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EUROPEAN COMMISSION FOR THE CONTROL OF FOOT AND MOUTH DISEASE

Research Members of the Standing Technical Committee

MINUTES

of the Meeting held in Brescia on 10 - 11 March 1960

The research members of the Standing Technical Committee met in Brescia on 10-11 March 1960. In addition to Drs. Ubertini, Galloway and Michelsen, there were present Drs. Willems and Moosbrugger from the OIE Commission on Foot-and-Mouth Disease, Drs. Kimron, Israel, van Bekkum, Holland and Nardelli, Brescia. Dr. Fogedby, Secretary of the Committee and Sir Thomas Dalling, who was appointed Chairman, were also present.

This meeting was arranged in Brescia at the request of the research members and on the invitation of Dr. Ubertini, in order that he could demonstrate large scale cultivation of foot-and-mouth disease virus on kidney monolayer cells which he described at the meeting of the group in Lindholm in 1959.

A considerable part of the meeting was occupied with demonstrations arranged by Dr. Ubertini and discussions on technical aspects of the subject while the demonstrations were in progress. Demonstrations on the concentration of the virus were also given and here again, discussions took place.

Following the demonstrations, discussions took place on a number of subjects concerning foot-and-mouth disease vaccines: the following are short summaries. A full report will be circulated to the participants in due course.

There is a strong impression that the vaccines in use in European countries have a lower immunizing value than those available when vaccination against the disease was first introduced. The evidence for this seems to be a longer period before vaccinated cattle develop a serviceable immunity and a shorter duration of this immunity. No definite reasons have been propounded for this and opinions differ on probable causes. The reasons may be associated with the strains of virus used in vaccine production: the same strains have been used for many years in many institutes and are preserved by deep-freezing. The effect of vaccination, especially on extensive scales, may have some influence and better results may follow the use of current field strains of the virus. The tendency has been to reduce the amount of the antigen and the volume of the dose but it seems that even with large amounts similar reduction in immunizing value has been observed. Research work on the whole subject is needed.

Inactivated vaccine prepared from virus cultivated on kidney monolayer cells has been the subject of tests for immunizing value. At Brescia, satisfactory results have been obtained in many guinea-pigexperiments. Vaccine prepared in Brescia from strain A virus is being tested in cattle at Lindholm. A preliminary test with the vaccine sent to Lindholm was carried out in six cattle about one year old at Brescia. When challenged about a month after vaccination, generalisation occurred in the control and in five of the six

vaccinated animals only some localised lesions develop in the mouth. At Lindholm, three cattle were used to show the innocuity of the vaccine. No lesions developed following injection of the vaccine into the tongue. Challenge tests resulted in localised tongue lesions only in two of the three animals. Thirtysix cattle, 2-6 years old, have now been vaccinated at Lindholm and groups will be challenged at different periods. Serological tests are also being made.

It was reported that a considerable number of cattle had been treated with inactivated vaccine prepared from Strain Asia I similarly cultivated. The field results were not entirely satisfactory. Breaks in immunity have apparently occurred.

Arising out of the discussions on the production of vaccine and the methods of challenge, consideration was given to a number of technical points.

There is an "optimum" amount of natural virus in a dose of inactivated vaccine: larger amounts do not appear to give rise to a better or a larger immunity. It was stated that this optimum amount is 15-20 centigrams per dose..

Much consideration has always been given to the infective titre of the virus used in the preparation of vaccine. It does not always follow, however, that the use of virus of high titer produces high value vaccine. In natural virus, the stage of the infection decides the amount of the virus in the vesicular epithelium and old lesions may contain little virus but may have high immunizing value.

In challenging vaccinated animals, different methods are used. Some workers inject virus introdermally into the tongue, other combine these injections with subcutaneous or intramuscular injections: contact with actively infected cattle is also used. The results of some experiments were given. A group of vaccinated animals was tested, some by tongue injections and some by contact: 30% of the tongue-treated cattle developed lesions while none of those exposed to contact showed any lesions. In a similar experiment 50% of the tongue-treated animals and none of those exposed to contact showed lesions. A further example concerned a group of animals which, three years previously, had recovered from the disease. They were challenged in three groups with the following results:- tongue-injected - severe localised lesions but no generalisation; intramuscular injected - no lesions; contact - no lesions.

Differences of opinion were expressed on the tests which should be used for both innocuity and potency of vaccine. Some felt that the simultaneous injection of virus into the tongue and subcutaneously or intramuscularly might tend to interfere with the development of lesions because of the early production of specific antibodies.

It was agreed that in the preparation of vaccine, more satisfactory results followed the use of filtered virus especially with natural virus, following which a more homogeneous product is obtained. Loss of virus during filtration may be prevented by saturating the filter with serum before filtration of the virus is carried out.

Deaths in mice which receive intraperitoneal injections of vaccine or virus, from apparent non-specific causes, were reported. Discussions, centred around damage which might be caused by the aluminium hydroxide in the vaccine and the PH of the vaccine. Some of the aluminium hydroxide in use contains amounts of ammonia which may have an irritant effect.

The time after preparation when vaccines should be tested for innocuity and potency was referred to. There were differences of opinions. Some felt that a period of time should elapse in order that "ripening" of the virus should occur. Others felt that vaccines should be tested immediately after preparation following which it could be concluded that, after "ripening" they would be of higher value than the earlier tests indicated.

Modified or attenuated virus

A short description of the work on these vaccines and their use in the field in Israel was given to the meeting. Their use in the field followed the observation that during the present epizootic caused by virus Asia I, the infection appeared in a group of 23 cattle, vaccinated some four months previously and 40 non-vaccinated animals. In only three of the 23 vaccinated animals were some slight lesions seen while in all 40 non-vaccinated cattle, extensive lesions occurred. Vaccination in the field with the attenuated Asia I vaccine has been carried out on a large scale in the following order - (1) infected settlements in infected areas; (2) non-infected settlements in infected areas; (3) settlements in non-infected areas. A total of some 87,000 cattle in grade herds has been vaccinated between November 1959 and February 1960. (A settlement has from 20 to 200 herds; a herd has an average of 20 cattle; herds are separated from each other by about 30 meters.)

In infected settlements the disease continued to spread for about 8 days and then there was no further spread. In non-infected settlements, no infection has occurred. No spread from vaccinated animals was observed.

Following vaccination, no reactions have been seen in young animals. In adult cattle some mild lesions have been noted, mainly on the udder and teats, in about ½% from the 3rd to the 7th day following vaccination. All the vaccinated animals continued to feed well.

The Asia I strain used was isolated in the 1958 outbreak. Attenuation was carried out first in chick embryos and the vaccine for field use is prepared in kidney cell cultures or in mice.

This vaccine is stable in that no spread of infection has been noted from vaccinated to contact animals under experimental or field conditions.

The lesions which occurred on the teats of somevaccinated animals were examined. No virus was transmitted to cattle or mice nor could it be cultivated in tissue culture. The virus was, however, cultivated in the chick embryo and at this stage could infect cattle and mice and developed in tissue culture. The lesions produced are identical with those following vaccination and no spread takes place.

The virus is not filtered. Two herds are being subjected to serological tests.

A short account was also given of the work on attenuated viruses at the Pirbright Institute and of the experiments with Asia I virus in Thailand and of SAT II and SAT III strains in South and East Africa. The main objects of these experiments is to determine the types of reactions which may follow the injection of the vaccine into different types of cattle, as found in the regions and in buffaloes in Thailand as well as their immunizing values under the conditions of these various parts of the world.

A short discussion took place on the use of different adjuvants in the preparation of vaccines. While it is mostly considered that the value of aluminium hydroxide is to adsorb the virus, to cause some local reaction and to release virus slowly with consequent continued stimulation of the antibody-producing mechanism, it was felt that it may also have some other functions, such as the stimulation of production of non-specific immunity.

The meeting was informed of some research work on the use of some other types of adjuvants in vaccine for use in pigs. There are some indications that such vaccines are of value for the immunization of pigs, but more work, now in progress is necessary.