pointed out, to severe ptosis of the transverse colon, the splenic flexure remaining fixed, and sometimes to unexplained muscular weakness of the distal part of the transverse colon. If such cases are examined by means of a barium enema it is generally found that the fluid run in from the rectum passes without difficulty into the transverse colon; moderately large enemata without the aid of drugs or other treatment, with the exception of an abdominal support if ptosis is present, are then often successful. In two of my cases, however, all medical treatment failed to give relief, and Mr. F. J. Steward effected an anastomosis between the lowest part of the transverse colon and the pelvic colon in one instance, and between the two limbs of the splenic flexure in the other, with satisfactory results.

The comparatively rare cases in which the whole of the bowel is involved are generally amenable to treatment by diet, massage, and drugs. I have up to now only seen a single case, out of the very large number I have examined with the x rays, in which the whole of the colon was involved and in which, in spite of every form of medical treatment I could devise, the patient became steadily more and more poisoned and suffered from more and more pain. Mr. Arbuthnot Lane was good enough to operate on this case for me in December, 1911, and the relief, which was almost instantaneous, has proved permanent and complete. I am therefore convinced that when the whole of the colon is involved, and when thorough and prolonged medical treatment has proved completely ineffective, the operation of ileo-sigmoidostomy is the only rational treatment.

Conclusion.—Ptosis of the intestines does not lead to stasis, except in rare instances at the splenic flexure, a pelvic caecum and a pelvic transverse colon being compatible with perfect health and normal intestinal action. In most cases of constipation a single part of the bowel, such as the rectum, pelvic colon, ascending colon, or splenic flexure, is alone involved, and treatment should therefore be directed to the affected part only. In those cases in which the whole of the colon is involved medical treatment almost invariably succeeds, but when it does not, ileo-sigmoidostomy, with or without colectomy, is indicated.

THE BACTERIOLOGICAL EVIDENCE OF INTESTINAL INTOXICATION.

BY

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My interest in the question of alimentary toxæmia is naturally confined to the bacteriological and biochemical evidence which has been advanced by the school of Metchnikoff in support of their master's thesis. That thesis, as has frequently been explained in previous contributions to this discussion, asserts that the poisons elaborated by the micro-organisms of the intestinal tract, and particularly those harboured by the large intestine, are the most potent factors in the production of a long array of symptom-complexes loosely grouped under the term "autointoxication," and further, that these same poisons are the essential causes of the sclerotic changes in the organs which accompany old age. The thesis, as you can understand, is, therefore, a perfectly straightforward one, and one which ought to admit of both observational and experimental bacteriological proof. In the absence of proof capable of satisfying the bacteriological critic the thesis must remain little more than a fascinating hypothesis. It will be my purpose, therefore, to discuss as briefly and succinctly as the time at my disposal permits the main bacteriological evidence which Metchnikoff and his pupils have brought forward during the past four years in support of the theory of intestinal intoxication. This evidence has been sought for in the following types of research:

1. An investigation of the flora of the large intestine or of the faeces, with a view to the classification and identification of the various bacterial groups and their biochemical properties.

2. Experiments on the toxic action of filtrates of special groups of these micro-organisms in animals.

3. Analogous experiments with substances of definite chemical composition, especially indol.

4. Alteration in the intestinal flora as the result of food changes, constipation, and operations undertaken for the removal of the large intestine.

In connexion with the first of these lines of research the main work has been done by Metchnikoff himself and his pupils, especially Distaso, who have built on the earlier work of Tissier, and I would here point out that French authors are too prone to the assertion that our knowledge of the intestinal flora has been in the main the outcome of French work. Such, of course, is by no means the case. In fact, the chief contributions to our knowledge of the coliform group have come from workers in this country and in America. It is, however, to the anaërobic flora particularly that Metchnikoff and his pupils have directed their attention, as it is these proteolytic anaërobic which they specially incriminate as playing the chief rôle in what they call "intestinal putrefaction." It would be out of place to enter into a description of these various anaërobic, as I am convinced that the question of the classification and identification of these groups is far from settled, and there are probably far more names than bacteria to correspond.

It is doubtful if much that is new on this subject has emerged from recent French work. The chief putrefactive organisms whose cultural and biochemical properties have been studied in connexion with intestinal putrefaction have been *B. perfringens*, *B. sporogenes*, and *B. putrificus*, but it cannot be said that we have yet accurate methods of differentiating anaërobic. One must also mention the acidophile or acetogenic organisms which by the French observers are regarded as highly beneficial organisms by virtue of the inhibitory effect exercised by their acid products on the growth and activity of the putrefactive types.

Of these acetogenic organisms which have the property of producing acid from lactose and of being able to grow in acid media the most important perhaps is the *B. bifidus* of Tissier. This author found that this organism is the chief representative of the flora of the breast-fed child, a statement which more recent work has confirmed. It may be noted that *B. bifidus* is a strict anaërobe, and is Gram-positive.

A very similar organism to which attention has been paid is the *B. acidophilus* of Möro. As the child passes on to more varied food there is a gradual change in the flora from the purely fermentative type represented by the acid formers above mentioned to a combined flora of the fermentative and putrefactive type, using the term "putrefactive" in the sense of ability to break down nitrogenous constituents to the stage of peptones and proteoses and mono and diamino acids. Further katabolism of these cleavage products is effected mainly by the representatives of the *coli* group, many of which have the power of producing indol from tryptophane, and some of producing phenol from tyrosin.

Now it is seen that in the adult normal human flora the Gram-positive acetogenic organisms, represented by *B. bifidus*, are rare, and never predominate as in the young child. The predominant group is that of the *B. coli*, and in addition there are the representatives of the putrefactive anaërobic group (*B. putrificus*, *B. perfringens*, *B. sporogenes*, etc.).

Indol is formed chiefly by coliforms, and only to a small extent by these putrefactive anaërobic. It is, therefore, all the more surprising that Metchnikoff and his school should have drawn so much attention to the anaërobic as the chief factors in intestinal putrefaction, while at the same time their energies should have been devoted to the investigation of the toxic action of indol, a product chiefly of coliform activity. How far the indican in the urine is an evidence or a measure of intestinal putrefaction by micro-organisms is not yet completely settled, but admitting for the sake of argument that it does come from the action of micro-organisms in the intestine, it is not at all clear why it should be regarded by Metchnikoff and his school as the chief toxic agent produced by their action. Indol, of course is a substance of definite chemical composition, while the known bacterial toxins are of unknown chemical composition. How far,

then, the Metchnikoff school is justified in taking a simple substance like indol as the toxic product *par excellence* of the action of putrefactive intestinal microbes is extremely doubtful. Recently the opinion has been revived by Emmerich that in cholera the symptoms of intoxication are not due to specific vibrio toxins but simply to the nitrites, which, as you know, the *V. cholerae* is capable of forming in the test tube.

Little support has been given to this view in the case of cholera, and it would therefore seem all the more gratuitous to regard indol as the main toxic product of putrefactive organisms the pathogenic action of which has been only very insufficiently studied.

Let us see, therefore, what has been the main result of the experimental work performed with these putrefactive anaerobes and with their presumed chief toxic product indol. In one of his earliest papers Metchnikoff tested the toxic action of filtrates of some of these anaerobes. Filtrates were tested intravenously on rabbits in doses of 7 to 8 c.cm. per kilo of body weight. These are very large doses. For an ordinary full-grown rabbit this would mean at least 20 to 25 c.cm., and it is not surprising that in some cases a fatal result ensued. Great variation, however, was apparent in the toxic power of these filtrates (*B. perfringens*). Nevertheless the result of these experiments led Metchnikoff to state that in the putrefactive organisms of the digestive tube we have a source of autointoxication. Further experiments on this line were performed by his pupil Korentschewsky, who tested filtrates of anaerobic organisms isolated from rabbits' faeces. Occasionally quite potent filtrates killing in 1.3 c.cm. per kilo were obtained, but in other cases doses of 20 c.cm. per kilo did no harm. The strongest filtrate was prepared from *B. perfringens*.

Experiments were also performed on rabbits by intra-rectal injection of filtrates, and there was some very slight evidence that antibodies to these organisms appeared in the blood serum.

In the case of dogs fed daily with broth cultures of *B. perfringens* (in very large doses, 200 to 500 c.cm.), progressive loss of weight occurred with slight anaemia, and when the animals were killed some evidence of sclerotic changes in the kidneys were found. It is surprising that nothing worse happened after such heroic dosing!

It must not be supposed, however, that the putrefactive organisms are the only defaulters. The flora of the large intestine is, according to Metchnikoff, wholly bad, and therefore we have other series of experiments with preparations of staphylococci, *B. coli*, etc.

According to Manouélian, atheromatous plaques appeared in the aorta of a large proportion of rabbits inoculated repeatedly with staphylococci (in 73 out of 86), and also in monkeys. These plaques occurred at the level of the arch of the aorta. It must be noted, however, that Weinberg found spontaneous atheroma in 4 to 19 per cent. of rabbits. More recently Bertrand and Berthelot have isolated from the faeces of patients suffering from chronic autointoxication an organism which, when grown on a special medium containing histidine, yields a highly toxic product apparently identical with β -imid-azoethylamine, a base previously obtained by Ackermann in the putrefaction of histidine, and also by Barger and Dale in ergot. The organism which yielded this toxic product belonged to the coliform group, and, according to the authors, was closely related biochemically to the *B. lactis aerogenes*. The authors make the statement that this particular organism was never found in the faeces of normal healthy people. This is a very important statement, and confirmation must be awaited before it can be accepted.

I turn now to the animal experiments performed with definite chemical substances which are understood to arise from the action of micro-organisms in the intestinal tract. In these experiments by Metchnikoff, Dratschinski, and others, potassium phenylsulphate and indol have been the chief substances whose toxic action on animals has been investigated.

With potassium phenylsulphate atheromatous changes in the aorta of rabbits, guinea-pigs, and monkeys were produced, and small cell infiltrates in the liver and kidney. Rabbits received by the mouth 0.04 gram of paracresol during a period of one to four months, and 61 per cent. of the rabbits showed atheromatous

plaques. Dratschinski gave similar doses of indol daily to guinea-pigs by the mouth, and obtained evidence of atheromatous degeneration of the wall of the aorta with chronic interstitial processes in the organs, such as the liver, kidney, and suprarenal capsules. These foci in the wall of the aorta invariably contained calcareous deposits, and the question to be decided was whether these foci met with in the animals intoxicated with indol were merely further stages in the development of the cartilaginous foci met with in similar situations in normal guinea-pigs, especially those of advanced age. Such foci were met with in 67.5 per cent. of normal guinea-pigs weighing 250 grams and over. The author was of opinion that hyaline and calcareous foci encountered in the intoxicated animals were distinct from the cartilaginous foci found in normal animals, and concluded that intoxication with indol was the exciting cause. It does not appear to me, however, at all proven that the indol, if it affected anything at all, did any more than hasten the calcareous transformation of these normal cartilaginous foci, and the question of the influence of indol in this connexion must still be considered as undecided.

I now come finally to discuss the changes which have been stated to occur in the composition of the intestinal flora in cases of intestinal stasis and in cases which have suffered resection of the large intestine. This question has recently been attacked by Distaso who had the advantage of obtaining material from Mr. Lane's cases.

Distaso roughly classifies the organisms of the intestinal tract according as they do or do not produce indol. In the normal adult man the faeces, as is well known, show a preponderance of indologenic organisms of the coliform group. In constipation, according to Distaso, there are practically no Gram-negative organisms, but there is a great abundance of spores, the indol-formers being now of the sporulating type. There is also an absolute diminution in the quantity of bacilli present. The conclusion drawn by Distaso that the flora of constipation is an index of intoxication is entirely unsupported by the evidence he adduces. In cases operated upon for removal of the large intestine it was observed that the flora showed not so much a qualitative change as a quantitative change with a consequent alteration in the functional activity of the organisms concerned. Before operation the flora was one typical of constipation, while after operation the indologenic organisms had largely given place to the acetogenic (that is, *B. bifidus* and *B. acetogenes*) which are regarded as highly beneficial. The effect of this change, according to the author, is that the acid produced by the latter organisms inhibits the activity of, or actually destroys, any putrefactive organisms present. The evidence on which this statement is based was the fact that, when the faeces were inoculated on a potato medium, marked acid formation took place, while growth on broth containing boiled white of egg only rarely was followed by proteolysis indicating an action on the part of the putrefactive organisms. It is very questionable how far it is legitimate to assume that the function of a flora in the body can be determined by an *in vitro* experiment of this rough order. To prove a change in flora of this character would require far more extensive bacteriological and biochemical research than has so far been devoted to the subject, and it is indeed remarkable that the author should make the astounding statement "that after this study the theory of chronic intoxication by the work of intestinal organisms cannot any longer be in doubt." As a matter of fact, it is not clear from the paper how often the faeces were examined in these cases, and whether samples were taken at operation from the bowel above the resection.

If, as stated, only two examinations of the faeces at a year's interval were made, the data so obtained would be of little value. Such cases would require to be examined repeatedly before and after operation, and under all conditions of diet.

Distaso further asserts that the intestinal flora of the normal adult is noxious, and yet he asks the reader to rejoice with him over the microscopical appearance of the faecal flora of one of these operated cases. This flora, of which a drawing is appended, is characterized as "*une des plus belles*," but certainly the flora of the constipated person—a drawing of which is placed alongside—seems far

the more attractive. With regard to the work done by the Metchnikoff school on the influence of food on the composition of the faecal flora, I would merely refer to certain experiments of Bertrand, who found that rabbits fed on potatoes always gave a marked indican reaction in the urine, while those fed on carrots gave no such reaction. When a carrot-fed rabbit was placed on potato diet indican appeared. The intestinal flora of the two groups did not differ qualitatively, but the potato-fed rabbits had more *B. coli* in the faeces. No quantitative data on this point are supplied. Bertrand's view was that in the potato-fed rabbit there was much less acid production from the fermentation of sugar than in the carrot-fed rabbit, and consequently there was nothing to inhibit the formation of indol by the coliforms present. Also it is stated that the flora of the potato-fed rabbit was very poor in amylolytic species, but data on this point are wanting. It cannot be said that work of this kind advances the subject far. One is tempted to ask why chemical examinations of the intestinal contents were not made at various levels, and accurate records kept of the organisms met with at these levels. In all the recent work on autointoxication and on sour milk therapy, it has to be remembered that the inhibition of intestinal putrefaction by milk and milk constituents, especially milk sugar, was known years before Metchnikoff popularized the administration of milk soured by lactic acid bacilli (see an excellent survey of this subject by Kendall, 1912, *Journal of Medical Research*, vol. xxv, p. 117), and, as pointed out by this author, the effect of such treatment may be due, not to acid produced by the bacilli supplied, but to that produced by *B. coli* acting on the sugar, which is generally increased in the diet. Protein is thus spared, and consequently protein decomposition products do not appear. A bacteriological basis for the view that the activity of lactic acid bacilli inhibits that of the putrefactive organisms in the intestine is still lacking.

In conclusion, I am of opinion that the investigation of the biochemical action of intestinal organisms yields a very large and promising field for future research, and may throw a flood of light on this question of auto-intoxication, but it does not seem to me that the results achieved in the types of researches so far published by the Metchnikoff school lend any very marked support to the thesis.

Memoranda :

MEDICAL, SURGICAL, OBSTETRICAL.

LONG SURVIVAL AFTER REMOVAL OF MAMMARY CARCINOMA.

This record may be of interest. A lady had a scirrhus of the breast removed in 1898. A recurrence was more widely removed in December, 1899. She lived to November, 1910, when she died of extension to the lungs, aged 68.

During the greater part of the interval she enjoyed very fair health, was able to travel abroad, to see her daughter married, and grandchildren growing up.

Putney, S.W.

JOHN GAY.

AFTER-HISTORY OF A CASE OF MYELOID SARCOMA OF THE FEMUR TREATED BY SCRAPING.

IN the JOURNAL of February 26th, 1898, I reported the case of myeloid sarcoma of the femur operated upon in 1895. Since then the patient has remained in perfect health, and recently writes, "My health is very good; my knee is sometimes painful, but is fairly strong; I cannot bend it. I am able to attend to my work (a wheelwright's), and have walked ten to twelve miles in a day. There is still a slight discharge from the wound, which I dress about once a week." Obviously this is a better result than that obtained by amputation.

Professor Bloodgood of Baltimore, in a paper published in the *Transactions of the American Surgical Association*, 1910, had collected two cases besides this one, which had been similarly treated, and had both done well.

From the discussion at the Surgical Section of the Royal Society of Medicine in November last, at which no example of treating myeloma of the femur by scraping was mentioned, it must be inferred that the method is not practised at the London hospitals. In the hope that surgeons will give it a trial I venture to again draw attention to the case which has been under observation for eighteen years.

FRANK HINDS, M.D.,
Honorary Surgeon, Worthing Hospital.

LARGE FIBROMYOMA OF THE URINARY BLADDER.

THE following case is interesting from the fact that fibromyoma is exceptionally rarely found in the bladder.

Mrs. H., aged 44, was admitted to the Walsall Hospital on February 2nd, complaining of retention of urine, pain over the region of the bladder—both of three months' duration—and of haematuria of one week's duration. The usual points of differential diagnosis were considered, and in order to facilitate the examination she was anaesthetized. On vaginal examination, a large, hard tumour was felt over the anterior vaginal wall. The uterus was freely movable and normal in size. It was decided to explore the bladder, and for this purpose the urethra was dilated until it admitted the forefinger. By this means it was ascertained that the tumour was occupying practically the whole of the bladder and was firmly fixed in the region of the trigone. Subsequently the bladder was opened suprapubically and the growth, which was the size of a closed fist, removed after ligating the pedicle. She made an uninterrupted recovery.

Microscopically the tumour was composed of interlacing bundles of smooth muscle tissue, with a small amount of stroma and well formed blood vessels. There was no evidence of malignancy.

I am indebted to Mr. Caddick for permission to publish this very interesting and extremely rare case.

Walsall.

J. D. SPEID SINCLAIR, M.B., Ch.B.

British Medical Association.

CLINICAL AND SCIENTIFIC PROCEEDINGS.

OXFORD AND READING BRANCH: MAIDENHEAD DIVISION.

CLINICAL MEETING.

At a well-attended meeting of the Maidenhead Division of the Association held at the Guildhall, Maidenhead, on March 27th, after Dr. G. E. MOORE, who was in the chair, had entertained those present to tea, Mr. ANGUS MACNAB, F.R.C.S., read a paper on *Recent operative procedure in glaucoma*. The inefficiency of iridectomy in the treatment of chronic glaucoma and the study of the pathological material available had combined to lead to the view that the criterion of success in the surgical treatment of this disease must be the establishment of a fistulous track between the anterior chamber and the sub-conjunctival lymph space. He described briefly and lucidly the methods of Professor Lagrange, Lieutenant-Colonel Herbert and Elliot, I.M.S., and paid a tribute to the skill of these surgeons. The detailed technique of Herbert and Elliot's operations was described, the speaker's preference being for Elliot's method by means of a special trephine. The important point in both these operations was that the aperture should be close up to the corneal margin. Mr. MacNab was heartily thanked for his interesting paper. Dr. J. J. PATERSON, D.P.H., followed with an amusing paper on *Quacks and their methods*. He had a regular Odyssey of adventure to relate in his personal experiences with some well-known quacks; and although some of the narratives might not perhaps be quite appropriate for a lady's boudoir, the success of his crusade in exposing some of these gentry was heartily appreciated. The meeting then adjourned.