PRELIMINARY OBSERVATIONS ON THE USE OF AN AUTOGENOUS LIVING VACCINE IN THE TREATMENT OF ENTERIC FEVER (SIX CASES).

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HAVING recently treated cases of enteric fever with vaccine, and obtained satisfactory results, it occurred to one of us (S. R.) that better results might be obtained by employing autogenous living vaccine for each case. The clinical notes and temperature charts of our first successive cases treated by this method, and the satisfactory results obtained, will, we hope, lead to this method being given a more extensive trial. Our cases have demonstrated that this method of injecting living bacilli in suitable doses is perfectly safe. The vaccine was injected subcutaneously, as a rule in the pectoral region, and was followed by very slight local reaction, but marked general reaction. No local or general complications were observed. The injection, as a rule, was followed by a rise of temperature within the first few hours followed by a marked fall within twenty-four hours of inoculation. Careful notes were made and in our minds there is no doubt that this treatment has a beneficial effect, and tends to cut short the duration of the disease. It promotes perspiration and the aspect of the patient is undoubtedly brighter after injection and the tongue becomes much cleaner.

The diagnosis was verified in all cases by blood culture. Several of the cases on admission to hospital gave one the impression that the attack would be a severe one; in this opinion, our consulting physician, Sir Wilmot Herringham, agreed. To him also we are indebted for valuable suggestions as to dosage, and frequency of administration of the vaccine.

PREPARATION OF THE VACCINE.

The disease was in each case diagnosed by means of blood culture. For this purpose 5 c.c. of blood was drawn from the arm and immediately transferred to one per cent sodium taurocholate. From this a broth culture was prepared and the purity and identity of the growth verified by agglutination and sugar fermentation tests. The broth culture was reinoculated into fresh broth and
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itself constituted the vaccine. No further preparation whatever
was employed. The age of the culture used was generally eighteen
hours, and the number of bacilli contained in it was obtained by a
direct method of counting which has been previously described by
one of us. The average number of organisms given for a dose
ranged from 60,000,000 to 300,000,000.

Effects of Inoculation.

The local reaction following injection was surprisingly small,
and was far less than is commonly seen after a prophylactic inocula­
tion using a killed vaccine. The general reaction on the patient
was on the other hand very marked. A sharp rise of temperature
was always observed. Frequently this was accompanied by
profuse perspiration.

These preliminary observations have demonstrated that a living
culture of the typhoid bacillus can be injected subcutaneously into
enteric patients, not only without any deleterious effects whatever,
but as far as the few cases show with decided favourable influence
on the course of the disease. Much remains to be worked out.
The dose and spacing of the dose will require many further cases
to determine. In conclusion, it is desired to draw attention to
the point of view that has dominated these experiments. The
vaccine treatment of enteric has many advocates. It is the
common experience of bacteriologists that all antigens are very
delicate substances, and any physical agency employed to kill the
enveloping bacillus acts deleteriously on the contained antigen.
If, therefore, the vaccine treatment of enteric is of use when
employing a killed vaccine, it should be of still greater use when the
living vaccine is used. More especially will this be the case if the
vaccine is autogenous. It has been the work of one of us during
the last few years to investigate the antigens of the plague bacillus.
In the case of this organism it has been found that the strain of
organism used for the preparation of an antigen is most important.
In the cases above related the strain used was in each case the
strain isolated from the patient.

It is hoped that these investigations will be continued by
others.

Autogenous Vaccine Case.

been inoculated for enteric. November 27: Headache and feeling
out of sorts. November 29: Had to fall out on parade and report
sick. December 2: Admitted to hospital. On examination patient
was tired and listless; pupils large; tongue dry, glazed, brown fur, tremulous; considerable cough, slight expectoration; breath fetid; abdomen no tumidity or tenderness; reflexes diminished; a few spots, marked diarrhoea with occasional vomiting after milk; spleen enlarged; knee-jerks exaggerated; chest breathing harsh moist rales; no dullness; promised to be a moderately severe case.

December 3: **Blood culture positive.** December 5: Abdomen more tumid, spots gone; 12 noon ½ c.c. vaccine; evening temperature 103°F. December 6: Slight local reaction, now almost gone; temperature 100°F., looks flushed, complains of headache; abdomen tender, more spots. December 8: Feeling better, sleeps well. December 11: 8 a.m., temperature 98°F.; ½ c.c. vaccine; 6 p.m., temperature normal. December 12: Considerable local reaction; temperature 97¾°F.; general condition excellent, was able to read newspapers. December 18: Temperature normal; general condition excellent; got up for two hours; was a bit weak on his legs; convalescent. One cubic centimetre vaccine contains 400,000,000 bacilli.

Serjeant C., No. 9443, 2nd Roy. Irish, aged 25.—Never been inoculated. December 20: Admitted to hospital; headache and general malaise; no definite symptoms; drowsy; face flushed; tongue moist, light brown fur; abdomen slightly distended and tympanitic, numerous rose spots. December 23: **Blood culture positive**; spleen enlarged; slight local reaction from autogenous vaccine; patient drowsy and does not feel so well. December 24: Patient feels very well and is much brighter; during the night has perspired freely. December 27: ½ c.c. vaccine; 5 p.m., complains of severe
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pain in left iliac fossa, which he states has been coming on ever since he has been inoculated: no signs suggesting any complications; same night 1 c.c. omnipon. December 28: Patient has had a good night; abdominal pain all gone, feels well, new patch of rose spots; tongue still coated and tremulous. December 31: ¼ c.c. vaccine. January 1: Moderate local reaction, temperature dropped considerably; patient had a good night and is in good spirits; perspired freely. January 4: ¼ c.c. vaccine. January 5: More local reaction than usual, but not as much as is usual after a prophylactic dose of Wright's vaccine; did not sleep so well and perspired freely; seems better this morning, says he feels well; tongue clean; no abdominal signs or symptoms; from this date convalescent, discharged to base January 7, 1915. One cubic centimetre vaccine contains 400,000,000 bacilli.

Sergeant A., No. 21681, A.S.C. 9 Co., aged 30.—December 7: Sudden attack of cold shivering and malaise; pains in back and headache; admitted to hospital. December 14: Temperature 101.4° F.; tongue thick white fur turning brown; patient is bright and talks well; chest increased resonance and vocal fremitus over lobe of right lung; heart increased second aortic sound; abdomen no pain or gurgling; rose spots; constipated. December 15: Blood culture positive. December 17: 8 a.m., temperature 101° F., autogenous vaccine ¼ c.c.; 6 p.m., temperature 103.8° F. December 18: 8 a.m., temperature 101° F., one more spot. December 21: Temperature has continued about 102° F.; patient seems bright; ¼ c.c. vaccine. December 22: No local reaction;
slight general reaction temperature; restless. December 24: Fairly comfortable; tongue cleaning; since vaccination has per­spired very freely. December 25: ¼ c.c. vaccine. December 26: No local reaction; patient cheerful and says he feels better.

December 29: ¼ c.c. vaccine. December 30: Had an excellent night, very slight local reaction; tongue moist and clean; wants to get up. January 1: Patient feels perfectly fit; temperature normal; tongue clean; no abdominal symptoms. January 2: Convalescent. One cubic centimetre vaccine contains 400,000,000 bacilli.

Driver F. B., No. 17703, A.S.C. 9 Co., aged 30.—November 22: Began to feel out of sorts, headache and malaise. November 25: Admitted to hospital; patient was flushed, tired and restless; severe headache and pain in back and legs; appearance of being a severe case with co-existent bronchitis; spat up a little blood; perspires freely and complains of thirst; eyes sunken; tongue tremulous; breath fetid; tongue coated with dry white fur; has not vomited nor bled from nose; restless with a tendency to delirium and sleep­lessness; heart sounds normal; pulse 108, and soft; temperature 105° F.; spleen not enlarged; no pain or distension in abdomen, no caecal gurgling; no spots. November 25: Blood culture positive. November 27: Temperature falling, 103° F. at 6 p.m.; diarrhoea has commenced; 7 p.m. ¼ c.c. autogenous vaccine injected into left arm; 8 p.m., temperature 103° F., pulse 94; 12 midnight, temperature 101°2° F., pulse 104. November 28: 7 a.m. temperature 102°8° F., pulse 104; 8 a.m., temperature 103° F., pulse 92; condition much same, very slight local reaction. November 29: Did not sleep, some delirium; does not seem so well; urinary incontinence.
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November 30: Temperature same; feeling brighter and had a good night. December 2: Temperature falling to 99.2°F., condition improved; 12 noon, 0.5 c.c. vaccine; 2 p.m., temperature 102°F.; 6 p.m., temperature 99.2°F. December 3: Slight local reaction; condition improved; still rather thick in the head. December 4: Very heavy and dull; tongue tremulous; still has a bad cough. December 6: 8 a.m., temperature normal; greatly improved; tongue cleaner and less tremulous; no further involuntary passage of water or stools. December 7: 8 a.m., temperature 99°F., has not passed water since last night, pain over bladder which is distended, hot fomentations no effect, catheter passed five pints urine drawn off; 3 p.m., temperature 102.6°F., 0.75 vaccine; 3 p.m., temperature 102.6°F.; 6 p.m., 103.8°F. December 8: Temperature 102°F., marked reaction after vaccine; no local reaction, though temperature went up pulse remained the same; has had a restless night but has not wandered in mind. December 9: 8 a.m., temperature normal; slept well and marked improvement; bowels open naturally, still being catheterized; has an old stricture which always gives trouble when he is ill. December 10: Seems tired but sleeps well. December 11: Feeling better; tongue steady; urine clear; no signs of cystitis; 8 p.m., temperature 103°F. December 12: 8 a.m., temperature 99°F., ½ c.c. vaccine; no symptoms to account for temperature; complained of feeling cold but had no rigor; 6 p.m., temperature 101.2°F. December 13: 8 a.m., temperature normal; feels distinctly brighter and talks; still unable to pass water; since this his temperature has remained about normal with exception of a rise on December 18 after some solid food. One cubic centimetre vaccine contains 400,000,000 bacilli.
Private D., No. 26473, No. 9 Co., A.S.C., aged 25.—December 10: Felt ill with headache; pains in shoulders and back; reported sick December 12; pains gone; pain now in stomach.

December 14: Admitted to hospital, temperature 104° F.; looks dull and listless; tongue dry brown fur; tremulous; slight bronchial catarrh; promises to be a severe case with marked chest symptoms.

December 15: Blood culture positive.

December 17: 8 a.m., temperature 102° F.; 1 c.c. vaccine; at 6 p.m. temperature 102.4° F.

December 18: Temperature 102.8° F. December 21: Temperature 100.4° F.; ½ c.c. vaccine; bright and cheerful; still has some chest symptoms. December 22: Had a good night; feels very well this morning; slight local reaction. December 25: ½ c.c. vaccine, slight local reaction. December 30: Feels perfectly well and is clamouring for food; wants to get up; temperature normal; tongue moist and quite clean; no abdominal symptoms. December 31: Convalescent. One cubic centimetre vaccine contains 400,000,000 bacilli.

Private A. S., No. 9761, 1st Lincolns, aged 19.—December 23: Reported sick with bad headache; pain in stomach and diarrhoea; diarrhoea has always lasted a week. December 26: Complains of headache, diarrhoea and malaise; tongue moist and covered with white fur; breath fetid; vomited a few times before admission. December 27: Very drowsy and listless, unable to sleep; no appetite; abdomen distended and tympanitic; tenderness over left iliac region, and tenderness and distension over splenic area; splenic dullness not enlarged; few rose spots. Blood culture positive. Bacillus paratyphosus B. December 28: Had a restless night, still drowsy and cannot be persuaded to take an interest in anything;
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One fresh spot. December 29: Seems a little better; still restless and sleeps badly; given $\frac{1}{10}$ c.c. autogenous vaccine (60,000,000); blood count 8,000; considerable local reaction; had a better night.

December 30: Distinctly brighter; tongue quite clean and not tremulous; still some local reaction; typical enteric stools.

December 31: $\frac{1}{10}$ c.c. autogenous vaccine 11 a.m.; by 6 p.m. some local reaction. January 1: Patient feels a little better; there is still some abdominal tenderness and a fresh crop of rose spots has appeared; diarrhōea has ceased. January 4: Patient looks well and feels much better; abdominal tenderness and distension have disappeared; tongue cleaner and not tremulous. January 6: Temperature down but unsteady; $\frac{1}{10}$ c.c. vaccine given. January 7: Patient has had a poor night; considerable local reaction, but he seems bright this morning. January 8: Patient much improved; tongue almost clean; no abdominal symptoms: temperature dropping. January 9: Temperature normal. From this date patient convalesced rapidly.