The O.I.E.
Foot and Mouth Disease Commission

Final Report
of the XVIth Conference
Paris, 14-17 September 1982

The XVIth Conference of the O.I.E. Foot and Mouth Disease Commission was inaugurated by Dr. J. Leunen, President of the Commission, at 10 a.m. on 14 September 1982, following the welcoming of participants by Dr. L. Blajan, Director General of the O.I.E., on behalf of the International Committee.

In his opening address, Dr. Leunen said that the Commission had been very fortunate to have the help, advice and support of Dr. J.B. Brooksby for the organisation of this Conference. He thanked him heartily on behalf of the O.I.E. Foot and Mouth Disease Commission, and said that the Commission deeply regretted that Dr. Brooksby had decided to step down from the presidency of the Commission that he had guided with such extraordinary competence and efficiency for fourteen years.

The first working session commenced immediately after Dr. Leunen's address.

Item 1: VACCINES

A. IMPROVEMENT IN ANTIGENIC VALUE

This session was chaired by Dr. R. Casas (P.A.H.O./W.H.O., Brazil) and the following points were emphasised:

In order to improve the antigenic value of vaccine preparations, Colombia indicated that all available knowledge is being applied to make best use of the 140 S particles. Workers in this country have demonstrated that to obtain one 50% bovine protection dose (BPD$_{50}$), 5.5 µg of virus per dose are needed (for O$_{1}$).

Argentina informed the meeting of a new procedure for virus inactivation by activating a virion-associated endonuclease. It was also noted that vaccines prepared by the private industry contain an average of about 7 BPD$_{50}$.
Kenya presented an analysis of the laboratory investigations on foot and mouth disease virus (FMDV) typing, subtyping, production and potency testing in cattle of vaccines produced from African virus types O, A, C, SAT 1 and SAT 2 since 1963. Vaccines from this laboratory are used in control programmes in countries of Eastern Africa and occasionally other parts of Africa.

The U.S.S.R. recorded the large-scale preparation of FMD vaccines using the Frenkel method. Very efficient vaccine preparations for swine using rabbit-adapted virus in oil adjuvant were also reported.

Great Britain presented the advantages of a semi-automated method for sucrose density gradient analyses for the quantitative assessment of antigens, and also a proteolytic enzyme assay which will be of value in predicting the integrity of the immunising protein VP 1.

Thailand described the production of FMD vaccine in BHK₂₁ rolling and suspension cultures.

Dr. Casas indicated that FMD-infected countries in South America are having more success in controlling the disease due to the availability of higher quality vaccines.

**B. ADJUVANTS**

This session was moderated by Dr. K. Dalsgaard (Denmark) and the following points were emphasised:

Several adjuvants can be used to increase the immunogenic capacity of inactivated viruses.

Crude or purified saponin with aluminium hydroxide is most regularly used. Its adjuvant capacity is evident; however, the antibody response in young cattle can be influenced by genetic factors.

With oil adjuvants, particularly when used in extensive cattle breeding in endemic areas in certain South American countries, the morbidity of foot and mouth disease appears lower than that observed in animals vaccinated with other classical vaccines. Some oil formulations are innocuous and can be recommended to immunise different categories of swine and they may also have some advantages in young cattle.

A new synthetic amino-lipid adjuvant, CP 20961, has been used in guinea-pigs with interesting results.

However, it must be emphasised that the antigen quality and quantity are still a priority.

**Item 2 : DIAGNOSTIC TECHNIQUES**

**A. VIRUS**

This session was moderated by Dr. J. Callis (U.S.A.) and the major issues were as follows:
The specificity of the reaction between the virus and its antibody has a vital role in diagnosis and identification of viruses causing outbreaks. The introduction of monoclonal antibody techniques together with the more sensitive methods such as RIA and ELISA means that highly specific and sensitive methods are available for the identification of viruses.

In the last two decades there has been an enormous increase in our knowledge of virus nucleic acids and proteins. The methods which are now available for the definitive analysis of these components have enabled us to examine viruses with considerable precision.

The four papers which were presented illustrated the value of some of these physico-chemical methods in the identification of viruses. In the papers by McCahon et al. and Lombard et al. examples were given of the application of isoelectric focusing of virus-specified proteins for the identification of type O viruses which have caused recent outbreaks in Europe, North Africa and the Middle East.

In this method, the proteins are separated according to their electric charge. Consequently any change in the charge of a protein resulting from the substitution of an amino acid by one of a different charge results in a detectable difference in the behaviour of the protein. The methods thus allow the ready detection of changes which occur in viruses during and between outbreaks.

In the papers by Brown and Underwood and La Torre et al., several examples were given of the value of ribonuclease T1 fingerprinting of the virus RNA to differentiate virus subtypes causing outbreaks in Europe and South America. In this method, the fragments of the virus RNA produced by hydrolysing with ribonuclease T1 are separated by electrophoresis in gels by making use of test differences in electric charge and size.

Each virus gives its own fingerprint. Viruses of different serotypes and subtypes of individual serotypes are clearly distinguishable. Even isolates belonging to the same subtype which could not be distinguished by the most common serological methods could be differentiated. The value of the technique lies in its precision in allowing very closely related strains to be distinguished.

All four papers showed that the addition of physico-chemical methods for analysing the virus RNA and proteins to the traditional methods of serology provides epidemiologists with powerful new tools for identifying viruses.

B. ANTIBODIES

This session was moderated by Dr. R.C. Knudsen (U.S.A.). The following points were emphasised:

The evaluation of the level of immunity in vaccinated animals continues to be of considerable importance. Virus neutralisation, complement fixation
and newer methods such as ELISA are used. Preliminary studies suggest that for large-scale routine use a partially purified FMDV antigen would be sufficient for ELISA. The technological ease of ELISA, its sensitivity and high correlation with VN assays suggest greater use of this assay in future studies. Mathematical evaluation of FMDV antibody levels of large and heterogeneous cattle populations appear to have great use in predicting the level of immunity. Effective immunisation of animals is directly dependent on the amount of 140 S antigen present in the vaccine, and the requisite amount of 140 S in vaccine is different for different virus strains.

Preliminary characterisation of murine monoclonal antibodies produced by hybridisation techniques demonstrated a number of antibodies that could neutralise the FMDV. Future studies with these antibodies in VN and virion VP 1 and 12 S particle binding assays should greatly aid in defining homologous and heterologous virus antigenic sites.

Item 3 : GENETIC ENGINEERING

A. PROSPECTS FOR THE USE OF VACCINES PREPARED BY GENETIC ENGINEERING TECHNIQUES

This subject was extremely well and clearly presented by the keynote speaker Sir William M. Henderson. He emphasised the following in particular:

« It must be recognised that the results obtained so far in recombinant DNA work and in nucleotide synthesis are preliminary and incomplete. It is premature to talk about a new vaccine being available. A new vaccine is unlikely to be in commercial production for a period of years. Experiments and field trials are bound to occupy a lot of attention during at least the next two, three or more years. Every change engineered by the molecular biologist in seeking to build a better antigen and every change in formulation in seeking to improve vaccine potency has to be checked in animals. These experiments take time. Success must be measured by the production of a vaccine at least as good as the present ones, although the complete safety of the new procedures is a considerable advantage. Extension of the duration of immunity would be a most desirable achievement but the major problem is caused by the characteristics of the mode of infection of the virus.

The recent scientific advances are most stimulating and praiseworthy. Those who have achieved them deserve to be congratulated. The brilliance of the work is such that there is every reason for optimism that the problem of successful development will be overcome even taking into account the need with this disease to have a stock of antigen of diverse type and variation. It must, however, never be forgotten that the best of vaccines to be effective must be put into the right animals, in the right place at the right time. »

In emphasis of the correct use of vaccines, attention is drawn to four cardinal points for the control and eradication of FMD:
1. A well planned, well organised and well financed field campaign based on the scale and the extent of the movement of animals and the epidemiology of the disease, all in the local situation.

2. A well trained, well equipped staff, adequate in disciplines and numbers supported by an efficient laboratory service.

3. If vaccination is part of the policy, the vaccines used must be of the highest quality.

4. Good international collaboration with programmes running in parallel within epidemiological areas.

B. ROUND TABLE:
GENETIC ENGINEERING AND FOOT AND MOUTH DISEASE

This round table was remarkably well organised and chaired by Dr. K. Strohmaier (Federal Republic of Germany), with the participation of the following specialists in this field: J. Asso (France), H. Aviv (Israel), F. Brown (Great Britain), J. Callis (U.S.A.), P.E. Highfield (Great Britain), H. Küpper (Switzerland), E. Pfaff (Federal Republic of Germany) and M. Rivière (France).

Sir William Henderson reviewed the prospects for the use of vaccines prepared by genetic techniques. He also discussed the newest development of vaccines based on chemically synthesised peptides.

The F.A.O. representative, while welcoming these new discoveries, proposed extreme caution in giving publicity to these methods, until their application under field conditions has been unequivocally demonstrated.

1. The conclusions of the discussion on bio-synthesised peptides were:

   (a) Clones of bacteria expressing the immunising protein VP 1 are available in several institutes.

   (b) The European types O, A and C with some subtypes including some of the South American strains and an Asia type are cloned.

   (c) Different promoters are used with equally good results. The expression of the fusion protein is about 0.5-1 gram per litre of bacterial suspension.

   (d) Normally an amino acid sequence from the vector is added beneath the immunising protein. No negative influence of the added sequence has been observed so far.

   (e) About 90% purification of the fusion protein is possible.

   (f) At least two injections of the expressed protein with adjuvants are necessary to elicit a sufficient titre of neutralising antibodies and to protect against challenge. The formulation and the method of application of the vaccine to animals should be investigated.
(g) In addition to the immunisation of cattle, swine and goats, several laboratory animal species have also been immunised.

(h) The type specificity of a fusion protein is expected to be about the same as in a conventional vaccine. For polyvalent vaccines, VP 1 corresponding to the different types will have to be used.

(i) In studies thus far reported, the bio-synthesised protein has been used with oil adjuvants.

(j) With such preparations immunity has been demonstrated for several months.

(k) In studies thus far reported, 200-500 µg of fusion protein has been combined with oil adjuvant to make a vaccine.

(l) Patents are pending for all of the protein producing plasmids.

(m) Vaccines from bio-synthesised peptides have not been commercialised but are expected to cost approximately the same as conventional vaccines.

2. Organically-synthesised peptides were also discussed:

(a) Two groups confirmed the location of the immunising portion of the protein VP 1 of FMDV between amino acids 141-160. Antigenic activity was also observed on the C terminus positions 200-213.

(b) Vaccines formulated with organically-synthesised peptides have been shown to immunise rabbits and guinea-pigs and to protect guinea-pigs against challenge with virus. Such preparations also produce significant levels of neutralising antibody in cattle.

(c) The peptides were linked to a potent carrier, haemocyanin which would not be practical for large-scale application. Other carriers are being tested.

(d) The comparative costs of bio- and organically-synthesised peptides were discussed but no conclusion could be reached since neither production process has been commercialised.

(e) The stability of peptide vaccines is expected to be superior to conventional whole virus vaccines.

Briefly, peptides have been produced in genetically-engineered bacteria and by organic synthesis. Experimental vaccines with peptides produced by both processes have been shown to induce an immune response in a limited number of animals. Neither process has been commercialised and large-scale production is not expected for several years. However, research is underway at several locations.

Public apprehension relative to the possible hazards of genetic engineering has diminished. However, precautions must continue to be taken when viral genetic material is moved from one location to another.
Item 4: EPIDEMIOLOGY AND VACCINATION CAMPAIGNS

This session chaired by Dr. R.F. Sellers (Great Britain) was divided into four parts corresponding to each geographical region of the O.I.E.

A. AMERICAS

The first part of this session was moderated by Dr. E.J. Gimeno (Argentina) and dealt with the situation in the Americas.

The continued control of FMD in South America (and later its future eradication) is not easy, particularly considering the extensive livestock industry involved.

However, it is not an impossible task if the countries follow a regular working programme which is well coordinated, using the best techniques and systems. To accomplish this goal, it was recommended that the following aspects be considered:

1. Improve the epidemiological control system by developing sentinel surveillance mechanisms in different areas to detect changes in disease incidence for each area, virus modifications and ecological relationships that may influence the spread of FMD infection in and within areas.

2. Improve the quality of vaccines by increasing the level of control standards in a progressive but permanent manner.

3. Promote more active participation of the livestock industry by various educational means. Their participation is essential for the success of the animal disease control campaigns. The implementation of these recommendations will enable progress in the control of FMD and the eradication of the disease from South America in the not too distant future.

B. EUROPE

The second part of this session was moderated by Dr. R.F. Sellers (Great Britain) and dealt with the situation in Europe.

During the past four years Europe has maintained its comparative freedom from FMD as a result of the control and vaccination campaigns from the 1950's onwards.

In the meeting, the outbreaks of FMD in Greece and the measures taken were described. An account was given of the control and vaccination procedures in France. The United Kingdom delegate described the epidemiology of the outbreak in the Isle of Wight and the eradication of the disease. The spread of disease and the measures taken for eradication were enumerated for the 1982 outbreak in Denmark.

The relationships of the recent type O strains in Europe and the Middle East were described.
In conclusion, it was recommended that the practice of prompt reporting of FMD, rapid identification of the type and subtype responsible and the provision of information to other countries be continued. The measures used in eradication should always be readily available in case of emergency.

It was also recommended that, in view of the rare occurrence of FMD, instruction in recognition of signs should be given to young veterinarians.

The usefulness of an epidemiological team in investigation of outbreaks was noted.

C. ASIA

The third part of this session was moderated by Dato Dr. Osman Bin Din (Malaysia) who presented a summary of his paper which dealt with the situation in Asia.

Papers submitted by Thailand, Malaysia and the Socialist Republic of Vietnam were discussed.

While there has been a general increase in the incidence of FMD in Thailand during the last seven years, a decline was observed in 1981. The outbreaks in Central and Northern Thailand were the result of FMD types O, A and Asia 1.

The occurrence of the disease in Southern Thailand and Malaysia, however, has been rather sporadic and inter-related from the epizootiological point of view. The outbreaks in 1973 were due to FMD type A22 and those encountered in 1978/79 and 1980/81 were the result of type O1 infection. Both Southern Thailand and Malaysia have been free of the disease since mid-1981.

In Vietnam, there has been no disease outbreak north of the 17th parallel. However, in the Southern region 16 out of 21 provinces were affected.

Although variations have been observed between O1 types isolated particularly in 1980 from Thailand and Malaysia, it is felt that they are not significantly different. Nevertheless, field isolates are regularly screened against vaccine strains.

Those showing significant variations in relationship will be studied thoroughly including composite relationship and cross-protection tests.

Cattle and buffaloes were consistently affected in all outbreaks while infection in pigs was most serious in the 1980 outbreaks experienced in Southern Thailand and Malaysia. While goats and sheep were in close proximity to large ruminants, clinical signs were only observed once in goats in Malaysia. This was proved by virus isolation.

The outbreaks in 1973 and 1978 in Malaysia have been brought under control through the « stamping out » method and more recently through
mass vaccination coupled with strict movement control in Thailand and Malaysia. Bilateral cooperation between Japan and Thailand as well as between Thailand and Malaysia has played a significant role in the control of the disease in these areas.

Control in Vietnam is ensured through regulatory measures since 1975 and through the use of polyvalent vaccine from the U.S.S.R. since 1978. Since 1979, only six provinces have been affected.

Plans for the eradication of the disease in Thailand include improvements in quality and production capacity of FMD vaccine as well as mass vaccination of susceptible animals. In Thailand plans consist in the vaccination of cattle and buffaloes three times a year in disease-free zones and twice in other parts of the country. Malaysia will continue to enforce strategic vaccination with priority to cattle and buffaloes along routes of movement, in areas surrounding abattoirs and in intensive livestock rearing areas.

Efforts towards education of farmers, improvements in quarantine facilities and check points will be intensified to enhance vaccination programmes in both countries.

The need for personnel training in FMD control as well as the establishment of a FMD laboratory were emphasised by the Delegate from Vietnam.

In conclusion, the Conference considered the need for vaccination and systematic control of livestock in FMD enzootic areas, better disease surveillance and the improvement of existing control measures and other services.

It was recommended that:

1. More effective programmes should be implemented in order to achieve the desired results.
2. Training programmes should be organised for personnel of all categories involved in FMD control.
3. Support should be granted for the establishment of an FMD laboratory in Vietnam.

D. AFRICA

The fourth and final part of this session was moderated by Dr. M. Mannathoko (Botswana) and dealt with the situation in Africa.

Papers presented by Nigeria, Togo and Botswana described the FMD situation, epidemiology and control programmes in Africa. In West Africa, outbreaks of FMD, mostly types A, SAT 1 and SAT 2 have been closely associated with the movement of livestock along marketing routes from the northern states and countries to the consumer areas in the south.

A lack of diagnostic facilities in the area has prevented studies of the viruses to determine virus strains which could be used to produce vaccines with adequate potency to prevent and control outbreaks in Nigeria. However,
Nigeria is thinking of establishing FMD diagnostic facilities in the near future. Nigeria is also thinking of establishing a trial FMD-free zone through routine vaccinations and movement control.

In Southern Africa the predominant FMD is caused by SAT viruses. The African buffalo is the carrier of the virus in the region. Control programmes in the region are based on regional cooperation through SADCC and SARC-CUS, movement control and vaccination.

The Botswana Vaccine Institute is used by the region for diagnosis, subtyping and production of potent vaccine against FMDV, SAT 1, SAT 2 and SAT 3. The vaccine has been used successfully to eliminate FMD in livestock from Botswana, South Africa and Zimbabwe. The use of potent vaccine and effective movement control in the region has enabled beef exporting countries in the region to export beef to Europe and other areas of the world.

The major factors in FMD control in Africa were considered as follows:

1. Adequate diagnostic facilities to identify and compare serological relationships between various FMD viruses especially with vaccine strains.
2. Good vaccine coverage and the use of potent vaccines maintained at 4°C until vaccination.
3. Control of livestock movement through movement permits, natural and artificial barriers and quarantine systems.
4. Surveillance to enable early discovery of outbreaks.

Finally, Dr. Sellers, Chairman, and Dr. Leunen, President of the FMD Commission, made the following comments:

Significant gaps still existed in the reporting systems of various areas. It was recommended that together with an improvement in prompt reporting in all areas, FMDV strains from field outbreaks should be sent to the World Reference Laboratory in Pirbright, England on a regular basis so that the laboratory could maintain a library of strains available to all.

**Item 5: REPORTING OF FOOT AND MOUTH DISEASE**

The following points of the paper presented by Dr. L.V. Meléndez, Head of the Technical Department of the O.I.E., were emphasised:

It will never be possible to have prompt and accurate animal disease reporting without the organisation and establishment of adequate structures for epidemiological surveillance by the Animal Health Services and/or Veterinary Services of the Member Countries.

Through adequate international reporting, countries without particular animal diseases may be aware of the disease situation in infected countries, the movement of their animal products, the level of efficiency of their disease
surveillance structures, their capacity for prompt diagnosis and capabilities to control diseases in emergency situations.

It is with this knowledge that it is possible to best coordinate the necessary intergovernmental cooperation to control animal diseases that might easily spread beyond national borders.

Developed countries must do their utmost to provide the means for less developed countries to establish adequate reporting systems for animal diseases irrespective of their epizootic or enzootic character.

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The Final Report was presented to and adopted by the assembly on Friday, 17 September 1982.

In closing the meeting, Dr. Leunen, President of the Commission, expressed his satisfaction with the active and interesting discussions between the 110 participants from 36 different countries and three International Organisations. After highlighting the importance of this Conference for veterinary science, Dr. Leunen thanked all participants for their valuable contribution to the activities of the O.I.E.