On the Intestinal Secretion in Dogs in the Interdigestive Period.

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Now we acknowledge through a work of Ooisi²⁸⁾ that the pancreatic juice in dogs flows out in the interdigestive period, but discontinuously under some careful experimental conditions, and the time relations between the active and the inactive periods are never regular, otherwise expressed, the term, the "periodical" secretion, as expressed by Boldyreff, cannot be applied for this kind of the digestive juice.

It is then a natural sequence to try other kinds of the digestive juices along the same line of thought.

In fact there is a number of the reports, which have some bearings upon the intestinal juices in the interdigestive period, and they are in number not a whit less than those on the pancreatic (literatures in Muto²⁷⁾ and Ooisi²⁸⁾), as reviewed in the present essay.

I.

Methods, etc: As the experiments in all the previous reports, which dealt in any way with the periodic secretion, were carried out exclusively on dogs, the present writer prepared the Thiry fistula in three male dogs: Dog C (25. XI. 1943; 16.5 kg), Dog D (11. I. 1944; 15.3 kg) and Dog E (7. X. 1944; 15.5 kg). After the separation of the small intestine at a point of about 10 cm distal from the duodeno-jejunal flexura, the fistula was prepared with a distal portion of the gut of various lengths, such as 15 cm in Dog C, 10 cm in Dog D and 5 cm in Dog E.

In the experimental room the dog, which took no food usually for twenty hours, was placed on the table for five hours or longer; no food was given there, and the writer himself never fed the animals. No particular manipulation with a purpose to make the animal dislike the experiment was not attempted, contrary to the cases of Ooisi. The juice was measured for each 5 minutes.

How to collect the juice in this kind of experiments is clearly illustrated in Paragraph III in the paper of O o i s i. In reality a 15 minute interval has been adopted by most previous experimentalists, but a shorter period, such as a 5 minute is highly recommendable. It is merely absurd to rely on a longer interval, such as 30 minutes or further 60 minutes. 54 experiments were run in toto.

II

A: Without catheterization.—At first the enteric juice was collected without placing any catheter into the fistula, then we came across several instances the distinctly remittent tide of secretion, as given in Figg. Exp. 4, Exp. 45, Exp. 50.

Apart from small fluctuations (secretion of small velocities and non-secretion), there are periodical accelerations in the secretion rate of enteric juice; the rate in those periods is incomparably large. The time interval of large output was commonly about 10 minutes in all the dogs, and that of small or no output was about one hour, a half hour and one and a half hours being the limits. The figures are taken up from typical cases, as the curves given here and some similar ones. To give the acceleration period as 10 minutes depends partly on the fact that the collection was done for each 5 minutes, but it is not unfair to take it as the mode in viewing all the data, we obtained, altogether.

By way of precaution it may be mentioned that lengths of "almost or no output" period are commonly somewhat dissimilar in one and the same experiment, although they are almost regular in the curves, here given, and the amount of juice, taken in the large output spells was rather uniform, that is, the maximum amount scarcely tripled the minimum.

In this series of experiments where no catheter was inserted, there are cases where no "large output" period appeared and as a consequence the whole curve appears similar to Dog D, Exps. 43 & 37, originated from the experiment with a glass catheter; only in these cases there are commonly wholly quiescent spells.

Ignoring irregular cases, the whole feature of the present outcome apparently duplicated well that of Boldyreff, well known as the "periodical" secretion of digestive juice.

Now let us examine whether the numerals or the phenomena observed by Boldyreff on one side and those by us on the other completely identical or not; that author is right in giving the term "periodical" to his findings, so far as his description and the curves constructed show that the active period and the inactive alternate surprisingly punctually (4, 192 ff; 8, Figs. 1 & 2; 16, p. 488.).

It must be noted, however, that there are in his second review some descriptions betraying recantation of the strictness of the periodicity. Compare the

description on p. 192 in (4) and the second foot-note on p. 488 in (16). Further it is rather strange to hear from him the complaint that many younger experimentalists without experience in this field, have missed the regularity of periodic act while we must complain on the contrary, many young workers too readily accept the term of "periodic" secretion with the results, rather characterized with irregular waves in the secretion rate, such as the authors (21, 22, 25, etc.). Over believe in the authority! In fact Komarov¹²⁾ related to the high degree of authority of the laboratory of Pavlov, notwithstanding it is to us out of question that the results of himself assuredly differ from those of Boldyreff. The "periodic secretion of digestive juices," as termed by Boldyreff is originated vocabularily and substantially from himself, as thoroughly studied by himself biographically (16, p. 529).

The duration of the active period and the inactive period is given in the first review of Boldyreff⁹⁾ as 30–35 minutes and 2.5 hours in the cases of longer cycle and as 15–20 minutes and 1 hr 20 minutes in those of shorter. (Similar figures in (4).) In the second review,¹⁶⁾ appeared about twenty years ago, he formalized them as 10–15 minutes and about 75–120 minutes respectively.

The figures or the length of periods of Boldyreff are therefore two times as ours. It is quite unreasonable to take both figures as identical.

Further let us then examine the data given in the hands of previous experimentalists. Here we shall take into account only those indicating some regular fluctuations in the secretion rate, while many authors were in reality able to see such fluctuations only in exceptional instances. If they were even to be termed as "periodical" secretion, the term such as *pulsus irregularis* should be wit off from medical vocabularies.

One cycle of fluctuation is 75–90 minutes in Brynk,⁷⁾ 60–135 m. in Komarov,¹²⁾ 45–120 m. in Matsubara,¹⁸⁾ 60 m. in Kokura.²⁰⁾ Orbeli reported similar figures to those in the second review of Boldyreff. Further, if we take into account the portion with most regular appearances only from these figures, the mode of one cyle will be 75 minutes.

This numeral, 75 minutes depends partly on the fact that the juice was collected for each 15 minutes interval, and consequently it should be taken as indicating a little longer interval than 60 minutes and further it is difficult to say the length of the active period on the same reason. It should be noted that such regular portions are given only in a few papers such as Brynk,⁷⁾ Komarov,¹²⁾ and this fact indicates that most of previous observers were able to have only irregular output of intestinal juice from the Thiry or Vella fistula, despite of they call it "periodical" secretion.

Of ratio between the active and the quiescent period, it will be further noted the findings or the view of Kratinoff¹⁷⁾ (movements only) are opposite to those of Boldyreff (secretions too). Thus the periods of "output" and "quiescent" of intestinal juice from the fistula, which were

obtained by previous observers seem to be adequate to speak of some regularity and check well with ours, but never with those of Boldyreff.

How the latter author came to see the periodicity of an astonishing degree in such a phenomenon as digestive juice secretion, was tentatively suggested by Ooisi in a study on the pancreatic secretion. It is noteworthy that Boldyreff modified the figures in the second review, which was oversights in that paper of Ooisi regrettably.

The dog is standing, sitting or in motion at a distance of a half to 1 meter from the experimentalist, i.e. the present writer, who came to notice rumblings in the bowels which soon appeared me as holding some relationship to the output of juice from the fistula, a matter noted by some authors, as Komarow,¹²⁾ etc.

I did neither attempted to go nearer to the dog nor endeavoured to listen rumblings, but simply noted them on the protocol as I heard them.

Then it appeared as if there are some intimate relationships between rumblings and the large output of the juice. Rumblings were however seldom audible when there were small ejections only, and further it must be added that much small rumblings were not noted in the present experiments. The juice coming out at the beginning of active period is thick and rich in mucus. It is rather astonishing that no drop of juice was obtainable from the Thiry-Vella fistula of a dog in the interdigestive period in the hands of Molnar.⁶⁾ N.B. In Exp. 4 on Dog C neither rumblings nor characters of juice were noticed.

III.

Any one who pays some attention upon intestinal movements or rumblings in bowels simultaneously with secretion or output of enteric juice, will come soon to note some associations between both phenomena. Of whether they are causally related or not, different views are still prevailing. Boldyreff and Sinelnikoff¹³⁾ against Babkin.^{9) 15)}

With a purpose of solving this interesting problem we tried to collect the juice from the fistula by means of a catheter, at first of gummi and then of glass. A gummi catheter of 5 mm thick and 5 cm long (1 cm more out of fistula), and that of respectively 7 mm and 11 cm (1.5 cm), and bent glass catheter of 5 mm and 5 cm (1 cm), and that of 10 mm and 11 cm (2 cm) were employed according to the size of intestinal fistulae.

Use of a catheter causes a large flow of the juice from the fistula as a matter of course; in Dog D, for example, juice flowed out in one hour in an amount of 0.7 cc when no catheter was inserted, of 1.7 cc on a rubber catheter of 5 cm, 2.1 cc on that of 10 cm, and 1.5 cc on a large glass catheter.

In Dog C with a fistula of about 15 cm, a short and a long gummi catheters were used, afterwards a gastric fistula was placed for recording gastric move-

ments. One and a half months later the Thiry fistula prolapsed, and eventually died thereof. In Dog D, with a fistula of 10 cm, gummi catheters of 5 cm and of 10 cm and a glass catheter of 11 cm were placed in the fistula, and in Dog E with a fistula of 5 cm, catheters of 5 cm of gummi and of glass were used.

Typical cases from each set of experiments are displaced in the accompanying figures.

On the one hand there are cases qualified with some periodicities in the output rate, as shown in Exps. 5, 11, 19, 52, etc, while there are cases where intestinal juice flowed out incessantly, as given in Exps. 12, 16, 43, 37, 54, 47 & 51.

And the former occurred frequently when rubber catheter was shorter than the length of fistula; the shorter and the thinner the catheter the more distinct the periodicity. If a catheter of 5 cm is inserted into the Thiry fistula of 10 or 15 cm, the intestine segment which remains untouched thereby is capable of moving freely.

A comparison of the data, given in the figures for demonstrating the general tendencies and not given here, it seems justifiable to assume that intestinal juice comes from the orifice of the Thiry fistula with a periodicity, roughly speaking, if the intestine is allowed to move freely; but if the movements are restricted the periodicity of output becomes obscure and finally completely disappear.

And this modus of dependence of intestinal juice output upon the intestinal movements can be also illustrated in the manner how the juice is ejected from the fistula orifice, as given in the following notes.

Exp. 3. Dog C, 26, XII. '43. 16.6 kg. 5°; no food was given for about 20 hrs. No catheter was inserted. In the relative quiescent period a water clear fluid flowed out of fistula orifice at a rate of a drop in 5 to 30 minutes, seldom no outflow in 1 hour or longer. The active period set in with appearance of a yellowish-whitish thick mass, like condensed milk, in the orifice as to stop it. About 10 seconds to 1 minute later it was pulled out in a rush. Similar output occurred three, four times or so with an interval of about 10 seconds to 1 minute. The fluid became thinner and thinner, and the force of output weaker and weaker; at last it flowed out with intervals of 3-30 seconds.

Exp. 52. Dog E. 10. XI '44. 16.4 kg, 12°; no food for 19 hrs. Rubber catheter. Distinctly rhythmical outflow was noticed. The rhythm corresponds to that of the peristalsis, viz. 15-20 per min. as the writer noted on another occasion and also in a paper of T a n a k a.¹⁹⁾ At first mucus-like mass flowed out, then turbid fluid flowed out rhythmically rather abundantly. In five to ten minutes the outflow became little and seldom, the rhythm being noted as one-half to one forth as before, and then gradually irregular. Finally the fluid flowed out continuously but scanty along the catheter.

The fluid flowed out in the quiescent period looked very clear.

The juice flowed out thus rhythmically contained a trace of blood in this dog, while no blood was witnessed in the other dogs (C,D).

These examples definitely prove also that the output of intestinal juice from the Thiry fistula is brought about by intestinal movements.

The output or secretion, as so called, of intestinal juice, which is chiefly dealt with above and in the papers here quoted, is that called forth by a group of these rhythmical movements with a rhythm of about 20 per minute, which lasts for ten minutes on the whole. The quiet spell is about one hour. The outflow in the so-called active period of intestinal secretion is the sum of the ejections set forth by rhythmical movements of intestinal loop.

Otherwise expressed, the intestinal juice is secreted rather continuously; the rhythmical outflow from the intestinal fistula such as Thiry or Thiry-Vella fistula is occasioned by the intestinal move-

ments. If the ejection is to be followed precisely in proper experimental conditions one can observe that it is brought about by each intestinal movement, and if intestinal movements are to be more or less depressed by proper measures, such as use of gummi or glass catheter of suitable size and length the periodical output, observed by several experimentalists, is rendered aperiodical or continuous.

That the periodical secretion of intestinal juice is always accompanied by periodical movements of intestines is a fact to which several authors, such as Babkin, Sawitch,¹¹⁾ paid keen attention. The findings of Rabinkowa and Eberle,¹⁴⁾ that the gastric secretion has no periodicity, is worth while of note here.

Further, the writer came sometimes to notice that during the active period the dog behaves quite still as if it is thinking about something, probably quite different from the experience of Sinelnikoff (p. 687).¹³⁾

In terminal it may be added that the inflammatory state of intestinal loop brings about an

abundant outflow of enteric juice, as noted in our dog C (Exp. 20). Some previous references exist.^{1) 2) 3)}

SUMMARY.

From a Thiry fistula provided in dogs, enteric juice was collected either without inserting any catheter or using catheters of gummi or glass of various size and length.

When no catheter was inserted or catheter of smaller size or length, compared with those of fistula, periodical output of the juice was observable though not always, but rather frequently. And the periodicity was more regular in comparison to previous experimentalists, while it was not so regular, or otherwise expressed, not so strictly periodical as the

description of Boldyreff. The active period was usually noted as ten minutes and the quiescent period as one hour as a mean, or from a half hour to one and a half hours, and the figures are about the half of those of Boldyreff. The figures given in the reviews of that author, one in 1911 and the other in 1929, are somewhat different from each other.

When catheters of large size and length were used, the output of juice inclined to lose its periodicity, that is there were fluctuations in the output rate, but it was irregular and of insignificant magnitude, so that finally it has no periodical character at all.

The results show clearly that the so-called "periodical secretion," or strictly spoken, "periodical output" of enteric juice, observed by means of Thiry, Thiry-Vella fistula or something like procedures, can be abolish-

ed by restricting influence of intestinal movements: that is, the latter act to push out periodically the juice, which is secreted highly probably continuously.

And further, the writer had opportunities to observe the output of juice in a rhythm of about twenty times a minute, which corresponds to that of intestinal movements.

The periodicity, spoken by Boldyreff, especially in his first review in 1911, for example, also of the output of intestinal juice, is also of highly strictness. Such an exact periodicity is never found in the communications of other authors. How that author would come to see such a data has been suggested with right in a previous paper of Ooisi rê the pancreatic secretion.

Briefly concluded: The "periodical" output of intestinal juice in the interdigestive period in dogs, which is rather frequently observable, and has a periodicity of the active period of ten minutes and the quiescent period of one hour, roughly speaking, is due to the intestinal movements and not to having of its secretion the periodicity. There is no evidence of existence of periodicity in the secretion of enteric juice.

Further it is observable that the juice is ejected rhythmically according to the rhythm of intestinal movements, about twenty times a minute. Namely the output in the active period in the so-called periodical output is the summary of the rhythmical output or periodical output of second order.

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