ABNORMAL FAT ASSIMILATION ASSOCIATED WITH SOME DISEASES OF THE INTESTINE

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(Received June 29th, 1907)

The difficulties surrounding the study of the absorption of fat and the different views held thereon depend largely upon the limitation of knowledge regarding the various fats concerned, and the difficulties of the chemical technique connected therewith. Except in such conditions as the failure of the fat-digesting secretions to reach the intestinal tract associated with obstruction to the flow of bile and pancreatic juice, little is known of any abnormality of fat digestion. The present views of the digestion of fats is stated by B. Moore (1) as follows :—

‘It is now generally accepted that the neutral fats of the foods are completely split up in the course of intestinal digestion by the lipase of the pancreatic juice into free fatty acids and glycerine, and that the fatty acids are then rendered soluble by the bile salts and lecithin, either in the form of free fatty acids or as alkaline soaps, so that all the constituents formed in fat digestion are finally taken up in soluble form.’

In the same contribution this author points out that from solutions containing soaps and glycerine the living cell is capable of inducing the synthesis of neutral fat, and thus rendering the soaps capable of absorption.

The clinical and chemical observations recorded in this contribution tend to show that there are conditions in the intestines in which

certain soaps or other insoluble compounds of fatty acids are not absorbed by the intestinal mucous membrane, and that with the presence of these conditions certain diseases of the alimentary tract are related. The analyses here given show that true intestinal sand, appendix concretions, and some bodies formed in the intestines are largely formed of fats and soaps. The fats and soaps present are compounds of saturated fatty acids. The constitution of these bodies and their relation to each other in chemical constitution throws, in my opinion, much light upon the etiology of appendicitis and mucous colitis, and possibly upon the underlying factors in certain diseases accompanied by colic.

Investigations of other foreign bodies different from the above occurring in the intestine, such as concretions formed by inspissated faeces, by inorganic salts, gall stones, and *false* intestinal sands, have been made, but their chemical constitution shows that they have no relation to the pathological processes accompanying fat digestion.

In the following analyses determinations have been made of total ethereal extractive, free fatty acid and combined fatty acid, soaps insoluble in ether, iodine values of the fatty acids showing percentages of saturated and unsaturated fatty acid present (Hubl and Köttstorfer methods, non-saponifiable matter, cholesterine, etc.), and the bases present in combination with fatty acids and in organic combinations.

In the present state of our knowledge a systematic classification of fat is not possible. In the investigation of fats in faeces it is usual to determine the melting points, and to use these as expressions of their different natures. A more correct classification for practical purposes, as the results of these observations show, appears to be obtained by using their iodine values. This value expresses the amount of iodine which 100 grammes of fat are able to take up and combine with, and divides the fatty acids into two main groups, the saturated and the unsaturated. Of the saturated fatty acids palmitic and stearic acids, and of the unsaturated fatty acids oleic acid, occur in the animal fats.

INTESTINAL LITHIASIS

Cases in which intestinal sand has been passed in the stools have been recorded from time to time, the most noteworthy being the one recorded by Duckworth and Garrod (2). In this as in others the amount of organic and inorganic material, with the nature of the latter, has been recorded. I have only been able to find one observation which calls attention to the presence of fat in the material, Roesser (3) reporting that 10 per cent. of his specimen contained fatty substance soluble in ether.

The sand is found as a 'gravel' adhering to the bottom of the vessel from which the faeces have been emptied. It varies in colour from grey to brown, and is often mixed with small quantities of faeces which tend to hide its appearance as an abnormal constituent. When the specimens are washed and dried they in all cases show the characteristic appearance of the sand. This looks much like ordinary sand, but has not the same gritty feeling, but rather feels like soap, and in well-marked cases I have observed fair-sized particles appearing and feeling like ordinary soap. My attention was first drawn to this material by Professor Vaughan Harley, at whose request I examined it in his laboratory.

The first specimen examined was intimately mixed with numerous small green leaves, and microscopically show vegetable fibres in abundance. False intestinal sand consists of the remains of undigested vegetable food, and thus this specimen suggested some possible relation between the two forms. In two later cases of the true sand a few vegetable fibres were found, mixed with the material.

The true sand was found to be insoluble in water. On heating with Millon's reagent some of the particles became faint red in colour.

By analysis it was found to contain—

					Per cent.
Organic material and water	...	...	...	...	55'6
Inorganic material	...	...	...	...	44'4

The ash after combustion contained—

	Per cent.
CaO	65·65
Fe ₂ O ₃	6·5
MgO	0·15
P ₂ O ₅	23·1
CO ₂	3·3
SO ₄	1·3
Cl	Trace
Total fatty acids in specimen	18 per cent.

Of the total calcium present, only 34·1 per cent. is present as calcium phosphate. The remaining 31·5 per cent., as is seen from the above table, has no inorganic acid with which it could be combined.

An investigation was therefore made to find the combination in which this calcium existed. The material on being burnt showed a smoky white flame, which suggested the presence of fat. The original material was accordingly treated with ether, and 10 per cent. of its total weight was found to be soluble.

This ethereal extract was found to contain :—

22·5 per cent. free fatty acid	} estimated as oleic acid
13·4 „ combined fatty acid	

The iodine value of these fats was found to be 18 per cent.

After all the fats soluble in ether had been removed the material was treated with hydrochloric acid, and again extracted with ether, when a further 8 per cent. was found to be soluble. This was found to be free fatty acid, the hydrochloric acid having therefore split up the calcium soaps and liberated their fatty acids.

The iodine value of these fatty acids was found to be 13·3 per cent.

The above values show that the fats present in the material were of the saturated type (palmitic or stearic, or both).

During the past year, in the wards of the Royal Infirmary, Liverpool, I have seen several specimens of faeces containing particles resembling sand. I have been able to collect seven well-marked specimens, and in these I have found the same constitution as that noted above, all showing presence of fat soluble in ether and soaps

insoluble in ether, all the fatty acids from these being of the saturated type. To obtain the material from well-formed stools they were allowed to stand under a slowly-running tap to disintegrate them, and then carefully emptied, the sand remaining at the bottom of the vessel.

The nature of the cases is shown in the following brief summary. Cases I and II will be referred to in greater detail later :—

Case I.—A female, aged twenty-two, under the care of Sir James Barr. The patient's appendix had been removed one year previous to admission to hospital on account of repeated attacks of abdominal pain. The pain recurred one month after operation. On admission she was suffering from abdominal pain with much mucus in the stools.

Case II.—Under Mr. Paul's care. A male, suffering from symptoms suggesting the presence of gall stones. The patient had colic.

Case III.—A female, aged sixteen, under the care of Sir James Barr. The patient had a large ovarian cyst. On admission she was suffering from abdominal pain, constipation, and vomiting. The vomiting had no relation to food. Intestinal sand was found in the stools both before and after the operation for removal of the cyst.

Case IV.—Sir James Barr's case. A female, aged thirty-four, suffering from colic. She was markedly constipated. Purgatives relieved the pain after the passing of faeces containing intestinal sand. The appendix vermiformis was felt to be thickened.

Case V.—Sir James Barr's case. A female suffering from thrombosis of the femoral vein following parturition. The patient was very ill and the leg much swollen and very painful.

Case VI.—A male, under the care of Dr. Bradshaw, suffering from ulcerative colitis, with pus and blood in the stools.

Case VII.—A female, under the care of Mr. Paul, suffering from malignant disease of the caecum. The caecum was removed. Intestinal sand was found both before and after operation.

Harley and Goodbody (4) state that the sand is not uncommonly found in the stools if looked for. On many occasions, in addition to the seven typical cases mentioned above, I have been able to find small quantities of similar material by placing the faeces in a bag with an open top, made of several layers of muslin, and allowing it to hang in running water until most of the faeces had been washed away. The material when present in any quantity was found in cases where there was abdominal pain of a colicky nature, and it may hence be suggested that the material acted as a chemical irritant,

giving rise to painful contractions of the intestine to eliminate it. The richness of these intestinal sands in calcium, iron, and phosphoric acid, and also in fatty constituents which are all usually described as constituents of the secretion of the intestinal mucous membrane, point to their originating in the intestine as a result of some excess in secretion or defect of absorption.

Duckworth and Garrod investigated the pigments in their case, and from the relatively large amount of urobilin and the small amount of unaltered bile pigment present, believed it to be formed in the upper part of the colon.

APPENDICITIS

Concretions occurring in the appendix when dried cut quite easily; they appear almost always to be white, and the cut surface has a smooth appearance like soap. This is quite different from the section of a faecal concretion, which is deeply pigmented and has a gritty feeling to the touch.

Analyses of these concretions show them to be very similar in constitution as regards fat to the specimens of intestinal sand, both containing fats soluble in ether and soaps insoluble in ether.

The following tables show the nature of the fats contained in three concretions obtained from the appendix:—

FAT SOLUBLE IN ETHER

	Amount	Combined fatty acid	Iodine value
Specimen A ...	14·97 per cent.	73 per cent.	4 per cent.
„ B ...	16·2 „	all	16 „
„ C ...	7·1 „	all	18 „

FATTY ACIDS FROM SOAPS INSOLUBLE IN ETHER

	Amount	Iodine value
Specimen A ...	15·6 per cent.	4 per cent.
„ B ...	2·1 „	low
„ C ...	1·2 „	low

The amount of calcium in each concretion was found to be—

A, 3·3 per cent. B, 3·6 per cent. C, 3·2 per cent.

A faecal concretion from the intestine examined at the same time for comparison was found to contain *only* '68 per cent. of calcium.

The extraction of fat from several faecal concretions was undertaken for comparison, but the amount and nature could not accurately be determined owing to the amount of pigment always taken up by the ether interfering with the reactions—another point of difference between an appendix concretion and one formed of inspissated faeces.

Further facts which point to the fact that appendix concretions are not, as they are almost invariably called, faecal concretions are the following :—

Appendix concretions are usually of sufficient size to markedly dilate the terminal portion of the appendix, and to do this it would presuppose an abnormal amount of force acting from the caecum to so distend the narrow lumen, a condition of affairs impossible to understand with the lumen of the caecum so large to carry away the faeces acted on by such a force did it conceivably exist. The appendix concretions are invariably concentrically laminated, proving conclusively that they are formed by successive depositions on all sides, the terminal as well as the proximal, and that they are formed *in situ*.

That the appendix has a secretion which, under abnormal conditions, could form these concretions, is to be seen in any appendix in the post-mortem room. Sir William Macewen has demonstrated the presence of such a secretion during life. Schmidt (5) states that the intestinal mucous membranes excrete inorganic salts, such as those of iron, calcium, and phosphoric acids, and also fatty substances. Hermann (6) has shown that a loop of intestine separated from the intestinal tract, sewn up in the form of a ring, and restored to the abdomen, soon becomes filled with a mass resembling faeces.

It is probable that the faecal-like masses found in the appendix are formed in a similar manner ; this would explain their containing fat and calcium in such large quantities.

In a case in the Royal Southern Hospital, under the care of Mr. Newbolt, I was able to collect a glairy mucoid-looking material which was being excreted by a loop of intestine shut off from the

rest of the alimentary tract and discharging on the surface. This contained 3·8 per cent. of fatty substance which contained saturated fatty acids (iodine value 12·2 per cent.). This shows that the fatty substances excreted by the intestinal mucous membranes are of the saturated type.

The above facts are evidence to show that the concretions in the appendix containing insoluble calcium soaps of saturated fatty acids are formed by the secretion of the appendix itself.

It is generally agreed that these concretions, when they occur, play a definite rôle in the pathogenesis of appendicitis. Of a case observed, Nothnagel (7) states :—

‘The appendix after removal was opened while still warm, and while the muscular fibres were still contracting. The mucous membranes were pale and perfectly normal in appearance except at the distal extremity in the immediate vicinity of a hard rounded calculus, the size of a cherry stone, where it was injected, and light red in colour. An observation of this kind conclusively shows, to my mind, that the localised catarrh, which was unquestionably due to the presence of the faecal concretion, would have ultimately led to other and probably grave results.’

Though the majority of cases occur without the formation of a concretion, it may be suggested that the same pathological processes which allow of their formation may have a deleterious effect even before a concretion is formed. The appendix normally tends to become obliterated as the result of age. Zuckerkandl (8) shows this to be the result of involution changes :—

‘The mucous membrane undergoes atrophy, the glandular structures desquamate, and the opposing layers of the inner surface of the organ grow together. At the same time, or occasionally before this time, the submucous coat undergoes thickening, and *fat* accumulates at this part of the wall. The muscular coat does not necessarily show any changes, but may also reveal an accumulation of fat.’

The lumen of the appendix is so small that the slightest swelling of its wall leads to its obliteration. I have cut open several appendices

not containing concretions immediately after their removal by operation and placed them in osmic acid. The walls stained black, but on the surface of the lumen there remained a layer which did not stain, this layer being the secretion adherent to the walls. This is significant, as the saturated fatty acids—palmitic and stearic acids—do not stain with osmic acid, whereas unsaturated fatty acids such as oleic acid do. I would therefore suggest that these fat compounds secreted or excreted by the tubular glands may under abnormal conditions block the lumen of the gland, and so render them liable to be more easily infected by micro-organisms than they would be if carrying out their normal functions.

The close relationship between appendicitis and colitis has been frequently suggested. Harley and Goodbody (9), in discussing the etiology of mucous colitis, do not admit that it is generally consequent on appendicitis. A great number of cases undoubtedly follow appendicitis, but this fact does not necessarily imply that the appendicitis is responsible for the condition. The underlying pathological condition which caused the appendicitis is probably the same as that which caused the colitis.

Intestinal lithiasis is, according to Nothnagel, usually associated with mucous colitis, and may be prolonged over many years.

He also states that it has been regarded as due to a lithogenic catarrh of the bowel, and might be compared to the process which gives rise to the formation of concretions in the vermiform appendix.

In relation to the above views, Case I, mentioned above, is of interest.

The appendix was removed in November, 1905, on account of repeated attacks of abdominal pain. The patient stated that one month afterwards the same pain recurred, and continued intermittently until December, 1906, when she was admitted to Sir James Barr's wards. Colic was present at this period, with attacks of nausea and vomiting. The vomiting was unrelated to food. The patient was of a neurotic temperament. In the stools were found much mucus and quantities of intestinal sand. The sand was not immediately obvious, and was gathered by the methods mentioned

above. It was analysed and shown to be true intestinal sand. After some weeks' treatment the symptoms and stools were much the same as on admission. With the view of relieving the symptoms the patient was placed on a diet containing much unsaturated fat (olive and sardine oils, both of which have very high iodine values). After a week on this diet the amount of sand and mucus in the stools was very much diminished. On the patient resuming a diet containing butter fat and meat fats (saturated), the sand and mucus increased very definitely in quantity. The stools were carefully collected under these conditions, and are being subjected to special examination for separation and determination of the different saturated and unsaturated fatty acids. After three months' treatment with olive oil, the pain is much less, and there is very little sand or mucus in the stools.

The fact that unsaturated fats might be of value was suggested by obvious theoretical considerations, the formation of more soluble and more easily split-up soaps. This is borne out in a case related to me by Dr. Thomas Clarke, who, many years ago, had a patient suffering from abdominal symptoms, with which was associated intestinal lithiasis. Treatment for a very considerable time failed to relieve the patient until she was placed on a diet containing olive and salad oils, when the symptoms and sand both disappeared in a few weeks.

French authors (Dieulafoy, Matthieu, Talamon, Reclus, and others) attach special importance to a peculiar form of catarrh as being the cause of the formation of intestinal sand, a catarrh which they consider to stand in close relationship to enteritis membranacea or also to gout, and which, according to some, is also the cause of appendicitis. Dieulafoy (10) has called attention to the number of patients suffering from muco-membranous typhlo-colitis who are operated on for an appendicitis which they have not got. He described thirteen cases, all suffering from abdominal pain. It has frequently occurred that patients have been operated on for appendicitis when they have had entero-colitis, and Dieulafoy has observed the painful crises to recur at the same spot and with the same intensity

after the operation. Bottentuit (11) has similarly collected twenty-two cases who have suffered from muco-membranous typhlo-colitis, or intestinal lithiasis, who have been operated on for a non-existent appendicitis.

It is therefore possible that the observations recorded above may afford a solution to the suggestions which have been made as to the relations between appendicitis and mucous colitis on the one hand, and mucous colitis and intestinal lithiasis on the other, and go still further to suggest a possible relation between the three diseases, they having in common some abnormality in the conduction of the processes associated with the digestion and absorption of fat, and the production of calcium salts of saturated fatty acids.

FAT CONCRETIONS IN THE INTESTINE

That these are not the only conditions in which pathological fat processes are associated with disease is seen from the following cases :—

From a patient suffering from acute intestinal obstruction Mr. Paul removed a mass which was causing the obstruction. It was situated in the small intestine in the upper part of the jejunum. Recognizing the unusual character of the mass, Mr. Paul kindly sent it to me to examine. It was about the size of a small Tangerine orange. In the centre was a raisin, around which was a bright yellow pultaceous mass held together by stroma of vegetable material. The exterior was stained by faecal material.

The nature of the fat was found to be—

Amount	Combined fatty acid	Iodine value
34·1 per cent.	74 per cent.	18 per cent.

The unsaponifiable material was isolated, and proved to be cholesterine. That this was not a concretion such as is sometimes formed by the administration of large quantities of olive oil was proved by the nature of the fat.

In another case of Mr. Paul's, a male, the symptoms suggested the presence of gall stones. Intestinal sand was found in the stools.

When operated upon there were found in the bile passages and neighbouring portions of the intestines numerous very small brownish-red granules, but no stones. An analysis of these granules showed that they contained fat in quantity.

This specimen is of interest in relation to the site of formation of intestinal sand, as the presence of the sand in the stools with the numerous fat granules in the duodenum suggest some relation between the two by their synchronous appearance in the same patient.

Duckworth and Garrod (12), in their specimen of intestinal sand, found very little unaltered bile pigment, showing that their specimen was probably formed lower down in the intestine.

The fact that the fatty acids present in all the above conditions are saturated—such as palmitic and stearic—is of high interest, for it is well known that these fats, when given alone, are only absorbed in very small quantities, from 86 to 91 per cent. remaining as residue in the faeces, whereas, when given mixed with unsaturated fatty acids, such as oleic, they are absorbed to a higher degree. Olive oil, when given alone, is almost all absorbed, only 2 per cent. remaining in the faeces.

Equally interesting, from the point of view of the value of the various fats in human food, is the fact that human milk contains a very high proportion of unsaturated fatty acids compared with the milk of the cow. The fact that unsaturated fatty acids aid the absorption of the saturated suggests that in the above conditions, where insoluble compounds of saturated fatty acids occur, the administration of olive oil might be of value in aiding the absorption of these deleterious products.

Observations which are being made tend to show that the nature of the fats in the diet have some effect in producing the conditions mentioned in this paper.

My thanks are due to Professor Vaughan Harley, in whose laboratory the work was commenced, and to Mr. Thelwall Thomas for many valuable specimens. To the surgeons and physicians of the Royal Infirmary, Liverpool, I am indebted for the use of their cases,

for specimens, and for the time to conduct these researches. The work was conducted in the Bio-Chemical Laboratory of the University, under the direction of Professor Benjamin Moore. My thanks are due to him for his valuable advice, and to my colleagues in the laboratory for much kind assistance.

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