancreatic Secretion plays in the process of digestion are somewhat perplexing, it is Satisfactory to think that we have, at least, by the way, attained to some degree of Certainty with regard to the Nature of the Fluid itself and the laws of it's Secretion. *De Graaf imagining that the Secretion ought to be constant and in Equal quantities at all times - endeavoured to account for the origin of Intermittent and other fevers by Abnormalities in this respect - Modern observation has shown that in this supposition he was completely wrong - for *Bernard @Bidder & Schmidt, ^Weinman, †Kroeger and others, who have experimented for the purpose of collecting the fluid, all agree that Active Secretion only takes place during digestion or with the presence of some Special Stimulus in the Stomach - And that during the intervals of digestion it either altogether or almost entirely ceases. The Gland itself, during fasting, appears of a pale yellow colour - relaxed and withered-like - after feeding on the other hand it is found to be turgid and of a dark red colour as if intensely hyperaemic - The Secretion is accordingly in the former State, given off very sparingly - only in drops at considerable intervals - While in the latter it sometimes flows in a continuous stream - Relative to this matter Weinman inducted the following General Laws

from

from a series of Observations made on dogs in whom he had established a Pancreatic fistula: —

1° That the Secretion is continually going on; — yet

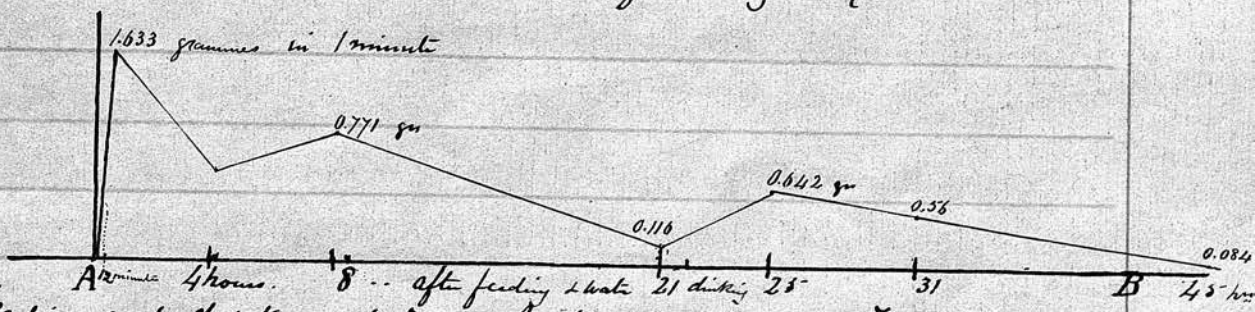
2° Not with equal vigour at all times — for it varies: —

3° Reaching its <u>Minimum</u> (a) after long fasting; (b) after vomiting; (c) from the effects of the Operation of establishing the fistula

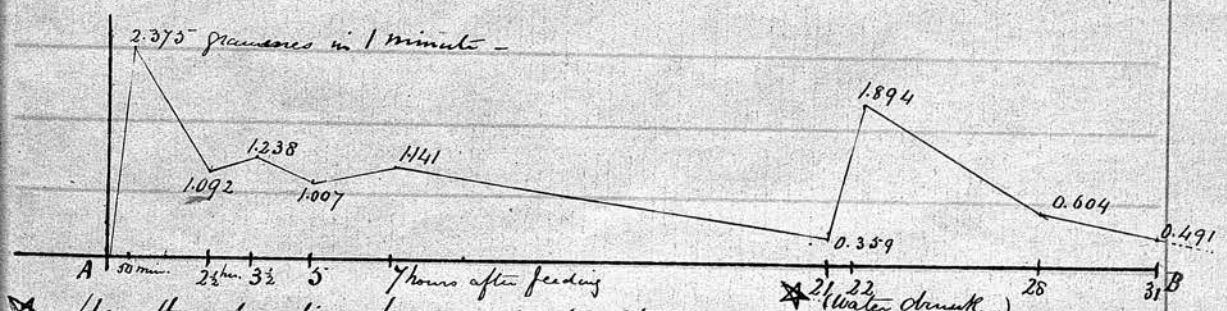
4° Reaching its <u>Maximum</u> after feeding — and moreover after drinking water

It was observed to reach its Maximum in one instance in 12 minutes after feeding, in another in 30, and in a third in 13 minutes

By referring these to <u>axes of Coordinates</u>, the Variations in the Secretion are readily illustrated in the following way.



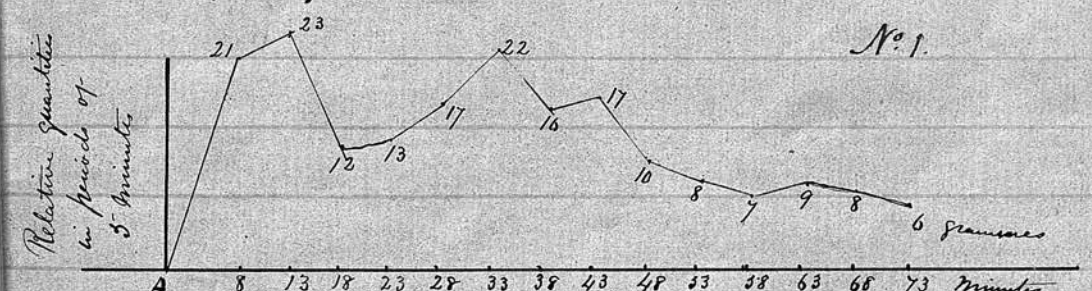
Feeding and drinking at A and fasting till B — : The quantities of the Secretion as given in <u>one minute</u> at the Specified periods, are marked in <u>fluid grammes</u>; —

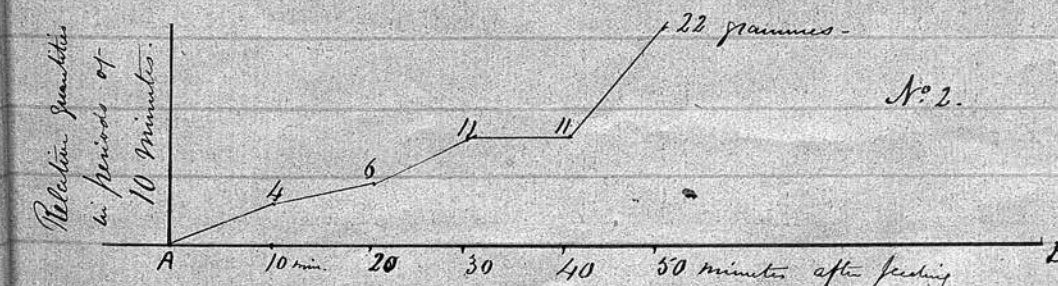


☆ Here the Secretion having reached its Maximum in 50 minutes after

After feeding - was diminishing rapidly towards its minimum, when at the 21st hours - the Animal having drunk some water - the secretion suddenly rose again in quantity nearly as high as after feeding - This phenomenon as well as that of the sudden decrease of the secretion after Vomiting or from the effects following the establishment of a Pancreatic fistula leaden it highly probable that the immediate exciting cause of the secretion is a reflex nervous action, dependent upon the presence of alimentary matters in the stomach - It was found by Bernard that galvanism applied to the Solar ganglion would not increase the flow while the presence of Ether in the stomach in the same animal had decidedly this effect. With regard to the anatomical relation of the nerves to the secreting structure of the Pancreas we are as yet unacquainted. —

Again following the same plan - we have the relative quantities secreted in equal successive periods - thus : —





※ Loc. cit.

The total quantity of Pancreatic Fluid secreted in a day – has been variously estimated by Bidder & Schmidt – Weinman – Krüger – *Kölliker & Müller and other Observers: – and while some of these closely approximate to each other – others are widely different – Thus: – Bidder & Schmidt having introduced a Canula into the Ductus Choledochus immediately before its entrance into the Duodenum – the following quantities were obtained – the Animal (a strong dog weighing 20 Kilogrammes) having previously eaten copiously of flesh.

	Grammes	
In 1 hour – 15 min –	1.614	The whole animal gave
– 1 hour – —	1.528	Afterwards in
2 hours – —	2.131	in 1 hour – 0.9527 grammes
1 hour – 30 min.	1.108	∴ By the proportion
2 hours – 30 min.	1.480	then is produced for
Total in 8 hours – 15 min	= 7.860	1 Kilog. per hour 0,0476 Grammes.

Adding to this what must have flowed from the Ductus Choledochus whose diameter is to the greater 1 : 3 and whose Calibre ∴ 1 : 9 nearly And also reckoning that only one half of the Secretion was allowed to flow out of the gland we have roughly – in 8 hours about 16 grammes. and ∴ in 24 hours about 48 Gr. Hence they calculate that a full grown man weighing 64 Kilogrammes secretes about 150 grammes of Fluid per diem. Bernard's Observations agree with these nearly – On the other hand Weinman found that for each Kilogramme of total weight of the animal

there is

there is secreted 1.466 grammes per hour - which is an very much higher proportion than the previous one - Thus -

		per hour	Calculated per diem
Kröger obtained from a dog (Wt. 9 Kilogs.)		43.952	1054.84 grammes
— — — —	dog (Wt. 18 Kilogs)	50.348	1208.35 —
— — — —	dog (Wt. 26 Kilogs.)	70.120	1682.88 —
Weinman — from a small	dog	18.06	433.44 —
— — —	dog (Wt. 30 Kilogs.)	43.98	1055.52 —

These observations, it is to be remarked, were made not immediately after the establishment of the fistula - And it is a fact, which Bernard first called attention to, viz. that for a short time after this operation the secretion remains normal - then that, for some time, it becomes immensely increased in quantity and at the same time of low specific gravity - and finally, if the animal survive, returns to its original state - This doubtless is the explanation of the difference - and therefore we hold the calculation of Bidder & Schmidt - which nearly agrees with that of Bernard, as the correct one - Whatever be the absolute quantity of the fluid secreted - we should probably find, on comparing these widely different figures, that the absolute quantity of solid matter, secreted within a given time, is the same in both cases. Thus Kölliker & Müller who agree with the above calculations of Weinman & Kröger, found that a dog weighing 18 Kilogrammes secreted 691.84 grammes of fluid - whereof 14.153 grammes were solid matter - the rest fluid - On the other hand Bidder & Schmidt

& Schmidt calculate that 0ut of 150 grammes of fluid, no less than 15 grammes are solid matter - It is therefore an induction to which all physiologists yield assent that "the concentration" "of the Pancreatic fluid on the whole is in inverse ratio to the" "quantity of the secretion in a given time."

The Characters of the Normal Pancreatic Juice are the following: - ✱ It is a completely clear, colourless, viscid, transparent fluid without odour, - having a slightly saline taste analogous to that of blood serum - It reacts strongly alkaline - coagulable almost en masse by Heat & strong acids (e.g. Nitric and Sulphuric) — Metallic salts - gall nuts - and alcohol of 85° per cent precipitate it - While weak organic acids have not this effect and do not sensibly disengage Carbonic acid - Alkalies hinder the precipitate and re-dissolve it when formed. The flocculent precipitate given with alcohol, when washed out and re-dissolved in water to a fluid of the consistence of the original is found to have all the digestive properties of the Pancreatic fluid itself and contains besides Organic matter a small quantity of Carbonate of Lime. —

The Specific Gravity of Normal Pancreatic Juice, from the dog is stated by Bidder & Schmidt (at +15° Centigrade in vacuo) as 1.0306 & by Bernard (at 10° Centigrade — —) as 1.0401

When examined under the Microscope, it exhibits no morphological elements - except now & then epithelial cells in process of

* Hist. de la Dégestion Paris 1825.

of solution. It is exceedingly liable to undergo decomposition Bernard found that it can be kept however for a considerable time, [redacted] if preserved at a temperature below +10° Centigrade but that above this it soon begins to change — losing its transparency and forming a flocculent precipitate — which under the microscope shows nothing peculiar — Chlorine precipitates it when fresh, but develops no peculiar colour — When it is somewhat decayed the precipitation is less complete and at the same time a red colour is formed, which disappears on excess of the reagent — When the decomposition has advanced some way, this colour is no longer produced by Chlorine but is by H,NO_6 —

The relative quantities of solid matter in the Pancreatic Juice has been variously stated by different observers — and this is, no doubt, (as already remarked) mainly dependent on the state of purity or concentration of the fluid obtained — as well as on the kind of animal from which it was got —: — Thus — —

Liedemann & Gmelin found the proportion in the dog to be 8.7 per cent. of the whole

— — — — — — — — — Sheep from 3.7 — 5.2 — —

* Lenret & Lassaigne — — — — — — horse 0.9 per cent

Reichs — — — — — — — — — — — — ass — 1.62 p.c —

Weinman — (when Secretion small, reach a maximum) dog 3.6 p.c

Kolliker & Muller — — — — — — dog 2.11 p.c

Bidder & Schmidt (Observ.tn 1°) — — dog 11.56 p.c

— — — — — (Observ.tn 2°) — — dog 9.924 p.c.

Accepting therefore the data of Bidder & Schmidt as probably correct - we may roughly estimate the proportion as 10. per cent - A Quantitative analysis of this gave the following results: - In 1000 parts of normal Pancreatic Fluid there is contained -

Water - - - - - - - - - - - - - - - -	900.76 parts
Solid matter (not evaporated at 120° Centg.)	99.24 - -

Of these -

Organic
- Insoluble in Alcohol
  - Re-soluble in Water - 64.25
  - not re-soluble in HO - 4.00
- Soluble in Alcohol - 22.12

Inorganic.

Chlorine	4.47	KO, SO_3	0.02
SO_3	0.06	NaO, SO_3	0.00
PO_5	0.24	NaCl	7.36
K,	0.01	2NaO, PO_5	0.45
Na,	3.32	NaO	0.32
O (of alkalis)	0.13	CaO	0.22
CaO,	0.22	MgO	0.05
MgO,	0.05	Fe_2O_3	0.02
Fe_2O_3	0.02	Total	8.54

Here we find the Inorganic matter equal to about $\frac{1}{12}$ part of the Whole Solid matter - While of the 1.62 per cent of solid matter found by Frerichs as the proportion in the Pancreatic fluids of the Ox - not less than 1.1 was Inorganic or about $\frac{2}{3}$ of the whole - Again of the 14.153 grammes of Solid content found by

Kölliker

* Archiv für Pathol. Anatomie &c. (Virchow) Band XI. Heft 1. 1857.

Kölliker & Müller in 691.84 grs. of Fluid – 6.083 were inorganic – (the last organic) or about $\frac{1}{2}$ nearly – Thus showing that Abnormal Pancreatic Juice diminishes in Specific gravity by a deficiency in its' Organic Elements – And since it is from these elements that it derives it' active digestive properties – the phenomenon is thus explained, Why such diluted fluid exhibits so feeble digestive power, even when the Inorganic salts are not absolutely diminished or very slightly so.

Among the Organic elements, there exist besides Common Albumen – also Leucin & Tyrosin – as has been distinctly demonstrated by Kölliker & Müller &c &c – Also Bernard found certain peculiar crystals which he took at first for crystals of Stearine and Margarine – but which on further examination proved to be Lactate of Lime – So that Lactic acid is present. Special attention however having not been given to this particular ation of these elements we still are uninformed of their quantity &c Besides these elements normally present in the Pancreatic secretion Hoppe has recently noticed the occurrence of Urea in it – in one instance – This case was that of a patient who died in the Charité (Hospital) in Berlin with symptoms of icterus – in whom – on section – besides distension of the Gall bladder and duct – Also the Pancreatic duct was found cylindrical and in some of it chief branches even widened into Ampulliform sacs which were found to contain a nearly gelatinous clear fluid – Of this 5.655 Grammes were collected

And Analyzed - giving the following results -

Element	Found - (Grammes)	Proportion
Urea	0.007	0.12 per cent
Fatty Matters	0.001	0.02 "
Alcohol Extract { Leucin / Na Cl }	0.049	0.87 "
Watery Extract { Tyrosin / & Na Cl }	0.030	—
Insoluble Residue	0.028	0.49
Inorganic Salts	0.032	0.57
Total Solid Matter	0.147 Grammes	= 2.60 per cent
Water	5.508	= 97.40
Pancreatic Juice	5.655 Grs.	100.00

This is to be regarded however as an abnormal fluid - yet here we may observe the remarkable fact already noticed - viz. that while the total amount of solid matter is only about 2½ p.c. of the whole fluid - (or only one fourth of what we consider with Bidder & Schmidt as normal) - this decrease is entirely on the part of the organic elements - for if we add to the inorganic salts the Na Cl - from the Alcohol & watery solutions - we bring the quantity of inorganic matter up to about 1.— p.c. of the whole ~~fluid~~ which is exactly that found in normal fluid —

With these remarks on the Physical and Chemical characteristics of the Pancreatic secretion - we now pass to the

Consideration

* Comptes rendus de l'Acad. des Sciences Naturelles —

Consideration of its action on the chief Alimentary principles.

III. Of the Functions ascribed to the Pancreatic Juice as a Digestive Agent.

These we shall divide into two - viz.

I°. Its action on Carbonaceous Substances - including
A. Starch and B. Fatty matters -

2°. Its action on Azotic or Nitrogenous Substances - including
Albumen, Fibrine, Casein &c -

1°. With regard to the first of these viz. its action on
A Starch - Valentin appears to have been the first to discover that this Fluid possesses the power of rapidly causing the transformation of Starch into Dextrin & Grape sugar And all subsequent observations (Bouchardat & Sandras &c &c) have confirmed this. This action which it possesses in Common with the Saliva (discovered by Leuchs - Poggendorffs Annalen 1832.) as well as with Fibrine, Gluten &c other Animal Substances when undergoing decomposition - is, however, much more energetic than ~~with~~ any of these others - Moreover, while the Saliva does not possess this property of itself, but seems to require the Commencement of decomposition to its development - the Pancreatic juice alone Contains the ferment originally - and at the same time its action is much more speedy than in the case of any other Substance possessed of the property - Thus Fleriches found

that

that ordinarily the action is completed in 1½ hours - And that on mixing equal quantities of Starch solution (Concentrated) and Pancreatic fluid - the whole became almost instantly more fluid - reacted alkaline - and reduced the Tartrate of Copper test, immediately and completely - While no blue colour was given with Iodine - This action was not impeded by the presence of Gastric fluid & Salt in the mixture - Bernard further found that when Starch has been transformed into Sugar by the action of any of these other substances - (e.g. Saliva &c) - and the decomposition of the mixture is allowed to proceed - in all, the Lactic fermentation is the result (viz. with disengagement of H & N gases) - which in that with pancreatic fluid alone, does the alcoholic take place.

In passing on to the action of this fluid on the next class of substances viz. B - Fatty Matters - we enter upon a subject about which so much dispute exists - and upon which so much has recently been written that to discuss fully all the experiments performed, and all the arguments used to prove the truth of contending opinions, with regard to it - would vastly exceed our present limits - We propose therefore, to refer only to the more important of these in so far as they serve to prove or disprove the doctrine held by M. Bernard on this matter - And here I beg to state, that as these experiments instituted to try this proposition, have been performed on such a scale and with so extreme care - by men of the most

practised

* Physiol. der Verdauung. p. 78.

practised skill – I have not attempted to repeat any of these
from myself – convinced in the first place – that any such results
would be of little value compared with the facts already laid
down by theirs;– and secondly that enough has already been
done, by way of experiment, to guide us, on a fair consideration
to a proper conclusion on the subject.

While the difficulty of accounting for the passage of fatty mat-
ters through animal membranes by the ordinary law of Osmosis
had long ago occurred to Physiologists – nothing was calculated
to be received with greater interest by them than the discovery
announced by Eberle in 1834 – that the Pancreatic Juice pos-
sesses the power of emulsioning them and so directly removing the
difficulty to their absorption. Unacquainted with Eberle's researches
M. Bernard shortly afterwards from numerous experiments made
with this view – arrived at a similar conclusion with regard
to this use of the Pancreatic fluid – In the course of these
experiments he has sufficiently established the fact that 2 parts
of fresh Pancreatic Juice mixed with 1 part of oil, Butter or
Lard form an emulsion completely (when shaken together) &
that this emulsion is not subsequently destroyed on standing.
Compared with this, he found the action of Bile and Intestinal
Mucus much less prompt in this respect – emulsioning a much
smaller quantity of fat, while at the same time it is less com-
plete and less persistent when formed – This emulsioning property
is in

is in direct ratio with the Sp. Grav. of the Fluid – a fact, which is of the utmost importance, in considering the relative value of the results obtained by different observers. Further, in the living body, Bernard found that the Chyle vessels begin to assume a white milky aspect, and Fat to be emulsioned, just below the point where the Pancreatic duct opens into the duodenum. In confirmation of this, when both ducts were tied in the dog, Fat was found in the bowel unchanged – and the Chyle vessels were no longer of a milky aspect.

Again, M. Bernard, observing that tho' an alkaline reaction exists at the time of forming such an emulsion, by and bye an acid reaction is developed and, when fresh butter was used, that the odour of Butyric acid is evolved, holds the opinion that the action of the Pancreatic Fluid on Fatty matter in digestion is to separate the Fatty acid from it's base – as well as form an Soap with the former – in which state alone he holds that it can be absorbed. These doctrines are founded (as already stated) upon numerous experiments – of which the following are examples.

Experiment No. 1 (in conjunction with M. Berthelot) – 8.7 Grammes of fresh Pancreatic Juice were mixed with 6.5 grammes of Oil (Olive) – An emulsion took place instantly, reaction alkaline – 3 hours afterwards, it was distinctly acid – next day still more so – After 48 hours standing in the cold, it was agitated with

with Ether – a flocculent White matter separating – The Ether solution was separated and evaporated in the Sand bath – the residue treated with alcohol and filtered – This filtrate treated with NaO, CO_2 was entirely saponified in the Cold This soap further treated with HCl gave a White fatty acid – solid – spongy, which boiled with HO did not fuse, but when heated more strongly at last fused into small liquid drops. The Glycerine was separated in the following way – The liquid after decantation of the Ether solution and extension in water was then filtered to separate the undigested from the emulsioned part of the fat – This was then evaporated in the water bath to dryness, in presence of an excess of Oxide of Lead – and the residue treated with absolute Alcohol cold – This was extended in water, treated with HS, filtered and the filtrate again evaporated to dryness in the water bath – from which was obtained a syrup, slightly sweet – then saline in taste – leaving no doubt from its characters as to its being Glycerine.

The emulsion with Albumen of the Egg was found to cause this acidification too – While no such action could be obtained with the parotid or submaxillary Saliva – nor with Bile even though the mixtures stood 9 days. With the Gastric Juice not even an Emulsion was formed. In these experiments it was sought to separate the fatty acids (taking

for granted

for granted that they were set free) but only the mono-butyrine was found unchanged.

Experiment. No. 2 - An artificial anus having been formed in a dog - about 60 centimetres below the opening of the duct (Pancreatic) and the animal kept fasting - on the 31st day after 32 centilitres of Lard were injected into the stomach by the mouth and 20 centilitres into the bowel below the anus - On killing the animal 4 hours afterwards - the Chyle vessels all along the Duodenum and Small intestine (above the anus) were found White and gorged with emulsioned fat - While, below the anus, the mucous membrane was contracted and the fat found lying on it in statu quo - the Chyle vessels being not at all White or only slightly Opalescent -

From these and many similar Experiments M. Bernard concludes "that the Pancreatic fluid is absolutely indispensable" "to the Emulsion & Absorption of Fatty Matters."

With regard to their acidification in the living body - ——

Experiment. A dog having been fed on Mutton fat for 8 days (120 Grammes per diem - last day 240 Grammes) was Killed by section of the Rachidian bulb - The Chyle in the Thoracic duct was found not acid - Contents of Stomach & Small intestine acid - Hence he concludes - "that this decomposition (into acid & base)" "is not, perhaps, necessary to the digestion of fat - that though" "it be formed in the intestine it may be neutralized in the Chyle by

the Bile

"the Bile or Pancreatic Fluid itself." Moreover it is the opinion of Bernard that the Absorption of fat cannot take place in the Stomach or large Intestine but only in the small Intestine Whether from peculiarity of the lining Epithelium or of the termination of the Chyle vessels is uncertain. In the Opinion above stated, regarding this function of the Pancreatic fluid M. Bernard became confirmed by his experiments in Extirpating the pancreas. In 9 such experiments performed on dogs all died of peritonitis except the last - this one having survived the Operation, which consisted in destroying the Pancreas by injecting the ducts with Lard, began to eat on the 3rd day after and was fed on food containing a large quantity of fat His excrement showed always an oily envelopement which became solid on cooling - the whole decolorized of a clay colour - and other matters undigested - When flesh had been eaten - the excrement was very foetid - with potatoes no odour at all - but starch was detected with Iodine - part of the starch however had been digested, for Starch sugar was found afterwards in the bowel - On the 17th day following the Operation, he began to get more lively, and still more so till the 22nd - Showing a tendency to return to his normal state. On the 24th he was fed with food containing fat - and then Killed - The Sections Showed the following - - (a) Stomach filled with aliments partly softened - acid reaction - walls normal - (b)

in duodenum

(b) in duodenum nothing particular – some fat partly emulsioned (c) in ileum intestine – reaction alkaline (opposite of Normal) wall not much altered – (d) in large intestine & Coecum a fine blood exudation on the surface, with small ulcerations. Pancreas – much diminished in volume – both horizontal & vertical portions – duct dilated containing a gummous substance like coagulated milk – not completely obstructing the passage. – part of the gland in the centre still entire, which had secreted some juice into the bowel by the small canal. Liver – sound – duct widened – decoction contained much sugar. Besides this experiment – M. Bernard – brings Pathological observation in support of his Theory – viz: 1°. Case quoted from Lloyd & Elliotson (Med. Chir. Trans. Lond. vol 18. for 1833) 2°. American case reported by Dr. Gould (Anat. mus. Catalogue of Boston Soc. for 1847) 3°. Dr. Bright's Cases (Lond. med. Chir. Trans. vol XVIII) – Also 4°. Case reported by Mr. A. Clarke to the Lancet Aug. 15th. 1831) — In all of which, the symptoms during life were – emaciation and voracity – discharge of oily matter with the stools (which became coagulated on standing) after food containing fat – stools of a pale clay colour – bloody stains – all as observed in the above experiment – From these facts M. Bernard concludes that the extraordinary phenomena observed in these cases which, he says, were not at all understood by their observers at the time

* British & For. Med. Rev.; Vol

⊗ Loc. cit.

at the time, are now clearly and sufficiently explained by referring them to a disease of the Pancreas - Now, as Dr. Gairdner has pointed out,* the diagnosis arrived at by Dr. Bright in the cases reported by him, was, by a singularly ~~faithful~~ exclusion of all other causes, exactly this, viz: that the phenomena in question must be attributable either to disease of the Pancreas or upper part of Small Intestine - and on reviewing the objections of M. Bernard's opponents on this theory of Fat digestion, we shall find that this diagnosis is now fully borne out by modern observation than even the opinion of M. Bernard - above expressed.

While all observers agree with Bernard as this property possessed in an eminent degree by the Pancreatic fluid of emulsionizing Fat, by far the greater number of them however dissent from the opinion that it is the sole digestive agent in this respect -: for, on the one hand, others of the fluids secreted into the Alimentary Canal have been clearly proved to possess a similar property though comparatively in a minor degree - and on the other hand - it has been found that Fat can actually be emulsioned & digested without the intervention of the Pancreatic Fluid -

Thus in the first place - Bidder & Schmidt found that an emulsion can be formed with Bile as well as with the Intestinal mucus - And that this emulsion was not destroyed by standing - Bernard having failed to accomplish this with Bile by using too little of it and not having experimented at all with the Intestinal Fluid -

Again

✡ De adipis concoctione et absorptione 1831.

⊕ (Verdauungsäfte u. den Stoffwechsel) -

T (Physiol. der Verdauung - Wagners Handwort.)

I (Physiol. des Menschen. -

⁂ Physiol. Chemie -

Again Lenz, Bidder & Schmidt, Heriehs, Dowders & others by many and varied experiments have shown that Fat is emulsioned and absorbed when absolutely no Pancreatic fluid was present in the bowel. Thus Lenz & Bidder in a series of experiments on ~~dogs~~ cats, having tied the Pancreatic duct - and then waited 3 or 4 days so as to allow any Pancreatic fluid in the bowel to be Absorbed, injected melted butter into the stomach of the animals and found at least in 9 cases out of 33 - ~~the~~ the Fat absorption perfectly distinct - the Chyle vessels and Thoracic duct being filled with a milky fluid which was found to be emulsioned fat. In the other cases there were, in general, traces of the absorption - and the partial failure in these - as well as in Bernard's similar experiments - is attributed by Lenz - and also by Heriehs to the inflammation induced by the ~~operation~~. Further, - Bernard's experiments on the rabbit, which was performed in presence of a Commission of the French Academy (Magendie, Edward & Dumas) - was repeated several times by Lenz along with Bidder and Schmidt - but with different results from Bernard. - In the first of these - 6 hours after feeding with fatty matter - ~~the~~ none of the Chyle-vessels above the entrance of the Pancreatic duct (which in the rabbit enters 35 Centimetres below the Common Choledoch duct) were found White - below this much White - The 2nd experiment agreed with Bernard's - The 3rd, when the animal was killed 4½ hours after feeding yielded similar results with the first. Lehmann obtained similar results in the same experiment - and hence Lenz concludes that

☆ Loc. cit.

● Physiol. des Menschen. (Bedauung.) p. 260.)

✻ Gazette Med. de Paris — Avril 1837 - Tom XII. idem
Bulletin de l'Acad. Imper. de Med. 1837.

that Bernard failed to observe them White Chyle-vessels above the orifice of the duct from waiting too long, or until they had been again emptied of their contents - Bernard however states that he found, in his cases, fat, Milk in the Stomach and bowel above the duct - and argues that the appearances observed by Leuf* was due to Pancreatic fluid - which had flowed toward the Stomach - With this suggestion* Dowders cannot agree for when he injected fat into the Stomach of the rabbit every 2 hours - 4 or 5 times in succession - he Milk found White Chyle vessels above the orifice of the Pancreatic duct - while evidently no flow of Lymph could in this instance have taken place towards the Stomach -

Finally, the results obtained from the extensive experiments of M.M. Bérard & Colin, during the last year - acting with others as a Commission of the French Academy appointed to inquire into the subject, appear to me to have completely put an end to all doubt in this matter - leading to the conclusion that "though" "the Pancreatic fluid may be necessary - yet it is not" "indispensable to the Emulsioning & Absorption of fat in" "the Organism" - These experiments of M.M. Bérard & Colin, which have been conducted on a most extensive scale - including both Carnivora & Herbivora - no fewer than 36 dogs, 3 horses, 3 bulls and 4 cows having been used - (besides many other dogs & other animals since) - have been performed either by diverting the Pancreatic secretion by establishing a fistula - or

by

39.

* Bulletin de l'Acad. Imper. de Med. 1854.

by extirpating the gland altogether -
Thus in one Experiment upon a Bull - a Pancreatic fistula having been established so that not a drop of the fluid could pass into the Duodenum - the Animal ate and ruminated as if nothing had happened - It having been previously observed that in only 4 out of 14 cases, a very small accessory duct joined the Ductus Choledochus - it was presumed that none existed here - And in order to remove any suspicion of digestion being carried on by any Pancreatic fluid still in the Duodenum - it was waited till the third day after the formation of the fistula - When - the Animal having eaten of oleaginous vegetables - One of the great branches of the Thoracic duct having been opened and a Silver Canula introduced - in 24 hours, 40 litres of Chyle (White) were obtained which on being dried and analyzed by M. Wurtz was found to contain 11 per cent of fatty matter -
Still more conclusive if possible are the results of the Experiment for extirpation of the Pancreas - This was practised in many instances by M. Colin on Young Dogs - and in nearly all successfully - the whole gland being destroyed - The animals not only survived the Experiment but were observed to thrive and gain greatly in weight, like others - as they grew older - The same Experiment was repeated on pigs - and in all the results were sufficiently clear to prove that the Theory of M. Bernard is untenable - We doubt not however that the Pancreatic Fluid

though not

⁂ Bulletin de l'Acad. Supér. de Med. Nov: 1837

though nor absolutely indispensable, is yet accessory to the emulsioning and absorption of Fat. This we might be led, a priori from its composition, to expect - for it abounds both in Albumen and Alkalies - either of which have individually the power of forming an emulsion with fatty matter. It is a well known fact observed first by Aschenson (Muller's Archiv for 1840. p. 49) that when fluid fat & fluid albumen are shaken together - an emulsion is formed - The same takes place by using a solution of an alkali or alkaline carbonate instead of albumen - Thus ※ M. M. Leaned & Mousel have recently shown that 5 Centigrammes of Carbonate of Soda or Potash are sufficient to emulsion permanently 8 grammes of oil in 100 grammes of distilled water - And of this fact I have assured myself - not quantitatively - but of the fact generally - that a few drops of a solution of KO, HO added to a few drops of melted butter or oil extended in distilled water - cause this to form an emulsion. Now the Pancreatic fluid is not only the richest in albumen of the Digestive fluids - but also has the strongest alkaline reaction - in virtue of which it ought to be the most powerful emulsive agent.

So much for this quoad vim - We come now consider

2°. The action of the Pancreatic fluid on Azotic or Nitrogenous substances - A function, which has been denied by ~~Bernard~~ who have experimented with regard to it - but which on

Careful

☆ Gazette Hebdomadaire. Avril et Mai. 1834.

⊕ Loc. cit.

※ Koreff's notizen – tom. I. 214.

Careful consideration of the Experiments and Results recently made known by M. Corvisart — as well as from my own observation — I am inclined to believe to belong as much to this substance as either of the functions already noticed. To conclude the existence of such a function we might be led a priori — For how can we account for the much greater comparative size of the gland in Carnivora than in Herbivora unless we suppose some other function to belong to it than those already discussed — (the pancreas in the Rabbit weighing only $\frac{1}{600}$ part the weight of the whole body — while in the Cat it is $\frac{1}{300}$ part — exactly double the other in proportion) Moreover Bidder and Schmidt observed that, in the case of dogs when the pancreatic duct had been shut for some time, the contents of the thoracic duct did not as usual coagulate in a few seconds but required several hours to do so — and even then this was incomplete — As the digestion of Nitrogenous substances has generally been referred exclusively to the stomach — in virtue of its acid reaction — tho' Eberle (Physiol. der Verdauung p. 78) had announced that a liquid prepared from any mucous membrane whatever and acidulated with HCl or Ac, will dissolve animal substances as well as Gastric juice — and Purkinje & Pappenheim had discovered the same property in an acid solution of the tissue of the pancreas — yet these observations have been allowed to remain undeveloped — And the above observation

⁂ Memoire sur le Pancreas.

☆ Gazette Hebdomadaire - Avril & Mai 1857 -

Observation of Bidder and Schmidt did not lead them to any further inquiry as it might well have done. * Bernard indeed found that Coagulated Albumen is dissolved by the Pancreatic Fluid - but as the Solution soon passed into a State of decomposition, he considered the action a simple putrefaction - Casein and Gluten he found also to be soluble - and that without putrefying - but nevertheless, no special notice was given by him to this action, engaged as he was with its action on Fatty matters. ☆ Twelve months ago however M. Corvisart published his researches on this subject - the results of which go to prove that not only is the Pancreatic Fluid a digester of Albumen and Fibrine - but is more powerful in this respect than the Gastric Juice or any other Fluid of the Animal body.
1° With regard to the digestion of Albumen he found that
"The Pancreatic Fluid dissolves and transforms Coagulated "
"Albumen from the Egg exactly like the Gastric Juice into "
"Albumino Peptone ; the two digested products appearing "
"identical in their properties, in spite of the different agents "
"to which they owe their origin - The following are examples
of his experiments for determining this -
1st Experiment - A young dog weighing 15 Kilogrammes, having been kept fasting for 24 hours previously - had his abdomen opened without wounding the Pancreas - The duodenum was cleansed with a stream of water at 38° Centig. - thrown in by an opening at its

at it' upper end and allowed to escape by another at the lower end – Communication with the stomach having then been intercepted by a ligature placed round the pylorus – 78 grammes of boiled, absolutely insoluble albumen were introduced by the lower Opening into the duodenum which was then closed by a ligature. – 18 hours afterwards the animal was killed by strangulation – there was found 325 Cub. Centgrs. of fluid (alkaline reaction) in the bowel, with morcels of albumen floating in it, undissolved – On weighing these and deducting from the original – it was found that 50 grammes had been dissolved – Besides the Pancreatic juice, there must have been present Bile & Intestinal mucus in small quantities – as the former could not be detected with NO_3 –

2nd Experiment – Similar to the above – dog weighing 22 Kilogs. received 65 grammes of Coagulated albumen whereof 55 were digested. In this case the Common Bile duct was tied –

Further – Artificial digestions were made with infusions in water of the Pancreas of each of the above dogs, ~~from~~ These digestions were carried on for 5 hours at a temperature of 40° Centig. And the result, as in 8 several such experiments, was that such an infusion of the tissue of the Pancreas, dissolved from 40 to 50 grammes of Coagulated albumen – The same result was obtained – when from such an infusion the active principle was isolated by HS or alcohol – and this re-dissolved in water

used

* Corrosivo Sublimato.

used as the digestive agent. It has been already stated that Albumen dissolved is identical in Character with the Albumen transformed into Albumino-peptone by the Gastric Juice - i.e that the action is not simply Solvent but digestive - Among other points of resemblance between the two products of digestion - they are both found to deprive Grape sugar of the power of reducing the Tartrate of Iron & potash - a fact first discovered by Longet with regard to the Albumino-peptone of the Stomach and hence called Longet's test - Comparison of the two is made in the following Table -

Reagents / Reaction	Albumen digested in the Stomach — acid Liquid	Albumen digested in Neutral Pancr. Juice — Neutral Liquid	Alb. digested in acidified Pancr. Juice — acid Liquid
KO gave	nothing	nothing	nothing
$A\bar{c}$ —	nothing	nothing	nothing
NO_5 —	nothing	nothing	nothing
acide picrique	nothing	nothing	nothing
Al_2O_3, SO_3 —	nothing	nothing	nothing
$PtCl_2$ —	nothing	nothing	nothing
$\ddot{H}gCl$ —	precipitate	precipitate	precipitate
$PbO, A\bar{c}$ —	precipitate	precipitate	precipitate
AgO, NO_5 —	precipitate	precipitate	precipitate
Longet's test —	nothing	nothing	nothing
Bile —	Troubling or precipitate soluble in excess	nothing	Troubling or precipitate soluble in excess
Aspect before filtering	milky	Lymphy	Lymphy

N.B. The quantity digested by acidified Pancreatic fluid is somewhat less than by neutral fluid or alkaline - And the Albumen of the blood is not quite so readily digested as that from the egg. Of the latter, it was found, that 100 Grammes of Gastric Juice could digest 30 grammes - the pancreatic fluid or infusion of the Pancreas from the same animal could digest at least 40 grammes.

2°. Fibrine (of the blood) — (A.) When acted on by Gastric Juice is dissolved & turned into Fibrine-peptone: (100 Grammes of Gastric Juice being sufficient to transform 30 Grammes of Fibrin) — This is similar in properties to albumino-peptone - but differs in this respect that it is precipitated with $PtCl_2$ If the Fibrine be in too great quantity for the Gastric Juice - it may be all dissolved while the digestion is not entirely accomplished - being coagulable by heat, like albumen in like cases.

B. Fibrine acted upon by the Pancreatic fluid turned singly into the duodenum during an experimental digestion - as above - or the watery solution of an entire pancreas in an artificial digestion - is dissolved and transformed to the extent of about 30 grammes. — This transformed fibrine has a striking resemblance to that similarly changed by the Gastric Juice - while both resemble albumino-peptone in hindering the reduction of Lougets' test.

The resemblance between fibrine variously digested may be observed by reference to the following table of their reactions -

Reagents / Reaction	Fibrine digested by Gastric Juice - acid -	Fibrine digested by Pancreatic Fluid - (Acidified) -	Fibrine digested by Pancreatic Juice - alkaline
Longet's test	not reduced	not reduced	not reduced
KO, HO	nothing	nothing	nothing
$NO_5 H$	nothing	Troubling	Troubling
Al_2O_3, SO_3	nothing	Troubling	Troubling
$Pt Cl_2$	precipitate	precipitate	precipitate
PbO, Ac	precipitate	precipitate	precipitate
$Hg Cl$	precipitate	precipitate	precipitate
Acids pierique	precipitat	precipitate	precipitate

With these results generally my own observations lead me to agree - I took the pancreas from an ox - immediately after the animal was Killed - and having cut it down into very fine pieces - and infused it in 2 or 3 times its volume of distilled water for 6 hours at a temperature of 50° Fah. - Strained the fluid thro' a fine cloth - and into this put the coagulated albumen of an egg cut into small pieces - This mixture having been Kept for 10 hours at a temperature of 100° Fah. was found at the end of that time to contain only a very few small pieces of undissolved albumen - & nearly the whole having been dissolved - Similar digestions were made of Blood - Fibrine (freshly prepared) and Caseine (from skim-milk cheese) - nearly the same quantities of each being employed -

The fibrine

The Fibrine was almost entirely dissolved - While about $\frac{5}{6}$ths of the Caseine was also. The expressed fluid in all cases was of a faintly acid reaction - Yet When this was rendered alkaline by KO,HO the action (on Fibrin at least in which Case only it was tried) was the same - and so was the Characters of the product in both cases. The Characters of these digested products in the Case of Fibrine - as compared with that of the expressed fluid before digesting the Fibrine - are to be seen in the following table -

Reagents / Reaction	Pancreatic solution as obtained by expressing the tissues	Fibrin digested in Pancreatic solution Acid -	Fibrin digested in Pancreatic solution rendered alkaline by KO,HO
Boiling	Dense coagulum -	no change	no change -
$A\bar{c}$ -	Copious granular white precipitate	nothing	nothing
NO_6H	Flocculent & curdy white precipitate	nothing or faint mottling	nothing or very faint troubling
AgO,NO_5	almost wholly solidified and blackened	rendered somewhat gray in colour - not distinct precipitate	rendered grayer in colour but not distinct precipitate
KO,HO	nothing	nothing	nothing
$PbO,A\bar{c}$	Granular white precipitate	very faint white precipitate	very faint white precipitate
Al_2O_3,SO_3	Granular white precip.	faint gray precipitate	faint gray precipitate
Colour	reddish brown	reddish brown	grayish brown -

Again, it will be found that this table bears a close resemblance to that of Corvisart in its results - clearly establishing the fact that in this process of digestion something more than a simple solution has been accomplished -

This

This conclusion is borne out by the results obtained in the case of the Albumen and Caseine – whose characters in the manner are laid down in the following table – Compared again with those of the solution used in the Experiment.

Reagents	Aqueous Solⁿ of Pancreas	Albumen digested in Pancr. Solⁿ	Caseine digested in Pancr. Solⁿ.
Reaction	acid	acid	acid.
Boiling	Dense Coagulum	Copious fibrinous precipitate	dense granular precipitate
$A\bar{c}$ –	granular white precip.	faintly granular gray precipitate	rendered opalescent or very faintly granular
NO_6H	Flocculent curdy White precip.	slight granular precip.	slight granular precip.
KO, HO	Nothing	nothing.	nothing.
$PbO, A\bar{c}$	precip granular White	dense white curdy precip.	dense white curdy precipitate
Al_2O_3, SO_3	precip. granular White	dense granular white precip.	dense granular white precip.
K_4FeCy_6	precip. granular White	※ no precip. but changes to pale green	※ no precip. but changes to pale green
$Hg\,Cl$	precip. dense curdy white	dense granular white precip.	dense granular white precip.
AgO, NO_5	rendered almost solid & blackened.	dense granular white precip	dense curdy white precip.

※ (No precipitate at first, but changed to pale green – after standing 3 hours a troubling appeared in both – and after 12 hours a small green granular precipitate was deposited) – — From this it appears further that digested Caseine closely resembles Albumen digested by the Pancreatic solution – I have not yet experimented with this Fluid upon Gluten or any other Azotic substances besides these three – but so far as I have gone, it appears to me

to me, that no function yet ascribed to the Pancreatic Secretion has been more clearly established than this - if we are to believe the foregoing results - I endeavoured also to assure myself of this action within the organism - by performing a similar experiment to that of Corvisart's, introducing by an opening in the lower end of the duodenum in a Cat - a quantity of Coagulated albumen - and separating this from the Stomach by a ligature at the Pylorus - The Animal unfortunately died within 6 or 7 hours after the completion of the operation - (Corvisart observing his results after 18 hours digestion) - yet I found the Contents of the duodenum from being pieces of solid albumen - reduced to a soft pulpy mass - showing that the action had so far advanced towards completion -

Besides these results - let me further add, that Corvisart found 1° "that when the Gastric Juice has completely trans- "
"formed the Fibrine into Fibrine-Peptone - this is a definite "
"product which has no more to undergo from the digestive "
"influence of the Pancreatic Juice & therefore is not affected "
"by its action" - 2° that "though the Pancreatic & Gastric "
"Juice fulfil the same end in the Digestion of Albuminoid "
"matters, it is necessary that they act separately. In this con- "
"dition each fulfils its function - If they meet in the same "
"state - so far from the digested product being doubled it is "
"possible that they reduce themselves to nothing - for in each "

non-physiological

"non-Physiological circumstances the two ferments (Pepsine & Pancreatine) destroy each other" Thus 100 grammes of Gastric Juice + 100 Grs. of Pancreatic Juice - instead of digesting 13 grammes of dried fibrine - were found to digest only 5.75 grs - Again - the following experiment was performed - 6 different mixtures were formed (each containing 6 grammes of Pancreatic Juice & 12 grs. of Fibrine) with varying quantities of Gastric Juice added - Them being placed on the stove in the most favourable circumstances for digestion with a heat of 40° Centigr. - Thus -

	Grammes	Grs.	Grammes
1st mixture contained	6 of pancr. Juice	+ 12 Fibrin	+ 1 Gastric Juice
2nd	6 ———	+ 12 —	+ 2 —
3rd	6 ———	+ 12 —	+ 6 —
4th	6 ———	+ 12 —	+ 18 —
5th	6 ———	+ 12 —	+ 24 —
6th	6 ———	+ 12 —	+ 36 —

In the 1st 12 grammes were transformed — While in the last scarcely the half or only 5.75 were digested - This hindrance to the action of the Pancreatic Juice by mixing it with Gastric Juice - cannot be due to the acid contained in the latter (Lactic or Hydrochloric) for as we have already seen the reaction matters not to its action - It must be, therefore owing to a direct action of the two ferments upon each other wherein they are to a certain extent mutually destroyed -

The

the importance of this fact when we regard the possibility of its occurrence in the Living Organism is Considerable — By what means is it avoided? This question we do not intend to enter upon — probably the Bile is the direct agent in the prevention of such antagonistic action —

Other functions besides those here discussed have been ascribed to the Pancreatic Secretion — Thus Frerichs supposes that it assists in decomposing the Bile into insoluble products and thereby facilitates it's more complete elimination from the body — This, with many other Conjectures which have been hazarded on this subject, we cannot here enter upon — having only proposed to ourselves to Consider the more important of it's functions — and that not in an extended form, but only by way of "Remarks" on what has been recently advanced on this interesting branch of Physiological Research.

James Whitelaw B.A. Edinburgh.
Scotus