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KONINKLIJKE AKADEMIE VAN WETENSCHAPPEN TE AMSTERDAM.

PROCEEDINGS OF THE MEETING

of Saturday December 30, 1899.

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The following papers were read:

Physiology. — "*The resorption of fat and soap in the large and the small intestine*". By Dr. H. J. HAMBURGER.

(Read November 25, 1899.)

Introduction.

While investigating the distribution of fat in the bloodcorpuscles and plasma under the influence of respiratory gas exchanges, I tried some experiments which may be said to prove that the large intestine probably possesses the power of resorbing fatty matter by

means of its blood vessels [1]). I have thought it necessary still further to pursue these preliminary experiments, as they touch on a question which, both from a theoretical and a practical point of view, seems to be of the greatest importance. From a theoretical point of view, because some light may, at the same time, be thrown on our present, in many respects, very inadequate knowledge of the resorption of fat in the more complicated small intestine; from a practical point of view, because the problem of rectal nutrition with fat has not yet been satisfactorily solved.

In this domain, indeed, there has hitherto been but little investigation. In 1874 CZERNY and LATSCHENBERGER [2]) tried two experiments on a man to whom an anus praeternaturalis had been applied. They brought into the fistula a known quantity of some fat emulsion, then by rinsing out the contents after some time and ascertaining how much fat they contained, they determined how much emulsion had been absorbed.

In 1891 MUNK and ROSENSTEIN [3]) administered some rectal injections of oil emulsion to a girl who had chyle fistula on her leg, and by quantitative determination of the fat in the issuing chyle ascertained how much fat had been absorbed. They found, as CZERNY and LATSCHENBERGER had also done, that the resorption was insignificant.

DEUCHER [4]) and PLANTENGA [5]) injected into persons with a normal intestine a clysma consisting of the yolk of an egg and milk; here too fat appeared to be resorbed, but the resorption was insignificant.

Though these experiments of MUNK and ROSENSTEIN have unquestionably shown that from a clysma fat may be resorbed, it has not yet been proved that this resorption takes place in the large intestine. What proof has there been afforded that, in the above mentioned experiments, a part of the clysma has not passed the valvula Bauhini?

And as for the experiments of CZERNY and LATSCHENBERGER,

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[1]) Verhand. d. Koninkl. Akad. v. Wetensch. Dl. III N° 10. 1894. p. 31.

[2]) CZERNY und LATSCHENBERGER, Physiologische Untersuchungen über die Verdauung und Resorption im Dickdarm. VIRCHOW's Archiv B. 59. 1874. S. 179.

[3]) MUNK und ROSENSTEIN, Zur Lehre von der Resorption im Darm, nach Untersuchungen an einer Chylusfistel beim Menschen. VIRCHOW's Archiv B. 129. 1891. S. 230 en 284.

[4]) DEUCHER, Ueber die Resorption des Fettes aus Klystieren. Deutsches Archiv f. Klin. Medizin. B. 58. 1896. S. 260.

[5]) PLANTENGA, Der Werth der Nährklystiere. Diss. Freiburg i/B. 1898.

they were only two in number, and, from more than one point of view, they are questionable.

If we consider that, as yet, no hypothesis even has been formed as to the way in which the fat is resorbed in the large intestine, an investigation of this subject will not be deemed superfluous.

In the first place we wish to know with certainty whether the large intestine is indeed able to resorb fat.

I. *Does the large intestine possess the power of resorbing fat?*

A loop is taken out of the large intestine of a dog in a state of narcosis, is cleaned out inside, and by means of strings tied round it is divided into three equal parts *a*, *b* and *c*. An emulsion of lipanine (olive oil with 6.4% of oleic acid) in a solution Na_2CO_3 of $^1/_2$% is then introduced into the middle part *b*; nothing is introduced into the exterior parts *a* and *c*. The intestine is then replaced, the central cavity closed, and four hours later the intestine is removed and by administering more chloroform the animal is killed.

The mucosa of the central part *b*, which contains no more fluid is prepared and cut into small pieces. As a means of control the mucosae of the two outer pieces are also cut into small pieces, placed in two small receptacles, and as much emulsion added as was injected into *b* at the beginning of the experiment. The fat in the three receptacles is then with the utmost precaution determined.

EXPERIMENT I.

Length of the pieces of intestine *a*, *b* and *c* 9 cM. Into *b* 12.5 cc of a 5 pCts. lipanine emulsion in Na_2CO_3 of $^1/_2$% is injected. Four hours later the intestine is eliminated. Isolation of the mucosae, cutting into pieces. To the mass *a* and *c* 12.5 cc of the emulsion is added. After it has been dried the extract of ether yields the following results:

Ether residu of intestine *a* (mucosa + emulsion) = 0.635 Gr.
" " " " *c* (" ") = 0.659 Gr.

Mean . . . = 0.649 Gr.

Ether residu of intestine *b* (mucosa + not resorbed fat = 0.499 Gr.

This proves that 0.649—0.499 = **0.150** Gr. of fat has been absorbed out of the intestine *b* during these four hours.

Another experiment on another animal resulted in a resorption of **0.182** gr. of fat in four hours.

These two experiments and many others of which we shall speak

later (cf. page 293), *have decisively proved that the large intestine does really possess the power of resorbing fat.*

It was remarkable that the piece *b*, on being opened, proved to be nearly empty, and *that big drops of fat clung to the mucous membrane.* This gave rise to the suggestion that the Na_2CO_3 solution had probably been rapidly resorbed and the emulsion thus destroyed; the fat had got into a condition in which it could not be absorbed at all, or but very slightly.

This agrees with the views of MUNK and ROSENSTEIN, viz., that of an emulsion of 15 gr. lipanine in a Na Cl solution of 0.4 pCt., in $7\frac{1}{2}$—9 hours, 0.55 gr. of fat issues from the chyle fistula, but that the quantity amounted to 1.1, that is to say about double as much, when emulgent fluid Na_2CO_3 was used. Now it is known that with a Na_2CO_3 solution fat remains suspended much longer than with a Na Cl solution. It appeared then that on using Na_2CO_3 the lipanine remained longer in an emulgent state in the intestine than on the application of Na Cl.

Having obtained this result, which was confirmed by further experiments, we thought it of importance to employ, instead of the Na_2CO_3 solution, a fluid in which the emulsion would remain still longer existing in the intestine. It had therefore, to be a fluid of great emulgent power and moreover not rapidly absorbed in the wall of the intestine. For years clysmata of the yolks of eggs, of cream, and of milk have been used for these purposes. As these are compound mixtures these forms of emulsion seemed to me less fit; it is especially the albuminous investment of the fatglobules by which new factors are introduced into the problem of the resorption of fat. Besides DEUCHER and PLANTENGA had already shown that the quantity of fat which a man resorbs from such emulsions amounts but to about 10 gr. per 24 hours.

It now occurred to me to try a fluid which also in the small intestine exercises an important influence on the physiological emulgent, viz. a solution of soap.

After a preliminary experiment had shown that in a solution of sapo medicatus, the lipanine forms an emulsion which remains long in the intestine, and from which in the long run much fat is resorbed, we wished to determine the influence of soap on the large intestine. Such a research in itself seemed to us not destitute of importance, as under normal circumstances no inconsiderable quantities of soap occur in the contents of the large intestine and we are unacquainted with its functions in this part of the tractus intestinalis.

II. *Resorption of soap in the large intestine.*

In order to ascertain whether soap is resorbed in the large intestine we pursued three methods.

1st. Into a loop of the large intestine tied in two places we introduced a solution of soap. The loop having been replaced in the ventral cavity, it is left to itself for a few hours. From the quantity of soap still present we infer how much has been resorbed [1]).

2nd. From a dog in a state of narcosis a loop of the large intestine is ligatured at one end, and at the other furnished with a tube which is connected with a funnel that may be adjusted at different heights. A solution of sapo medicatus is introduced into the funnel and the intestine filled.

From time to time it is now necessary by replenishing, to raise to its original height the level of the fluid descending in consequence of resorption.

At the end of the experiment the contents of the funnel, connecting tube and intestine are rinsed out, and the quantity of soap contained in this and in the mucosa is determined. If we deduct this quantity from the whole of the soap solution used, what has been resorbed remains.

3rd. The large intestine is cut through close to the coecum. The free ends are attached to the ventral wall [2]). After a cure has been effected we dispose of a separate piece of the large intestine. Into this large quantities of a solution of soap are now introduced through the rectum. By ascertaining how much soap, after a limited time, still remains in this portion of the intestine, we can determine how much has been resorbed.

All the three methods agree in showing unanimously that the large intestine possesses in a large measure the power of resorbing soap.

III. *What happens to the soap resorbed?*

The researches of J. MUNK [3]) and of J. MUNK and A. ROSENSTEIN [4]) have shown that the fatty acids taken into the body are

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[1]) We cannot enter into particulars here; they will be found in a paper which will appear in the Archiv f. Anat. u. Physiol. Physiol. Abth.

[2]) Dr. FOLMER, surgeon, was so kind as to attach this intestine fistula for me.

[3]) J. MUNK, Zur Kenntniss der Bedeutung des Fettes und seiner Componenten für den Stoffwechsel. VIRCHOW's Arch. B. 80. 1880 S. 10.

[4]) l. c.

converted into fat, and as such appear for a great part in the chylevessels. The last is opportune; for as MUNK first observed, the presence of relatively small quantities of soap in the blood circuit is dangerous to life; an intravenous injection of 0.12 gr. of soap per kilogr. of the weights of the rabbit already caused death.

These experiments made it highly probable that already in the *mucosa* of the small intestine the fatty acids combine [1]) with glycerine into fat. And the preliminary experiments of EWALD [2]) with finely minced mucosa of the small intestine have confirmed this hypothesis.

Now as there is no ground for assuming that the soap which is absorbed in the large intestine passes without injury into the blood it seemed to me not too hazardous to conjecture that the oleic acid in the large intestine is also converted into fat.

To test this hypothesis by observation, we made experiments in three directions.

1st We examined whether the mucosa of a loop of intestine which has been some time filled with a solution of soap shows an increase of fat. (As is known, some fat can always be extracted from the normal mucosa).

2nd We examined whether the formation of fat stated under 1st does indeed continue after the intestine has been taken out of the body and is left to itself at the temperature of the body.

3rd We inquired whether the fresh and still warm mucosa of the intestine, after having been minced fine and then saturated with a solution of soap in which was a little glycerine, was still able to convert soap into fat.

This proved to be really the case. The conversion, however, could no longer be observed when the mucosa had previously been heated to 80°. Hence this suggests fermentation.

There can be no doubt, then, that soap resorbed in the large intestine is, partially at least, converted into fat in the mucosa.

IV. *Resorption of fat from lipanine-soap emulsion.*

It having thus been established what happens to the soap resorbed in the large intestine, we went back to our point of departure and inquired whether, according to our theory, laid down at page 290,

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[1]) The origin of the glycerine is still uncertain.

[2]) C. A. EWALD. Uber Fettbildung durch die überlebende Darmschleimhaut. Archiv. f. Anat. und Physiol. Abth. 1883. Supplem. S. 302.

more fat is resorbed from emulsions with solutions of soap then from emulsions with Na_2CO_3.

In order to answer this question, a loop was produced from the large intestine and by means of a string tied round it, divided into three parts, of equal length. Into the central part *b* a lipanine-Na_2CO_3-emulsion was introduced, into *a* lipanine-soap-emulsion. The two emulsions contain 20 cc lipanine to 80 cc emulgent fluid (soapsolution 5 % and Na_2CO_3-solution $^1/_2$ %). The piece of intestine *c* serves as a control and does not contain anything.

Five hours afterwards the intestine is eliminated. On opening *b* there is no trace of emulsion to be observed; this section is empty, but a mass of fat is found lying against the mucosa. In *a* there is still a fine emulsion present; of a fatty mass or of drops of fat against the mucosa there is no trace.

The contents and mucosa of the two sections are taken in hand for the quantative examination of the fat still present.

The mucosa is also removed from the controlling section *c* and its fatcontents determined; but before proceeding to the last, we add, in order as much as possible to avoid mistakes the same quantity of lipanine-soap-emulsion as was injected into *a* in this case, thus, 20 *cc*.

The first experiment showed that from the lipanine-soap-emulsion **0.558** Gr. of fat had been resorbed, whereas, in the same time, only **0.156** Gr. of fat had been resorbed from the lipanine-Na_2CO_3-emulsion.

Further experiments yielded the same results.

Though it had hereby become certain that more fat is resorbed from lipanine-soap-emulsions than from lipanine-Na_2CO_3-emulsions and the power of the large intestine to resorb fat has hitherto been rated too low, yet, in order to form an idea of the resorbing power of the large intestine, it seemed desirable to compare it with that of the small intestine.

In making this comparison, the necessity of reducing the extent of the resorption to equal surfaces of mucous membrane, presents no little difficulty. If, however, in preparing the mucosa we make a circular incision which penetrates to the mucosa, and then strip off serosa with muscle from the mucous membrane, it is very easy to ascertain the surface of the mucosae of the two pieces of intestine to be compared.

The experiments have now shown that, for fat, the resorptive

power of the large intestine is, under the given circumstances, not inferior to that of the small intestine.

I say: "the resorptive*power*," by which I do not mean, of course, that in normal life the large intestine resorbs as much, per unit, of the surface of the mucous membrane, as the small intestine. Nor is that the case. For the fat is supplied to the small intestine in a pulpy, sometimes almost liquid mass, whereas the large intestine must absorb the fat from a more solid condition, which is, of course, done with less facility. Moreover, on reaching the large intestine, the contents have already rejected the greater part of the fat, and consequently what, in normal life, the large intestine absorbs in fat will amount to less than what the small intestine resorbs.

What our experiments teach us is this: that when the lipanine-soap-emulsion is supplied to the unit of the surface of the mucous membrane, an almost equal quantity of fat is resorbed.

Besides in detached pieces of the intestine, we have now also studied the resorption of fat in a fistula of the large intestine. In somewhat over a day we saw from a lipanine-soap-emulsion about 10 gram of fat arrive at resorption in 12 hours.

If we consider that this quantity is about the same that PLANTENGA in the course of twenty-four hours could bring *in maximo* to resorption in a human being whose large intestine possesses a much larger surface of mucous membrane than that of the dog, it then becomes highly probable that also in man, if we also employ lipanine-soap-emulsions we shall be able to bring about a much more considerable resorption of fat than we have hitherto obtained with other emulsions.

The emulsion with soap solution yields another practical advantage, viz. that resorbed soap contributes as such to the absorption of fat, for, as we have seen, the soap is converted into fat.

From a practical point of view it would be of importance systematically to examine what will be the most favorable proportion of lipanine and soap-solution, and also what concentration must be given to the soap-solution in order to make the resorption as great as possible. We shall have further to discover how much the extent of the resorption depends on the volume of injected emulsion and, therefore also on the respective times of injection.

We have, however, not pursued the subject further in this direction.

We have occupied ourselves with another problem, viz. what path does the fat take in the mucosa.

V. *What way does the fat take in the mucosa?*

We may *a priori* assume that the particles of fat after leaving the epithelial layer of the Lieberkühns glands and entering the lymphducts, will, for a part at least, be carried off with the current of lymph. The remaining fat would then have to follow the path of the blood capillaries situated in the lymphducts, and seeing that in the mucosa of the large intestine the system of lymphatic vessels is relatively only slightly developed, it would not even be improbable that the blood capillaries form the principal channel of conveyance.

Meanwhile the question might be raised: has a transition from fat into blood capillaries ever been observed in other places? And this then suggests in the first place, the small intestine. That a great part of the fat there follows the way of the lymphatic vessels, few will question; but whether the blood capillaries are also responsible for a part of the transport has not hitherto been decided.

According to CLAUDE BERNARD the serum of the v. porta in mammalia during digestion looks as white as milk. On the other hand, comparative investigation of the blood of the v. porta and of the a. carotis, undertaken by BORNSTEIN [1]) at the instance of HEIDENHAIN showed that the fat contents of the portal-blood are less than those of the a. carotis.

The experiments of ZAWILSKI [2]) also seem to argue against a direct absorption of fat by the blood capillaries. Eighteen hours and a half after partaking of a rich meal, while the resorption of fat was still in active operation, the contents of the ductus thoracicus where drawn outside so that the blood no longer received any chyle. The fat contents of the blood amounted only to 0 05 %; to no more, then, than in a state of hunger.

Over against the results obtained by ZAWILSKI and BORNSTEIN we must set those of VON WALTHER [3]) and of FRANK [4]). VON

[1]) HEIDENHAIN, Beitrage zur Histologie und Physiologie der Dünndarmschleimhaut. PFLUGER's Archiv Suppl. 1888. S. 95.

[2]) ZAWILSKI, Die Abfuhrwege des Fettes. Arbeiten aus der physiologischen Anstalt zu Leipzig. Jahrg. XI. 1876.

[3]) VON WALTHER, Zur Lehre von der Fettresorption, DU BOIS-REYMOND's Archiv. 1890. p. 328.

[4]) FRANK, Die Resorption der Fettsauren der Nahrungsfette, mit Umgehung des Brustganges. Ibid. 1892. p. 497.

Derselbe, Zur Lehre der Fettresorption. Ibid. 1894. p. 297.

WALTHER showed that *only a very small portion* of the whole quantity *from* 40 to 50 gr. *of the resorbed fat* is transported through the ductus thoracicus. And FRANK observed that, after ligaturing the ductus *thoracius*, the resorption of fatty acids in the small intestine was considerable. „These observations", HAMMARSTEN says rightly in his *textbook* on physiological Chemistry, hardly seem, however, under *normal circumstances*, capable of being transferred to the resorption of neutral *fats in man*". MUNK and ROSENSTEIN in their investigations on a *girl* who had a lymphfistula in the leg, could find again in the chyle scarcely more than 60% of the fat administered *per os*.

It will be seen that there is still little agreement with respect to the direct transition of fat into the blood capillaries. It appears to me that I have succeeded in showing with certainty that *in the small intestine of the dog the blood capillaries have a considerable share in the resorption of fat.*

The experiment was as follows.

In a large dog in a state of profound narcosis a loop of the small intestine was produced by means of an incision in the linea alba. In consequence of a rich meal (bread with a great deal of lard) which the dog had received the night before the chyle vessels were splendidly injected. At distances of 17 cM. strings are thrust through the *mesenterium*, close to the attachment of the intestine. By means of these strings pieces of the intestine will be shortly afterwards detached. The chyle vessels of the central piece of the intestine *b* are carefully bound together. Those of the adjoining parts *a* and *c* are not. The whole loop is then well rinsed with a tepid solution of Na Cl-solution of 0.9 %. The strings are then tightened and the loop divided into three equal parts. Into each of the three parts is injected 25 c.c. of a lipanine soap-emulsion, consisting of 200 cc. sapo medicatus of 5 % + 50 cc. lipanine. When from the side of *a* and *c* two pieces *a'* and *c'* had after rinsing been untied, everything was again restored to the ventral cavity, which was then closed.

Five hours later the intestine was removed from the animal, which was still in a state of narcosis and was now killed.

The determination of the percentage of *the fat of the contents* of the loop inclusive of the mucosae showed that in *b*, where the chylevessels were bound together, still 0.419 gr. was resorbed; whereas in *a* and *c*, that is to say in chyle-vessels not bound

together, 0.714 gr. and 0.697 gr. respectively of fat were absorbed. Three more experiments yielded the same result.

There can be no doubt, then, that the blood capillaries possess in a large measure the power of resorbing fat.

This result agrees with that of MUNK's and ROSENSTEIN's experiments, which showed that only about 60 % of the fat resorbed flows out through the chyle vessels.

With respect, now, to the experiments of other investigators who deny that the blood vessels have a direct share in the resorption, it seems to me, that considering the present state of our knowledge, those of ZAWILSKI are no longer conclusive. Of later years it has been shown that in the blood ferments occur (lipolytic ferment of COHNSTEIN and MICHAELIS, lipase of HANRIOT) which possess the power of converting fat. When ZAWILSKI finds that on the effluence of chyle the blood does not contain more fat than about what is found in a state of hunger, this does not exclude the absorption of fat through the blood capillaries; owing to the slow resorption the fat always undergoes, what had passed into the blood-circulation could be regularly analyzed.

On the same grounds, comparative determinations in different sorts of blood, such as were made by BORNSTEIN cannot be decisive in this question. Moreover in these experiments no notice has been taken of the significance of the relative volume of blood corpuscles and plasma in the composition of the total of blood in the two cases.

It may now be further asked whether the fatglobules as such are absorbed in the blood capillaria, or not until they have first perhaps, been converted into a soluble combination.

CLAUDE BERNARD's experiments suggests, indeed, the first hypothesis, but it does not exclude the second.

On this question I hope soon to make some communications.

It has already been shown *that the blood capillaria take a direct part in the resorption of fat in the small intestine; and may also most probably do so in the large intestine.*

Summary.

1. It may now be considered as proved that the large intestine of the dog has the power of resorbing fat.

2. Contrary to the opinion hitherto held, this power is considerable, and is not inferior even to that of the small intestine.

3. In order to bring about a resorption so considerable, it is necessary to take an emulsion that can stay a long time in the intestine.

The usual $Na_2 CO_3$ is not well adapted for the preparation of such an emulsion and the Na Cl still less so, because both are rapidly resorbed and with them the emulsion neutralized. A solution of sapo medicatus, however, seems to answer the requirement.

4. As to the soap solution itself, it appears that this is resorbed, though much more slowly than the $Na_2 CO_3$, and during the resorption is, at least for a part, converted into fat already in the mucosa.

This conversion continues in the intestine that has been cut out; nay it is effected even when the mucosa has been minced fine. Heating to 80°, however, neutralizes the said property.

5 As to the path taken by the fat in its resorption in the large intestine, it is highly probable that a part of it is transported through the blood capillaria. The experiments described above have at least shown with certainty that this is the case in the small intestine.

Physics. — "*Some Observations concerning an Asymmetrical Change of the Spectral Lines of Iron, radiating in a Magnetic Field*". By Dr. P. ZEEMAN.

1. In observing spectral lines resolved into triplets by the action of the magnetic field, one is certainly struck by the symmetrical position and the equal intensity of the outer components of these triplets. There are especially in the case of iron not a few of the stronger lines, which seem to represent ideal cases of triplets, as originally predicted by LORENTZ's theory. It is only after more attentive inspection that several faint triplets are seen in which one of the outer components is apparently more intense than the other. On a former occasion [1]) I pointed out that there were reasons for expecting triplets with a more intense lateral component toward the

[1]) Proceedings Royal Academy of Sciences Amsterdam, June 1898. Astrophysical Journal, Vol. 9. Jan. 1899.