supposed there was no doubt whatever that strychnine quickened the reflex reaction, but he thought that, theoretically, that quickening might take place in a number of different parts of the reflex arc rather than at the synapses. Perhaps the nerve-cells might act more quickly, and his idea of the action of strychnine was that it stimulated nerve-cells rather than terminations of the nerves.

The PRESIDENT said he understood that it was only by a summation of stimuli that one judged whether there was a synaptic resistance. He thanked Dr. Stoddart for his very interesting and suggestive paper, which would remain in their minds as a definite contribution on obscure confusional insanities.

Dr. STODDART, in reply, said that there was definite improvement after the injections, but he did not recommend it as a treatment except when the hallucinations were such as to cause much mental disturbance. It was not intended as a cure. For such a purpose one had to improve the general health. He only brought forward the effect of strychnine as a support to his thesis. He had kept up the injections for two or three days, and they very much lessened the excitement. The point was that the anæsthesia was apparently due to increased resistance at the synapses, because it could be overcome by multiple stimuli of various kinds, whereas a block due to disease of the neuron itself could not be overcome, so far as was known, by having a multiple stimulus, or a stronger stimulus. He had previously come to the same conclusion from a study of the nature of hallucinations.

The Treatment of Melancholia by the Lactic Acid Bacillus. (1)

By J. GEORGE PORTER PHILLIPS, M.B., B.S. (Lond.), M.R.C.S., L.R.C.P., Assistant Physician, Bethlem Royal Hospital.

MELANCHOLIA, with its attendant constipation and faulty alimentation, lends itself at once to a dietetic form of treatment.

Whether the constipation is dependent on defective innervation and is a direct symptom of melancholia or is the initial cause of this mental disturbance, it matters not so far as our endeavours in treatment are concerned.

It is obvious that the melancholiac, in the acute stages of his illness, struggles against great odds owing to the following facts: His alimentation is defective, his excretions are diminished, and, moreover, his whole system is in a state of auto-intoxication. In other words there is a general clogging of the metabolic processes. The disturbance of the alimentary tract tends to form a vicious cycle hindering the nervous system from obtaining an efficient and pure food supply.

We have ample evidence of this impaired metabolism with its toxæmia. The patient has a sallow, muddy complexion, a dry skin, a parched, furred tongue, a high-tension pulse, brittle nails and lustreless hair, a scanty high-coloured urine

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containing an excess of ethereal sulphates and fæces deficient in quantity and moisture and very offensive in odour.

Ranging from a mild attack of depression to a severe case of melancholia one finds the hub of the disturbance centring itself in the alimentary canal. For this auto-intoxication free purgation and administration of chemical antiseptics will afford relief but are not satisfactory.

An item of treatment which pre-eminently suggests itself is one which will not only inhibit the growth of the proteolytic organisms, the common cause of the abnormal putrefaction and consequent auto-intoxication, but will also obtain a biological intestinal antisepsis.

By the ingestion of vigorous cultures of the lactic acid bacillus under suitable conditions of diet one is able to produce this desired inhibition of these putrefactive processes. That this takes place is proved experimentally by the diminution of the daily urinary excretion of the ethereal sulphates and by alteration in the character and quantity of the stools. There is also a decrease in the number of the Gram-negative organisms and a great increase in the Gram-positive. This process of inhibition is probably due to the lactic acid formed in the intestine in a nascent state, this being dependent on the fact that the growth of putrefactive organisms which grow favourably in an alkaline medium is arrested by an acid-producing organism in a saccharine medium.

It is not my desire to write a monograph on the lactic acid organisms, but I think it is desirable cursorily to discuss the leading varieties.

An exact classification of the true lactic acid forming organisms has not met with any great degree of success. The soured milks used in Bulgaria, Egypt, Turkey and other eastern countries contain bacteria which are peculiar to themselves.

Kern, in 1881, described a milk-curdling organism which he isolated from the Russian Kefir, but this was found to be a spurious form of the lactic acid bacillus.

Rist and Khoury later investigated the Egyptian soured milk called Leben raib and described two kinds of organism—(1) *Bacillus lebenis*, (2) *Strepto-bacillus lebenis*. Grigoroff, working in Professor Massol's laboratory at Geneva, isolated, three years later, from the Bulgarian yohourth, two varieties of

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the organism, and these he called "Bacillus A" and "Strepto-bacillus C." These appear to be identical with the two strains described by Rist and Khoury, the strepto-bacillus in each case forming a smaller percentage of the lactic acid than the long bacillus—*lebenis* or A. In 1906, the bacillus A, or bacillus of Massol, was carefully described by Cohendy, who has done much work on the lactic acid organisms. Duggeli was the first to demonstrate the granule-staining in certain strains of lactic organisms. He obtained his cultures from the Armenian sour milk called Mazun.

The strain we have been using at Bethlem is the long bacillus of Massol, and we have noticed that this variety at certain times assumes the strepto-bacillary form, and occasionally shows this metachromatic staining with methylene blue.

From this observation I have formed an opinion that the two different varieties described are simply the result of a temporary deviation in the morphology of one organism. It is from 2 μ to 50 μ long and 1 μ broad. It is non-motile and does not form spores. Viable bacilli are Gram-positive, whilst dead are Gram-negative. Cultivation is very difficult on ordinary media, and at most is feeble. It is both aërobic and anaërobic, and grows best at 38° C. to 40° C., optimum temperature being 45° C., and minimum about 25° C. On whey agar the colonies are circular, irregular, a greyish-white in colour and curled at edges. Gelatine is not liquefied and potato gives no growth. The lactic acid formed is either inactive or else lævo-rotary.

No peptonisation of the curd takes place. It is non-pathogenic, and may be given even to infants.

The following distinctive characters of the two varieties may be of use:

Type A (long bacillus): Stains homogeneously with methylene blue, 2·7 to 3·7 *per cent.* of lactic acid formed, and is inactive.

Type B (strepto-bacillus): Metachromatic granules with methylene blue, 1·2 to 1·6 *per cent.* of lactic formed, and is lævo-rotary.

It is important that a vigorous strain of bacillus should be obtained, as weakly ones are easily inhibited and tend to die out quickly.

Now as to the methods of preparing and administering

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the bacilli, they may be administered (*a*) in *solid* form—tablets, powder, and gelatine whey; (*b*) in *liquid* form—bouillon of various kinds and curdled milk. The tablets and powder are quite unsatisfactory, owing to the small number of living organisms present in some brands and the total absence of living organisms in others. The lactic gelatine whey, when carefully and freshly prepared, is an admirable method of administration, especially to melancholiacs who refuse the milk or to other patients who are already well nourished, but there is no other special advantage in adopting its use.

In the liquid form we have various fluid media at our disposal: (*a*) milk, (*b*) lactose whey, (*c*) maltose whey, (*d*) malt extract solution.

In order to prepare the lactose and maltose whey one must proceed as follows: To each litre of milk add 1·5 c.c. of HCl and boil carefully for five minutes; in this way the casein will clot and separate. The whey may now be filtered through a piece of fine-mesh muslin. To each 100 c.c. of whey add two grammes of the sugar, maltose, or lactose. The most reliable sugars are those manufactured by Messrs. Kahlbaum.

Curdled or soured milk has now become so popular a panacea that the prescription has found a prominent place in the pharmacopœia of convention. Every dairyman has of late been initiated into the craft of bacteriology, and now claims to supply a pure sour milk, curdled by means of the real Bulgarian bacillus, the names of Professor Metchnikoff or Professor Massol being tacked on to assure the public that the organism employed is the one advocated and used by these pioneer scientists respectively. Many dairy companies manufacture and offer for sale a genuine and reliable sour milk, the whole process being carried out under scientific control. The chief objections to this source of supply are the expense, and, in outlying districts, the trouble entailed in obtaining a fresh daily supply.

For purposes of treatment of a number of hospital patients it is only necessary to obtain an incubator working at 37° (or a little higher), and a set of vessels for daily distribution. An ordinary-sized bacteriological incubator of Hearson's manufacture is sufficiently large for supplying curdled milk for twelve patients. Hearson's have a special form of incubator for this process, but the ordinary pattern suffices.

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There are various kinds of bottles used for the distribution of the milk, but after practical experience of the different patterns I have found an Erlenmeyer flask of 300 c.c. capacity the most useful and serviceable. This holds about half a pint. The advantages are that, being made of thin glass, it is easily sterilised in a hot-air oven at high temperature without cracking, and the tapering neck with its moderately wide mouth lessens the chances of contamination, the aperture being readily plugged with cotton-wool.

The preparation of the curdled milk is quite simple, but good results are only obtained when a strict ritual is observed, the keynote being *efficient sterilisation*.

The milk to be perfectly sterile should be brought up to a temperature of 120° C. Not only is it difficult to obtain this temperature by ordinary means, but also it imparts an unpleasant flavour to the product. For ordinary purposes it is sufficient to bring the milk up to the boiling-point for five minutes, as by this method all organisms are destroyed with the exception of the spores of the *Bacillus subtilis* and the *Bacillus butyricus*.

The flasks, having been washed with warm water and soap, are drained, plugged with cotton-wool and sterilised at a temperature of 140° C. for twenty minutes in a hot-air sterilsier. This procedure should be carried out on the daily return of the empty flasks from the wards. By having a duplicate set of flasks for each patient this method of cleansing and sterilisation can be adopted with ease and advantage. The cotton-wool plug is removed from each flask and the sterilised milk poured in, the plug being at once re-inserted. It only remains now for the cooling to take place and the inoculation to be made.

The most convenient way for perpetuating a healthy and vigorous culture of the bacillus is to keep a couple of sterile flasks specially for the stock cultivation of the organism. These are filled with sterile milk and inoculated with a few c.c. of the original or initial culture, purchased, or otherwise obtained from some reliable source. After incubating for twelve hours we have a stock culture, from which one is able to obtain a plentiful supply for inoculation purposes. Fresh stock cultures should be prepared every two or three days. Five to ten c.c.'s of this culture are taken up in a sterile pipette and ejected into each flask. The wool-plugged flasks are now

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placed in the incubator for eight or ten hours, at the end of which the milk in a curdled state is ready for distribution to the wards.

A daily bacteriological examination should be made to investigate the growth and purity of the culture.

One meets with various difficulties in the process, and the following points are useful to be remembered: (1) Failure of the organism to grow. This may be due to the presence of antiseptics in the milk (this is likely only in summer), or to a weak or dead culture being used for purposes of inoculation. (2) Contamination. This may be due to careless sterilisation of milk or flasks. These sources of failure should be sought out and rectified, especially the latter, as pathogenic organisms, *e.g.*, streptococcus, staphylococcus, *Bacillus enteritidis sporogenes*, *Bacillus typhosus*, etc., may be present in a sample of milk. From this fact it is self-evident how important it is to sterilise the milk efficiently before putting it into an incubator, where under more favourable conditions multiplication of the harmful organisms takes place before the inhibiting effect of the lactic acid can be exerted.

Two flasks, each holding about half a pint of the preparation, are sent into the ward for each patient, one portion being taken at 11 a.m., and the other at 4 p.m., or, if preferred, at breakfast and supper, the milk being whipped up with a little cream and sugar. In this way the whole contents of each flask are used up at each separate meal, and there is no fear of contamination, as the flask is not used again until it has been washed, drained and sterilised.

During the treatment it is necessary to adopt a strict regimen. At the onset the patient is placed on—

Diet A.—Suppress all food with the exception of milk, malt extract and *sugar of milk solution.* After two days give in addition gruel, milk puddings, custard, bread-and-butter biscuits.

After three to seven days adopt—

Diet B.—Avoid meat and all soups or gravy. Give yolks of eggs, milk, cream, bread-and-butter, potatoes, milk puddings, fruit and vegetables. After one week allow fish every other day.

By this means the pabulum for the growth of proteolytic organisms is reduced to a minimum whilst that suitable for the multiplication and acclimatisation of the lactic acid bacillus

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is increased. Although the lactic organism can be demonstrated in the fæces a few days after its regular administration, it takes at least a week or ten days before it becomes properly acclimatised. After acclimatisation it continues to thrive for twelve days longer without another dose being taken, and after that it tends to disappear.

During the early part of the treatment, in a few cases where the large intestine is in a state of atony, intestinal spasm may occur giving rise to colic. I have also noted headache, tinnitus, itching of the skin and nausea as unpleasant concomitants.

A somewhat marked feature in many of the cases noticeable at the end of the first week is the aggravation of the constipation. Some means has to be taken to combat it. Boiled vegetables and fruit greatly aid the regular evacuation of the bowels, and figs, prunes and boiled apples should be given freely in the dietary until the constipation lessens in severity. Some cases are so obstinate that medical treatment has to be resorted to; for these I have found the morning use of a glycerine enema or a nightly dose of treacle (1 or 2 tablespoonfuls) very efficacious. Even after a few days' treatment one is able to notice a difference in the appearance of the patient. The complexion is clearer and he wears a happier expression. The dry, furred tongue becomes moist and clean, and an increasing desire for food gradually appears.

As stated above, the constipation, although obstinate at first, tends to decrease. The fæces increase in quantity, become softer, and of regular consistency, and the offensive smell diminishes. Objectively with these changes the daily excretion of ethereal sulphates in the urine becomes less.

In order to check the quantity of fæces passed Schmidt's method should be adopted. This consists of separating off the stools of three days by means of a small meal of charcoal biscuits. In this way it has been found that a healthy person will pass during the three days a quantity of fæces which when dried will weigh 60 grm., whereas that passed by a habitually constipated person will not average more than 30 grm.

For the determination of the amount of ethereal sulphates excreted in the urine Salkowski's method is the best. The inorganic sulphates are precipitated by means of an alkaline solution of barium chloride. Barium sulphate is formed, which is filtered off, and the filtrate, after being acidified with HCl

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is heated just up to boiling-point. This results in the decomposition of the ethereal sulphates, which immediately combine with the barium salts present in excess. The precipitate is now collected on a filter-paper of known weight, ignited and weighed.

Coincidently with the amelioriation of these symptoms a marked increase in the patient's weight takes place. Usually from about the fourth or fifth day the patient puts on weight steadily, and I have record of a case in which the weight increased at the rate of nine pounds in nine days. For the purpose of control I have had patients weighed in the usual way on admission, put on ordinary diet, and their weight and symptoms noted at intervals of a week. In the majority of these cases only a slight increase, and in others no alteration in weight was noted, and the symptoms were in no way amelioriated. After a few weeks, or in some instances much longer, the patient was put on the lactic acid bacillus treatment.

In all cases which subsequently proved to be the genuine forms of melancholia, and not depressed states of other mental conditions, a decrease of the symptoms and an increase of bodily weight ensued.

The increase of body-weight was registered weekly and the results placed on special weight-charts.

The *weekly iucrease* varied from 1 to 5 lb., and the *total increase* during the whole duration of illness ranged from 12 to 28 lb.

Up to the present we have been discussing chiefly the physical side of these cases. Now let us view the mental side of the picture.

As described above, the patients undergoing treatment gradually lost their depression and accompanying delusions, and the state of lethargy present in so many cases became one of activity, the rigidity of the large joints soon disappearing. The patients suffering from delusions without hallucinations were the most amenable to treatment. Those cases in which hallucinations appeared showed slower recovery. *Eighteen* male cases were treated; of these, two who are still on treatment are returned as improved, the final decision as to cure or otherwise being unable to be legitimately given. Of these eighteen cases eleven have *recovered*: two still on

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treatment have *improved*; four un-cured (one of which proved subsequently to be a general paralytic); one died (agitated). In every case treated the body-weight increased considerably.

I wish here to acknowledge the valuable assistance which has been rendered me by Mr. Philip Crowe, our pathological assistant.

CONCLUSIONS.

The lactic acid bacillus has a decided beneficial effect on cases of true melancholia with disturbance of the alimentary canal: (*a*) By diminishing the amount of toxins absorbed from the intestinal tract; (*b*) by promoting a rapid and easy assimilation of food material—a very important factor, as in the majority of cases the previous history shows there has been great decrease in body-weight. It certainly shortens the duration of illness and increases the chance of recovery. The percentage of recoveries is increased from 46 *per cent.* to 61 *per cent.*

From a careful study of numerous cases I am convinced that a large number of them could be mitigated by early treatment with the lactic acid bacillus.

Its value in correcting defective alimentation suggests that it might be used with great advantage in other mental conditions.

(1) A paper read at the Spring Meeting of the South-Eastern Division, held at Hanwell, on April 26th, 1910.

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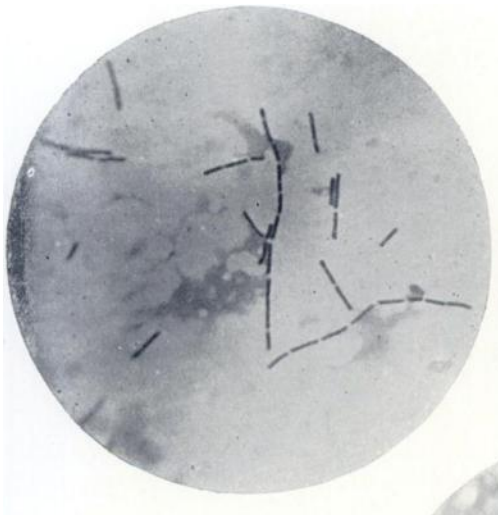

FIG. 2.—*Strepto-bacillus.* × 600. Showing chain formation, and resembling *Bacillus anthracis.* Stained by Gram's method.

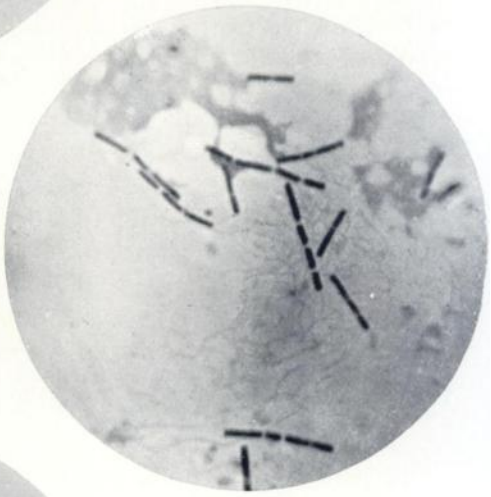

FIG. 3.—*Strepto-bacillus.* × 1000. Stained with methylene blue, which makes organism appear thicker.

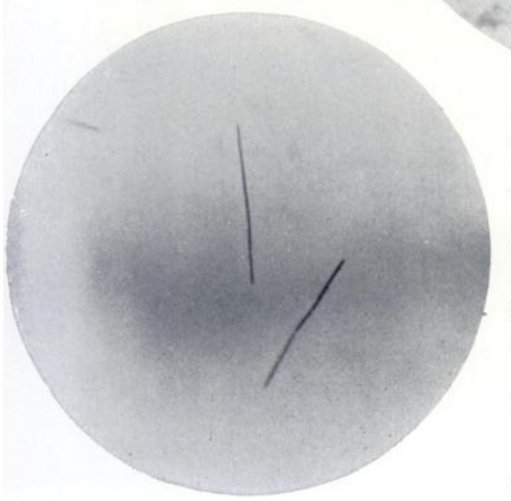

FIG. 1.—*Long bacillus of Massol.* × 600. Stained by Gram's method.

To illustrate Mr. J. George Porter Phillips's paper.

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