NOTE ON THE TREATMENT OF PERNICIOUS ANAEMIA.

By BYROM BRAMWELL, M.D., F.R.C.P.E.,

SENIOR ORDINARY PHYSICIAN TO THE EDINBURGH ROYAL INFIRMARY, ETC.

DURING the past year I have met with two cases of advanced pernicious anaemia in which, after a certain degree of improvement had taken place under arsenic, arrest of the improvement occurred, and in which the administration of iron was then attended with very marked and rapid alteration for the better.

It has for long been recognized that in typical cases of pernicious anaemia, in which the colour index is above the normal and each individual red blood corpuscle contains more than the normal amount of haemoglobin, the administration of iron is usually unattended with benefit, and is in many cases apparently injurious. This certainly has been my own experience; but I have met with some exceptions, amongst which the two cases to which I have just referred are perhaps the most striking. The notes of one of the two cases are as follows:

Mrs. P., aged 54, was admitted to the Edinburgh Royal Infirmary on September 1st, 1908, complaining of weakness, bleeding piles, and swelling of the feet.

History.

The patient stated that she had been a strong, healthy woman until three years previously; she then had an attack of what she termed "jaundice"; this lasted for seven weeks; she has had two other attacks of the same sort since, the last about a year ago. For thirteen years she has been troubled off and on with bleeding piles; for some months before her admission to hospital the piles had been worse.

Condition on Admission to Hospital.

Temperature 99.2°, pulse 108, respirations 32; extremely pale and anaemic. The face had a yellow tinge, but there was no jaundice; the feet were swollen. The patient was not emaciated, but stated that she had lost a good deal of flesh lately.

The blood showed all the characteristic features of advanced pernicious anaemia. The red corpuscles numbered 545,000 per cubic millimetre, the haemoglobin equalled 15 per cent., the colour index was 1.2, the white corpuscles numbered 3,800 per cubic millimetre. The differential count was as follows: Polymorphs, 73 per cent.; small lymphocytes, 19 per cent.; large lymphocytes, 7 per cent.; eosinophiles, 1 per cent. The red corpuscles showed marked poikilocytosis; no normoblasts or megaloblasts were found.

The appetite was poor; the patient complained of thirst. The bowels were constipated. All the teeth were absent. The patient stated that she had had no teeth for three years, and that she had for a long time only had one or two teeth; she further stated that she had not suffered from dental caries or from a sore mouth; her teeth simply dropped out, and did not decay.

The tongue was slightly furred; the liver was considerably enlarged, projecting $3\frac{1}{2}$ in. below the costal margin; the spleen was somewhat enlarged.

The patient was very short of breath and suffered from palpitation, and at times faintness. The pulse was 108, soft and weak; the blood pressure 120. Blowing systolic murmurs were heard in all the cardiac areas, most marked at the apex.

The urine contained a trace of albumen but no casts or other abnormal constituents.

There were no haemorrhages in the retina; the fundus oculi was pale, the optic discs normal.

Treatment.

Gradually increasing doses of arsenic, commencing with 2 minims of Fowler's solution three times daily, increased every fourth day by 1 drop. The maximum dose which the patient was able to take was 10 drops three times daily.

Progress and Result.

Under this treatment great improvement rapidly took place. On October 1st, the patient was looking and feeling very much better, and the condition of the blood showed a marked improvement—the red corpuscles were 1,800,000, the haemoglobin 50 per cent., the colour index 1.2. From October 1st to November 10th, although the general condition improved, there was no alteration in the state of the blood. On November 11th Robertson's Bland's pill capsules—one No. 3 capsule (equal to three Bland's (pills) three times daily—were prescribed. Under this treatment striking improvement in the condition of the blood immediately took place. On November 20th, the red corpuscles equalled 3,000,000, the haemoglobin 60 per cent., and the colour index 0.9. On November 21st the patient was discharged from hospital, and advised to continue the iron. On January 13th, 1909, when she was last seen, she stated that she was perfectly well. She looked very well—many years younger than on her admission to hospital. The blood examination showed the red corpuscles 4,100,000, the haemoglobin 65 per cent., and the colour index 0.7.

It is important and interesting to note that the iron produced a marked and rapid increase in the number of red corpuscles, and that after the administration of iron the colour index fell from 1.2 to 0.8.

Table showing the Condition of the Blood at different Dates.

	Red Blood Corpuscles.	Haemoglobin.	Colour Index.	White Blood Corpuscles.
		Per cent.		
September 3,* 1908 ...	545,000	15	1.2	3,800
" 6, " ...	580,000	16	1.2	—
" 12, " ...	890,000	25	1.2	3,600
" 16, " ...	1,200,000	30	1.2	—
" 29, " ...	1,600,000	40	1.1	2,200
October 6, " ...	1,900,000	45	1.06	3,200
" 16, " ...	1,800,000	50	1.2	5,500
" 29, " ...	1,800,000	45	1.1	3,000
November 3, " ...	1,600,000	45	1.2	3,200
" 10,† " ...	1,800,000	50	1.2	6,000
" 20,† " ...	3,000,000	60	0.9	5,000
December 2, " ...	2,900,000	55	0.8	—
January 13, 1909 ...	4,100,000	65	0.7	7,600

* Arsenic prescribed.

† Iron prescribed.

‡ Patient discharged from hospital on November 21st.

The fact that the patient had had no dental caries and no glossitis and that there had been no oral sepsis is an interesting point. I have met with and recorded some other cases of pernicious anaemia in which the same fact has occurred. I consequently doubt whether oral sepsis has the important influence in the production of the disease which some authorities have suggested. I am disposed to think that the glossitis from which many patients who are affected with pernicious anaemia suffer is a consequence rather than a cause—due, presumably, to the same toxin, whatever it may be, which is the cause of the anaemia.

SOME REFLECTIONS REGARDING THE FREE USE OF BACTERIOLOGICAL CULTURES FOR THE DESTRUCTION OF RATS AND MICE.

By DR. J. DANYSZ,

THE PASTEUR INSTITUTE, PARIS.

OWING to the general use of certain microbic cultures for the destruction of rats and mice, field mice, rabbits, and other small rodents, the question of a possible danger which these cultures may present with regard to the health of human beings has lately been raised.

The destruction of vermin is of course most important, both from a hygienic and an economic point of view. Rats and mice are the principal propagators of the plague, and probably of many other contagious diseases; we know, also, that rats and mice in warehouses, etc., and mice and voles in the fields, are often the cause of enormous damage. In France, for example, in the year 1903, field mice did nearly a million pounds worth of damage to the crops, and the scourge was only stopped by applying in the fields a virus prepared at the Pasteur Institute in Paris at the request of the French Government. In Great Britain, according to recent estimates, the damage caused by rats amounts to as much as £10,000,000 per annum.

It is incontestable that the introduction of raticide viruses has played a most important part in the campaign against these animals, nor must we forget that the application of these bacteriological methods for practical purposes is only of recent date, and that they have not yet been brought to complete perfection. It will readily be admitted that it is only since the introduction of these methods that the systematic and scientific study of the destruction of rodents has begun, and that it is solely by persevering in this direction, and by taking advantage of

every resource offered by science, that serious and lasting results can be obtained.

It would, therefore, be most undesirable in the general interest, if the free development of this science and of this new industry were prevented, as we should thereby be denied the advantage to be gained by practical experiments and trials with biological methods, in the campaign against destructive animals. It would be most unscientific to do this without sufficient reason.

The viruses of Loeffler, Danysz, Issatschenko, Neumann, and Dunbar belong to the group of microbes called *Salmonella* or *Bacillus enteritidis*. According to the most recent investigations, two types are to be distinguished among these bacilli, differing from each other in several biochemical characteristics.

Type I, to which belong the bacillus of Loeffler, of hog cholera, and of psittacosis, all apparently identical with the *Bacillus paratyphus* B.

Type II, to which belong the bacilli of the viruses of Danysz, Issatschenko, Neumann, and Dunbar, which seem to be identical with the *Bacillus enteritidis* of Gaertner.

The bacillus of psittacosis, discovered by Nocard during an epidemic among parrots, must be placed in a special category, as it appears to be very dangerous to man. All the other bacteria belonging to the *Salmonella* group call for special examination. The bacillus of hog cholera was for a long time considered to be the cause of this disease, but we now know with certainty that, although this bacillus is often found in the excreta and in the blood of pigs affected with cholera, yet it is in reality another microbe, invisible under the microscope and able to penetrate porcelain filters, which is the real agent of the disease. The visible microbe is a concomitant of no importance, unable to cause hog cholera in pigs. I lay great stress on this point, as it has a most important bearing on the subject.

The investigations of the American bacteriologist, Salmon, have incontestably shown that if the blood or the serum of a pig that has died, or is ill with cholera, are filtered, and if another pig is inoculated with these liquids, freed from all visible organisms, it will become infected with the disease, whilst inoculation with the visible bacillus, which has up to the present been looked upon as the sole agent of hog cholera, produces no appreciable effect. Thus we have a microbe which has for many years unjustly borne a bad reputation, and it is only now, since the existence of microbes invisible under the microscope has been established, that we are able to do it justice and declare it to be quite inoffensive.

Is it not possible that similar circumstances may obtain with respect to the microbes of Flüge and Gaertner, and particularly with those of the raticide viruses, which, whilst bearing great resemblance either to the *Bacillus paratyphus* B or to the *Bacillus enteritidis*, differ considerably from them as regards their biological characteristics, especially in their virulence?

Cases of infection through food are comparatively rare, as appears evident from the very small number of cases reported in medical literature in the course of a year, and yet, surprising as it may seem, large quantities of preserved meats, smoked or salted hams, sausages, etc., and even smoked sturgeon, contain bacilli belonging to the groups *Paratyphus* B and Gaertner.

Valuable light has been thrown on this question by the recent investigations of Drs. Muehler, Dahm, and Fuerst at the Institute for the Study of Infectious Diseases in Berlin.¹ They bought at random, in the shops of Berlin, fifty-seven specimens of preserved meats, and subjected them to minute bacteriological examination. Some white mice were also fed with portions of each. The results were quite unexpected; forty of these portions of meat gave characteristic diseases to the mice, which in the majority of cases proved fatal, but upon the autopsy of the mice cultures identical with *Bacillus paratyphus* B and the Danysz virus were found, while in the meat none of either the one or the other of these microbes could be traced.*

Since Conradi and Uhlenhuth first drew attention to the frequent presence in Nature of paratyphic bacilli they

* This fact does not prove that there were no pathogenic microbes in the incriminated samples, but it proves in an incontestable fashion that preserved meats may produce serious accidents in connexion with which *Bacilli enteritidis* may be found in the blood of the victims, while at the same time it may be impossible to discover these microbes in the articles of food which have caused the illness.

have been found everywhere—in articles of food and in the excreta and the urine of perfectly healthy persons and animals. Huebener² found *Bacillus paratyphus* B in various kinds of *charcuterie*, fresh and preserved, of which he and his family partook without the slightest evil effects. Rimpaud³ found the *Bacillus paratyphus* B in the excreta and the urine of eleven perfectly healthy individuals, none of whom had come into contact with persons suffering from disease. Uhlenhuth, Huebener, Xylander and Bohtz⁴ have frequently found the bacillus of hog cholera or *Bacillus paratyphus* B in the normal contents of the intestines of pigs.

It should be noted that in 1903-4 nearly 600,000 litres of cultures of the Danysz bacillus were distributed in France, in different departments, for the purpose of destroying field mice; that for more than ten years some hundreds of litres of virus have been distributed every week for the destruction of rats, and that consequently more than a million persons have handled this virus without taking any special precaution, and that, in spite of that, no appreciable case of illness has resulted, either in man or among domestic animals.*

CONCLUSIONS.

The following points should receive special attention:

1. Mice die after having eaten meat, and show the presence of the *Bacillus paratyphus* B or Gaertner's bacillus in the blood, whilst these microbes could not be discovered in the meat itself. (Muehler, Dahm, Fuerst.)

2. Small and large quantities of food containing the *Bacillus paratyphus* B or Danysz virus have been eaten by human beings, without the slightest evil effects being apparent. (Huebener, Danysz.)

3. *Bacillus paratyphus* B is often found in perfectly healthy human beings. (Conradi, Uhlenhuth, Rimpaud, and others.)

The following conclusions would, therefore, appear to be justified:

1. That the microbes of the *Salmonella* group are extremely widespread in Nature.

2. That, if these microbes are found frequently in cases of poisoning through food, it is far from being proved that they are the active agents in these occurrences.

It is much more probable, as maintained by Professor Marx,⁵ that they are due to ptomaines or other poisons emanating from foodstuffs more or less tainted, and that the microbes in question are only inoffensive concomitants, as in the case of hog cholera.

In the course of the above-mentioned investigations Drs. Muehler, Dahm, and Fuerst have once more confirmed the value of the raticide viruses; they found notably that the Danysz bacillus killed more than 50 per cent. of wild and over 90 per cent. of domestic rats.

I think, therefore, that microbic cultures which have been handled for more than ten years by more than a million individuals, and which have been scattered broadcast on bread or grain in many parts of the world and placed within reach of domestic or other animals without causing any serious accident, cannot reasonably be considered dangerous.

REFERENCES.

- ¹ *Centralbl. f. Bakt.*, October 10th, 1908. ² *Deut. med. Woch.*, 1908, No. 24, p. 1044. ³ *Ibid.*, No. 24, p. 1045. ⁴ *Berliner militär-ärztliche Gesellschaft*, May 21st, 1908. ⁵ *Centralbl. f. Bakt.*, 1908, orig. October 10th, p. 29.

* With a view of showing the many opportunities of infection which were afforded by the methods adopted when applying the virus over large areas, it may perhaps be of interest to describe in detail the manner in which it was distributed. For an area of 1,000 hectares (2,500 acres approximate) a quantity of 1,000 litres (225 gal. approximate) of the virus was employed, and from 1,200 to 1,500 kilog. (2½ to 3½ cwt. approximate) of crushed grain was soaked with it. If sufficient receptacles were not to be had to contain all this grain and liquid, the grain was put on the floor of a schoolroom, a barn, or the large room of an inn, the virus poured over it, and the mixture effected by means of spades. The bait, thus prepared in the morning, was distributed in the fields during the afternoon. For the purpose of distribution, a large number of the inhabitants of the village were requisitioned—men, women, and even children of over 12 years of age. Each person received some of the soaked grain in a basket or some other receptacle, and they used their hands to place it where required. One man was able on an average to lay the necessary bait for 1 hectare (2½ acres) in a day, and as the work had to be finished as quickly as possible, many persons were thus occupied for several days in succession. The bait was apt to stick to the hands, to the garments, to the baskets, and to everything with which it came in contact. The peasants, and especially the children, absorbed it more or less; the animals on the farms, game, and birds ate considerable quantities of it. The inhabitants of about 1,000 parishes in France were thus brought into contact with the virus.