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COMPTON 57
COMPTON (G.W.R.) STATION



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

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at Edinburgh 2/12/49.

Dear Professor Fisher,

The Brucellosis Committee met at Compton on Friday, 25th November and on hearing your comments it was agreed that I should consult you further about the plan of the experiment and later inform them of the result.

As to the second paragraph of your letter, I agree there would be serious objection in principle to the use of animals as controls of a different origin or different age from those used for vaccination. In this case however, the factor to be compared is one of resistance or susceptibility to Brucellosis infection and we know that animals which have remained negative to the agglutination test, and which have been reared in the Brucellosis free environment at Superity Farm throughout their lives, remain susceptible to infection. We have available 420 calves born in Scotland during June, July and August reared on milk from cows free from Brucellosis infection. To these may be added 30 calves born at Compton during the same period and reared on the same type of milk as those from Scotland, in fact, reared on colostrum from the same cows. I submit therefore that these can justifiably be included amongst the animals available for the experiment making a total of 450. Stratified samples of the whole of this material would be used to form the groups of vaccinated and control animals. The experiment might be limited to these animals but if we wish to increase the numbers in the vaccinated groups it would be possible to draw 20 cows each year over a period of 6 years to act as controls, from the Brucellosis susceptible herd at Superity Farm, Compton. These cows could not be included in the vaccinated groups because they are at present either too old to survive the period of experimentation or else they are not yet born. They would however be susceptible material to prove the infectivity of the infective dose used to test vaccinated animals and their susceptibility could be proved



ROYAL SOCIETY

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- 2 -

if necessary now by selecting some pregnant cows from this herd and subjecting them to the test infection.

The criterion of measurement in all our work has been either the development of infection or its complete absence when the test infection is applied. It may be argued that Superity cows are naturally either more susceptible or less susceptible than the Scottish calves but this could be parried by including a few Scottish calves in each group of controls to show that, like Superity cows, they all develop infection when the test dose is applied.

As to the third and remaining paragraphs of your letter, present evidence, imperfect though it be, suggests that we may expect a useful degree of ~~production~~ protection, following one vaccination, up to the second pregnancy and probably longer after more than one vaccination.

It is not known what may happen after that but it is probable that immunity will begin to decline at the third pregnancy in animals vaccinated once only. Once the level falls below 80% protection it would not be regarded as good enough for veterinary practise and if it becomes clear during the course of the experiment that immunity in any group of vaccinated animals has fallen below this level then revaccination could be adopted to raise the level of immunity in subsequent pregnancies.

If I am interpreting your suggestion correctly it appears that you would prefer to use small numbers of animals for test in say the first two pregnancies when immunity is expected to be good, increasing the number used in the critical period when there are indications of a fall in immunity and later using smaller numbers again when immunity is likely to



ROYAL VACCINATION

- 3 -

have fallen below the 80% level. That method appeals to me but I require your advice as to the numbers to be placed in the groups.

The committee agreed that it was desirable to have the following groups if possible:-

- (i) One vaccination at average age 6 months.
- (ii) One vaccination at average age 18 months.
- (iii) Two vaccinations at average age 6 months and 12 months.
- (iv) Three vaccinations at average age 6 months, 12 months and 18 months.

If there are not sufficient animals to do this satisfactorily group (iv) might be excluded but if we drop this group and two vaccinations fail to protect to the 5th or 6th pregnancy we will never know if three vaccinations might have done so.

With the material available, therefore, I would tentatively suggest the following basic plan:-

| | |
|-------------|--------------|
| Group (i) | 100 animals. |
| Group (ii) | 100 animals. |
| Group (iii) | 100 animals. |
| Group (iv) | 100 animals. |

| | |
|-----------|----------------------------------|
| Controls. | 50 Scottish and Superity calves. |
| | 50 Superity cows. |

If you can accept Superity cows as controls it permits 50 or more animals to be included in the vaccinated groups. At the first pregnancy, and thereafter until there is an indication of immunity waning, groups of 10 or possibly less could be used rising to 20 or even 40 per group at the critical period. After

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- 4 -

a fall in immunity has been established conclusively we could revaccinate the remaining animals in the group and continue to test them at subsequent pregnancies.

I hope this provides the additional information you require and I will be happy to add more where necessary and to meet you when suitable. I have to visit Cambridge soon and could see you then if that would save your time.

Yours sincerely,

W. S. Gordon.

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