Culling versus vaccination: challenging a dogma in veterinary (FMD) science

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Summary
Outbreaks of FMD can either be controlled by stamping-out or (circle) culling, or by (ring-) vaccination around the outbreak area, or by a combination of the two methods. The pros and cons of the two methods are discussed. A major draw-back – next to many other disadvantages - of the massive circle culling is its contribution to spreading disease.
We challenge the dogma that "vaccination against FMD will prevent the symptoms but will not eradicate the disease". Where outbreaks were controlled by consistent vaccination with a qualified vaccine the disease did not re-occur. Also, there are no documented cases where cattle vaccinated with a qualified vaccine, caused new outbreaks. Therefore, the risks posed by vaccinated carriers must be an acceptable, "close to zero" risk. Certainly, if used in combination with an anti-NSP test, vaccination should become the major tool in controlling outbreaks of FMD, without additional negative consequences for export trade.

Introduction
The oldest way of controlling outbreaks of FMD is by stamping-out, the killing and disposal of all susceptible livestock on infected farms. Already in 1892 a United Kingdom Act of Parliament stipulated that all susceptible animals must be killed and also, that the farmers would be financially compensated.

Although from 1940 onwards vaccines have been developed that protect against the disease, so far the U.K., Ireland, Scandinavian countries, the USA, Canada and some other countries have always stuck to the stamping out policy. Circle culling – invented by epidemiologists/computer modellers – and applied during the 2001 outbreaks, can be considered an extension of the stamping-out approach.

Another method of controlling outbreaks is by (ring-) vaccination. However, in 2001 vaccination had considerable drawbacks for export trade unless vaccination was declared "suppressive" and the vaccinated animals were successively killed.

Here, we first consider the effectiveness of the two methods in controlling outbreaks. Then we will discuss risks of eventual carriers remaining in the vaccinated population and, what became almost a veterinary dogma that "vaccination against FMD will prevent the symptoms but will not eradicate the disease". We will also discuss whether it is justified to punish – in terms of export trade - the use of (limited) ring- vaccination for controlling FMD outbreaks.

Stamping-out
Traditionally, in FMD free countries, stamping-out has been the first option to eradicate the disease. As a first line of defense it is often quite successful, at least if the disease has not yet spread too widely and if the density of livestock in the area is relatively low. Also, during the first days of an outbreak a proper vaccine might not be available. The choice of the stamping-out option should depend as well on the possibility of tracing dangerous contacts, political will and available resources.

In general, stamping-out consists also of the killing and disposal of all susceptible livestock of the outbreak farm and of "contact" farms that are most likely infected, followed by thorough cleaning and disinfection. If the outbreak farm is located at some distance from other farms and without intensive contacts, the slaughter of only infected premises - with surveillance of neighboring farms - might be adequate. In general, however, one must be "ahead" of the disease and, to that end, also slaughter "dangerous contact farms". However, the latter are difficult to define and decisions can create feelings of arbitrariness and unfairness.
In the U.K. and in some other countries in the past the carcasses were burned or buried, however, this creates environmental problems and, therefore, rendering is preferred.
If stamping-out of the disease succeeds in a relative short period of time it may be the most economical way of dealing with the outbreak.
If the disease is already widespread or occurring in an area with a high-density livestock population it becomes increasingly difficult to bring an outbreak under control and "classical" stamping-out has the following drawbacks:

- Staff must be available for detecting where the virus came from and where it might have spread in the mean time. Active and intensive surveillance is required in order to be "ahead of the disease" and to detect infection at an early stage. Such surveillance in itself represents a risk of spreading disease.
- Heavy equipment used in these operations is difficult to decontaminate and might be a source of infection e.g. by contamination of roads when being driven to another job or back home.
- Large numbers of contractors are involved who are not trained in disease containment. Most of them will be from rural areas and might even live next door to farmers. By having social contact in the farming community they can themselves spread disease.
- Disposal of cadavers also presents a risk since virus in lesions, excrements and excretions is not rapidly destroyed and might be disseminated by transport of cadavers, by pyres, at burial sites or rendering plants. To our knowledge, neither existing transport systems for carcasses, nor the handling of the carcasses at the rendering plants are bio-secure (Barteling 2002).
- High speed of operations is needed with logistics that are very much dependent on local circumstances. This can hardly be foreseen in contingency plans and, therefore, in the beginning of outbreaks it will take time before the required speed is reached. This will matter more if during a number of years (e.g. ten years or more) a country had no experience of outbreaks or, like in the U.K. the disease is already widespread when it is detected.

Ring- (circle) culling
So-called circle culling around infected premises (I.P.) as has been applied in the UK (and in the Netherlands) can be considered as an extension of usual stamping-out procedures. It has been "invented" by epidemiologists-modellers who make use of computer models on how

(fast) the disease spreads (Ferguson et al. 2001; Keeling et al. 2001). The aim of the circle is to eliminate incubating infections that may have spread from the outbreak farm(s) and to create a “fire break” zone around the outbreak. The diameter of the circle was based on the analysis of spread of FMD during the outbreak using computer models. However, the calculated distance of spread must include spread due largely to the culling process itself (see above). Also, important parameters such as virus dissemination by the involved species, number of animals involved, important parameters for the farms at risk (see below) and other factors are not incorporated.

The advantage is that the decision-making is simple and circle culling reduces much of the need for “tracing and anticipating” and surveillance. When the outbreaks are successfully brought under control, the current (economic) advantage is that the FMD-free OIE status can be obtained shortly after completion of the operation.

However, there are major draw-backs with respect to rapid disease control and other elements:

- Even more than for “classical” stamping-out a military organization is needed to implement all the logistics for the required speed.
- For the creation of a fire-break zone most of the culled farms will not be infected. However, some will be in the (undetected) pre-clinical infection stage. Because of the massive nature of the culling these farms and the equipment used for the hauling and destruction will not get the necessary attention for disinfecting with all the risks of further spread of disease.
- Most culled farms within the circle are not infected and do not represent a risk of further spread of the disease and, therefore, are culled unnecessarily. Consequently, one outbreak may cause the unnecessary deaths of large numbers of animals. For example, in The Netherlands there was an outbreak on a calf-fattening farm just outside the main infection zone. Although there was no single indication of virus spread, not even on the farm itself (approximately 500 calves), within the 2 km zone 70,000 animals had to be killed.
- The strict application of circle culling poses a threat to zoological collections and valuable (rare) breeding stock as well.
- The small risk represented by hobby farms and smallholdings is not taken into account.
- Massive killing and destruction of livestock is usually not done with adequate respect for animal welfare and bio-ethical principles.
- In contrast to control by vaccination (see below), in the outbreak area (s) the duration of a campaign cannot be predicted. A long drawn-out campaign is very disruptive for the rural society as a whole and includes also sectors like tourism. The rural community may fear the control measures more than the disease, and, because their animals are not protected by vaccination, will live under this fear for several months after the last case.
- An enormous serological surveillance exercise is often required to detect residual infection since new cases could easily restart the epidemic at its tail-end, particularly if movement controls are prematurely lifted.
- Last but not least, many culls represent a human tragedy and a traumatic experience not only for farmers and their families, but for many veterinarians and others in the rural societies as well. The risk-avoidance behaviour of farmers leads to social isolation and breakdown of the social-economic and trading patterns of rural communities.

If stamping-out is the method of choice, it should be based on the evaluation of *how* virus spreads (known risk factors). Certainly, the disease will not spread in a circular manner. The principal routes of virus spread to be considered are by:

- animal movements from the farm, during the pre-clinical phase;
- estimated virus aerosol production (species and number of animals involved) and weather conditions (temperature, humidity, wind direction) on the days preceding the outbreak (Donaldson et al. 2001);
- animal proximity at farm boundaries, e.g. grazing in adjacent fields;
- size and animal species of neighbouring holdings e.g. a large cattle holding (large air sampling volume) represents a greater risk of inhaling a minimal infectious dose" (Sellers 1971) and becoming a new generator of disease than a few sheep or goat of a nearby hobby farmer;
- people (veterinarians, inseminators, visiting farmers, cleaning and disinfecting crews, etc.)
- vehicles (e.g. animal transport, machinery) contaminating roads that are used by the farmer's family and associates;

Because, in principle, every culling may represent a human and animal welfare tragedy each farm should be judged on its own (risk) parameters. If possible, it would be very helpful if epidemiological factors and associated risks could be incorporated into a computer model to enable rapid risk assessment and decision making for each farm

Ring vaccination

Instead of killing all susceptible livestock around an I.P. a "fire break zone" can be created by vaccination.

The factors determining expected spread (as mentioned above) also should determine the size of the "ring" or area around an IP. In addition, to get "ahead" of the disease one must anticipate the natural spread over the period that is needed to organize the vaccination. In general, this will be a few days plus 4-5 days needed before animals become protected by the induced immunity.

In comparison to culling the method is relatively cheap and, therefore larger areas can be vaccinated in a relatively short period of time.

The logistics of a vaccination campaign are rather simple. It can be carried out on a large scale by a limited number of (trained) staff under full bio-safety conditions or by farmers and trained farm hands as is common practice in South America. The latter method has the advantage that there will be no risk of cross-contamination between farms caused by the visiting vaccinators.

When a potent vaccine is used, outbreaks in the vaccinated zone/ring will usually cease within a week when effective herd immunity is reached.

Therefore, ring-vaccinations should be performed without delay and should include all susceptible species. Preferably, the vaccination should be carried out from the outside of the "ring" towards the centre, the I.P. To protect the most endangered farms as soon as possible, vaccination should proceed simultaneously from the I.P. towards the outside. In the immediate vicinity of the outbreak farm, the large (cattle) holdings should be vaccinated first because potentially, those are the largest “aerosol collectors” and, therefore, will be most at risk.

Ring/emergency vaccinations should be included in any contingency plan:

- to stop the disease from spreading;
- to avoid all of the above mentioned disadvantages of stamping-out;
- to prevent the suffering of animals as much as possible;
- to ensure that a few weeks after vaccination life in the affected area can resume its normal course, with minimal socio-economic consequences.

Concerns have been raised with regard to human consumption of meat or other products from vaccinated animals. However, there is not any reason to object to human consumption of the meat of vaccinated animals. In Europe meat from vaccinated animals has been consumed for over fifty years, including the meat originating from South America.

Ring vaccination followed by slaughter (“suppressive” vaccination)

Fear of carriers among vaccinated animals has led to the idea of ”suppressive” vaccination. In that approach, vaccination is used to control the outbreak(s), but all vaccinated animals have to be killed before the FMD-free status can be regained. Vaccination was used in the Netherlands in the main outbreak area to control the 2001 outbreak. In accordance to OIE regulations, the FMD free status was regained 3 months after serological surveillance and after the slaughter of the 160.000 vaccinated animals. As indicated above the period would have been one year if the vaccinated animals were not slaughtered.

Vaccination works well to get rid of the disease. However, when vaccination is declared to be “suppressive” several of the problems mentioned for the circle culling remain. An advantage is that the vaccinated animals can be killed over a more extended period.

It is interesting to note that, although vaccinated pigs do not become carriers they still must be slaughtered as well!

Screening for anti-NSP antibodies

In non-vaccinated herds foci of hidden infection can be traced by screening for antibodies against the virus. Vaccination will also raise such antibodies and, therefore might frustrate such tracing; another reason for a primary ban on vaccination. However, virus infection raises antibodies not only against the virus particle but also against non-structural proteins (NSP), the proteins that are needed for virus multiplication. These anti-NSP antibodies are also useful indicators of a past infection and, consequently, of potential carriers.

After a single vaccination with a non-purified vaccine, a-NSP antibodies will, in general, not be raised. However, after multiple vaccinations such antibodies might be induced as well. In contrast, vaccines prepared from purified FMD antigens, such as those in the EU vaccine banks, will raise antibodies to the virus particle only. Even upon repeated vaccination no antibodies against non-structural proteins will be raised and past infection can still be traced. Such vaccines, in combination with tests for antibodies against non-structural proteins, will perform like a “marker” vaccine, enabling discrimination between vaccinated animals that are infected (potential carriers) and vaccinated animals that are not infected.

Although in individual animals the tests to detect a-NSP antibodies are not 100% sensitive, they perform very well if used for screening on a herd basis. If required, testing for the presence of virus e.g. by probang tests or PCR can further reduce the risk of missing an individual animal. Thus, the concern that vaccination blurs the distinction between vaccinated and infected carrier) animals, is no longer founded if purified vaccines are used. Tests to discriminate between potential carriers and vaccinated animals have already widely been used by South American countries to support their claims (at OIE) of freedom of FMD.

Dogma

The statement that "Vaccination against FMD prevents the symptoms but does not eradicate the disease" has become what one might call a dogma in veterinary science. That dogma was born after it was detected that vaccinated cattle could be carriers as well (Van Bekkum, 1959). Also in that period in many countries (e.g. South-America) the vaccines used were often of poor quality, were sometimes not properly inactivated, and were not always consistently applied. This resulted in "silent", sub-clinical transmission of FMD and re-occurrence of disease. However, to our knowledge over the past 15 years there are no examples where after consistent vaccination with a qualified vaccine, disease re-occurred. There are, however, many examples that FMD has been eradicated by consistent vaccination:

1. In the sixties The Netherlands suffered from large-scale outbreaks in the non-vaccinated pigs first of type C and later of type O. The virus entered from Germany where general vaccination was not yet applied. The routine Frenkel-type vaccine that was used for cattle did not sufficiently protect the pigs. On the (mixed) outbreak farms the vaccinated cattle were well protected and were left alive, and many of them became carriers (Straver et al. 1970). When the outbreaks were under control, by the application of (expensive) concentrated Frenkel-type vaccine - restrictions on transports and markets were lifted. Also, the vaccination of the pigs (in the outbreak area) was - because of the costs – discontinued. Because of their high turn-over rate, the pig population soon became fully susceptible again. Although at the time there were many mixed farms (with cattle and pigs) no further outbreaks occurred of either "pig-o-phylic" type C or type O strain.
2. The Italian outbreaks of 1985-'86 and of 1987 of type C and type A respectively were controlled by stamping –out of infected premises and additional vaccination. One of the last outbreaks in 1987 occurred in a large pig holding (approximately 5,000 pigs). Because of limited rendering capacity the authorities decided to vaccinate the whole lot with a potent aluminium hydroxide vaccine emulsified in oil. The other vaccinated pigs were left alive and later went for (normal) slaughter for human consumption. Of these pigs 35 were followed for possible virus reproduction by nasal swabbing at regular intervals. Only from one pig at 7 days post vaccination a minimal amount of virus was isolated probably caused by captured virus aerosol from the environment. Active virus multiplication has not been demonstrated (Panina et al.). The same approach was successfully followed in 1989 on another large pig holding. That was the end of types C&A in Europe.
3. Like described above in South Africa in 2000 vaccination was used to protect the non-affected cattle on a very large cattle holding (about 18.000 cattle) where an outbreak of SAT1 virus occurred. Also there, vaccination worked very well and the SAT1-type FMD did not re-occur (Bruckner et al. 2002).
4. Argentina, large parts of Brazil, Chile, Uruguay, and several other states in the southern cone of South-America became free of FMD by vaccination of the cattle population only and were able to cease vaccination.

5. After reintroduction of the disease in Argentina, the State of Rio Grande do Sul and Uruguay, the disease was rapidly eradicated, again by vaccination of the cattle population only and even without the slaughter of infected animals (Sutmoller et al., 2002).
6. Israel completely relies on (consistent) vaccination only. During the first 2 years of their life cattle are vaccinated twice a year, after that once a year with a tri-valent vaccine. Sheep are vaccinated once a year only against type O. At the borders sometimes outbreaks of FMD occur in the (nomadic) sheep and sometimes also in the outbreed meat cattle, in the not yet or once vaccinated calves. The infected animals are left alive and in the outbreak area the Israelis simply apply an additional round of vaccination. There are no indications that outbreak strains re-occur.
7. Other examples of recent outbreaks controlled by vaccination without re-occurrence of the disease are: Russia 1995, Albania and Macedonia 1996, South Africa 2000 and 2001, Turkey (Thrace) 2001 (Leforban 2002).

Thus it can be concluded that consistent vaccination – no holes in the "vaccination blanket" – with the application of a qualified vaccine can eradicate FMD. Also, that the statement/dogma that "Vaccination against FMD prevents the symptoms, but does not eradicate the disease" does not hold true.

There may be an exception for SAT-type viruses. There was circumstantial evidence that vaccinated carriers caused new outbreaks in Zimbabwe (in the late eighties and early nineties) of SAT-type virus (Thomson, 1996). Those outbreaks were on farms in the northern districts while the outbreak strains were related to SAT strains occurring in central Zimbabwe. It may be due to the fact that SAT-type viruses occurring in southern Africa have a special survival mechanism via (wildlife) carriers – buffaloes in particular – that is not known for other FMD sero-types. In addition, one could question whether the vaccines that were used were of undisputed quality and whether it really were the vaccinated carriers which caused the outbreaks.

The cattle concerned were moved around from central Zimbabwe to farms in the northern districts and they certainly were not the only animals that were moved around. However, the fact that the strains were related to a strain occurring in central Zimbabwe supported the theory that carriers were involved. However, can introduction of sub-clinically infected animals as a possible cause be excluded? Were all the Lorries that bridged the central and northern districts well disinfected? Were there no other contacts between the central districts and the Northern provinces that may have caused transmission of disease? Thomson (1996) also suggests the possibility that "sexual transmission" - from carrier bulls to cows - might be involved. From the few cases with evidence that carriers introduced FMD into "virgin" herds, bulls were involved as well. (Fogedby, 1961; Sutmoller et al., 2002). Therefore, the possibility of sexual transmission of FMD by carrier bulls might well be object of further studies.

Anyhow, the Zimbabwe argument is in our view not sufficiently strong to weaken all the evidence that consistent vaccination can eradicate FMD. Also the Republic of South Africa became free by systematic vaccination and remains free because it is protected by a vaccination zone around the Kruger Park where FMD is endemic in buffalos.

Because in all those cases where outbreaks of FMD were controlled by vaccination the vaccinated animals and their products went into the normal consumption circuit without causing new outbreaks it can also be concluded that products from vaccinated animals do not represent a risk, or at least an acceptable, “close to zero” risk (Sutmoller & Casas 2002, OIE paper in press).

The (possible) presence of vaccinated carrier cattle must also represent an acceptable “close to zero” risk. We base that on the fact that there is no evidence that the large numbers of vaccinated (A, O, and C-type) carriers that in the past must have been around in Europe and in South America, did not hamper the eradication of FMD. In those countries vaccination was no longer needed and could (successfully) be discontinued.

However, the assumed risk represented by (vaccinated) carriers puts a heavy penalty on the use of vaccine against FMD in the form of import/export restrictions of animals and animal products, even if for the control of outbreaks only a limited fraction of the cattle population has been vaccinated (pigs don’t become carriers). Therefore, countries with an important export of livestock will omit to use vaccination and will – like in the U.K. – try to control the outbreaks by stamping-out.

The question is, whether the presence of some (vaccinated) carriers and the risk they represent justifies regulations that in fact exclude a major and simple method to control outbreaks. So far a proper risk assessment has not been made. Also, the possibility to detect carriers by serological tests against non-structural proteins (see below) has so far not been accepted as a further assurance of an – in our view - already acceptable risk.

Conclusions

Stamping-out of outbreak and “contact” farms can be used as a first approach to control outbreaks, however, should be based on a proper evaluation of epidemiological and risk factors for each individual contact farm.

Massive circle culling will likely contribute to further spread of disease and, therefore will extend the duration of an epidemic. We also have pointed out several other reasons why it cannot be justified as a method to control outbreaks.

We have shown that the statement – almost a dogma in veterinary science – that “vaccination against FMD will prevent the symptoms, but will not eradicate the disease” will not hold true. We also gave evidence that the risk of vaccinated carriers causing new outbreaks must be negligible. Anyhow, the current regulations are not based on proper risk assessment also not for the situation after control by stamping-out.

In our view both stamping-out and vaccination should have the same consequences for trade, at least, as long as only a limited fraction of the livestock population is vaccinated.
If outbreaks are numerous and widespread the risk for trade partners increases anyhow whether they have been controlled by stamping-out or by vaccination.

If vaccination can be used without additional punishment, dairy farmers, hobby farmers, and others that have nothing to do with export trade (e.g. zoos) can have their valuable animals protected against a terrible disease.

Threatened pigs should be vaccinated anyhow because they might become generators of further spread of disease and, on the other hand, do not become carriers.

If the above policy is implemented, the ministries of agriculture and livestock industry can select the best options for eradication of the disease that cause the least disruption of social and economic life at the least cost to the community. The demonstration– after an outbreak has been controlled - that the country is free of active FMD and that serological surveys were carried out rapidly and efficiently would demonstrate to the international community the existence of a well-organized veterinary services that takes the eradication of FMD seriously.

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