Selection of vaccine strains of foot and mouth disease virus for use in Southern Africa *

D. FARGEAUD **

Summary: In the countries of Southern Africa, types SAT 1, SAT 2 and SAT 3 (SAT: Southern African Territories) of foot and mouth disease (FMD) virus are the most widely represented, especially the SAT 2 virus. Since 1982, examinations have been conducted on 139 isolates of these virus types. Other viruses, types O and A, have been detected in the north of this area.

The typing and sub-typing of viruses with the complement fixation (CF) test can be improved by using panels of monoclonal antibodies (MAbs), which provide an accurate antigenic profile of a new strain. A total of 33 SAT 2 strains have been investigated using MAbs, and the results enable the classification of viruses into groups presenting the same profile.

The author presents comparisons of isolates and vaccine viruses using conventional methods of serotyping – CF and virus neutralisation (VN) tests – as well as profiling the isolates using MAbs. Both manners of analysis provide information on the relationships between the viruses. The CF and VN tests give details on how animals responded against a particular isolate and how this antibody response would recognise another isolate; from this, the serological relationships can be proposed with respect to how different isolates might induce a humoral immune response. With MAb profiling, details of antigenic relationships between the isolates are obtained, enabling the identification of individual epitopic variations. These analyses can provide the potential to place different isolates into 'antigenic' groups. When compared with vaccine viruses, one can attempt to identify the vaccine virus with the closest profile to the isolate group. Immunological analysis (e.g. using the CF tests employed in this paper) can provide further information on the relationship between a particular vaccine and an antigenic group identified by MAb profiling. Of course, this MAb profiling can provide essential information in a very short time, which is of particular benefit in an emergency situation. Confirmation of the conclusions from the profiling would then be forthcoming through the serological analyses. Such combined analyses offer a more extensive identification of antigenic and immunogenic relationships between FMD virus isolates, as well as between isolates and vaccine viruses.

KEYWORDS: Africa – Antigenic variants – Foot and mouth disease – Monoclonal antibodies – Vaccines.

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** Botswana Vaccine Institute, Broadhurst Industrial Estate, Private Bag 0031, Gaborone, Botswana.
INTRODUCTION

One of the most important functions of a Regional Reference Laboratory for foot and mouth disease (FMD) involves giving advice on vaccines to be used for prophylaxis and control of outbreaks. In order to produce an effective vaccine which is appropriate to the field situation, it is necessary to have a good knowledge of the field strains. The virus strains used in vaccine manufacture must be suitable for the countries in which the vaccines are employed. Many countries rely on imported vaccines for FMD prophylaxis and, very often, they are not in a position to control all the parameters on which the success of vaccination depends. The degree of protection in the vaccinated population depends on the quality of the vaccine used, the storage conditions, the skills of the vaccination staff, and also the antigenic homology between vaccine strains and field strains. Two of these parameters, namely the selection of vaccine strains and the formulation of the vaccine, are the concern of the Reference Laboratory.

The updating of vaccine composition with respect to the characteristics of the field strains requires the constant co-operation of Veterinary Services in collecting and despatching fields isolates to the Regional Reference Laboratory.

In the Southern African countries, types SAT 1, SAT 2 and SAT 3 (SAT: Southern African Territories) viruses are most widely represented, especially the SAT 2 virus. Despite an effective control policy to combat the disease, the risk of cross-transmission of FMD between livestock and wildlife, particularly buffalo, still remains. Thus any new FMD outbreak in cattle must be investigated immediately.

Antigenic variability of the FMD virus is so great that a vaccine prepared from one isolate will not necessarily always afford protection against infection with other isolates from the same serotype. In a first stage, identification of virus type and preliminary sub-typing by serological tests may give a rapid indication of vaccines to be chosen, especially if the geographical origin of the FMD outbreak is known or suspected. The classic serological studies compare viruses using homologous and heterologous sera. These studies can be improved by the use of monoclonal antibodies (MAbs) against neutralising epitopes, which provides a powerful method for epidemiological investigations. The antigenic profiling of the field virus with a panel of MAbs should provide an accurate tool to determine the relationship with previously-isolated viruses.

Viruses used for vaccine production are selected on the basis of sub-type classification and immunobiological characteristics. The latter are determined by cross-immunity tests in cattle using existing vaccines against the most important new FMD virus field strains. The field virus is compared with the reference vaccine strain, using sera from animals which have been vaccinated once or twice. A reciprocal virus neutralisation test may be conducted with sera from convalescent animals. Re-evaluation of suitable vaccine strains can be obtained only through cross-immunity tests in vaccinated cattle challenged with the new virus.

MATERIALS AND METHODS

FMD virus isolation on cell culture

Isolation of FMD virus from samples submitted to the Regional Reference Laboratory for FMD was performed in tissue cultures, using either a pig kidney cell-line or secondary lamb kidney cells, to obtain a sufficient quantity of the new field virus for studies and storage.
FMD virus typing and sub-typing

Methods and reagents for typing and sub-typing using the complement fixation (CF) test have been described previously (7).

FMD antibody detection

The virus neutralisation (VN) test was performed on secondary lamb kidney cells in a microassay. Titres were expressed as the log_{10} dilution of the serum giving 50% protected wells.

Monoclonal antibodies

Six-week-old BALB/c mice were primed intraperitoneally (i.p.) with inactivated purified SAT 2 viruses BOT 04/80 and ZIM 07/83 at 50 μg per mouse, using virus emulsified in Freund’s complete adjuvant. This was followed by two booster injections (i.p.) at two weeks and three weeks, with the same amount of antigen. The final injection was given intravenously three days before the fusion. SP2/O myeloma cells were fused with spleen cells of mice as described by Allen (1). Hybridoma supernatants were screened for antibody reaction with purified preparations of FMD viruses using a sandwich enzyme-linked immunosorbent assay (ELISA). Monoclonal antibodies (MAbs) were produced in pristane-treated mice by passaging the hybridomas as ascitic tumours.

ELISA characterisation using a panel of MAbs

The sandwich ELISA was performed as described below. Wells of microtitre ELISA plates were coated with pre-titrated dilution of a mixture of rabbit polyclonal anti-SAT 2 sera. After washing, virus samples were added at a constant dilution. After incubation and washing, dilutions of each MAb were used, starting at the last dilution which gave the maximum optical density previously determined in that system. The anti-mouse (specific of the Fab fraction of IgG) peroxidase conjugate was then added, and the test was developed by the addition of the substrate solution containing o-phenylenediamine (0.4mg/ml) and hydrogen peroxide (0.012%) in citrate buffer (pH 4.5).

Vaccines

Vaccines used were prepared with viruses inactivated by ethylenimine (3). Each batch of vaccine adjuvanted with aluminium hydroxide and saponin was tested for safety in cattle (2). The activity of the vaccine was tested on groups of cattle which were inoculated with serial dilutions of vaccine and challenged by intradermalingual inoculation of virulent virus (10^8 ID_{50} [50% infective dose]) (8).

RESULTS AND DISCUSSION

Serological analysis

One of the first tests to be conducted on the new field strain is typing as one of the seven recognised serotypes of FMD virus.

When FMD appears in a previously disease-free area or vaccination failures are observed, the purpose of sub-typing is to determine whether the outbreak is due to the appearance of a field strain with new antigenic characteristics.
Preliminary sub-typing by one-way serological test (giving \(r\) values) may provide a rapid indication of whether the virus strain used in the stock vaccine is appropriate for the area in which the outbreaks occurred.

Since 1982, various FMD outbreaks have been monitored in most countries in Southern Africa (Fig. 1). The SAT 2 type has occurred more frequently than the SAT 1 and SAT 3 types. Type O and type A strains have been isolated in countries as far north as Malawi, Tanzania, Kenya and Ethiopia. A total of forty-four SAT 1, eighty-one SAT 2, fourteen SAT 3, six O and six A virus isolates have been examined since 1982.

**Fig. 1**

*Origin of the foot and mouth disease virus field isolates examined at the Botswana Vaccine Institute (1982-1994)*

Figures in brackets indicate the number of field viruses examined.
In the Southern African area, SAT 1, SAT 2 and SAT 3 types are usually involved. Types O and A were found only in the north of this area. Types C and Asia 1 have never been found in this region.

All these viruses were adapted to grow in cell culture, to obtain a sufficient quantity of virus for characterisation purposes.

Among the most recent FMD outbreaks in Southern Africa, the SAT 1 virus (Fig. 2) from the outbreak in Zambia in July 1992 appeared close to the SAT 1 virus isolated in Zimbabwe in 1989; most of the r values between the antisera and previous strains were lower than 0.50.

The r values between SAT 2 strains are generally higher than those between SAT 1 strains. Antigenic similarities have been found between the SAT 2 isolates from the Zimbabwe outbreaks of 1983, 1987 and 1989, and also with the outbreak strain from Botswana in 1980 (Fig. 3). The strains BOT 04/80 and ZIM 07/83 show the closest relationship.

The antigenic profiles of the virus isolates from the three separate SAT 2 outbreaks in Namibia in 1989, 1991 and 1992 are similar, except for the homologous serum SAT 2 NAM 04/92 which has low reactivity with the two previous strains (Fig. 4).
Comparison (r values) of results of serological analysis by complement fixation test of foot and mouth disease virus type SAT 2 isolates from Zimbabwe with the most recent SAT 2 field strains from Botswana (1978-1980)

The SAT 3 virus from the outbreak in Zimbabwe during 1991 is closer to the strains from 1981 and 1983 than the 1984 strain (Fig. 5).

Antigenic analysis using MAbs

The polyclonal antisera used in the CF test have limited ability to distinguish between viruses which do not differ greatly. Nucleotide sequencing of the viral genome is the main test for identifying minor differences between two viruses. But this technique analyses only a very short sequence of the structure of epitopes, and consequently gives an incomplete picture of the immunogenic properties of the field virus.

As presented by Crowther (5), MAbs can provide the link between chemical structure and antigenic and immunogenic properties. For example, the substitution of only two amino acids could totally modify the immunological properties of the strain (4).

The value of MAbs lies in their specificity for epitopes and in the fact that they are totally consistent reagents between laboratories. MAbs recognise specific sites, and
Comparison (r values) of results of serological analysis by complement fixation test of the foot and mouth disease virus type SAT 2 isolates from Namibia

The two isolates from East Caprivi (1989 and 1991) have similar profiles, and both differ from the 1992 isolate.

FIG. 4

Comparison (r values) of results of serological analysis by complement fixation test of the foot and mouth disease virus type SAT 3 isolates in Zimbabwe

The sera and corresponding r values are as follows:

FIG. 5
non-reactivity of a particular MAb therefore indicates an antigenic difference between strains. Reduced (i.e. 0-50%) MAb binding reflects a change in the affinity of the virus for an epitopic region due to a change in amino acid sequence.

A panel of MAbs has been produced against two distinct SAT 2 isolates of FMD viruses (BOT 04/80 and ZIM 07/83). Sixteen hybridomas which secrete anti-FMD virus antibodies were expanded and injected into pristane-treated mice to produce ascites fluid containing a high concentration of MAbs. Fourteen of the sixteen MAbs neutralised the virus with a titre of 1.4-3.0 \( \log_{10} \). The patterns obtained by ELISA reactivity for each MAb with 33 different SAT 2 strains were compared. The MAbs were then classified into ten different groups. The MAbs included in each group showed exactly the same pattern, each group representing a specific reactivity and probably different epitopes (Table I).

After the specificity was established, the panel of MAbs was used to compare the isolates and thus assess differences between the virus strains involved in the various FMD outbreaks, and to compare these with the vaccine strains. The panel of anti-SAT 2 MAbs was used, in conjunction with the ELISA, to characterise 33 representative strains of FMD virus SAT 2 serotypes isolated in the field since 1977 in different parts of

**TABLE I**

<table>
<thead>
<tr>
<th>SAT 2 virus*</th>
<th>Group **</th>
<th>Designation</th>
<th>Isotype</th>
<th>Neutralisation ***</th>
</tr>
</thead>
<tbody>
<tr>
<td>BOT 04/80</td>
<td>A</td>
<td>410D2-1</td>
<td>IgG1</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>411E1-3</td>
<td>IgG1</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>412E9-3</td>
<td>ND</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>419G7-1</td>
<td>IgG1</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>415B4-1</td>
<td>IgG2</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>511H7-1</td>
<td>IgG1</td>
<td>0.7</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>512F6-1</td>
<td>ND</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>519E9-4</td>
<td>IgG2</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td>G</td>
<td>519H7-1</td>
<td>IgG1</td>
<td>2.9</td>
</tr>
<tr>
<td>ZIM 07/83</td>
<td>H</td>
<td>707B10-5</td>
<td>IgG2</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>810G4-3</td>
<td>IgG1</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>813G1-5</td>
<td>IgG1</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>814D11-6</td>
<td>IgG2</td>
<td>2.9</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>813C8-1</td>
<td>ND</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>814E8-1</td>
<td>IgG2</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>J</td>
<td>858B5-2</td>
<td>IgG2</td>
<td>2.7</td>
</tr>
</tbody>
</table>

* origin of the SAT 2 virus used to prime mice
** group of MAbs showing the same ELISA pattern for the 33 different FMD isolates
*** defined as the reciprocal \( \log_{10} \) dilution of monoclonal antibody which causes 50% neutralisation of virus infectivity in a plaque-reduction assay (30 plaque-forming units/well)

ND: not determined
ELISA: enzyme-linked immunosorbent assay
Southern Africa. Figure 6 shows different ELISA reactivity patterns obtained for the 33 isolates with the panel of ten MAbs. The reactivity of MAbs is highest with the SAT 2 BOT 04/80 strain, and lowest with the SAT 2 BOT 03/77 strain. The other patterns are between these two figures. In each of these patterns, one or more isolates could be included which have the same pattern. In particular, SAT 2 BOT 04/80 and SAT 2 ZIM 07/83 are virtually identical, despite having been collected at an interval of three years in two different countries. Four SAT 2 isolates from the outbreak in Zimbabwe in 1989, namely ZIM 05/89/B1 (Gweru), ZIM 06/89A (Bulawayo), ZIM 06/89C (Bulawayo), and ZIM 07/89 (Gweru) present an identical pattern, although they were collected over a period of three months, suggesting that the outbreaks were probably caused by the same virus strain. This profile is different from SAT 2 BOT 04/80 or SAT 2 ZIM 07/83.

The SAT 2 virus isolated at Mutorashanga, Zimbabwe, in 1989 (ZIM 05/89) has a profile close to that of SAT 2 ZIM 04/87 (from an outbreak in Filabusi in 1987); only one MAb reacted differently to these two isolates.

The SAT 2 virus isolated from an FMD outbreak in Côte d’Ivoire in 1990 (CIV 11/90) shows a surprisingly similar pattern to that of RSA 11/88, isolated from impala in the Kruger National Park (South Africa) in 1988.

The most recent outbreaks in Southern Africa have been caused by SAT 2 viruses which are generally closer to the BOT 04/80 and ZIM 07/83 strains than to the older BOT 08/78 and BOT 03/77 strains.

Finally, it is interesting to observe that antigenic profiling of the viruses with MAbs allows a more accurate analysis than antigenic analysis by the CF test using polyclonal sera (Fig. 7).

**Immunological analysis**

The virus neutralising antibody response in cattle has been shown to be a reliable method for estimating protection against FMD virus (6). The comparative titration of antibodies reactive with vaccine and field virus in sera from vaccinated cattle gives reliable results. Sera from convalescent animals collected in the field may prove adequate for reciprocal serum neutralisation (SN) tests.

The SN test results for the SAT 1 ZAM 07/92 virus show a high heterologous titre in comparison to the reference vaccine strains (Table II). There is a discrepancy between these results and those obtained in the CF test (Fig. 2). According to the SN test results, these strains appear to be more closely related than indicated by the CF test results, particularly when using serum after a booster vaccination. The previous strain originating from Zambia, i.e. ZAM 11/87 (Table II), showed a low antigenic homology with the SAT 1 BOT 01/77 vaccine strain \( r = 0.12 \) by the SN test. This result was confirmed by the CF test \( r = 0.17 \). The results quickly led to checking the efficiency of the vaccine strain in use, BOT 01/77, after challenge with the ZAM 11/87 virus (Table II).

Despite the weak serological and immunological relationships, good protection may be obtained, particularly against SAT 1 viruses (Table II).

These results may differ, however, with the SAT 2 type virus. Weak antigenic and immunological relationships between a new virus and the vaccine strain must be carefully considered, in view of the risk of immunity failure, regardless of the quality of the vaccine in use. As an example, Figure 7 shows the different relationships in the immunological and serological reactions against three vaccine strains successively proposed between 1978 and 1992, SAT 2 BOT 08/78, RHO 02/79 and ZIM 07/83.
Comparison (%) of results of monoclonal antibody (MAb) analysis (by ELISA) of foot and mouth disease virus type SAT 2 isolates in various African countries

For each isolate, the absorbance values of the different MAbs binding are expressed as the percentage value (%) of a cross-reactive polyclonal antibody
Comparison (%) of results of monoclonal antibody (MAb) analysis (by ELISA) of foot and mouth disease virus type SAT 2 isolates in various African countries

For each isolate, the absorbance values of the different MAbs binding are expressed as the percentage value (%) of a cross-reactive polyclonal antibody
Heterologous challenges on each vaccine prepared with these three strains showed insufficient heterologous protection, thus confirming the *in vitro* results (Table III). In contrast to the SAT 1 viruses mentioned above, there is a better correlation between *in vitro* and *in vivo* relationships for the SAT 2 viruses. This illustrates the extreme caution required when a new field strain emerges, particularly of type SAT 2 virus.

Very often, an immediate booster with the stock vaccine will considerably improve the immunity, particularly the heterologous immunity. For example, during the recent SAT 2 outbreak in Namibia, serum neutralisation values for the relationship between strain NAM 04/92 and the vaccine strains in use were 0.22 and 0.28. After a booster with the ZIM 07/83 vaccine strain, the r value increased to 0.63, indicating expected protection to the cattle expressed in terms of increased heterologous neutralisation of the virus (Table IV).

Nevertheless, in most situations, FMD outbreaks appear in non-vaccinated animals or in those which were vaccinated a long time previously. In these cases, animals would have insufficient immunity. Thus, if the new field virus is too different from the vaccine
TABLE II

Comparison (r values) of results of serological analysis, cross-neutralisation and protection of foot and mouth disease virus isolates SAT 1 ZAM 11/87 and SAT 1 ZAM 07/92, collected during the outbreaks in Zambia in 1987 and 1992, and the vaccine virus strains in use (SAT 1 BOT 01/77 and SAT 1 RHO 12/78)

<table>
<thead>
<tr>
<th>Comparison of results</th>
<th>r₁</th>
<th>r₂</th>
<th>r (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serological relationships</strong> *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAT 1 BOT 01/77 x SAT 1 ZAM 11/87</td>
<td>0.17</td>
<td>0.27</td>
<td>21.4%</td>
</tr>
<tr>
<td>SAT 1 RHO 12/78 x SAT 1 ZAM 11/87</td>
<td>0.29</td>
<td>0.39</td>
<td>33.6%</td>
</tr>
<tr>
<td>SAT 1 BOT 01/77 x SAT 1 ZAM 07/92</td>
<td>0.28</td>
<td>0.27</td>
<td>27.5%</td>
</tr>
<tr>
<td>SAT 1 RHO 12/78 x SAT 1 ZAM 07/92</td>
<td>0.29</td>
<td>0.26</td>
<td>27.5%</td>
</tr>
<tr>
<td><strong>Cross-neutralisation of cattle sera</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAT 1 BOT 01/77 x SAT 1 ZAM 11/87</td>
<td>0.12</td>
<td>0.27</td>
<td>18.0%</td>
</tr>
<tr>
<td>SAT 1 RHO 12/78 x SAT 1 ZAM 11/87</td>
<td>0.52</td>
<td>0.41</td>
<td>46.2%</td>
</tr>
<tr>
<td>SAT 1 BOT 01/77 x SAT 1 ZAM 07/92</td>
<td>0.30</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>SAT 1 RHO 12/78 x SAT 1 ZAM 07/92</td>
<td>0.40</td>
<td>ND</td>
<td>-</td>
</tr>
<tr>
<td>Protection of cattle primovaccinated with SAT 1 BOT 01/77 and challenged with SAT 1 ZAM 11/87 virus ***</td>
<td>Vaccine at full dose</td>
<td>Vaccine at 1/4 dose</td>
<td>Controls</td>
</tr>
<tr>
<td>No. of cattle protected/challenged</td>
<td>5/5</td>
<td>4/5</td>
<td>0/2</td>
</tr>
</tbody>
</table>

* measured by complement fixation
** result obtained using cattle serum after a booster vaccination
*** PD₅₀ (50% protective dose) content of the vaccine after challenge = 5.57 per dose
ND: not determined

r₁: ratio between the heterologous and homologous reactions for the first antigen
r₂: ratio between the heterologous and homologous reactions for the second antigen

strain, a homologous vaccine may be prepared using the field strain (particularly with the SAT 2 isolates).

This procedure was adapted in Zimbabwe in 1983 (for vaccination against SAT 2 ZIM 07/83) and in Namibia in 1992 (SAT 2 NAM 04/92).

This emergency procedure should remain exceptional, however, and should be applied only in countries which have well-organised and regularly-monitored programmes for the implementation of FMD prophylaxis.

The reason for this restriction is that other important features contribute to the choice of the vaccine strain, in particular the growth capacity of the virus on cells in culture, the dominance of the strain (7) and the stability of the vaccine.

Throughout the process of vaccine manufacturing, qualitative and quantitative criteria must be considered in order to monitor the in-process control testing. For the vaccine strain, all values of each quality control procedure (as well as their confidence limits) are well known, thus ensuring the consistent quality of each batch of vaccine.
Table III

Antigenic and immunity relationships (r values) between three foot and mouth disease virus type SAT 2 vaccine strains

The in vitro and in vivo results are in agreement

<table>
<thead>
<tr>
<th>Comparison of results</th>
<th>$r_1$</th>
<th>$r_2$</th>
<th>r (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serological relationships *</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 RHO 02/79</td>
<td>0.39</td>
<td>0.44</td>
<td>41.4</td>
</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 ZIM 07/83</td>
<td>0.29</td>
<td>0.10</td>
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<tr>
<td>SAT 2 RHO 02/79 x SAT 2 ZIM 07/83</td>
<td>0.38</td>
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<td>33.2</td>
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<tr>
<td>Cross-neutralisation of cattle sera</td>
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</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 RHO 02/79</td>
<td>0.23</td>
<td>0.23</td>
<td>23.0</td>
</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 ZIM 07/83</td>
<td>0.10</td>
<td>0.10</td>
<td>10.0</td>
</tr>
<tr>
<td>SAT 2 RHO 02/79 x SAT 2 ZIM 07/83</td>
<td>0.26</td>
<td>0.43</td>
<td>33.4</td>
</tr>
<tr>
<td>Protection of vaccinated cattle challenged by inoculating 10,000 ID$_{50}$ in the tongue (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 ZIM 02/79</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>SAT 2 BOT 08/78 x SAT 2 ZIM 07/83</td>
<td>80</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>SAT 2 RHO 02/79 x SAT 2 ZIM 07/83</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

* measured by complement fixation

ID$_{50}$: 50 infective dose

$r_1$: ratio between the heterologous and homologous reactions for the first antigen

$r_2$: ratio between the heterologous and homologous reactions for the second antigen

In the case of potency testing, correlation has been established between the percentage of protection in cattle (protection after challenge), serum neutralising antibody titre and ELISA antibody titre (6). The data used in this correlation were compiled over many years. This correlation is very useful in estimating the likelihood of protection, through testing sera from vaccinated and re-vaccinated cattle during a serological survey.

Table IV

Comparison (r values) of results by serum neutralisation of sera from cattle vaccinated with the foot and mouth disease (FMD) vaccine strains in use and the recent FMD virus type SAT 2 isolates in Namibia

<table>
<thead>
<tr>
<th>Bovine post-vaccination sera</th>
<th>SAT 2 viruses</th>
<th>BOT 08/78</th>
<th>BOT 04/80</th>
<th>ZIM 07/83</th>
<th>NAM 11/89</th>
<th>NAM 04/92</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAT 2 BOT 08/78 *</td>
<td></td>
<td>1.0</td>
<td>0.17</td>
<td>0.10</td>
<td>0.49</td>
<td>0.29</td>
</tr>
<tr>
<td>SAT 2 BOT 04/80 *</td>
<td></td>
<td>0.14</td>
<td>1.0</td>
<td>0.63</td>
<td>–</td>
<td>0.22</td>
</tr>
<tr>
<td>SAT 1 ZIM 07/83 *</td>
<td></td>
<td>0.10</td>
<td>0.91</td>
<td>1.0</td>
<td>0.33</td>
<td>0.28</td>
</tr>
<tr>
<td>SAT 1 ZIM 07/83 **</td>
<td></td>
<td>–</td>
<td>–</td>
<td>1.0</td>
<td>–</td>
<td>0.63</td>
</tr>
</tbody>
</table>

* bovine post-vaccination sera after primovaccination

** bovine post-vaccination sera following a booster vaccination
CONCLUSION

The occurrence of an FMD outbreak always creates an emergency situation, as the disease spreads rapidly if uncontrolled. This economically disastrous situation requires urgent action: a major dilemma arises, however, concerning the choice and application of a suitable vaccine.

Among the parameters for the selection of the vaccine strain to be used in the field, identification of the new virus type and preliminary sub-typing by serological tests must be performed within a short time. The results could provide a rapid indication of vaccines to be chosen, especially if the geographical origin of the FMD outbreak is known or suspected. Some results obtained between 1982 and 1994 are presented and discussed above. Recently, the antigenic profiling of the field virus using a panel of monoclonal antibodies has provided an accurate tool for determining possible relationships with previous viruses.

In the short term, the results of these tests suffice for emergency treatment. Subsequently, in vivo examinations (e.g. virus neutralisation testing of cattle) must be completed, especially in the case of SAT 2 viruses. The data presented above show that, despite a low serological relationship between the SAT 1 field virus and the vaccine strain, protection could be attained after primovaccination. These results may differ from those given by SAT 2 viruses, for which the level of protection after primovaccination is in accordance with the serological or seroneutralisation relationships between the vaccine strain and the field virus.

The choice of a vaccine strain, however, is not determined exclusively by a single FMD outbreak. It is motivated principally by the necessity of large-scale immunological coverage. For this purpose, thorough epidemiological background information is necessary from all the countries involved in the FMD control programme. Experience has shown that, during a major epidemic, more than one strain may be present in the field at the same time. In two recent cases (Botswana in 1980 and Zimbabwe in 1989), several FMD outbreaks occurred within a short period of time, which led to the assumption that the same virus strain was the cause. In both cases, sub-typing showed that two different strains were, in fact, present at the same time. In such situations, a large number of field isolates must be examined.

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SÉLECTION DE SOUCHES VACCINALES DU VIRUS DE LA FIÈVRE APHTEUSE EN AFRIQUE AUSTRALE. – D. Fargeaud.

Résumé : Les types du virus de la fièvre aphteuse les plus répandus en Afrique australe sont le SAT 1, le SAT 2 et le SAT 3 (SAT : Southern African Territories), avec une nette prééminence du second. Depuis 1982, 139 isolats de ce type de virus ont été étudiés. D'autres virus, de type O et A, ont été découverts dans le nord de la région.

Le typage et le sous-typage des virus par l'épreuve de fixation du complément peuvent être améliorés grâce aux anticorps monoclonaux qui permettent de déterminer le profil antigénique exact de souches nouvelles.
L'application d'anticorps monoclonaux à 33 souches SAT 2 a ainsi permis de les classer en plusieurs types de profils.

L'auteur présente des comparaisons entre isolats et souches vaccinales selon les méthodes traditionnelles de sérotypage (épreuves de fixation du complément et de neutralisation du virus) ainsi que le typage des isolats à l'aide des anticorps monoclonaux. Les deux méthodes donnent des informations sur les relations entre les virus. Les épreuves de fixation du complément et de neutralisation du virus fournissent des indications détaillées sur la manière dont les animaux répondent à un isolat particulier et sur la nature de leur réponse immunitaire face à un autre isolat. A partir de là, des relations sérologiques peuvent être proposées, liées à la façon dont différents isolats seraient capables d'induire une réponse immunitaire humorale. Le typage à l'aide des anticorps monoclonaux permet de mieux connaître les relations antigéniques entre les isolats et d'identifier chaque variation d'épitope. Grâce à ces analyses, on peut classer les isolats en différents groupes "antigéniques". Il est ainsi possible d'identifier la souche vaccinale présentant le profil le plus proche du groupe d'isolats étudié. L’analyse immunologique (notamment par l'épreuve de fixation du complément utilisée dans cette étude) fournit des données supplémentaires sur la relation entre un vaccin particulier et un groupe antigénique identifié par la méthode des anticorps monoclonaux. Certes, cette dernière méthode, qui permet d'obtenir très rapidement des renseignements essentiels, offre un avantage certain dans les cas d'urgence ; mais les conclusions du typage ainsi effectué doivent ensuite être confirmées par l'analyse sérologique. La combinaison de ces deux méthodes permet une identification plus large des relations antigéniques et immunogéniques entre les isolats du virus de la fièvre aphteuse et entre ces derniers et certaines souches vaccinales.

existentes entre los diversos virus. Las pruebas de FC y de NV revelan detalles sobre la forma en que los animales han respondido a la presencia de un virus concreto y sobre cómo sus anticuerpos podrían responder ante una cepa diferente; a partir de ello es posible determinar sus relaciones serológicas en lo que concierne al modo en que distintas cepas podrían inducir una respuesta inmunitaria humoral. El perfil obtenido mediante anticuerpos monoclonales, por su parte, permite obtener detalles sobre las afinidades antigénicas existentes entre los distintos microorganismos aislados, y con ello la identificación de variaciones epitópicas individuales. Estos análisis brindan la posibilidad de clasificar las diversas cepas salvajes en grupos «antigénicos», cuya comparación con las cepas empleadas en la producción de vacunas permitirá identificar el virus de vacuna provisto de un perfil más afín al del grupo salvaje que interese. El análisis inmunológico (por ejemplo, con las pruebas de FC utilizadas en el caso de este artículo) puede suministrar información adicional sobre la relación existente entre una vacuna concreta y un grupo antigénico identificado mediante la técnica de los anticuerpos monoclonales. Por supuesto, el empleo de estos anticuerpos para establecer el perfil de una cepa puede proporcionar datos esenciales en un plazo muy corto, lo que resulta especialmente útil en situaciones de emergencia. Las conclusiones de este tipo de análisis por anticuerpos monoclonales pueden confirmarse más tarde mediante pruebas serológicas. Semejante combinación de técnicas analíticas hace posible una identificación más amplia y exhaustiva de las relaciones antigénicas e inmunogénicas existentes entre distintas cepas salvajes del virus de la fiebre aftosa, así como entre cepas salvajes y virus utilizados en la producción de vacunas.


REFERENCES


