



ROYAL COUNCIL

AGRICULTURAL RESEARCH COUNCIL,  
FIELD STATION,  
COMPTON,  
Nr. NEWBURY,  
BERKS.

19th November 1949

Dear Professor Fisher,

You will recall the discussions which we had in 1944 when an experiment to test duration of immunity to Brucellosis in cattle after vaccination with S 19 was first contemplated and now, in 1949, we have obtained the animals for the job and the buildings are rapidly being completed for the work. Now comes the final planning of the experiment and I have been asked by the committee to consult you regarding its lay-out, especially the constitution of the control group and the practicability of introducing into the experiment animals from Superity Farm, Compton, which has been maintained free from infection since it was taken over by the Council in 1938.

Enclosed are A.R.C. 11223, and 11224, submitted to the Brucellosis Committee on 23rd September, A.R.C. 11240 which is the draft minute of the discussion which took place, and A.R.C. 11403 which gives on page 1, a summary of the series of experiments at Compton from 1943-49, and on page 2, a note by Dr. A.W. Stableforth prepared since the committee met on 21st September 1949.

The questions which await an answer are:-

- (1) What is the duration of immunity following a single vaccination with S 19 applied to calves when 4 to 9 months old?
- (2) If cattle are vaccinated more than once before they reach breeding age (18 months to 2 years old) is the immunity produced superior and of longer duration than (1) above?

It is desirable to find a method of vaccination which avoids the need for vaccinating lactating cows which are liable to suffer a drop in milk yield if vaccinated



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vaccinated/  
while producing milk. Further, it is hoped that the information obtained from the experiment will determine the method of immunisation suitable for nation-wide use.

At present the method adopted by the Ministry of Agriculture is one of vaccinating calves when 4 to 9 months old, but duration of immunity is not known though it is believed to be effective at the first pregnancy and possibly longer.

Ministry of Agriculture veterinary inspectors visit dairy farms in connection with routine duties at intervals of approximately 6 months, and for that reason I suggested a plan of experiment which allowed for vaccination at the average age of 6 months, 12 months and 18 months, so that it would coincide with routine visits. Since putting forward this plan I have been pondering over some of the difficulties and have discussed the matter further with Mr. Stablesforth. His views, like mine, have changed since the committee meeting, and are given on page 2 of A.R.C. 11403.

The strongest objection I have to the first plan is the absence of a vaccinated control group to prove the efficiency of the vaccine we are testing. Experiment 5, page 1, A.R.C. 11403 illustrates this point. When planned, this experiment was to have two vaccinated groups, one vaccinated subcutaneously with 0.2 ml. of S 19 applied subcutaneously, the other 0.2 ml. of S 19 intradermally. It so happened that when we did the experiment I was able to obtain sufficient cattle to include a group vaccinated, as we had always done previously, with 5.0 ml. subcutaneously. Had this group not been included we might have been tempted to think that 0.2 ml. subcutaneously and 0.2 ml. intradermally were both inferior to 5.0 ml. subcutaneously which, in fact, was not true and was



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opposed to our conclusion after experiment 4. Experiment 5 is the only one in our experience in which 3 19 did not give a good protection, but in this case the animals were vaccinated when they had been pregnant for 2 to 3 months. Previously we applied the vaccine before the animals were mated.

In the experiment now contemplated, it seems to me to be necessary to have vaccinated controls, i.e., animals vaccinated before mating, with 5.0 ml. subcutaneously, because we believe this to give a good protection in the following pregnancy and we can compare the efficiency of other methods with this proven method. We also require non-vaccinated controls and after that we have to use the remaining animals to the best advantage.

I think we can rely on starting with about 450 calves made up of 420, purchased in Scotland and reared with precautions to avoid infection with Brucella abortus, and 30 born in approximately the same period in the Brucella free herds at Compton. If non-vaccinated controls have to be provided from the 450 Scottish calves it will reduce the numbers in vaccinated groups and it would be a great help if we could use Brucella free animals from Superity Farm as controls. The main difference between these animals and vaccinated animals would be one of age at the time of testing. It could be, however, so arranged that they were older than the vaccinated groups at the time of applying the test infection so that if there is any increase in resistance to infection with advancing age, then the controls would be less susceptible to infection than vaccinated.

I think it desirable to have groups of not less than 20 because there are many factors liable to reduce the effective



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effective/  
 numbers in the groups as the experiment progresses such as sterility, infertility, accidents at calving, deaths, etc. There are several ways in which the experiment might be planned with the animals available, and that set out by Dr. Stableforth, while attractive, provides only 14 animals in each group which is a smaller number than I would like. An alternative which, unfortunately, would exclude the three dose method and would include as controls 30 Scottish calves and 90 Superity cows, is as follows:-

Dose of Vaccine	Time of Vaccination	Number to be tested at each pregnancy						Spares	Total
		1st	2nd	3rd	4th	5th	6th		
5 ml. S.C.	6 months old	20	20	20	20	20	20	20	140
	18 " "	20	20	20	20	20	20	20	140
	6 & 18 " "	20	20	20	20	20	20	20	140
Controls	Scottish calves	10	10	10					30
	Superity cows	10	10	10	20	20	20		90
									540

The Brucellosis Committee meets at Compton on Friday, November 25th, and it would be most helpful to the Committee if you could find it possible to attend. I would be happy if you would stay the night with me on Thursday, 24th November, and as I have to be in London that day, I could

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meet you at Dean's Yard at a time to suit your convenience, and we could travel to Compton together. If this is not suitable for you, could you possibly let me have your comments by Friday, 25th November, or failing that, could I visit you at Cambridge on December 9th, 12th or 13th to discuss the plan.

Yours sincerely,

*W. S. Gordon.*

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