to the front position in man, thus attaining recently acquired stereoscopic vision. Has not this change been brought about by diminishing action of thyroid on the fœtus and weakening of the pull on Landstrom's muscle, which, in adult hyperthyroidism, gives rise to Mœbius's sign? Myopia is widely prevalent amongst the human species, and recently has been shown to be caused by the slight divergence of the eyes. The inner muscles of the eyes in trying to correct this are subjected to strain which produces myopia. Many cases of myopia are now being reduced and many others have been entirely cured by the use of prismatic glasses, which restore the parallelism, and allow the eyes to remain in their natural slightly divergent position.

May not this divergence of the eyes in myopia be due to an incompleteness of this most recent attainment of evolution, and result from antenatal hyperthyroidism causing contraction of Landstrom's muscle in the fœtus?

Other conditions as well as mongolism, *e.g.*, fœtal monstrosities, have by some authorities been attributed to endocrine disturbances, by others to "reversion." It is more likely that a theory which incorporates both views is the correct one, and if thyroid acts on the human fœtus, when ontogeny is at the gill stage, in a similar way to its action on the gill stage of the frog, monstrosities can easily be explained. In view of the fatty and cholesterin changes brought about in spermatoblasts by thyroid it is possible that hydatid mole is an analogous condition. The problem of the mongol and the thyroid is wrapt up with the problem of evolution and of gland balance. Positive proof of my view seems as yet impossible, and no excuse is required for the speculative nature of the views expressed in this paper, which, if not immediately acceptable, will be of use if they call attention to the application to general medicine of some of the findings of experimental embryology, tissue culture and thyroid feeding.

Bacterial Change in Mental Disorder: Preliminary Note on Morgan's Bacillus. By F. H. STEWART, M.A., D.Sc., M.D., D.P.M., Major, Indian Medical Service (retired), Cheddleton Mental Hospital.

IN a previous communication (*) it has been shown that among intestinal bacteria of the coliform group *Bacillus paracoli* and *Bacterium coli mutabile* are at least four times more common in the insane than in the general community, and that they are to be

* *Vide* "Bacterial Changes in Mental Disorder: Coliform Group," by the same author, *Journ. Ment. Sci.*, 1928, p. 59.

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found in great number in at least one-half of the former during acute phases of illness. It was suggested that both the illness and the increase of these bacteria might be due to a third factor, namely, to the action of some other intestinal organism, since certain workers had found that colon bacilli when grown on phenol varied to the ***mutabile*** type, and it is well known that phenol is formed in the intestine by certain bacteria.

Following up this suggestion, and in the first place considering Tissier's statement (*Bull. Inst. Pasteur*, p. 363, 1923) that *B. lactis aerogenes* and *B. aminophilus* produce phenol, the question was investigated whether *paracolon* and *mutabile* occurred in greater number in stools which contained many saccharose-fermenting bacteria. No such association was found, and at the same time none of the strains of *B. lactis aerogenes* isolated in this laboratory were found to yield phenol.

In the second place the question was examined whether the natural mixture of bacteria present in fæces produces phenol in cultures containing tyrosine. (Tyrosine fluid cultures were inoculated direct from the stool, incubated two days, distilled and tested.) Out of 101 specimens examined (from 69 persons), 95 gave phenol and only 6 did not; of the 95 positives 71 were from mental patients and 24 from sane controls, while of the 6 negatives 4 were from patients and 2 from controls. There was, therefore, no difference so far between the sane and the insane. But cultures from some of the patients gave higher phenol readings than any from the controls; of 41 cultures with phenol above 0·015% 40 were from the former and only 1 from the latter.

The next step in the investigation consisted in plating out the bacterial mixtures in the above primary cultures, and in trying to isolate the bacteria which were responsible for the phenol production. In this we were successful in specimens from only 17 individuals.

The bacteria isolated belonged to the following species:

Bacillus Morgani (No. 1, Morgan, 1906) from 14 individuals, of whom 12 were patients and 2 were controls.

Bacillus phenologenes (Berthelot, 1918) from 3 individuals—2 patients, 1 control.

Bacillus paracoli (Gilbert and Lion, 1893) from 1 patient.

(In all, 325 isolated strains were tested, of which 28 produced phenol.)

B. Morgani was found in the stools of 12 out of 48 mental patients (25%), and of 2 out of 21 sane controls (9·5%); of the 2 neither was in robust health, and both were attendants who were constantly exposed to infection from their patients. None of the

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individuals examined was suffering from diarrhœa, and 3 of the 12 patients were recent admissions in whom asylum infection was not likely to have taken place. Animal experiments also showed that the strains isolated from our cases had no specific action on the bowel, and that in this they differed emphatically from Morgan's original strain in the National Type Collection.

B. phenologenes, Berthelot, is merely a collection of strains belonging to the colon group (*B. acidi lactici*, *B. coli communis*, *B. lactis aerogenes* and *B. coli communior*), which have this character in common that they can form phenol from tyrosine. It was found in 2 out of 48 mental patients, and in 1 out of 21 controls, but the latter was a young man who had recently spent several weeks in bed with a broken leg.

To come directly to the question whether the bacteria, *B. Morgani* and *B. phenologenes*, can be held responsible for the mental illness of the patients, we will firstly consider previous literature. *B. Morgani* has, as far as I am aware, been recorded only from cases of diarrhœa and dysentery. Phenol-producing bacteria, while they produce phenol from tyrosine in alkaline media, form tyramine in the presence of carbohydrates when the medium goes acid (Hanke and Koessler, 1924). There is, of course, an extensive literature on the *rôle* of amines in the production of disease, with which I will not deal at present.

The only satisfactory proof that an organism is the cause of a disease is the cure of the disease by removal of the organism, but of course many such cures must take place before the proof can be complete. In this hospital 65 cases have so far been treated with autogenous Morgan vaccine. There seems little doubt that efficient vaccination will remove the bacterium in question, but to be effective the vaccine must be given intravenously after a short hypodermic course.

Brief notes of these 6 cases will now be given.

(*In what follows "phenol %" means the percentage of phenol in a tyrosine bouillon culture inoculated from fæces and incubated for two days. "Agglutination" is the reaction of the patient's serum to his own B. Morgani.*)

CASE 1.—Male, æt. 15, admitted 10.xii.27. Typical dementia præcox; he is dull, cannot concentrate, very slow in answering, introverted, mischievous and sly, hallucinated and with delusions of poisoning; very pale in the face, mitral systolic murmur; weight 43 kilos. Duration of illness two months. Causes—too heavy work and neurotic heredity.

13.xii.27: Phenol 0·02%. *B. Morgani* present, from which a vaccine is made.

5.i.28: Agglutination negative. Mentally unchanged. Weight 42·3 kilos.

9.i.28: Phenol 0·008%. *B. Morgani* not found. Vaccine ½ c.c. hypodermically. Marked local reaction.

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16.i.28: Vaccine 1 c.c. hypodermically.
19.i.28: Phenol 0·003%. *B. Morgani* not found.
27.i.28: Vaccine ½ c.c. intravenously; reaction to 100·8° F.
31.i.28: Blood count—reds 4,790,000, hæmoglobin 79%, leucocytes 8,600. Weight 45·9 kilos.
2.ii.28: Agglutination 1/125.
4.ii.28: Vaccine ½ c.c. intravenously; reaction to 100·8° F.
9.ii.28: *B. Morgani* present.
11.ii.28: Agglutination 1/1000.
22.ii.28: Phenol 0·025%. Vaccine 1 c.c. hypodermically.
29.ii.28: Phenol 0·004%. *B. Morgani* not found. Vaccine 1 c.c. hypodermically. Mental improvement begins. Weight 50·3 kilos.
7.iii.28: Vaccinated 1 c.c. hypodermically.
19.iii.28: Practically normal in mind. Good colour in face; organic mitral murmur still present. Working in garden. Weight 51 kilos.

CASE 2.—Male, æt. 26. Admitted 23.ix.27. Dementia præcox; dull, nearly mute, apprehensive, refuses food, some echolalia; bodily, ashen grey complexion, trace of albumen in urine.
23.x.27: Horrible smell from mouth although no gum or throat disease. Weight 55·7 kilos.
25.x.27: Four epileptiform fits; vomited repeatedly; temperature 102° F.
29.xi and 2.xii.27: Phenol 0·02%. *B. Morgani* present; vaccine made. 53 kilos.
16.xii.27: Constant violent attempts to escape. Pallid and unhealthy.
19.xii.27: Agglutination negative. Vaccine ½ c.c. hypodermically.
24.xii.27: Vaccine hypodermically, 1 c.c.
31.xii.27: Vaccine 2 c.c. 53·6 kilos. Mentally quieter, better colour in face, no ozæna.
2.i.28: Phenol 0·008%. *B. Morgani* not found.
7.i.28: Agglutination 1/50. Vaccine 2½ c.c. hypodermically.
14.i.28: Phenol 0·001%. *B. Morgani* not found.
16.i.28: Vaccine 1 c.c. intravenously; reaction to 103·2° F.; albumen and casts in urine for 36 hours.
23.i.28: Vaccine 1 c.c. intravenously; reaction to 100·8° F.
30.i.28: Agglutination 1/1000. Much less troublesome; working. 53·8 kilos.
13.ii.28: *B. Morgani* not found. Works outside under supervision.
23.ii.28: Phenol 0·003%. *B. Morgani* not found. Vaccine 1 c.c. hypodermically.
27.ii.28: Phenol 0·002%. *B. Morgani* not found.
29.ii.28: Vaccine hypodermically, 1 c.c. Weight 60 kilos.
3.iii.28: Phenol 0·001%. No further mental improvement.
5.iii.28: Phenol 0·004%.
8.iii.28: Vaccine hypodermically, 1 c.c.
13.iii.28: Vaccine intravenously, ½ c.c.; no febrile reaction, but marked excitement for 24 hours.
20.iii.28: Vaccine ⅝ c.c.; reaction to 99·4° F. Has quite lost ashen-grey septic complexion.

CASE 3.—Male, æt. 23. Admitted 1922. Recurrent mania; periods of excitement lasting 10–14 days with intervals of 7–22 days; during intervals slightly weak-minded.
28.xi.27: 17th day of an interval; phenol, % *nil.*
4.xii.27: Manic relapse begins.
7.xii.27: Phenol 0·02%. *B. Morgani* present. Vaccine made.
15.xii.27: Manic relapse ends.
19.xii.27: Phenol 0·001%. *B. Morgani* not found.
31.xii.27: Weight 54 kilos.
4.i.28: Manic relapse begins.
5.i.28: Agglutination negative.
7.i.28: Manic relapse ends.
9.i.28: Vaccine ½ c.c. hypodermically; marked local reaction.
16.i.28: Vaccine 1 c.c.
18.i.28: Phenol 0·003%. *B. Morgani* not found.

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21.i.28: Vaccine 2 c.c.
22.i.28: Manic relapse begins. *B. Morgani* not found.
27.i.28: Vaccine ½ c.c. intravenously; reaction to 102°6° F., with profuse outbreak of herpes around mouth and on right temple. 52·8 kilos.
2.ii.28: Agglutination 1/500.
4.ii.28: Vaccine 1 c.c. hypodermically.
11.ii.28: Manic relapse ends. Agglutination 1/1000. *B. Morgani* not found.
20.ii.28: Phenol 0·006%. *B. Morgani* not found.
27.ii.28: Manic relapse begins.
27.ii.28: Phenol 0·035%, *B. Morgani* not found. *Proteus anindologenes* present, which, however, does not form phenol.
29.ii.28: Agglutination 1/500. Weight 53·5 kilos.
2.iii.28: Phenol 0·02%.
3.iii.28: Manic relapse ends.
5.iii.28: Vaccine ½ c.c. hypodermically.
8.iii.28: Phenol 0·0005%. *B. Morgani* not found; *Paracolon phenologenes* present.
10.iii.28: Vaccine ½ c.c. intravenously; reaction to 101·4° F.
15.iii.28: Vaccine ½ c.c. intravenously; reaction to 99° F.
20.iii.28: Agglutination 1/1000. Weight 51·3 kilos.

CASE 4.—Male, æt. 27. Admitted 17.ii.28. Melancholic dementia præcox. Was invalided out of the army in 1920 for neurasthenia, tremulous, frightened, with præcordial pains; has been the same with ups and downs since. Leg broken in accident xi.27; two and a half months in hospital; became suicidal.
On admission intensely suicidal; face extremely pallid; unconsolidated fracture of leg. Weight 50 kilos.
20.ii.28: Phenol 0·02%. *B. Morgani* present; vaccine made.
23.ii.28: Phenol 0·03%. *B. Morgani* present.
7.iii.28: Vaccine ½ c.c. hypodermically; reaction to 100° F., and marked local.
12.iii.28: Vaccine ½ c.c. hypodermically; reaction to 102·2° F., and marked local.
14.iii.28: Phenol 0·0002%. *B. Morgani* not found; *B. pyocyaneus* present.
20.iii.28: Has been sleeping better, less emotional, not suicidal, less pallid in face. Agglutination 1/50.
22.iii.28: Vaccine ½ c.c. hypodermically; no reaction.

CASE 5.—Male, æt. 28. Insanity with epilepsy since age of 14. Muddy septic complexion. Number of fits in successive months of 1927: 8, 3, 4, 3, 9, 8, 9, 5, 10, 15, 6, 1.
16.i.28: Phenol 0·008%. *B. Morgani* not found. Fits during January, 0.
10.ii.28: *B. Morgani* present; vaccine made.
23.ii.28: *B. Morgani* present; phenol 0·03%.
27.ii.28: *B. Morgani* present; phenol 0·06%.
29.ii.28: Vaccine ½ c.c. hypodermically. Fits during February, 11.
5.iii.28: Vaccine 1/10 c.c. intravenously; no reaction. Phenol 0·03%. *B. Morgani* not found.
10.iii.28: Vaccine 1/5 c.c. intravenously; reaction to 101·2° F.
15.iii.28: Vaccine ½ c.c. intravenously; reaction to 102·2° F.
20.iii.28: Agglutination 1/500. Complexion less muddy and septic. Fits during first three weeks of March, 15.

CASE 6.—Male, æt. 57. Admitted 19.i.28. Melancholia, 3 months' duration. Trace of albuminuria; arteries not palpable.
24.i.28: *B. Morgani* present; vaccine made.
7.ii.28: Vaccine ½ c.c. hypodermically.
9.ii.28: *B. Morgani* present.
16.ii.28: Vaccine 1 c.c. hypodermically.
21.ii.28: Phenol 0·02%.
22.ii.28: Vaccine 1 c.c. hypodermically.
29.ii.28: Vaccine 1 c.c. hypodermically. Phenol 0·02%. *B. Morgani* not found.
8.iii.28: Vaccine $\frac{1}{10}$ c.c. intravenously; reaction to 99° F.; small amount of albumen and hyaline casts in urine.

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15.iii.28: Vaccine $\frac{1}{10}$ c.c. intravenously; reaction to 102·4° F.; some albumen and casts in urine for 48 hours.
20.iii.28: Agglutination *nil*. Patient up and about, but little change mentally.

The remaining cases in which *B. Morgani* was found but which have not been treated by vaccine are as follows:

Post-traumatic delirium, 1; manic-depressive insanity, 2; melancholia, 1; acute dementia præcox, 1; imbecility with epilepsy, 1.

Of the 6 cases treated by vaccine 5 have responded by forming agglutinins. Of these, 1 has recovered mentally, 1 shows marked bodily and some mental improvement, 2 are beginning to improve although still in the early stages of treatment; 1 (Case 3) is doubtful. One case (No. 6) has not formed agglutinins, but his physical condition makes it impossible to push the vaccine; he shows little mental change.

Characters of the Bacteria Isolated.

Bacillus Morgani.—Very fine, Gram-negative cocco-bacilli, forming dewdrop colonies ½ mm. in diameter on McConkey or agar plates after twenty-four hours' incubation. In sugars they give acid slight gas in glucose, lævulose and galactose; no change in lactose, saccharose, maltose, mannite or dulcite; alkali in litmus milk. Some strains give no acid in glucose, but these are serologically identical with others from the same patient, which give acid and gas. Indol and phenol are formed from peptone, and phenol from tyrosine.

Virulence and toxicity.—Living bacteria kill a mouse in a dose of 0·04 c.c. of a forty-eight-hour bouillon culture. Endotoxin: The dead bodies of the bacteria are toxic to the individuals who carry the bacillus, as will be seen from the records of vaccination given above. There is some indication of idiosyncrasy, as in Case 4, where a second hypodermic injection of ½ c.c. caused marked local reddening and a temperature of 102·2° F., although ¼ c.c. hypodermically seemed to have no effect on a mouse. One sixteenth part of a three-day agar 10 cm. plate culture, killed, ground, filtered through paper and injected intravenously, killed a large rabbit in forty-eight hours. Soluble exotoxin: Cultures in tyrosine bouillon with marmite, of our local strains and of Morgan's original strain from the National Type Collection, were incubated for one month and filtered through Berkefeld candles. The N.T.C. culture was injected in 10 c.c. doses to two guinea-pigs and caused blood-stained diarrhœa; one animal died, the other recovered after a month; 1 c.c. doses caused similar diarrhœa in two mice. The filtrate from the local strains was given in 10 c.c. doses to three guinea-pigs, of which one died in five hours; the other two were manifestly ill; there was, however, no diarrhœa or blood.

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Technique.

The best method of isolating the bacillus appears to be as follows: Inoculate a tube of tyrosine bouillon from the fæces and incubate forty-eight hours; plate this culture on maltose-mannite McConkey's medium and pick off any small white colonies.

Estimation of Phenol.

I am indebted to my friend Mr. Robison for advice as to the demonstration and estimation of phenol in cultures. The method is as follows: The culture is distilled over into a test-tube and tested with Millon's reagent, which gives a red colour on heating if phenol is present. If a series of standard dilutions of phenol are made and treated in a similar manner with Millon's reagent, the percentage of phenol in the distillate can be estimated by colour comparison.

I wish to acknowledge my indebtedness to Mr. W. F. Gifford, senior assistant in this laboratory, for great help in the investigation described, not only in the daily cultural and experimental work, but in the manufacture of the tyrosine, which formed our principal medium.

Summary.

(1) If a tyrosine bouillon tube is inoculated with fæces from a healthy person, incubated for forty-eight hours and distilled, it will be found to contain phenol of not more than 0·008%, or at the most 0·015%. If, on the other hand, similar cultures are made from mental patients, they will contain 0·02 to 0·03% in half of the specimens examined. (It is not suggested that the phenol is of pathological importance; it is only important as indicating what bacteria are present in the culture.)

(2) At least one quarter of mental patients who are acutely ill carry *B. Morgani*; a smaller proportion carry *B. phenologenes*, Berthelot, and a still smaller proportion a phenol-producing paracolon. *B. Morgani* is the important phenol-producing bacterium of the insane.

(3) The strains of *B. Morgani* found in these cases do not cause diarrhœa, but the dead bodies of the bacteria are toxic to man, causing marked local, and in some cases general reaction, when moderate doses are injected hypodermically. After intravenous injection of minute doses they cause pyrexia, and if the dose is larger or the kidneys already diseased, a transient nephritis.

(4) As far as it is possible to judge by the very few cases treated, efficient vaccination (hypodermic followed by intravenous) can remove *B. Morgani* from the bowel. Such removal is followed by improvement in bodily health and possibly improvement of the mental condition.

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