Experiments on Pasteur's protective inoculation against anthrax in Hungary / by Aladár von Rószahegyi.

John Simon Esq. C.B.

M. with the authors respect.

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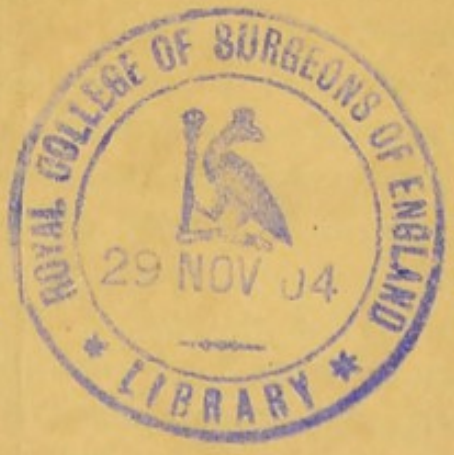

workman whom others do not like seems to me to be unjust; and, like most unjust actions, to be a blunder as well. A combination against a master whose workshops were badly lighted, or who wished to diminish the wages of men who wore spectacles and who could see as well with them as others without them, seems to me to be a proceeding which would be justified by science, by common sense, and by humanity; all of them allies of great practical value in the attainment of any ends with which they are associated. It is part of the business of this Health Congress to teach those who attend its meetings to take proper care of their bodies; a course which, with most men, is an essential preliminary to taking proper care of their souls. If my words to-night have at all assisted you to perceive the practical importance of taking care of one small organ, I shall feel that my time has indeed been well bestowed.

EXPERIMENTS ON PASTEUR'S PROTECTIVE INOCULATION AGAINST ANTHRAX IN HUNGARY.

BY DR. ALADÁR VON RÓSZAHEGYI,

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AFTER the publication of Pasteur's experiments on protective inoculation, the Royal Hungarian Ministry of Agriculture, Commerce, and Manufactures, requested him to demonstrate his mode of proceeding here. As Pasteur himself could not leave Paris, he sent one of his assistants, M. Thuillier, with the necessary material and apparatus for inoculation, to Buda-Pest, where a committee, consisting of nine members, was appointed by the Ministry to inspect the experiments.[1]

The inoculation experiments were performed in September and October, 1881, and the committee has reported on the

[1] The members of the Committee are:—From the University, Professors Fodor, Korányi, and Plósz; from the Veterinary School, Director Tormay and Professors Arary, Csákó, Liebermann, and Thanhoffer, and University Docent, Dr. von Rószahegyi.

results to the Ministry. The generally diffused and intense interest with which the subject of protective inoculation is followed by scientific circles in every country has induced me to make an attempt to communicate to the profession in foreign lands the chief results of the experiments performed in Hungary. The original report, with Appendices, will be published by the Ministry.

M. Thuillier's call to Hungary had the double object of getting him to demonstrate, (1) the protective power of Pasteur's inoculative substances on animals, and (2) the mode of preparing the matter for inoculation. Pasteur did not agree to the latter, as he could not spare M. Thuillier for so long a time as was required for the cultivation of the inoculative matter, and because he considered that our laboratories were not properly constructed for it. I am, therefore, only able to give authentic information upon the results of the experiments on inoculation. Although the origination of the methods and the preparation of the infective material have been already published by Pasteur himself, yet for foreign readers the oral communications which Thuillier occasionally made here may not be uninteresting, and I therefore reproduce them in order in the following pages.

Pasteur starts from the observation that when a number of animals are inoculated with a substance containing the anthrax microzymes, for example, with the blood of a sheep which has died from the disease, the greater part of such animals die, but some recover from the complaint and are no longer susceptible to infection by the anthrax poison. If, therefore, we could succeed in producing only temporary disease in all animals, their immunity would be secure. For this purpose the unmodified anthrax microzymes, those as in the blood just mentioned, or earth containing spores, are not adapted, because they produce a still greater mortality than the epizootic anthrax itself. It is therefore necessary to endeavour to weaken the infective power of the microzymes so much that they will produce only a slight attack of anthrax. For this purpose Pasteur took advantage of the conditions which he had observed in artificially cultivated anthrax bacilli kept at different degrees of temperature. The bacilli developed and multiplied in beef-tea best at 25° to 40° C. Above and below these temperatures their development was

retarded, and at 15° and 45° was completely arrested. These extreme temperatures could not be applied, since the object was not to arrest completely the development of the bacilli. On the other hand, from those temperatures at which the development took place with difficulty, corresponding diminution in the virulence of the bacilli might be expected. His ideas were confirmed by the fact that birds, and especially birds of prey, are little, if at all, affected by anthrax, and by his experiments, which indicated that this condition was due to the high temperature of these animals, which reaches 42° to 43° C. Pasteur accordingly cultivated some blood taken from an animal just dying of anthrax, and containing the *bacilli anthracis*, at 42° to 43° C. in beef-tea, and found that the bacilli no longer formed resting spores, but only grew into long homogeneous threads. The longer the fungi were kept at this temperature, the more did their virulence decrease, and while the original blood killed all the sheep inoculated with it, samples taken from the cultivated material on the twelfth day only killed half of the animals inoculated, and samples taken on the twenty-fourth day killed none of them, but caused in all a slight rise of temperature, which came on sooner or later after the inoculation and lasted for some days. In the fluid which was kept at from 42° to 43° C. the microzymes remained alive and capable of further inoculation from four to six weeks. At the end of this time they died.

The desired diminution in the virulence of the microzymes was therefore reached in the specimens taken on the twenty-fourth day from material cultivated at 42° to 43° C. Animals inoculated with this material were still killed when inoculated with the completely virulent original microzymes. On the other hand, a sample taken from the material on the twelfth day of cultivation caused no death amongst those animals already inoculated with material cultivated for twenty-four days, but only produced a slight feverish disturbance, after which they were altogether insensible to the completely virulent microzymes.

Herein is the scheme of the whole proceeding. First, inoculation with anthrax microzymes, whose virulence had been nearly destroyed by continued cultivation for twenty-four days at a

temperature of 42° to 43° C. After the disturbance consequent upon the inoculation had run its course, which it may with certainty be assumed to have done after twelve days, a second inoculation is made with microzymes whose virulence has only been diminished one half, by cultivation at the same temperature for twelve instead of twenty-four days. After twelve days more the fever which succeeds the second inoculation has run its course in all the animals, and they are now completely protected. Before this method could be rendered practically available, two great difficulties were to be overcome —the preparation of inoculative material on a large scale, and its preservation. The material cultivated at 42° to 43° C. retains its vitality at from four to six weeks, and if a single drop be taken from it at any time during this period, put into pure beef-tea, and kept constantly at 35° C., the microzymes quickly multiply, and this second crop possesses exactly the same virulence as the first one possessed at the time when the drop was taken from it. The secondary crop thus obtained from material taken on the twelfth day of cultivation will therefore kill only the half of uninoculated animals, and would not kill any which had already been inoculated with material cultivated for twenty-four days. Conversely, this secondary crop is completely protective against virulent microzymes.

No less important is it that the secondary crops cultivated at 35° C. begin to form resting spores after forty-eight hours, and after several days they are entirely changed into this resting condition. A definite degree of virulence is preserved in these spores, so that the inoculative material in the spore condition can be sealed up in tubes and preserved for any desired time and conveyed to any distance. This is not the case with the cultivated material in the form of threads, because these threads die when air is excluded, and it is impossible to send them about in open tubes on account of the contamination to which the material would be exposed. Whenever and wherever it is desirable, these spores can be cultivated in pure beef-tea, and a small quantity of them yields any required amount of inoculative material of the same strength.

After the degree of virulence required for protective inoculation has been once attained, and to a certain extent fixed in the

spore condition, the protective inoculations are carried out with matter which has been weakened to any desired extent by successive cultivation through any number of crops. In accordance with the practical application of the method, Pasteur has called the material obtained from the crop on the twenty-fourth day of cultivation the first inoculative material (*premier vaccin*), and that obtained from the crop on the twelfth day of cultivation the second inoculative material (*second vaccin*).

What I have said so far is gathered from the statements of Thuillier regarding the preparation of the inoculative material. I will now proceed to describe the experiments in inoculation which he performed in Buda-Pest, and in the province Puszta Öntés, near Kapuvár (County Sopron).

(1) The experiments at Buda-Pest were performed in the veterinary school there. The Ministry placed at the disposal of M. Thuillier ten cattle—six oxen and four calves, and sixty sheep—thirty merinos and thirty Wallachian. One half of these animals were to be inoculated with the anthrax microzymes weakened by previous cultivation, and the other half were not to be so inoculated. In order to ascertain the result, the whole of them, inoculated and non-inoculated, were to be finally infected with the virulent anthrax poison. The animals intended for experiment were of course completely isolated from the other animals in the institution, and special rooms were set apart for them, the cattle being kept in single stalls, the sheep being located in one common room, inoculated and uninoculated mixed together. During the whole duration of the experiments, the animals were fed on the same hay, which might be regarded as free from anthrax spores, as it caused no symptoms of anthrax in the numerous other animals in the same institution which were fed upon it. The cattle were poorly nourished, but healthy. Two of the sheep suffered from catarrhal stomatitis, and ten or twelve others were cachectic, probably in consequence of distoma and strongylus. The general health of the animals was, however, quite sufficiently good for the purpose of the experiments.

The material for inoculation, which M. Thuillier brought with him from Paris in sealed tubes, consisted of fluid containing spores. Four sheep were inoculated with this material just as it was. The other sheep and the cattle were inoculated with

material yielded by the crop which M. Thuillier obtained from these spores by cultivating them at 35° C. in the veterinary school here in sterilized beef-tea contained in sealed flasks which he had also brought with him from Paris. This cultivated material, at the time of its inoculation, contained homogenous and spore-forming threads.

The first protective inoculation with the completely weakened material (*premier vaccin*) was carried out on the 23rd September, on one half of the animals.

Into 30 sheep (15 merinos and 15 Wallachian) $\frac{1}{6}$ of a cubic centimetre was injected with a subcutaneous syringe into the inner surface of the thigh, which is nearly free from wool. Into 4 of these 30 sheep the spores were injected, and into the other 26 the cultivated threads. Into 5 cattle—three oxen and 2 calves, $\frac{1}{3}$ of a cubic centimetre was injected at the shoulder with a subcutaneous syringe. After this inoculation no symptoms of disease could be perceived either in the cattle or the sheep, and the latter did not once show a rise of temperature during the first two days. At M. Thuillier's desire, thermometric observations were then given up, and were not kept at all in the later inoculations. On the eighth day (Oct. 1) one sheep died suddenly, and at the post-mortem examination, made seven hours after death, bronchial catarrh and catarrhal pneumonia were found to be present, as well as a tape-worm (*Taenia expansa*) in the smaller intestine, and a catarrhal condition of its mucous membrane. A rabbit was inoculated with blood taken out of the femoral vein, and with the splenic pulp, which were introduced by an incision in the skin of the back with a negative result. M. Thuillier attempted to cultivate this blood, but obtained no anthrax microzymes from it.

After twelve days (Oct. 5), the animals which were still alive—29 sheep, 2 calves, and 3 oxen—were inoculated with the material whose virulence had only been half diminished (*second vaccin*), in the same quantities, which were injected in corresponding spots on the other side of each animal. This time, also, 4 of the sheep were inoculated with pure spore material, and 25 with the cultivated threads. After this inoculation, likewise, no marked symptoms appeared in any of the animals with the exception of one sheep, which died on the third day

(8th Oct.). The post-mortem examination was made seven hours after death, and showed chronic catarrh of the stomach and intestines, with tympanites, some swelling and softening of the spleen, and bacteria in the blood which resembled those contained in the inoculative material. As it was impossible to be certain from the post-mortem appearances whether or not the animal had died from anthrax, further experiments were performed. The bacilli which were contained in the blood developed, in a solution of isinglass, exactly like the *bacilli anthracis*, and these crops, obtained by cultivation, were injected subcutaneously into two rabbits, producing death by anthrax. The blood of the sheep was also inoculated into two rabbits by an incision in the skin of the back. One of them was found dead on the third day (10th Oct.). It exhibited hyperæmia of the respiratory passages, and œdema of the lungs. In the blood were found bacteria which were shown to be *bacilli anthracis*, both by their form and by the course of their development when cultivated in isinglass. The other rabbit remained alive, and exhibited no symptoms of disease. Finally, two sheep were inoculated with the weak inoculative material (*premier vaccin*), and after nine days one of them was infected with the blood of the sheep which had been kept in a sterilized tube with admission of air. Virulent anthrax microzymes were subcutaneously injected into the other, which died on the third day, of anthrax, but the first remained alive. All these experiments do not definitely decide what the cause of death in the sheep was, although they increase the suspicion that it was due to anthrax.

In the meantime twelve days had passed since the second protective inoculation; the inoculation was therefore complete, and the control experiments could now be begun. These consisted in the subcutaneous injection of a crop of unmodified virulent anthrax microzymes into all the inoculated animals, and into an equal number of uninoculated ones. M. Thuillier had brought with him anthrax spores which had been kept for nearly five years in Pasteur's laboratory. From these he prepared here, in Buda-Pest, a crop by cultivation in beef-tea; of this he injected one-sixth of a cubic centimetre into 25 inoculated and 25 uninoculated sheep, and half a cubic centimetre into

5 inoculated and 5 uninoculated cattle (in each case 2 calves and 3 oxen), in the usual spots under the skin.

We will now consider in groups the results of these control experiments on infection.

Among the sheep, the 25 inoculated ones exhibited no symptoms of disease on the days succeeding the virulent infection, but on the seventh day (Oct. 23), one died, and on the nineteenth day (Nov. 5), a second died. The post-mortem examination showed in the first excessive anæmia and distoma hepaticum, and in the latter alterations in the lungs due to strongylus filaria. No appearances of anthrax were present. Among the inoculated sheep one died in the first thirty-six hours, and others in the following order:—

First day	Oct. 17	0
Second day	,, 18	0
Night between second and third day	,, 18—19	8
Night between third and fourth day	,, 19—20	6
Fourth day	,, 20	4
Fifth day	,, 21	3
Sixth day	,, 22	1
Eighth day	,, 24	1
		23

The post-mortem appearances corresponded to those of anthrax in twenty-two cases, but in most of them were not sufficiently characteristic. In the samples of blood which we examined, rod-like and thread-like bacteria, and, exceptionally, also moveable bacteria, were found. In the twenty-third animal no symptom of anthrax was discovered. The blood was watery, did not coagulate, and contained no bacteria. The liver was greatly altered by distoma.

Among the cattle, the only thing that was observed was in the uninoculated calves, in which a rise of temperature to 41°·7 C., loss of appetite, dry muzzle, and constipation, were noticed. On the fourth day these animals were also well. The inoculated calves, as well as both the inoculated and uninoculated oxen, exhibited no symptoms of disease whatever.

The results of the experiments performed in Buda-Pest may be thus summed up. Among the sheep, one died after the first

inoculation with catarrhal pneumonia. After the second, one died with gastro-intestinal catarrh. The protective inoculation did not certainly cause any death from anthrax. After the control experiments one animal died of distoma hepaticum, a second of strongylus filaria. Consequently, among the inoculated animals, the virulent control inoculation caused no death which was certainly due to anthrax. There was no death among the uninoculated sheep during the time that the protective experiments were being carried out on the others. After the control inoculation eighty-eight per cent. died of anthrax within eight days, and one (four per cent.) died excessively anæmic. The cattle stood the protective inoculation without loss, and even without any illness. After the control infection there was only some fever of short duration amongst the uninoculated calves. The inoculated calves, as well as all the oxen, were unaffected by the infection.

(*To be continued.*)

Department of Public Health.

EXPERIMENTS ON PASTEUR'S PROTECTIVE INOCULATION AGAINST ANTHRAX IN HUNGARY.

BY DR. ALADÁR VON ROSZAHEGYI,

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(*Continued from p.* 160.)

(2) I will now proceed to the experiments made at Kapuvár, which were carried out on three groups of animals.

(*a*) The first experiment was arranged exactly like the one at Budapest. Out of 100 rejected sheep, 50 were subjected to double inoculation, and the others were not, and finally, all were infected with virulent anthrax poison, several of these animals were very cachectic, the cachexia being due to the pericarditis and peritonitis which rage in this district. During the experiment the animals were kept in the stall, and fed with hay, straw and turnips. The first protective inoculation with the *premier vaccin* occurred on Sept. 28, and was not followed either by general symptoms of disease nor by any local symptoms at the spot of inoculation. The more powerful matter (*second vaccin*) was inoculated on Oct. 10, when the following deaths occurred, exclusively amongst those animals which had been inoculated:—

First day	Oct. 10	0		
Second day	,, 11	0		
Third day	,, 12	1	of anthrax.	
Fourth day	,, 13	1	,,	
Fifth day	,, 14	2	,,	
Seventh day	,, 16	1	,,	
Ninth day	,, 18	1	with pericarditis.	
		5	of anthrax.	
		1	with pericarditis.	

The control infection experiments were performed on the 44 inoculated animals which remained alive, and on the

time of anthrax, and none of any other disease. After the infection with virulent material of 44 inoculated animals, 3 (6·8 per cent.) sickened, and of these 1 (2·27 per cent.) died. Of the 50 uninoculated 48 (96 per cent.) were killed by the infection, and, as the post-mortem showed, with the exception of some cachectic individuals, all died of well-marked anthrax.[1]

Among the cattle, the first protective inoculation produced no marked results. The second caused in 1 animal (7·1 per cent.) a slight illness. After the infection with virulent material also, only a slight sickness was observed among the inoculated animals in 1 case (7·1 per cent.), and, on the other hand, among the 6 uninoculated, 4 (66·7 per cent.) were severely ill, and 1 of them (66·7 per cent.) died of anthrax.

We will now proceed to draw such conclusions as are allowable from the results of these experiments, which I have arranged in tabular form on the following page.

I will follow the example set in the report of the committee, and leave out of account the results obtained elsewhere by the same methods.

It must be regarded as a great gain for *scientific* pathology that we were able, in these experiments, by artificial cultivation, to diminish the virulence of microzymes, which are known to be constantly associated with a deadly infectious disease, to such an extent that they produced a transient sickness only in the organism into which they were introduced, and in which they multiplied, and at the same time deprived the organism of its susceptibility to the action of microzymes retaining their original virulence. Herein lies, on the one hand, a proof that bacteria are the actual causes of the sickness and death in anthrax, and, on the other, an explanation of the mode of action of protective inoculation, a matter which has already been used for a long time in other diseases, as, for instance, in small-pox, without our having known how its action was to be explained.

The *practical results* of these experiments are of still further importance, because here sanitation and agriculture—that is,

[1] As it was not definitely stated what was to be understood by this "some cachetic sheep," I have been obliged to take the whole percentage under the heading of anthrax. But in order to show that this heading includes animals which died without symptoms of anthrax I have marked it with a (?).

Percentage Mortality of Animals Experimented on.

Experiment.		After the protective inoculations.										After the control infection.				Total Mortality.	
		First Inoculation.				Second Inoculation.				Total.							
		Inoculated.		Uninoculated.		Inoculated.		Uninoculated.				Inoculated.		Uninoculated.			
		Anthrax.	Other Dis.	Anthrax.	Other Dis.	Anthrax.	Other Dis.	Anthrax.	Other Dis.	Inoculated.	Uninoculated.	Anthrax.	Other Dis.	Anthrax.	Other Dis.	Inoculated.	Uninoculated.
Sheep.	Budapest ...	—	3·33	—	—	3·45 (?)	—	—	—	6·78	—	—	8·0	88·0	4·0	14·78	92·0
	Kapuvár (*a*)	—	—	—	—	10·0	2·0	—	—	12·0	—	2·27 [1]	—	96·0 (?)	—	14·27	96·0
	Kapuvár (*b*)	1·12	—	0·45	—	3·79 [2]	—	—	—	4·87 [3]	0·45	—	—	—	—	—	—
	Mean... ...	—	—	—	—	—	—	—	—	6·05	0·33	4·35		94·7		14·53	94·0
Cattle.	Budapest ...	—	—	—	—	—	—	—	—	—	—	—	—	—[4]	—	—	—
	Kapuvár (*c*)	—	—	—	—	—[5]	—	—	—	—[6]	—	—[7]	—	16·7 [8]	—	—	16·7
	Mean... ...	—	—	—	—	—	—	—	—	—	—	—	—	9·1	—	—	9·1

Rate of Morbidity—[1] 6·8 per cent. [2] 8·33 per cent. [3] 9·4 per cent. [4] Calves = 100 per cent.; oxen = 40 per cent. [5 6 7] 7·1 per cent. [8] 66·7 per cent.

health and wealth—are in the highest degree interested. This fact must excuse my minuteness.

Pasteur places the immediate results of the control infection in the foreground, and, following his example, we find that in Budapest and in Kapuvár, after the control infection, out of 69 inoculated sheep a single one (1·45 per cent.) died, while out of 75 uninoculated animals 70 (93·3 per cent.) died of anthrax. The difference is so striking that it seems completely to exclude every doubt regarding the immediate practicability of general protective inoculations, and one runs a certain risk of being suspected of malevolence if one raises objections to these results. And yet there is much more to be learned from our experiments, if we consider the whole course and do not fix our attention solely upon the final results.

First of all, some of the animals died, even after the first protective inoculation, with symptoms of anthrax. Although it is doubtful whether the one death at Budapest was due to anthrax, and whether in the first three cases at Kapuvár the animals were not already affected with anthrax before the protective inoculation, it is nevertheless certain that fifteen animals at Kapuvár actually died of anthrax, which could only be attributed to the second inoculation. It is possible that the inoculative material here used was too virulent for the animals which had only been previously inoculated with the weakest material to withstand.

The possibility is also not excluded that in handling the inoculative material, or during the inoculation, impurities had been introduced, and that septic infection was thus added to the anthrax. But all this *cannot* be taken as an excuse, for we must not overlook the fact that we have here to do with *pattern experiments,* which were conducted with the greatest care in every particular, and to a certain extent for a theoretical demonstration, and we must not forget that every method, every theoretically defined procedure, and every appliance loses much of its purity and precision in its general application and everyday practice. *It is therefore still to be feared that in the practice of inoculation both infection with anthrax and septic infection may easily, and therefore frequently, occur.*

We cannot overlook the fact, also, that after the protective

inoculation the deaths from other diseases, or, more correctly, those in which the post-mortem appearances were those of other diseases—catarrh, pneumonia, distoma, strongylus, and pericarditis—and not those of anthrax, occurred exclusively amongst the inoculated animals. It follows from this that the fatal issue of other severe, but latent diseases, is accelerated by a protective inoculation.

From a practical point of view, it is pretty nearly the same whether the loss is caused by anthrax or other diseases, and therefore deaths from them should be added to those from anthrax. If we do this and add together all the deaths which occurred after the protective inoculation and the control infection, we get, as the chief result, that of the uninoculated animals 94 per cent., and of the inoculated 14·5 per cent. died. Even thus a very considerable difference remains, but nevertheless the mortality of the inoculated animals, 14·5 per cent., is by no means small. This mortality rate corresponded so closely in two experiments, 14·78 per cent. and 14·27 per cent., that it almost appears to be a rule, and therefore we must not asume that experiments carried out on a larger scale would yield a more favourable result. It must not be forgotten, too, that we have here to do with average numbers, while in practice we have to deal with single cases, and in such cases the mortality due to the protective inoculation mounted, for anthrax alone, as the preceding experiment showed, from 3·5 per cent. to 10 per cent. of the inoculated animals. When we consider all these facts, the fear seems not unfounded that in practice a still higher rate of mortality would be reached. On the other hand, from a practical point of view, we must set against this mortality, not the experimental mortality of 94 per cent. of the uninoculated animals, but only the rate of mortality which occurs among the cattle in districts affected with anthrax, and which is very considerably less.

It is unquestionable that the mortality, even of the 14·5 per cent., might be accepted since the yearly loss from anthrax in certain districts reaches as much as 60 per cent., if only certain protection were afforded from the natural anthrax contagion. In one of the experiments at Kapuvár, three of the sheep which had been subjected to double protective inoculation sickened

after the control infection with virulent matter, and one of them died. *The protection afforded by inoculation is therefore not a perfectly certain one.* Since these cases stand alone, they do not justify any further conclusions, but in summing up the results they will by no means lend support to the expediency of the general adoption of the method.

As a proof that the inoculation actually affords a protection against the true anthrax contagion, we are referred to the action of the control infection with the virulent matter on uninoculated animals. The course of the disease, the post-mortem appearances, and especially the bacilli which are present, leave no doubt that anthrax poison was used for the control infection experiments. But the observations that the cattle do not all sicken from it, and only exceptionally died from it, and further that, especially in Budapest, the mortality among the sheep extended over a long period, and that the post-mortem examination of these animals showed no well-marked symptoms of anthrax, appeared to indicate that the material which was employed for the control infective experiments was somewhat less virulent than the natural anthrax contagion. How far the protective power of these inoculations avails against the natural spread of anthrax-spores can only be decided after the termination of the experiments marked (*b*) at Kapuvár, where 254 inoculated and 221 uninoculated sheep are kept upon pastures known to be affected with anthrax. In the meantime, however, the epizootic anthrax has everywhere almost entirely ceased with the approach of winter, and only when warm weather comes will it assume such dimensions that its effect on those two groups of animals can be compared. Till then it cannot be regarded as proved that these inoculations protect as powerfully from the natural anthrax contagion as from the material used in the control infective experiments, which was cultivated from spores several years old.

The method, therefore, requires several modifications, in order that the protective inoculations themselves may give rise to no mortality, and absolute proof that it affords a certain protection against the natural anthrax contagion is still lacking.

There are still several doubts about the method from a public health point of view. The doubt that the protective power is

only exerted for a certain length of time is of minor importance, for if we only succeed in removing the other difficulties, the protective inoculations can be so comparatively easily and cheaply carried out, that in case of necessity they could be repeated every year.

Of great importance, however, is the question whether the meat, milk, &c., of inoculated animals can convey anthrax to man; and certainly before the protective inoculation becomes general, the question must be solved as to how long a time must elapse before the flesh and milk of inoculated animals could be allowed to be used as food.

When we consider that the inoculative material contains anthrax microzymes in colossal quantities, although of diminished virulence, and that the microzymes multiply to a gigantic extent in the organism of the inoculated animals, we see that the general employment of protective inoculations would spread these microzymes in inconceivable quantities through the whole country. Deaths will occur at all times, even among the inoculated animals, from other diseases, although fewer from anthrax. The possibility is not excluded that the microzymes which would be liberated from the dead bodies when they became scattered might regain, in some way or another, their original virulence, and that, despite all trouble and cost, they might in this round-about way affect men and other animals. This is all the more to be feared, as the carelessness with which people even now treat the bodies of animals which have died from anthrax, would then be as much as possible increased by the belief in the omnipotence of the protective inoculations.

Everything considered, I entirely concur in the opinion of the committee, that the *immediate* general application of Pasteur's method *in the form demonstrated to us here* would be precipitate, that it should, least of all, be recommended and disseminated under the authority of the State; and that, with regard to the other possible sanitary evils, the performance of protective inoculation by private individuals on their own accounts should be completely forbidden, and only allowed under the condition that such operations should be performed by a Government official acquainted with the subject, and under his superintendence.

The committee is very far indeed from finally rejecting Pasteur's method. It is of opinion that by strict sanitary regulations in regard to animals attacked by anthrax and to their dead bodies, much might be done to prevent the increase of the anthrax poison and the spread of the disease, but it also perceives the general utility of protective inoculations, especially in en- and epi-zootic occurrence of anthrax. With special reference to Pasteur's method, it is of opinion that the results already obtained justify the highest hopes of the possibility of its reaching perfection. On this account the committee has recommended to the Ministry that further experiments be made regarding the preparation of the inoculative material, regarding the most convenient modifications of the method, and the questions connected with protective inoculation. The committee placed themselves at the disposal of the Ministry for carrying on those further experiments, and recommended that a grant should be made for the purpose of defraying the expenses connected with them.

MALARIA.

BY DR. G. DODS, FLORENCE.

In the *Practitioner* for October I have read with great interest the article on Malaria by Professor Tommasi-Crudeli, and I am pleased to find that the opinions I formed on this subject during a lengthened residence in the East are confirmed by this distinguished observer. For a period of eighteen years I resided in the South of China, at Canton and Hong Kong, and was necessarily brought much in contact with cases of malarious fever.

I long since came to the conclusion that the production of malaria is not necessarily connected with the presence of marshes, ponds, rivers, or rank vegetation, but rather with a dry arid soil, more especially when denuded of vegetation. It is not confined to low-lying districts but may occur at a consider-