High potency vaccines induce protection against heterologous challenge with FMD virus

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Permanent cell line

Seed Virus

Amplify

Clarify

Inactivate (BEI) (I)

Inactivate (BEI) (II)

Purify and Concentrate

Store

Formulate DOE, Al(OH)₃

DOE, Al(OH)₃

Principle of current production method for FMD vaccines
Problems of current FMD Vaccines:

Gap between vaccination and onset of protection
Duration of immunity
Limited crossprotection
Still low level of virus transmission/carriers likely
No perfect DIVA vaccine
Production under high security conditions
Stability at ambient temperature
Criteria for the decision to apply protective vaccination

Population density of susceptible animals

Clinically affected species

Movement of potentially infected animals or products out of the protection zone

Predicted airborne spread of virus from infected holdings

Suitable vaccine available?

Origin of outbreaks (traceability)

Incidence slope of outbreaks

Distribution of outbreaks

Public reaction to total stamping out policy

Acceptance of regionalisation after vaccination

Economic assessment of competing control strategies

It is foreseeable that the 24/48 hours rule cannot be implemented effectively for two consecutive days?

Significant social and psychological impact of total stamping out policy

Existence of large holdings of intensive livestock production in a non-densely populated livestock area
Improved vaccine strain selection
WP5 of FMD_ImproCon

Heterologous challenge experiments vs. in vitro tests
EP - Challenge test

3 groups of 5 cattle

1 Dose
¼ Dose
1/16 Dose

2 Control animals

intradermolingual infection 21 d.p.i
<table>
<thead>
<tr>
<th>Virus</th>
<th>A 22 Irak</th>
<th>A 24 Cruzeiro</th>
<th>A Iran 96</th>
<th>A Iran 99</th>
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<tbody>
<tr>
<td>A 22 Irak</td>
<td>$\geq 32$ PD 50</td>
<td>2,64 PD 50</td>
<td>6,06 PD 50</td>
<td>3,84 PD 50</td>
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<td>A Iran 96</td>
<td>2,00 PD 50</td>
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<td>$\geq 32$ PD 50</td>
<td>10,56 PD 50</td>
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<td>A Iran 99</td>
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<td>18,38 PD 50</td>
<td>$\geq 32$ PD 50</td>
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</table>

A22 vaccine – A Egypt 06: 10,56 PD50
## Challenge Results

<table>
<thead>
<tr>
<th>Vaccine/challenge</th>
<th>A22/A22</th>
<th>A22/Air96</th>
<th>A22/Air99</th>
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<td>0.04</td>
<td>0.10</td>
<td>0.23</td>
<td>0.12</td>
<td>n.a.</td>
<td>0.10</td>
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</tr>
</tbody>
</table>
Homologous and Heterologous VNT-Titres, 21 d.p.v.

Log10 Neutralising Antibody (Final Dilution)

Antibody Against Virus Strain

A22 hom
A96 het
A22 hom
AEGY06 het
A22 hom
A99 het
A22 hom
A99 hom
A22 het
A99 hom
A96 hom
A99 het
A99 hom
A96 hom
A22 het
A96 hom
A99 hom
A96 hom
A22 hom
A96 hom
Definition r-value

$$r_1 = \frac{\text{titre of bovine reference serum against field isolate}}{\text{titre of bovine reference serum against homologous reference strain}}$$
Ferris and Donaldson, 1992:

$r_1 = 0 \text{ to } 0.19$: highly significant serological variation from the reference vaccine strain

$r_1 = 0.2 \text{ to } 0.39$ represent an area of concern. They show significant differences from the reference strain, but protection may be satisfactory if a sufficiently potent vaccine is employed.

$r_1 = 0.4 \text{ to } 1.00$ are not significantly different from the reference vaccine strain

Barnett et al, 2001:

$r$-values of $0.3 \text{ to } 1$ = indicative of reasonable level of cross protection
VNT and Protection

Log titre (Final dilution) vs. Log PD50

Equation: \( y = 1.5599x - 0.295 \)

\( R^2 = 0.7675 \)
Historical Data: VNT and Protection (homologous)

Ahl et al. 1990
Historical Data: LPB-ELISA and Protection (homologous)

Type ASIA

\[ y = 0.7135x + 2.3336 \]

\[ R^2 = 0.8988 \]
Conclusion:

High potent emergency vaccines offer cross protection within serotype A

But: Many vaccines won’t reach ≥32 PD50
Important new A strains arising should be tested
More data on correlation of titre and protection needed
Further Research is also needed because:

What’s true for „A“ may not apply to other serotypes, e.g. „O“

Are there strains that can overwhelm a vaccine that on the basis of serology should protect?
There are still gaps in fundamental knowledge on host immune responses and viral determinants of protection!
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Thank you for your attention!