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Original Articles

THE INFLUENCE OF FOOD AND OF EPITHELIAL ATROPHY ON THE MANIFESTATIONS OF SACCHARO-BUTYRIC INTESTINAL PUTREFACTION.

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In recent publications I have sought to establish the significance of the part played by anaërobic butyric-acid forming bacteria in chronic intestinal disorders and have advanced evidence to show that of these anaërobes, the *Bacillus aerogenes capsulatus*, or "gas bacillus," is the most important both on account of the frequency with which it is concerned and because of the intensity of its fermentative and putrefactive activities.¹ In assigning this place to the gas bacillus, I have not failed to recognize that other closely related, highly anaërobic bacteria, such as the bacillus of malignant edema and the *Bacillus putrificus* of Bienstock, are often associated with it. There are, in addition to these anaërobes, some butyric-acid forming aërobic bacteria which may thrive in the stomach and mouth, but there is no indication that in man they multiply abundantly in the large intestine, or in the small intestine, or that they are even moderately pathogenic for man. In some animals, as, for example, goats and pigs, large quantities of butyric acid are formed in the stomach by aërobic butyric-acid-forming bacteria taken in with the food and it appears likely that in them butyric acid is of importance in its relation to nutrition. These organisms, in fact, appear to be significant physiologically rather than pathologically, although we can not say that the continued persistence of a butyric-acid type of decomposition of great intensity may not exert some detrimental influence on the duration of life.

The human condition which I have described as one of saccharo-butyric putrefaction² is characterized by the persistent presence of excessive numbers of anaërobic butyric-acid makers in the large intestine and probably also in the small intestine. In fact, the persistent occurrence of this form of putrefaction is an indication of an intestinal infection through the agency of anaërobes.

CHIEF CHARACTERISTICS OF THE SACCHARO-BUTYRIC TYPE OF INTESTINAL PUTREFACTION.

It is desirable for the purpose of the present paper to describe briefly the leading features of the saccharo-

butyric type of intestinal putrefaction. The process in question is a chronic one. There are acute conditions in which there is a temporary increase of anaërobic butyric-acid makers, but in young individuals this condition is commonly of short duration—a few days or a few weeks—and is mainly of interest here as a forerunner of the more chronic type of infection. In chronic infection, the anaërobes have become adapted, at least partially, to the mucous membrane and its secretions. This is especially true of the large intestine where the putrefactive anaërobes may persist in very large numbers. The excessive numbers of anaërobic butyric-acid formers are readily demonstrable in the case of *B. aerogenes capsulatus* by (1) the large numbers of characteristic Gram-positive bacilli seen in the fecal fields; (2) the growth of characteristic colonies on anaërobic blood-agar plates with or without sugar; (3) the intravenous injection of fecal emulsions into rabbits incubated by the Welch-Nuttall method; (4) the subcutaneous or intramuscular injection of fecal emulsions into guinea-pigs, with the production of hemorrhagic edema at a distance as well as locally and by the spread of the bacilli (usually in pure culture) throughout the blood.³

How far into the ileum the organisms establish themselves in significant numbers is not yet clear. While they are continually present in the large intestine in excessive numbers, it is probable that in many cases their presence in the small intestine is less constant and that the upper level of the small intestine to which they attain is variable, depending on the state of the secretion of the digested juices, on the character of the food and on the state of the epithelium of the intestinal tract. In one instance, I have obtained experimental evidence of the upward wandering of the *B. aerogenes capsulatus* to a level at least as high as the middle of the small intestine. This was in a dog in which Dr. Carrel had resected the pancreatic and biliary ducts. There was, however, in this case an acute gastroenteritis, apparently induced by an experiment in diet (which will be referred to later). A comparison with other animals shows that exclusion of the bile and pancreatic juice is not necessarily followed by this upward wandering of the *B. aerogenes capsulatus*, but that this is likely to occur under certain pathologic conditions. In human beings with chronic anaërobic infections, there is usually a diminution in the numbers of colon bacilli in the feces—perhaps even a complete disappearance—which probably points to a diminution of these organisms at higher levels. If the chronic infection has been of only short duration, the colon bacilli may still be well represented, and, indeed, this is the case in some infections of many years' standing.

1. Bacterial Processes in the Intestinal Tract in Some Cases of Advanced Anemia, with Especial Reference to Infection with *B. Aerogenes capsulatus* (*B. Welchii*), Jour. Biol. Chem., II, p. 1, August, 1906; see also Common Bacterial Infections of the Digestive Tract and the Intoxication Arising From Them, The Macmillan Company, 1907.

2. I use the term putrefaction rather than fermentation to indicate that butyric acid is formed from protein as well as from sugar and because the most harmful products are those derived from protein; at the same time the adjective "saccharo-butyric" is a reminder that butyric acid is formed from sugar.

3. I expect soon to publish exact data regarding the virulence of the heated and unheated fecal suspensions from a series of cases, as I believe the virulence of *B. aerogenes capsulatus* (in the human tract) varies almost as much as its numbers.

In the saccharo-butyric type of intestinal putrefaction, there is an excessive production of butyric acid on an ordinary mixed diet. The amount of butyric acid recoverable in the feces depends in part on the proportion of acid that has been absorbed and is, therefore, greater, the conditions of diet remaining the same, when there is an increase in peristalsis from any cause, or when the epithelium has been temporarily or permanently denuded. It is usual in the saccharo-butyric type of putrefaction for the feces to have the odor of butyric acid, owing to the presence of a small amount of the free acid. This is especially noticeable on a diet rich in carbohydrates, but if the diet consists largely of meat the acid is neutralized wholly by ammonia or ammonia and other bases, and the odor of butyric acid is not pronounced. The quantity of butyric acid in one hundred grams of dried feces may reach 0.5 grams in well-pronounced examples of this type of decomposition. The formation of butyric acid from carbohydrates is attended by the liberation of hydrogen, carbon dioxide and methane, and this gas production accounts for the intestinal flatulence which is so persistent a feature in marked instances of the affection. The quantity of hydrogen sulphid produced is small and in several instances the quantity of hydrogen sulphid bound by the proteids of the feces has not been in excess of that observed in normal persons on a similar diet.

Often the expelled gases have a sickening odor, exactly like that which emanates from a rabbit that has been injected with a pure culture of *B. aerogenes capsulatus* and then incubated. The presence of gas gives a light color to the movements which are often unformed and soft and float on water. Through the active reducing agency of the putrefactive anaerobes there is a conversion of bilirubin into hydrobilirubin, the presence of which may be inferred from the pink or red color developed on the addition of a saturated solution of mercuric chlorid. This reaction is frequently intense. It fails, however, in those conditions in which the bile is excluded from the intestinal tract.

Another unusual reaction, dependent on some modified form of bile pigment (perhaps urobilinogen) is that which is manifested when an acid solution of dimethyl-amidobenzaldehyd is added to the filtrate prepared from a fecal suspension. The intense cherry-red color so obtained is like that yielded by indol. Hence in order to determine whether the reaction is due to urobilinogen it is necessary first to remove by distillation any indol which may be present. It is very common to find indol in the intestinal contents of persons suffering from chronic saccharo-butyric putrefaction, but the quantity may be small, and I have met with instances in which the feces contained a great excess of anaerobes, chiefly *B. aerogenes capsulatus*, but from which only traces of indol could be recovered, while the urine on repeated examination failed to contain indican.

I consider that two conditions have to be fulfilled in order that a saccharo-butyric putrefaction should be unattended by indol formation. The first is that the dominant anaerobe should not be an indol producer. This is frequently the case with *B. aerogenes capsulatus*. The second condition is that the colon bacilli, of which the intestine almost always contains many that are indol formers, shall not take part in the process of putrefaction. In other instances there is an abundance of indol produced, and consequently a strong reaction for indican in the urine. The explanation of the indol putrefaction must be sought either in the indol-producing properties

of the anaerobes concerned (properties which they sometimes possess in a very high degree) or in the active cooperation of indol-making colon bacilli in the putrefactive process. I have met with instances in which the colon bacilli have been so few, both in the feces and in material obtained by catharsis, that I have questioned whether they could have any considerable part in the indol production.

In this connection I would call attention to two facts relating to indol production which I think are not recognized. One is that when the bile and pancreatic juice are experimentally shut out from the intestine there may be a large production of indol in the upper half of the small intestine as well as lower down. The second point is that indol production may occur in the small intestine in the presence of a distinctly acid reaction to litmus, this reaction being due mainly to the presence of free fatty acids.⁴ Further reference will be made to this point in discussing the influence of the fats on manifestations of saccharo-butyric putrefaction.

THE PRESENCE OF SKATOL.

In many instances of pronounced saccharo-butyric putrefaction, skatol has been present in the intestinal contents. Contrary to the general belief, I have found that skatol is very often absent from the intestinal tract of normal people. I have never, under any circumstances, met with it in considerable quantities; that is to say, in quantities comparable to those in which one finds indol in cases of severe putrefactive decomposition, but the largest quantities I have observed (10 mg. in 100 gm. of fresh intestinal content) have been obtained from persons suffering from severe or long-standing forms of intestinal putrefaction.

In many of these instances, putrefactive anaerobes have been extremely abundant, and I have come to regard the presence of skatol as a usual accompaniment of the saccharo-butyric variety of intestinal putrefaction, although I admit that in small quantities skatol may be found where there is certainly no long-standing or intense decomposition of this sort. I have found it very difficult to determine the conditions under which skatol is produced by putrefaction rather than indol. In the study of individual putrefactive anaerobes I have found three which gave rise to considerable quantities of skatol on pepton-bouillon. These were certain varieties of the bacillus of malignant edema, some forms of *Bacillus putrificus*, and a butyric-acid-producing anaerobe sent to me by Dr. Theobald Smith.

I believe that skatol is only rarely formed, if ever, by the *B. aerogenes capsulatus* acting on pepton-bouillon. For these reasons it seems to me not impossible that when we find considerable quantities of skatol in the feces in the course of saccharo-butyric putrefaction this must be attributed to some associated anaerobe or to some special symbiosis rather than to *B. aerogenes capsulatus*.⁵ On the other hand, these considerations explain why it is that skatol is not always present even where there is pronounced saccharo-butyric putrefaction.

In many of the cases where skatol has been found in relatively considerable quantities, indol has been present

4. It is possible that in such cases there are minute portions of the intestinal contents that give a neutral or even slightly alkaline reaction to litmus, while the reaction of the contents as a whole is decidedly acid. This would explain the formation of indol, hydrogen sulphid and some of the putrefactive substances.

5. It is difficult to form a judgment on this point which takes account of the nutrient media found in the human intestine in these cases.

in smaller quantities or not at all.⁶ The ethereal sulphates of the urine are generally increased whether indican be present in the urine or not.

The presence of mucus in the feces in excessive amounts is a common occurrence. It is usually present in moderately excessive rather than largely excessive amounts and in rather small strings intimately intermingled with the feces. But frequently relatively large quantities may be found on the surface in some places, while in other parts there is no excess. Commonly, too, the microscope shows an abundance of epithelial cells in the feces, often associated with mucus, but sometimes independently distributed through the contents of the intestine. In some instances, particularly where there has been associated streptococcal infection, I have found an abundance of spheroidal masses of nuclear substance which I have suspected to represent leucocytes, but some of which were probably nuclei derived from desquamated epithelial cells.

In the early stage of chronic infection with putrefactive anaerobes constipation is common. This condition is, however, varied from time to time by diarrheal seizures in which the gas-holding intestinal contents are discharged in large quantities. I attribute the constipation of this period to diminished peristalsis, due to impaired innervation of the gut and diminished secretion of bile and pancreatic juice. It is often possible, even in this early period, to determine that there is impaired secretion of free hydrochloric acid into the stomach, and it appears likely that with this there is associated a diminution in the intestinal secretions.

At a later stage of the affection, usually after it has existed several years, diarrhea is of frequent occurrence and is significant as a factor in bringing about a distinct decline in weight and strength. Usually the diarrheal movements consist largely of coccal forms, colon bacilli and anaerobic putrefactive organisms. Relatively slight indiscretions in diet suffice to bring on diarrhea. This sensitiveness I attribute to a chronic condition of congestion of the small intestine with some associated desquamation of epithelium—a condition in which slight irritation brings on a temporary increase in the local congestion and an increase in peristalsis.

Dr. Houghton⁷ has lately made what I regard as a significant observation in a patient with pernicious anemia. The patient suffered with very marked manifestations of intestinal putrefaction (which, though not so described, appear to me to point unmistakably to a chronic infection with anaerobes) which it was attempted to relieve by an operative procedure which should permit free intestinal lavage.

At operation "the peritoneum resembled one subject to a low grade of inflammation without exudate. The color was darker than normal, the vessels injected, and that tissue itself very easily torn." I have long suspected that such a condition is a common occurrence in persons suffering from advanced forms of chronic excessive intestinal putrefaction, and now believe such chronic congestion will come to be recognized as a pathologic factor in many such cases.

It is not my intention to enter here on a full discus-

sion of the clinical manifestations of chronic saccharo-butyric putrefaction, but rather to emphasize such biochemical features of the condition as are at present recognizable. I wish, however, to refer briefly to certain derangements of the nervous system, the blood and the general nutrition that may be regarded as characteristic of the affection.

CLINICAL SIGNS OF EXCESSIVE PUTREFACTION.

Among the earliest signs of excessive intestinal putrefaction is a state of debility which is usually described as neurasthenic. The patients are indisposed for work, especially in the mornings, the tension of the pulse is low and fatigue sets in quickly. The extremities are usually cold, and it is only after vigorous exercise that a better distribution of blood occurs. It appears likely that these symptoms are in a measure dependent on anemia of the nervous system, which in its turn is referable to intestinal irritation, due to the micro-organisms concerned with the infection. These neurasthenic symptoms gradually increase and may ultimately be associated with considerable mental depression, especially in those cases where the saccharo-butyric type of putrefaction is associated with the formation of considerable quantities of indol and the excretion of indican in great excess. The pulse is commonly faster than normal in uncomplicated cases.

The influence of chronic saccharo-butyric putrefaction on the blood I have discussed elsewhere, especially in its relation to severe anemias. It is only necessary to say here that the long persistence of excessive saccharo-butyric putrefaction due to the *B. aerogenes capsulatus* is followed by some degree of anemia and that in some instances this anemia is extreme, even presenting the indications of the pernicious type of the disease. While I have been unable to bring forward convincing proof that the severe forms of anemia observed in cases of chronic excessive saccharo-butyric putrefaction are due exclusively to the agency of putrefactive anaerobes, I consider that certain clinical relationships which have been observed and the marked hemolytic action of the *B. aerogenes capsulatus* point to the latter organism as the one chiefly concerned in bringing about a degree of blood destruction which can not be adequately compensated by the blood-forming organs. A not infrequent association of chronic infection of the intestinal tract with the gas-bacillus is an infection with streptococcal forms, and where this exists it is not possible to say to what extent the blood destruction is due to this associated infection, since some of these streptococcal forms possess a hemolytic action. Not rarely patients develop a slight degree of cyanosis, especially noticeable in the extremities during cold weather or early in the morning. Even in the absence of distinct cyanosis the blood may have a darker appearance than normal.

The general nutrition of patients with chronic saccharo-butyric putrefaction gradually suffers. The persistent character of the diarrhea in the advanced stages of the disease contributes largely to this result, but even where exhausting diarrheas are absent nutrition is apt to fail. The nutritive failure is shown in subcutaneous atrophies of fat and connective tissue and gradual diminution in bulk of the muscles, which sometimes undergo fibrillary tremors, as in progressive muscular atrophies. These are changes which, for the most part, are to be expected in old age, and it is true that a premature senility is a feature of chronic saccharo-butyric putrefaction.

6. The presence of considerable skatol in the intestinal tract is apt to be associated with a strong reaction to dimethylamidobenzaldehyd. This reaction is strong, however, in all persons who eat meat to excess and such excessive use of meat is probably the explanation of the reaction in some persons with putrefactive disorders.

7. Apparent Recovery from Progressive Pernicious Anemia Following Cecostomy and Colonic Lavage, THE JOURNAL A. M. A., June 29, 1907, p. 2186.

Having sketched the leading clinical characteristics of chronic saccharo-butyric intestinal putrefaction, I wish to speak of the influence of the chief kinds of food-stuffs on the course of the fermentative and putrefactive aspects of the process. While there are still many questions regarding the influence of foods on intestinal putrefaction from butyric-acid forming anaërobes to which no answer can yet be given, there are facts of theoretical and practical interest which stand out so distinctly as to merit recording.

THE INFLUENCE OF CARBOHYDRATES.

The putrefactive anaërobe which attacks sugars with the greatest activity is *B. aerogenes capsulatus*. This organism decomposes dextrose, lactose and saccharose. Gas-production is in each case rapid and abundant. Moreover, boiled starch is inverted, though not quickly. The presence of at least a trace of sugar appears necessary to initiate the growth of this anaërobe, which does not multiply on sugar-free media containing proteins or proteins and starch. The gas formed through the decomposition of sugar is mainly hydrogen, the proportion of this gas to other gases formed being 2:1 or 3:2. Of the other gases formed, carbon dioxide is the chief, but a little methane is also made. Butyric and propionic acid are freely formed and acetic and even valerianic acids may probably be produced in traces.

I consider it noteworthy that patients with chronic saccharo-butyric putrefaction tolerate carbohydrates badly. In the early stages of the affection a meal rich in carbohydrates, whether in the form of sugars or starches, appears to make little difference (although there is some evidence that the sugars give rise to the most disturbance) causing moderate intestinal flatulence, abundant but formed stools, smelling of butyric acid, and perhaps also an increased frequency in micturition.

There is often a sense of drowsiness or dulness after an excessive carbohydrate meal, but seldom headache. In later stages of the affection, when the general nutrition has begun to fail and the patient falls below the normal weight, there appears an increasing sensitiveness to carbohydrate food which shows in the prompt occurrence of diarrhea and intestinal flatulence after any excess. Indeed, there comes a time when carbohydrates, even in amounts that would be called physiologic and moderate for a normal man, cause distress from gas and soft, ribbon stools, if not diarrhea.

This abnormal sensitiveness may be so highly developed that diarrhea becomes a frequent occurrence and through its frequency makes further inroads on the weight and strength of the patient. Under such circumstances a pronounced restriction in the quantity of carbohydrates becomes imperative, for every infringement of a rigid dietary is promptly followed by increased peristalsis, abdominal discomfort, unformed movements or watery diarrhea. Sometimes diarrhea promptly follows the error in diet, in the course of a few hours, but more often there elapses a period of twelve to eighteen or twenty-four hours. In the period following the excessive use of sugars or starches and before the onset of unformed movements, the subject of this affection may become lethargic or even prostrated to such an extent as to feel quite indisposed for work or exercise. I am disposed to attribute this temporary state of lethargy (which may be only an exaggeration of the habitual condition) to the increase in the chronic congestion of the intestinal mucosa, which, as already mentioned, I

assume to be a usual feature of the pathologic process in its advanced stage.

I consider the clinical phenomena just described as best explicable on the supposition that there has been an upward invasion of the small intestine by the gas-bacillus, although at the present time I have no proof based on early autopsies that this is actually the case in man. The presence of excessive numbers of gas-bacilli in the feces in diarrheal stools gives no positive indication of the level of the intestine at which they have actively multiplied, but in connection with the free formation of gas in the small intestine after carbohydrate food makes it reasonable to believe that these organisms are actively engaged in fermentative decomposition above the ileocecal valve, since no other bacteria found in the stools of these patients possess a gas-making capacity at all comparable with that of *B. aerogenes capsulatus*.

There is probably little simultaneous bacterial attack on the proteid food in the small intestine, for the gas-bacillus acts preferentially on the carbohydrates of the food. Nevertheless, free multiplication on carbohydrates prepares suitable conditions for subsequent putrefaction, as the gas-bacillus decomposes proteids more actively when carbohydrates gradually become scarce. Unless, therefore, the intestine be relieved of its proteids by the occurrence of diarrhea, gas-bacillus fermentation in the small intestine facilitates putrefaction at lower levels.

The maintenance of a strongly acid reaction is antagonistic to putrefaction, but alkali may be derived in sufficient quantity from the succus entericus of the pancreatic juice to neutralize such volatile fatty acids as fail to be absorbed. When the reaction of the intestine approaches neutrality to litmus the decomposition of proteid begins. This proteid decomposition yields both butyric acid and ammonia, and the latter may be sufficiently abundant to establish a neutral or even slightly alkaline reaction.

In the advanced stages of chronic saccharo-butyric putrefaction there is developed a marked sensitiveness of the digestive tract to acids, which may lead to diarrhea. The digestive tract may become so intolerant of acids that ordinary moderate quantities of kumyss or bacillac or zoolak cause increased peristalsis or diarrhea owing to the lactic acid they contain. An equal volume of water may stimulate peristalsis, but does not cause diarrhea. The intolerance to fruits which exists in these patients is due in part to the organic acids they contain, but in part, of course, to their content of carbohydrates which yield butyric and other volatile fatty acids. Indeed, the intolerance of this group of patients to carbohydrates in general is probably to be interpreted as an excessive sensitiveness of the mucous membrane of the small intestine to the organic acids formed from carbohydrate cleavage.

It is perhaps hardly necessary to add that this sensitiveness (due to chronic inflammation) expresses itself also in an intolerance for mechanical irritants, such as cellulose, the seeds of berries, etc. In some instances of this affection the mouth quickly develops an acid reaction from the use of carbohydrates. This is, however, due to other varieties of bacteria than the gas-bacillus and does not appear to be a constant occurrence. Moreover, this excessive acidity of the mouth after taking sugar may be observed in persons who do not show any definite indications of the saccharo-butyric type of intestinal putrefaction.

INFLUENCE OF FATS.

The effect of fat on the course of the saccharo-butyric process in the intestine has received little consideration and is at present only imperfectly understood. The fact that neutral fats are relatively resistant to the cleaving action of bacteria leads one to suppose that they play an unimportant part in digestive disturbances characterized by excessive fermentation and putrefaction. On the other hand, there is clinical evidence that in many disorders of digestion the fats are not well tolerated. The chief manifestations of such intolerance are:

1. A tendency to nausea or regurgitation (especially in children) or even vomiting.

2. Abdominal discomfort referred to the intestine.

3. An impaired absorption of fat from the intestinal tract.

Any or all of these manifestations may be observed in cases of saccharo-butyric putrefaction after a meal rich in fats, but none of them can be regarded as in any way characteristic of the process. It should, however, be stated that, although exact fat metabolism experiments are as yet wanting in cases of well-defined saccharo-butyric putrefaction, there is considerable clinical evidence to show that even where moderate quantities of fat are ingested many persons suffering from this putrefactive disorder show a larger percentage of neutral fats and fatty acids in the feces than is the case with normal persons on a similar diet. This holds true even where there is no increase in peristalsis, to which diminished fat absorption might reasonably be ascribed. The necessity for accurately conducted metabolism experiments in such cases is evident.

In relation to the saccharo-butyric type of putrefaction there are two questions in reference to the destiny of the fats which arise prominently: First, how do the putrefactive anaerobes act on neutral fats in regard to their cleavage into fatty acids and glycerin, and, second, what is the influence of the fats on the anaerobic putrefaction of proteins?

THE TECHNIC.

In order to determine the fat-splitting action of various intestinal bacteria on neutral fats, a number of observations were made on media containing a sample of olive oil containing less than 1 per cent. of free fatty acids. In the earlier experiments made the medium consisted of 50 c.c. of peptone bouillon, 20 gm. of olive oil, 20 gm. of ground boiled beef, 100 c.c. of water and a large excess of calcium carbonate. A flask containing this medium was inoculated with fecal emulsions containing an abundance of *B. aerogenes capsulatus*. This fecal material was from a dog in which the biliary and pancreatic ducts had been resected and which showed evidence of greatly excessive intestinal putrefaction. A second flask was inoculated with a fecal emulsion from a dog with a shortened large intestine, but otherwise normal, fed on meat. A third flask was inoculated with human fecal emulsion containing an abundance of *B. aerogenes capsulatus*. The period of incubation was forty hours. The first flask contained 45 per cent. of free fatty acids, the second 37 per cent., and the third 20 per cent.

As it was desired to extend these observations to a greater variety of bacteria, another series of cultures was made. In this series the medium so employed was, for the sake of convenience, used in test-tubes instead of flasks. Each test-tube contained:

Olive oil	2 gms.
Pepton-bouillon	7 c.c.
Boiled beef (ground)	5 gms.
Calcium carbonate	1 gm.

In addition to the control tubes, tubes inoculated as follows were placed in the incubator: 1, Tubes containing fecal suspensions of bacteria, among which *B. aerogenes capsulatus*

was abundant, the fecal material having been heated to 80 C. for 20 minutes to destroy vegetative forms; 2, heated fecal suspensions from another subject, containing *B. aerogenes capsulatus*, but in smaller numbers (this material was also heated to destroy vegetative forms); 3, fecal suspensions from normal breast-fed child, unheated; 4, *B. coli communis* (New York Health Board stock); 5, *B. putrificus* (Biestock) obtained from Kral.

The repeatedly sterilized media, after inoculation with the above material, were incubated for 40 hours. In all cases there was some separation of fluid into layers with an oily layer of varying thickness at the surface. The inoculated tubes also showed a varying quantity of yellowish, cream-like material. The tubes inoculated with human fecal emulsions all had a pungent putrefactive odor with a somewhat sickening sweetish quality. The odor from the culture-free material from the breast-fed child was slight and rather ammoniacal; the odor from the *B. coli* inoculations was faint and slightly putrefactive; the odor from the *B. putrificus* inoculations was moderately putrefactive with a slightly sweetish quality and not ammoniacal.

After incubation the fat was extracted (though not completely) by repeated shaking with ether. The ethereal extract was filtered through absorbent cotton to remove whitish particles suspended in the extract. The ethereal extract was then washed with about one-quarter its volume of water to remove acids other than fatty acids. The ethereal extract was placed in weighed vessels, evaporated to dryness in the water oven and weighed, and then dissolved in boiling alcohol and titrated with a decinormal alcoholic solution of potash with phenolphthalein as an indicator. In cases where some insoluble material unavoidably found its way into the ethereal extract, the vessels were dried and weighed again for the correction of this error after throwing out the substance soluble in ether. The results showed that in the tubes inoculated with human fecal emulsions there had been a high degree of fat-splitting—in one case 72 per cent.; in a duplicate, 59 per cent.; in a second case, 77 per cent. In the tube inoculated with the fecal extract from the breast-fed child the percentage of fatty acids was 4.2 per cent. In the tubes inoculated with colon bacilli and with *B. putrificus* alone, the quantities of fatty acids recovered were less than 2 per cent.

(To be continued.)

THE OPHTHALMO-TUBERCULIN DIAGNOSTIC TEST.

SOME CLINICAL OBSERVATIONS.*

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The early diagnosis of tuberculosis has so recently seemed to be appreciated as of vital importance that there has barely been time to extend the use of means other than physical examination into general use.

The tuberculin test, applied subcutaneously in small doses, is one of the most valuable confirmatory measures when a positive reaction is obtained, yet it still has terrors for those unfamiliar with it. Although rapidly coming into wider use, it is an unpleasant method and almost comparable to general anesthesia when employed for diagnosis. Moreover, when used carelessly or in overdoses it is as capable of doing harm as any of the poisonous alkaloids. These facts need not deter the general practitioner from its use when other means of diagnosis fail, yet it will doubtless not become popular. Any modification of the test which would do away with its unpleasant or dangerous features would, of course, be exceedingly welcome, provided it

* Read at the First Annual Meeting of the Fourth District Branch of the Medical Society of the State of New York, Saranac Lake, N. Y., Sept. 18, 1907.