naking a discovery when they had really only succeeded in exploiting at the concluding stages the pioneer work of others.

Soon after the publication of the constitution of atoxyl the writer met Ehrlich in Liverpool on his way to receive a medal at a sanitary congress being held in Douglas, Isle of Man, and congratulated him on his recent paper with Bertheim establishing the constitution of atoxyl, remarking that he had an able and energetic young man in Bertheim. The Geheimrath laughed heartily and said: "Energetic young man! Why he is a director of the Höchst Anilinfabrik, one of the greatest aniline dye works in Germany, and turned the whole staff on to the work."

It is in this combined team work, dealing with minute details, that Germany excels, and the history of the production of organic arsenical therapeutic agents is very similar to that of the aniline dye industry.

SUMMARY.

To conclude this brief sketch of the history of the therapy of protozoan diseases by the use of organic arsenical compounds, a history which only pretends to present the salient points and not to give any complete account of the literature, the following summary may be given:

Atoxyl, the mother substance, was discovered in France, the application to protozoan diseases was made by a Canadian working in a British laboratory, and the chemical nature of atoxyl was shown simultaneously in England and Germany; then German observers finessed amongst the derivatives to find the compounds best adapted for therapeutic use.

The details of production of the compounds were not revealed by Germany, and it is a matter for congratulation that these can now be manufactured in Britain.

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THE PREVENTION, SYMPTOMS, AND TREATMENT OF TETRYL DERMATITIS.

BY

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FOR the past nine months I have acted as medical officer to munition works employing about 250 women, where tetryl (tetra-nitro-methyl-anilin) is used.

This note, on the means used to avoid the dermatitis and other troublesome symptoms caused by handling this explosive, is written at the suggestion of Dr. Legge, H.M. Medical Inspector of Factories.

I. SELECTION OF WORKERS.

Experience showed that women with obvious eye or skin diseases should be excluded, and all workers should be taken on probation. It is quite impossible to foresee who will prove susceptible.

II. PROPHYLAXIS.

On entering the factory the workers remove their outdoor clothes, put on special overalls and slippers, and pass through a toilet room, where a responsible person sees that each worker hardens her hands in spirit lotion (filtered methylated spirit 20 per cent., water 80 per cent.) and dusts her face freely with powder (zinc oxide 1, starch 3).

In the rooms the workers are warned against touching their faces with their hands. The trays and tables are regularly wiped and the floors swept and scrubbed, so that the quantity of tetryl is limited. Tetryl-laden dust, or finely divided tetryl seems to be more injurious than tetryl in bulk. Some workers use veils or muslin across the mouth to avoid inhaling the dust. The rooms should be airy and cool, but not draughty. Hot, close weather increases the trouble, so that provision must be made for keeping the rooms cool in summer.

On leaving the works, the workers should wash their hands, using olive-oil soap or bran. Each worker should

have her own towel. The face is wiped free of powder and a simple greasy preparation may be used at the end of the day.

Washing of Clothes.—It should be noted that those living with workers get affected, especially if they wash the workers' clothes. All clothes should be soaked in cold water and paraffin and rinsed before being boiled, or the steam from the boiling clothes will be very irritating.

III. SYMPTOMS.

The hands of all workers are stained yellow, and in most of them the faces and hair. They are known in the town as the "canaries." The conjunctivae are never stained, nor the covered portions of the body, but the feet may get "yellow as duck's."

Dermatitis, by which almost all workers are attacked, consists, in its mildest form, of irritation and roughening of the exposed skin. More serious is a papular eruption; in the severest cases there is acute oedema of the whole face, closing the eyes and making the features unrecognizable; any variety of eczematous eruption may be seen. The attack may occur at any time, but usually after a fortnight's exposure.

Conjunctivitis may occur with or without dermatitis.

Nasal irritation manifests itself in excessive sneezing and in epistaxis, but is never severe enough to keep a worker at home.

Pharyngeal irritation has occurred in a few cases. Asthmatic attacks compelled two workers to leave.

Constitutional symptoms are almost absent. Insomnia perhaps occurs out of proportion to the cutaneous irritation. "Biliousness" at the monthly periods has been noticed. It has not been found necessary to give the workers rest days on this account. The appetite is excellent, and the general health of some delicate women has certainly improved.

TREATMENT.

If the symptoms are slight the worker is encouraged to remain at work, perhaps changing to a room where tetryl is not used. The symptoms will then, as a rule, subside in the course of a few days and not recur.

If the symptoms are more severe—if, for example, there is oedema or a papular eruption, or conjunctivitis of moderate degree—the worker must stay at home. She should not return until quite well, as a convalescent seems unusually susceptible. If, after recovery, the worker gets a second severe attack, I advise her to find other work. In some cases, however, where the worker has remained at her own risk, she has gradually improved, and the skin, apart from pigmentation, has become practically normal.

For the dermatitis, in the severest cases, steaming the face with subsequent application of wet cloths reduces the swelling and allays the irritation. Later on, and in less severe cases from the first, calamine lotion acts well, though some prefer an ointment composed of zinc ointment, lanoline, and castor oil, equal parts. I have avoided lead lotion, as lead has a dangerous affinity for tetryl.

For conjunctival irritation colloidal silver acts well, though it smarts on application. For nasal irritation we use liquid paraffin.

RELAPSING PARATYPHOID "A" INFECTION.

BY

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SINCE the outbreak of the war paratyphoid fever has received a considerable amount of attention, and, with the extension of bacteriological laboratories, further opportunity has been afforded for its study. So far as recognized, the cases have presented more or less definite clinical manifestations, and the diagnosis is usually confirmed by the bacteriologist. That the infection may present itself in anomalous or atypical forms seems very probable, yet, so far, there has been little reported on the subject.

The case of paratyphoid A infection herein recorded is one presenting several remarkable and unusually interesting features, and a correct diagnosis might not have been made had we not succeeded in isolating the organism from the patient's own blood.

The patient, aged 32, a private in the New Zealand Force, left Gallipoli about the second week of September, 1915. He stayed for seven days at Malta, and arrived in England in October. At the end of the previous June he had had an attack of diarrhoea lasting seven to ten days only, and not necessitating his being invalided, but, with this exception, he had been quite well until arrival here.

On October 10th, 1915, three days after landing in this country, he was taken ill with shivering, pains in the back and legs, and vomiting, and was admitted to the Royal Herbert Hospital on October 15th. On admission he was found to be fevered, with a temperature over 102° F., pulse 100, and respirations 24. He had headache and some vomiting but no diarrhoea, and there was nothing to be made out in any of the viscera; the spleen was not appreciably enlarged.

The fever persisted for eleven days. For the first five days after admission the evening temperature was always about 103° F., and there were morning remissions to 100° F. and 101° F.; thereafter the morning remissions became more marked and the evening rise tended to get less, so that the temperature curve resembled the defervescence of an ordinary typhoid fever. From the twelfth to the twentieth days after admission the temperature did not quite settle; the morning temperature was usually normal but there was a persistent evening rise to about 100°, and on two occasions it reached 102°.

From the twenty-first day after admission until the morning of the thirtieth day there was practically no fever, the evening temperature never being above 99° and the morning temperature always normal, and the pulse usually ran about 80.

On the evening of the thirty-fifth day of illness (that is, the thirtieth day after admission), the temperature rose to 101.2° F. and reached 103.8° F. the following night, and with occasional slight morning remissions the fever persisted till the forty-seventh day; on the thirty-ninth day the morning temperature was 104° and the evening 105.8°; during the next three days the temperature remained about 104°; on the forty-third day the morning temperature was 103° and the evening 104°; on the forty-fourth day the morning temperature was 101.8° and the evening temperature 103°. With increasing morning remissions the temperature gradually fell to normal on the morning of the forty-eighth day of illness. From the forty-eighth day until the fifty-seventh day of illness the temperature remained practically normal, except on the evenings of the fifty-second and fifty-third days, when it rose suddenly to 102° and 100° respectively.

On the evening of the fifty-eighth day the third relapse was ushered in by a rise of temperature to 102.4°; the following night the temperature reached 104.6°, and remained between 103° and 104° until the sixty-fifth day, when it again showed morning remissions with a gradually falling evening rise. By the seventy-fifth day the evening rise was only to 99.8°, and thereafter both morning and evening temperatures remained normal until the ninety-fifth day. On the evening of the ninety-fifth day a fourth and similar febrile attack was ushered in by the temperature rising to 103°. The following night it rose to 105°, and remained between 104° and 105° for two days longer; then it gradually fell by morning remissions as before until the hundred and eighth day, when the evening rise was only to 99° and the morning temperature 97°. The temperature touched 99° on the two following nights, but remained normal for the rest of the time that the patient was under observation—namely, forty-five days.

Taking the onset of the fever as dating from the onset of symptoms (shivering, etc.), we see that there was an attack of pyrexia lasting about sixteen days; this was followed by a period of eight days in which, although the morning temperature was normal, there was an evening rise to about 100°. An apyrexial interval of ten days followed, and this was succeeded by a second pyrexial attack lasting about fourteen days. Thereafter an apyrexial interval of nine days ensued, to be succeeded in turn by a third pyrexial attack lasting sixteen to seventeen days. A period of apyrexia lasting twenty days followed, and this was succeeded by the fourth and last period of pyrexia lasting fourteen to fifteen days.

The pulse throughout varied more or less with the temperature. During the first three attacks of fever it varied between 90 and 116, but during the fourth attack it tended to be faster, being usually over 100, and sometimes going up to 114–120. In the apyrexial intervals the pulse was normal.

The pyrexial attacks were all more or less alike—a fairly sudden onset, the fever reaching its height in about two days and persisting at its height for five to ten days, then falling by gradually increasing morning remissions like the lysis of ordinary typhoid fever. During the early stages of each pyrexial attack there were occasional rigors, headache was present more or less throughout the attack, there was occasional vomiting, and the defervescence was

associated with considerable sweatings. The patient was always quite clear mentally, and never really seemed quite so ill as the fever suggested. There was never any diarrhoea.

There was a slight leucocytosis during the first pyrexial attack, but practically none later. On the fifteenth day of illness, that is, about the end of the first attack, the leucocyte count was 11,200; about the middle of the second relapse the leucocytes numbered 8,800, and during the third relapse they only numbered 7,000.

On the second day of the second relapse (thirty-sixth day of illness) we withdrew 6 c.cm. of blood from a vein and made cultures in broth and in sterilized ox bile, and obtained a pure growth of an actively motile Gram-negative bacillus which proved to be *B. paratyphosus* A. It fermented glucose and mannite but with scanty gas production, gave no change in lactose, turned milk acid, and agglutinated strongly only with a specific paratyphoid A serum. During the third relapse and during the height of the fourth relapse we again obtained pure cultures of *B. paratyphosus* A from the blood. A point worthy of note is that the primary cultures required three and four days' incubation before growth became apparent.

On the thirty-ninth day of illness, during the height of the second relapse, we tested the agglutination reaction of the patient's serum against known organisms, using the macroscopic method, and found that it gave a positive reaction with *B. typhosus* up to 1 in 40 dilution, but with *B. paratyphosus* A a positive result could not be obtained beyond a dilution of 1 in 5. The reaction with *B. typhosus* was probably dependent upon two antityphoid inoculations which the patient received in November, 1914. On the fifty-second day of illness—that is, during the apyrexial interval after the second relapse—we tested the agglutination reaction of the patient's serum against a known strain of *B. paratyphosus* A, and also against the *B. paratyphosus* A isolated from his own blood, but failed to find any evidence of a positive result in a dilution of 1 in 20.

We prepared a vaccine from the organism isolated from the patient's blood, and two to three days before the termination of the third relapse administered an initial dose of 20 million. There were no ill effects, and three days later we gave a second dose of 40 million. Three days after the administration of the second dose of vaccine we estimated the agglutination titre of the patient's serum against the autogenous *B. paratyphosus* A, and found a partially positive result up to a 1 in 40 dilution. The supernatant fluid in the agglutinating tubes was not clear, but several small clumps floated about, and some were deposited. A week after the second dose of vaccine we administered a third dose of 80 million, and six days later found the agglutination titre of the patient's serum to his own *B. paratyphosus* A to be raised to 1 in 80, with a trace at 1 in 160. Nine days after the third dose of vaccine we gave a fourth dose of 120 million.

The administration of the vaccine was commenced shortly before the termination of the third relapse, and as the apyrexial period following this relapse—nearly three weeks—was much longer than either of the preceding intervals, we imagined that we had overcome the infection. Our hopes were dispelled, however, when the fourth attack set in. Nevertheless, during the fourth relapse the agglutination titre of the patient's serum to his own paratyphoid A bacillus was found to be considerably raised; a positive result was obtained up to a dilution of 1 in 600, with a definite trace up to 1 in 1,000.

Probably the dosage of vaccine was too small, but we were dealing with an acute case of unusual type, and had had no experience of paratyphoid A vaccine in treatment, so that we preferred to feel our way with smaller doses in the first instance.

The long duration of the illness, with pyrexia and apyrexial intervals, perspirations, and absence of diarrhoea, gave it a certain resemblance to Malta fever, and on several occasions we tested the agglutination reaction of the patient's serum against *M. melitensis* and *M. paratyphosus*, with uniformly negative results.

The faeces and urine were only submitted to us for bacteriological examination twice—once during the second relapse and once during convalescence, twenty-seven days after the termination of the last relapse. On both occasions we failed to recover any paratyphoid or other organisms of the typhoid-dysentery group.

We have not been able to determine the source of infection. We have made inquiries of the M.O.H. for the district in which the patient lived after arrival in this country, but cannot trace any possibility of infection there. If he contracted his infection in Gallipoli this would entail an incubation period of at least three and a half weeks, but it is, of course, possible that he acquired the disease at Malta or even on board ship.

Summarizing the principal features of the case, we note:

1. A relapsing fever, due to infection with *B. paratyphosus* A.
2. Cultivation of the organism from the patient's own blood during the relapses.
3. Absence of diarrhoea.
4. Little or no leucocytosis.
5. Attempt to treat the infection with autogenous vaccine.
6. Absence of agglutinins to the infecting organism until after inoculation of vaccine.

We desire to express our indebtedness to Lieutenant Home Ross, R.A.M.C., from whose notes and charts the above account of the clinical aspect of the case was made.

NEW APPARATUS FOR BACTERIAL FERMENTATION TESTS: FERMENTATION BULBS.

By S. DELÉPINE,

DIRECTOR OF THE PUBLIC HEALTH LABORATORY, MANCHESTER.

Soon after the beginning of the war the price of various sugars and other products used in fermentation tests was so high, and it was so difficult to get sufficient stocks of them, that it became at times impossible to carry out all the tests required for the identification of bacilli isolated from the very large number of cases which had to be examined bacteriologically in Manchester for the 2nd Western Military Hospital.

To meet this difficulty I adapted a method which I devised about sixteen years ago and have used from time to time for the purpose of studying, collecting, and measuring the gases generated by definite quantities of fermentable fluids. In order, however, to meet the difficulty mentioned above, I reduced the size of my apparatus to a minimum.

This small fermentation apparatus consists of a tube 4 to 5 cm. in length, with a 2 or 3 mm. internal

1. Burette containing one of the sterilized fermentable media. The medium has been sterilized in the burette. The capillary delivery pipe is protected by a glass sheath until it is going to be used.

2. Fermentation bulb (sterilized) ready to be filled with the fermentable medium through the capillary delivery pipe of the burette. (A long hypodermic needle is suitable for this purpose.)

3. Fermentation bulb in a sterilized supporting glass tube. Sets of these tubes containing series of fermentable media are kept ready for use in racks.

4. Fermentation tube taken out of its supporting tube and inoculated by means of a platinum or palladium* needle. A Pasteur's pipette of suitable shape can also be used in the same way, but care has to be exercised to avoid an excess of fluid.

5. Result of a test with production of gas and change of reaction of the medium.

*Owing to the difficulty of obtaining platinum at the present time, I have adopted palladium as a substitute for platinum, after ascertaining that this metal has no appreciable lethal action on bacteria.

bore. The closed end of the tube is in the form of a small bulb, measuring 7 or 8 mm. in diameter, and of a capacity not exceeding 0.5 c.cm. The tube looks very much like the bulb end of a thermometer. These little tubes are inserted mouth downwards into other glass tubes of suitable diameter, which are themselves kept vertical by being inserted into the holes of a wooden rack. The bulb of the fermentation tube closes the upper end of the supporting tube. The two tubes can be sterilized together

by steam. After sterilization they must be thoroughly dried in the hot-air oven.

To introduce the fermentable medium into the bulbs, special burettes are used provided with a capillary delivery tube which can be pushed down to the bottom of the fermentation bulbs.

Each burette contains enough fluid to fill about 100 fermentation bulbs. After the burettes have been filled with the fermentable fluid, they are sterilized with their contents, the delivery pipe being protected by a glass sheath. When the fermentable tubes have to be filled they are held vertical, mouth upwards; the delivery tube (after flaming it, if it has been exposed to contamination) is inserted to the bottom of the fermentation bulb, and enough fluid is allowed to flow to fill the bulb, and about 8 to 10 mm. of the stem. The tube is then inverted and placed again mouth downwards in the supporting tube.

A set of tubes with the various fermentable media can easily be arranged in the rack provided for the purpose. A great number of such sets can quickly be prepared.

It is best to place these racks with the fermentation tubes ready for use in the incubator at 37° C. for twelve hours previous to using them. At the end of that time any gas which may be in solution in the fluid will have separated in the shape of minute bubbles. This gas is got rid of by shaking the bulb like a clinical thermometer and heating the tube gently near the free surface of the fluid.

When the bulbs have been prepared in this way they can be kept for several weeks ready for use. The fluid remains in position, provided the tubes have been filled exactly as stated above. When the bulbs have to be stored for several days before being used, it is best to keep them with the bulb down, the mouth remaining protected by the supporting tube.

The fermentation tubes are easily inoculated by means of a platinum needle or loop brought in contact with the surface of the fluid, and gently shaken in it. The needle must be removed carefully, so as not to cause any of the fluid to be carried to the mouth of the tube. This does not happen readily if the tubes are kept mouth upwards during inoculation.

All the reactions which can be observed in other kinds of apparatus are observed clearly in my bulbs, which present important advantages over the Durham's tubes at present in general use:

1. The total amount of gas generated under aerobic and partly anaerobic conditions out of a certain amount of medium is collected.
2. The first stages of the reaction are easy to observe, can be detected very early, and can be easily timed.
3. The colour of the litmus, when this indicator is used, is not affected by sterilization as it is in the Durham's tubes.
4. The amount of fluid used is very small.
5. The fermentation bulb is not expensive.

The fermentation bulbs can easily be prepared in the laboratory, or they can be obtained from Messrs. Charles Hearson and Co.

Memoranda:

MEDICAL, SURGICAL, OBSTETRICAL.

TWO CASES OF TETANUS TREATED SUCCESSFULLY BY SUBDURAL INJECTIONS OF ANTITETANUS SERUM.

I HAVE treated many cases of tetanus in China, India, and, during the war, in France, but have hitherto been unable to save a single one of them.

Every treatment has been given a trial—magnesium sulphate intraspinally, Baccelli's carbolic acid injections, antitetanic serum intramuscularly, chloral, bromides, etc. Death was the result in every case. The success following on the administration of large doses of serum subdurally in two consecutive cases of tetanus is very gratifying, and, although no definite conclusions can be drawn from such a small number so treated, the result is at least encouraging.