8. *Conclusions from the above Series of Cases.*—In some cases it may be fairly concluded that tuberculin has done decided good; in others that it has been negative in its effects; and again, in others that it has probably been harmful. As to the selection of patients for treatment, provided that very advanced cases are excluded, the experience obtained by careful observations during the past seven months has thrown no light whatever upon the subject, and my colleague and I are still absolutely at a loss for data to determine beforehand what are and what are not suitable cases for treatment with tuberculin.

TREATMENT OF CONSUMPTION BY THE HYPODERMIC ADMINISTRATION OF GUAIACOL AND IODOFORM.

*Read in the Section of Therapeutics at the Annual Meeting of the
British Medical Association, held in Bournemouth,
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IN 1884 Dr. Roussel introduced a method of treating phthisis by injecting hypodermically solutions in sterilised olive oil of eucalyptol, thymol, and other antiseptic agents. Later, Shetelig, of Nervi, used creasote with olive oil, until finding that guaiacol might be used for the creasote, and that it was less irritating he substituted for it injections of pure guaiacol. These methods were asserted to be of great service in the treatment of this disease, but I cannot find that Roussel's method was ever used in this country, and Shetelig's method has disadvantages which must always make its use in consumption a serious consideration.

Professor Picot, of Bordeaux, published in the *Semaine Médicale* of March 4th of this year a paper upon the use of iodoform and guaiacol administered in solution in sterilised olive oil by the hypodermic method, and the SUPPLEMENT to the BRITISH MEDICAL JOURNAL of March 14th, page 85, gives a short summary of his statements. He had tried this method for two months in twenty-five cases of phthisis and tuberculous pleurisy, and his conclusion was that under no other treatment in his experience had he obtained such favourable results. Creasote has been favourably thought of in consumption for about sixty years, and iodoform was introduced by Dreschfeld as a valuable adjunct to our means of combating the progress of that disease ten years ago. Faith in their powers has, however, of late been seriously tried by the large quantity of these drugs which some of their advocates have employed and recommended. Fifteen minims of pure guaiacol once or twice daily, and 30 grains of iodoform daily for a month, do not seem to have achieved more than was claimed for much smaller doses. Picot's treatment goes to the opposite extreme apparently, for he commences with injections of one-sixth of a grain of iodoform daily, and less than a minim of guaiacol, and increases the dose gradually up to three times that quantity. It is only in contradistinction to these larger doses that Picot's appear small, however, until custom modifies the effect the smallest dose usually causes a flush of heat on the surface of the body, and profuse sweating within half an hour of the injection.

The success of Professor Picot induced me to give the method a trial.

The strength of the solutions used in the following cases was, according to Professor Picot's recommendation, 0.01 iodoform and 0.05 guaiacol in 1 c.c. of olive oil, increased to three times that proportion of the drugs by degrees. The plan followed was to begin with the weaker solution, at the seventh injection to use the second strength, and at the twenty-first the third strength, discontinuing at the thirtieth injection. In a few cases, after a short interval without injections, they were resumed at the request of the patients. In four cases less than the full number of injections were administered, owing to the irksomeness of the treatment to the patients.

Three of the patients were suffering from empyema, twenty-five from consumption. Of the latter some were in

the earliest stage, the majority had cavities in one or both lungs, two or three were so advanced that no improvement from treatment could well be expected.

In two cases operation had been performed for empyema. In one case thirty injections were given with reduction of temperature from 100.8° in the evening to normal after the sixth injection, diminution of cough and of discharge from the pleura, and general improvement in health. After a few days' interval the injections were resumed at the patient's request, and he continued to improve. He gained 11 lbs. during the first two months of treatment, and then lost 2 lbs. before leaving. In the other case, very similar except in the absence of pyrexia, the patient steadily improved and gained 7½ lbs. in weight during the first five weeks of residence. On the thirty-ninth day his temperature rose to 105° F., the injections were stopped, but other symptoms of tuberculous meningitis manifested themselves, and the patient died a few days later.

The cases of phthisis are classified into pyrexial and apyrexial cases, for the immediate urgency of a patient's condition is best estimated concisely by the daily excursion of his body temperature. The pyrexial cases were eighteen in number, some of them being only occasionally pyrexial and to a small degree, while others were of a more severe type.

Two of the cases of advanced disease with temperatures ranging to 103° F., were unwilling to continue the injections long enough to say that they had been fairly tried. In a third case of a temperature of nearly 104°, with a pleuritic exacerbation of the disease, nine injections were given and the temperature fell to normal, but became unstable when at the patient's request they were discontinued. In another similar case the temperature fell from 104° F. to normal after sixteen injections, the patient's appetite improved, cough greatly diminished; the expectoration, which had been about 1½ ounce daily, practically disappeared, and the patient remained well. In this case there was tuberculous affection of both apices with excavation on one side.

In two cases the pyrexia was not materially influenced; the patient's condition in one of these improving, however, as regards cough and expectoration, the latter being reduced in six weeks from 3iv 5j in twenty-four hours, to 5j 5j in that time.

In five other cases the pyrexia was of equally severe type. One was a very advanced case with large cavities and much crepitation in both lungs, with a pulse of 140 to 160 and diarrhoea. He was kept in bed at first owing to his high temperature and great feebleness. At the end of sixteen days—after use of ice bags, stimulants and quinine—his temperature was still 103.4°, though it had fallen on first commencing the ice-bags, and again on beginning with the quinine, but after a day or so it had again risen. Then the guaiacol and iodoform injections were commenced, and in five weeks the pyrexia had disappeared. He was able to be about. His cough and expectoration were much reduced and his appetite and strength improved. He left the hospital then, and we have lost sight of him.

In another similar case of hopelessly advanced lung disease with diarrhoea and laryngeal tuberculosis, the temperature fell a little, cough and appetite improved, and the expectoration was reduced from 8½ ounces daily to 3½ ounces. But while still making good progress pneumothorax occurred and the patient died. In a third case of less advanced disease the temperature fell to normal from 103° F., and the expectoration was reduced from 4½ ounces to 1½ ounce, when a pleuritic exacerbation occurred, and the temperature rose again to 103.2° F., and the expectoration to 3 ounces daily, but in six days the temperature was again normal and has continued so. In the other two cases of severe type the progress was somewhat similar; pyrexia disappeared, cough diminished, expectoration diminished greatly (in one case entirely ceased), and the general condition improved, with slight increase in body weight.

The progress of the other seven pyrexial cases was much the same. Sometimes only after prolonged treatment, sometimes more quickly, the pyrexia subsided, and other symptoms correspondingly improved; with one exception—a case of variable temperature of no great severity, with advanced disease of the left lung and serious laryngeal trouble—the expectoration increased from 2½ ounces to 4 ounces, apparently through the guaiacol, which he tasted, causing irritation of the larynx. The man's body weight, however, increased at the same time by 7 lbs., so that some improvement occurred even in these cases.

The apyrexial cases need little mention. They all, without exception, gained in body weight, but not more than might have been expected without the injections; if anything, perhaps less than is common at the Ventnor Hospital in apyrexial cases. One of these patients had a slight attack of hæmoptysis after he had had seventeen injections, and they were therefore stopped. No other untoward symptoms manifested themselves, nor was there any local trouble from the injections in any instance.

Of the cases of empyema one had burst into a bronchus and there was a daily expectoration of 10 to 12 ounces of foetid pus. In this case a stronger solution than that of Picot was employed and daily injections were given. Except for the necessary cough and the expectoration, this patient was pretty well. He had thirty injections in all, and during the period of their administration he gained 10 lbs. in weight. After they ceased he lost 6 lbs. while taking terpene hydrate in pill. No material improvement in the factor of the expectoration nor in its quantity occurred while the patient was in the hospital.

The conclusions which seem warranted from these cases are:—

1. That in empyema with free drainage the treatment does good in improving the general condition and in diminishing the discharge from the pleural cavity, but that without free drainage it is of uncertain value.

2. That in pyrexial phthisis, whether the disease is small in extent or so extensive that the case seems almost hopeless,

it is not an absolutely certain antipyretic, but it is commonly of decided advantage if persevered with in reducing the fever, and by so doing in diminishing the activity of the disease.

3. That even where it fails within a reasonable time to modify the fever, it is still serviceable in most cases in diminishing expectoration and in modifying the cough.

4. Though it is serviceable in limiting waste by reducing temperature and by diminishing expectoration, it cannot be said that this treatment is specially favourable to increase in body weight.

5. The treatment is without risk with ordinary precaution.

6. Its use does not prevent the development of other tuberculous outbreaks or extensions of tuberculous mischief, for tuberculous meningitis, pleurisy, hæmoptysis, pneumothorax have been shown to occur after many injections.

7. In interpreting the mode of action of these remedies, their antiparasitic action should not exclusively be thought of. It should not be forgotten that both remedies act, even in small doses, upon the patient himself; that so long ago as 1867 Headland, in his *Action of Medicines*, described creasote as a sedative, a stimulant of mucous membranes, and as a true astringent.

ON THE USE OF DOG'S SERUM IN THE TREATMENT OF TUBERCULOSIS.

Read in the Section of Therapeutics at the Annual Meeting of the British Medical Association held in Bournemouth, July, 1891.

By C. BERETTA, M.D.,
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In his most interesting address to the general meeting Dr. Lauder Brunton called the attention of the Association to the use of the serum of dog's blood, recently inaugurated in France by Professor Charles Richet. I propose to give a short explanation of this method of treatment, and a rapid sketch of the original experiments made upon animals, the way to procure the serum, the mode of using it, and the results obtained.

It is well known that the staphylococcus pyosepticus causes fatal septicæmia when injected into a rabbit, and only local suppuration when injected into a dog. Professor Richet and Dr. Héricourt, as far back as 1888, succeeded, by injecting a small quantity of dog's blood into the peritoneal cavity of a rabbit, in rendering this animal also refractory to the action of the same microbe. They noticed besides that the experimental immunity of the rabbit was still more marked when the injected blood belonged to a dog which had previously been inoculated with the staphylococcus. It was natural that the same method should be tried with other microbes, particularly with the bacillus of tuberculosis to which the rabbit is so liable, while the dog is manifestly refractory to it. The principal results successively announced by MM. Richet and Héricourt to the French Academy of Sciences and to the Paris Society of Biology may be summarised as follows:

First, a rabbit having been inoculated with a culture of the tubercle bacillus, the evolution of tuberculosis can be arrested by injecting dog's blood afterwards when the bacillus culture is not too virulent, but this evolution is only delayed when the culture is very virulent.

Secondly, the effective substances of the blood, which have not yet been identified, reside in the serum, and a small dose of the latter is sufficient ($\frac{1}{3}$ cubic centimetre per kilogramme of the rabbit).

Thirdly, the serum of dog's blood has a prophylactic action—that is to say, when injected into a healthy rabbit it prevents the development of experimental tuberculosis at a later period.

Fourthly, the serum of a dog which has been previously inoculated with tuberculosis seems to be more efficacious in a healthy rabbit, but, on the contrary, seems to aggravate the disease when injected into a rabbit already tuberculated.

These results encouraged several physicians to try the dog's serum, called also hæmocyste, upon human beings, of course, with all requisite precautions.

We had the gratification of showing in Paris to Dr. Lauder Brunton and to other members of this Association the process we use in Professor Richet's laboratory. The blood is taken aseptically from the carotid artery of a strong, healthy dog, and is received in sterilised receptacles closed with cotton wool. The serum quickly separates itself, and can the next day be drawn by suction into glass pipettes also sterilised, which are immediately shut at both ends by means of a gas burner. In this way are obtained flasks of this very convenient form filled with pure, clear, transparent serum more or less coloured by hæmoglobin. It must be employed as unaltered and as fresh as possible. Of course a careful necropsy is made of the dog; its blood is microscopically examined, and no serum is used for man, except from animals in a perfect physiological state of health. It is interesting to notice that we have now made hundreds of necropsies of dogs of all kinds without finding a single case of spontaneous tuberculosis in this animal. The serum has sometimes been given by the mouth, but, of course, its effects are much more marked when injected. Injections of one or more cubic centimetres are generally made every two days in the subcutaneous cellular tissue of limbs or trunk. They must be performed with strict aseptic precautions and with sterilised syringes. In this manner several thousands of hæmocyste injections have already been given without any serious accident. The temperature of the patient is as a rule only slightly increased after each injection of serum. It should, however, be mentioned that very often a peculiar local swelling does appear at the site of injection, which is accompanied by redness, sometimes pain, and even short fever, but never by suppuration. A more or less widespread urticarial eruption, probably of a similar nature to the nettle rash produced in some people by mussels, crustacea, or certain kind of drugs, is also common. I hasten to add that these phenomena are neither dangerous nor lasting. We have not yet been able to establish any relation between their appearance and the action of the serum.

I come now to the results obtained by using dog's serum, principally against tuberculous diseases. I shall not trouble you with the details of the numerous cases, both medical and surgical, observed in France by Drs. Héricourt, Langlois, St. Hilaire, Clado, Morel-Lavalée, Feulard, Laborie, Wehlin, etc., nor even with those I have myself followed at the Paris Hôtel Dieu, in Professor Verneuil's department. I need only describe the clinical phenomena usually noticed by different observers. In the first place, it must be acknowledged that in about one-third of the cases no apparent result was obtained. In the other two-thirds a real improvement, more or less marked, has been observed.

In all these cases it was remarkable to see how quickly the patient recovered his appetite, strength and power of movement, while his weight gradually increased. As a rule, after a few injections, the patient sleeps better, the digestive functions become more regular; in some cases we find that coughing, expectoration, sweating, and hæmoptysis, are diminished. Twice it was noticed in young women that long suppressed menstruation came on again. Lastly, in a number of cases, there has been a local improvement of the anatomical changes in the lungs, the larynx, the skin, bones, suppuration, etc. The favourable modifications were well maintained in several patients. These patients were in the first stage, or at most in the beginning of the second stage of the tuberculous evolution. Unfortunately, in most of the other cases the wonderful effects of the first days were not durable, and the tuberculous evolution has only been delayed for a few months.

To sum up: dog's serum, in men as in animals, does not seem to have a special curative action against tuberculosis, but it possesses a powerful action, if not against the microbe, at least against its effects. It seems to act as a powerful tonic, and indirectly by improving the general nutrition puts the patient in a better condition to overcome his terrible disease. The blood of steers, tried by MM. Bertin and Pique, the serum of sheep, tried by Professor Lépine, seems to give similar results.

Experiments upon animals' blood are very much *à la mode* now on the Continent, and I am very happy to see here present Professor Mosso, from Turin, who made such interesting experiments upon the blood of eels and other