

Guide to epidemiological surveillance for rinderpest

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Summary

The practical implementation of epidemiological surveillance programmes for rinderpest prescribed by the standards of the Office International des Epizooties (OIE) is described. The rationale of surveillance is discussed in relation to the stages of disease control, discontinuation of vaccination, clinical surveillance and serological surveillance. These stages lead to provisional and confirmed declarations of freedom from disease, and the confirmed declaration of freedom from infection. Practical methods of stratification of livestock populations, and selection of samples of herds and animals within selected herds are explained. The actions to follow any discovery of disease, or any clinical or serological signs of disease, are discussed. In the serological surveillance stage, balancing the number of herds and the number of animals within selected herds tested can result in considerable reduction in the overall number of serum samples to be tested. The methods used in rinderpest surveillance can readily be adapted to surveillance programmes for other diseases.

Keywords

Epidemiological surveillance – Freedom from disease – Freedom from infection – Rinderpest.

Introduction

This paper explains practical issues in the design and implementation of epidemiological surveillance programmes that can provide objective evidence, meeting standards set by the Office International des Epizooties (OIE), that countries or regions are free from rinderpest. These surveillance programmes are also used as the basis for planning and monitoring the Global Rinderpest Eradication Programme of the Food and Agriculture Organization (3, 8). Surveillance is implemented when it is believed that the disease is no longer present, and vaccination has been discontinued. It has two main objectives:

- to control the risk that foci of infection might remain, and ensure that they are detected before they can cause serious outbreaks in the increasingly susceptible unvaccinated population
- to provide internationally recognised evidence of the new disease status, which is important in international eradication programmes, and to facilitate trade in livestock and their products.

In practice, it is never possible to be absolutely certain that rinderpest does not exist in the animal populations of a region or country, since this would require that all the animals present be examined simultaneously by a perfectly accurate diagnostic procedure. However, it is possible to reduce the probability of failing to detect the disease to a very low and controlled level by testing relatively small samples of the susceptible animal species present. This requires that the sampling procedures be correctly designed and implemented.

It should be emphasised that these sampling procedures are complementary to, and not substitutes for, effective disease reporting systems. Any reports of rinderpest-like disease should be thoroughly investigated by field and laboratory methods to confirm or refute the diagnosis of rinderpest.

The steps leading to the eradication of, and the proving of freedom from, rinderpest infection are detailed in the OIE recommendations (6), and are summarised in the paragraphs below.

Disease control

If no rinderpest has been detected for at least two years, the risk of re-introducing infection is controlled, and vaccination has been discontinued, then it is possible to declare *provisional freedom from disease*.

Clinical surveillance

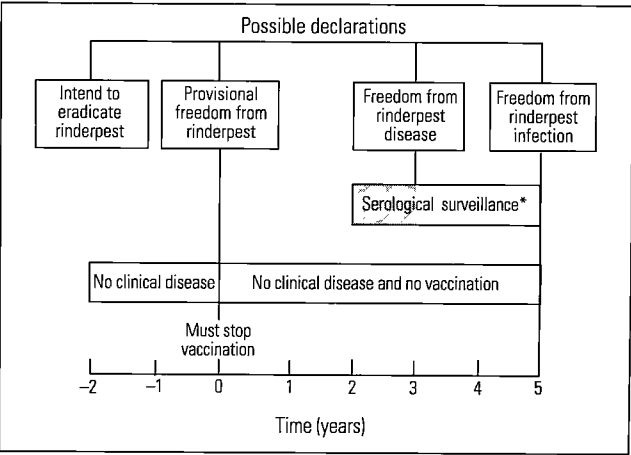
Clinical surveillance is necessary to ensure that any remaining infection is detected before it can cause serious outbreaks, and to provide objective evidence of freedom from disease. Random samples of cattle and other susceptible species are examined for clinical signs of rinderpest. The sampling and examination procedures must be designed to give a 95% probability each year of detecting rinderpest if clinical signs were present in 1% of herds or other sampling units in any stratum of the population of susceptible animals. Any cases of clinical suspicion must be subjected to full laboratory testing to confirm or refute the presence of infection. After three years, and subject to review of the surveillance programme and certain other requirements, the OIE may declare *freedom from disease*.

Serological surveillance

Serological surveillance is intended to confirm by serological methods that rinderpest virus is not circulating. Sero-surveillance is commenced at least two years after the declaration of *provisional freedom from disease* (one year before declaration of *freedom from disease*) and is continued for at least two years. These methods of detection of virus activity should be more sensitive than searching for clinical signs of the disease. They are subject, however, to confusion caused by vaccine-related and non-specific reactions, the frequency of which depend on the sampling and antibody detection procedures. No animal born since the cessation of vaccination should have rinderpest antibody, unless it has maternal antibody, which should not normally be present after the first year of life. This defines animals eligible for serosurveillance as those born after the cessation of vaccination, and which are more than one year old. Any animal in the eligible age group that has antibodies to rinderpest provides evidence of circulation of rinderpest virus, or the continued use of vaccine.

The sampling and testing procedures must be designed to give a 95% probability each year of detecting seropositive animals in the relevant age group if any are present in 1% of the herds or other sampling units in any stratum of the eligible population. Cattle and any other susceptible domestic animals must be included in the serosurveillance programme. Wild susceptible species must be sampled where possible, and domestic stock in contact with these animals should be sampled intensively. If no evidence of virus activity is found, and subject to review of the serosurveillance programme and certain other requirements, the OIE may declare *freedom from rinderpest infection*.

This sequence of steps is often referred to as the ‘OIE Pathway’ and is shown diagrammatically in Figure 1.



* If a country wants to be declared free from rinderpest infection at the end of year 4, serological surveillance of unvaccinated animals must be in operation at the end of year 2, in order to prove that there has been no seropositive case in the country for at least two years

Fig. 1 Requirements for the declaration of freedom from rinderpest disease and freedom from rinderpest infection

The timing and duration of these stages are as important in controlling risk as the detection probability and prevalence standards. It would not in general be possible to compensate for a reduction in the duration of the surveillance programme by increasing sample sizes. This is because the design of the standards takes into account the fact that the susceptible population will steadily increase after the cessation of vaccination, and with it the probability of detecting unsuspected foci of infection. Thus, as the risk of disease increases over time, so does the probability of detecting it. To reduce the duration of the surveillance programme would compromise the likelihood of detecting any residual disease foci before the declaration of *freedom from disease*.

Rinderpest clinical surveillance

General considerations

Epidemics of rinderpest are usually prevented or controlled by vaccination programmes in cattle (and possibly other susceptible species) which reduce the susceptible proportion of the population so that it cannot sustain the maintenance of infection. The rinderpest vaccine confers life-long immunity, and there is no known carrier state in which individual animals could act as long-term reservoirs of infection. If the proportion of immunised animals is brought to a sufficiently high level for an adequate period, then the infection will be eradicated. However, if the proportion of immunised animals in a population does not reach this level, then a situation may

arise in which the level of immunity is too high to allow the development of rinderpest epidemics, but too low to eliminate the infection completely. This can result in the creation of 'endemic foci'.

In such situations, the disease can persist for many years in relatively small populations of cattle. Most of the adults in these populations are immune, either by recovery from the disease or by vaccination, and the disease tends to occur in young stock with waning passive immunity. As these animals account for only a small proportion of the population, there are only ever a few cases of rinderpest at any one time. In addition, the disease can be very mild in such animals. The combination of low prevalence and mild disease make such foci very difficult to detect. Indeed, it is possible that the disease will only be detected if it moves out of such foci into more susceptible or sensitive populations. Therefore, reports of clinical rinderpest are not necessarily a good indication of the original source of infection.

It is the purpose of rinderpest clinical surveillance to confirm that no such foci of disease remain. This is achieved by clinical examination of samples of herds (or other population units such as village populations) for signs suggestive of rinderpest. The clinical signs of rinderpest are described by Plowright (7) and other authors (4, 9). Further guidance on the diagnosis of rinderpest is provided in the form of multimedia computer programs (1). If such signs are found, further investigation and diagnosis are required to confirm or refute the presence of rinderpest.

While it is the purpose of clinical surveillance to search for signs of disease, it is to be hoped that no rinderpest will be found. This situation can easily affect the motivation of the staff conducting the surveillance. It is of obvious importance that staff reporting signs of rinderpest, even if they prove to be due to some other cause, are not penalised in any way. It is inconceivable that clinical surveillance would disclose no signs, such as diarrhoea or ocular discharge, that might be due to rinderpest. Any such signs must be investigated, either to confirm a diagnosis of rinderpest or to provide an alternative explanation. It is important that records of these investigations be kept for the purposes of OIE verification.

No special equipment is required to conduct clinical surveillance: the vehicles that were used in the past for vaccination campaigns could be re-allocated for this purpose. Teams should include sufficient staff to handle the animals efficiently, and at least one member of each team should be competent to examine animals for the relevant clinical signs. The animals should be restrained to allow a careful examination for any clinical signs suggestive of rinderpest. Any dead animals should be examined for post-mortem lesions.

Sampling procedures

General considerations

The objective of the sample design is to keep the volume of surveillance work to a minimum, while demonstrating absence of the disease to the required level of statistical confidence. Typically, this involves less work than most field veterinarians would assume is necessary to demonstrate that the disease is absent. It does, however, require rigorous procedures for selecting the sample of the population to be examined.

In sampling an animal population or populations, it is essential to ensure that all sections of that population are included in the sampling procedure. If part of the population is excluded for any reason, then it is not possible to draw any objective statistical inferences about the disease status of that part of the population. It might be possible to make a subjective assessment of the risk of disease being present, but this could cause problems in international recognition of disease status. If part of the population is inaccessible for disease surveillance, then it is likely that it was also inaccessible for disease control operations.

Stratification

The first step in the sampling procedure is to develop a suitable system of stratification for the livestock population, which divides the population into a series of sub-populations or strata from which samples can be drawn. The reason for stratification is that if the disease were present it might be restricted to a certain sub-population. The prevalence within the affected sub-population could be at or above the minimum prevalence to be detected, while the prevalence in the whole population was below the minimum prevalence to be detected. In this situation, surveillance designed for the whole population could fail to detect the disease, even though the prevalence was above the minimum level in the affected sub-population.

A separate sample of herds is drawn from each stratum, so that the required probability of detection is achieved for all strata. However, the overall stratified sample size is larger than the sample size that would be used for the unstratified population by a factor of the number of strata. Therefore, stratification should only be used where necessary.

Any sub-population that could maintain the disease independently of the rest of the population over the period of the surveillance programme should be considered as a separate stratum. In the case of rinderpest, strata would normally be based upon geographical regions. Small ruminants are suspected of maintaining rinderpest independently of cattle in some countries. In this case, strata should also be defined by species or species group. Rinderpest would be unlikely to be maintained in one production system (e.g. dairy) while not infecting cattle in other production systems in the same area. Therefore stratification by production system would be unlikely in rinderpest.

surveillance, although it might be necessary for other diseases. Populations may be stratified by more than one factor; for example, by region and by species.

There is a degree of subjective judgement in defining strata. Knowledge of the livestock population structure, contact between sub-populations and the epidemiology of the disease is required. Considering the criterion of maintaining rinderpest independently of the rest of the population, few countries would need to define more than five geographical strata per species, and two or three strata per species would suffice for most countries. Stratification by species would only be necessary if it were suspected that the disease could be maintained for longer than the surveillance period (three years) in other species without spreading to the cattle population.

Sample units

Having classified the population to be sampled into the relevant strata, the actual units to be sampled must be considered. In most commercial and pastoral production systems the sample unit is normally the herd or flock. However, in smallholder mixed farming systems, where only a small number of animals are held by any one owner, it may be convenient to consider groups of animals on a village basis. In this case all animals owned by the villagers would be grouped together and classified as one ‘herd’. This word is used in the rest of this paper to refer to the sample unit, but it has a wider meaning than its conventional use.

Having defined the sample unit or ‘herd’, if a herd is selected for sampling, then all animals contained within the selected herd must be examined. In most production systems a herd would probably contain between 20 and 500 animals. If many herds would contain more or fewer animals than this, consideration should be given to re-defining the sample unit.

Sample size

Once the livestock population has been suitably classified into appropriate strata, the appropriate number of herds from each stratum must then be examined. The required sample size depends on the number of herds present, but is not a simple proportion. Required sample sizes can be obtained from published tables (2).

Table I shows the sample sizes that would be required from a particular stratum to achieve a 95% probability of detecting clinical rinderpest if 1% of the herds contain animals showing clinical signs of the disease.

To achieve this specified probability of detecting clinical signs of rinderpest in any stratum, a maximum sample size of 299 herds is required. Thus, if four strata are defined, then a maximum of 1,196 herds (299 from each stratum) need be investigated, irrespective of the size of the national herd.

Table I
Sample sizes required for 95% probability of detecting clinical rinderpest present at 1% prevalence

N	10	50	100	500	1,000	5,000	10,000	Infinite
s	10	50	96	225	258	290	294	299

N = total number of herds in the stratum
s = required sample size

The reliability of the clinical surveillance field work is of the utmost importance. Care must be taken to ensure that all animals within a selected herd are subjected to a detailed clinical examination. In a typical infected herd in an endemic focus of rinderpest, only one or two yearlings might be expected to show very mild clinical signs. The sample sizes are based on the assumption that surveillance teams would detect all animals showing clinical signs. If detection efficiency were only 50%, then the required sample size would have to be doubled.

In general, it would be prudent to use a sample size of 300 herds, irrespective of the total number of herds in the stratum. It is common for some of the selected samples to be unavailable for examination for legitimate reasons. For example, a selected village might be found to contain no livestock, or a selected herd might have been disbanded. Some additional ‘reserve’ herds should be selected to allow for such cases. The reserve herds should be used in the order that they were selected to replace missing sample herds. More reserve herds can be selected later if necessary. From the operational point of view, it might be more efficient to sample the reserve herds at the same time as the main sample, to avoid the possibility of having to travel long distances to find a few reserve herds after the main surveillance programme.

Sample selection
Random samples

For the purposes of objectivity and international recognition of the results of surveillance, it is essential that a proper random sampling procedure be used. While it might seem logical to focus the surveillance on populations considered most likely to be maintaining the disease, judgements as to the location of residual infection are very unreliable. The residual endemic focus of rinderpest, which is the target of surveillance, is unlikely to be found where it is expected: otherwise it would have been eliminated in the disease control programme. However, it is acceptable to undertake additional surveillance in populations considered at greater risk, or to sample additional herds if suspicion of disease arises during surveillance work. These herds must be added to those in the random sample, and not substituted.

Random samples are typically less evenly spread through the population than is the case with a sample selected to be ‘representative’. Sometimes, having selected a random sample of herds, it will be apparent that some part of the population considered to be important has been missed or

under-represented by chance. In this situation it is not permissible to abandon the sample and select another. It is, however, acceptable to add herds to the random sample. This could never decrease the probability of detecting the disease below the level achieved by the random sample alone. It will increase the probability of detection (but by an unspecified amount).

A serious source of potential bias in the sample is the willingness of livestock owners to allow examination of their animals. The uncooperative owner is most likely to have avoided vaccination and other control measures. Most countries have the necessary legislation to allow the veterinary service to inspect animals, but enforcement (once persuasion has failed) is often difficult. Unfortunately, this source of bias must be eliminated if the surveillance programme is to produce meaningful results. There is little point in searching for disease if the very herds most likely to be infected are missed.

In a random sample, every individual in the population must have an equal probability of being selected, and the selection of one individual must not affect the probability of another being selected.

The method to be used to select a random sample of herds depends on the information available when the surveillance is being planned. Ideally, random samples should be selected from a sample frame (a list of all herds in the population). When no sample frame is available, alternative procedures can be used, but these are designed to emulate sample frame selection. Therefore, the procedure using sample frames is described first, as it represents the ideal random sampling procedure that alternative procedures are designed to emulate.

Random selection using a sample frame

If reliable census data are available, then it may be possible to compile a list (sample frame) of all the herds within a particular stratum. It is important that sample frames should not be selected from incomplete or obsolete census data, since this may result in herds being omitted, and it is possible that these omitted herds may be at greater risk of disease. Furthermore, a herd should not appear more than once in the sample frame since this will increase its probability of being included in the sample at the expense of the other herds. However, no sample frame is perfect, and provided that erroneous entries, duplicates and omissions account for less than 5% of the total, a sample frame is likely to produce a better random sample than alternative random sampling methods. The sample frame should also contain sufficient information to enable a particular herd to be located within the country or region, should it be selected.

To select a random sample from a sample frame, the following procedure should be followed: each animal or herd should be assigned a number in the range 1 to N , where N is the total

number of animals or herds in the list. The allocation of these sequential numbers does not need to be at random: the position in the census list can be used. If a sample of X herds is required, then X different random numbers in the range 1 to N should be drawn. Each random number indicates the number of a herd to be included in the sample.

Random numbers can be obtained from tables, or can be generated by some scientific calculators. The advantage of using a calculator to generate random numbers is that they are generated in the range from 0 to 1. These numbers can be multiplied by N so that random numbers in the range 0 to N are produced. Most computer spreadsheet and database programs also have random number generator facilities, which can be used to automate the selection process if the sample frame data are stored in a computer file.

The process of selection can be illustrated by an example. Suppose one wished to select a sample of 300 herds from a stratum containing a total population of 2,500 herds: use the random number generator to produce a series of random numbers. These might be as follows: 0.15335, 0.07562, 0.78956, 0.65324, 0.69413, 0.99856, etc. Multiply these numbers by 2,500 (N) and take the next higher whole number (round up): 384, 190, 1,974, 1,634, 1,736, 2,497, etc.

The process is continued until the required 300 herd numbers have been selected. Any numbers that have already been selected should be discarded.

Random selection without a sample frame

If no sample frame is available, the most generally applicable method of selecting random samples of herds is based on random selection of map co-ordinates. A reasonably large-scale map is required, covering the area in which the entire population of the stratum to be sampled is contained. This should have a grid of longitudinal and latitudinal lines marked on it. Sometimes the grid lines will be identified by letters rather than by numbers, and in this case the lines should be relabelled with numbers. Using random numbers to identify co-ordinates, a series of random points should be marked on the map. The selection process is illustrated in Figure 2, which shows the position selected by the two random numbers 24 and 21. In general, the grid should be arranged so that there are at least 100 divisions in each direction, although it is not necessary to draw so many lines: the last digit of precision can be measured with a ruler.

All herds within a specified radius of the point must be included in the sample. If there were no herds within the specified distance, no animals would be sampled. It is important in this case not to take the herd nearest to the specified point, as this procedure would bias the sample to include too many herds from areas of low population density, and too few from densely populated areas.

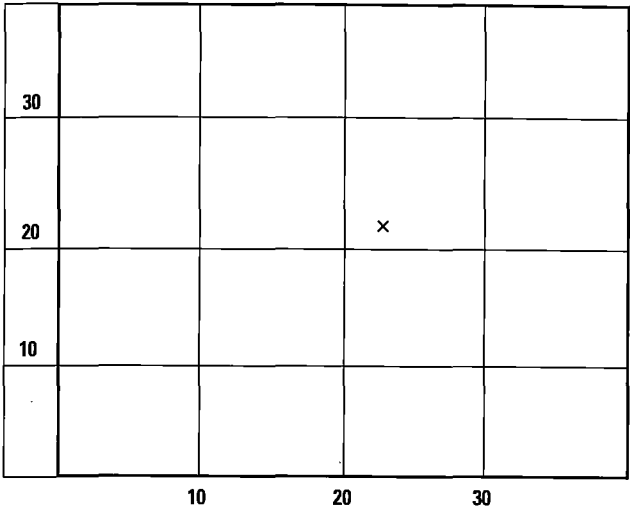


Fig. 2
Method of selecting random points on a map

The radius within which to include herds would be set to suit the distribution of the population in the area. If animals were concentrated in villages, a relatively small radius, perhaps as little as 50 to 100 metres, would be appropriate to obtain the required 10 to 500 animals. On the other hand, in rangeland conditions a radius of several kilometres might be used. The same radius must be used for all selected points in any population stratum, otherwise the procedure would approximate to the selection of the nearest herd which, as explained above, would bias the sample to areas of low population density.

When using this sampling procedure, it is likely that quite a high proportion of selected points will have no herds or animals within the specified radius. In such cases, it would be necessary to continue selecting points until the required total of 300 herds has been reached. Thus, it would usually be necessary to select more points than the number actually required. Strictly, to be sure of reaching the required level of confidence, where more than one herd is found in one radius, this should be counted as contributing only one unit to the sample size. However, this source of error is only likely to be important if more than 20% of the herds come from radii containing other herds.

Field procedures

All animals in the selected herds should be examined carefully for mouth lesions, ocular or nasal discharge, or signs of diarrhoea. The owner should be interviewed to ascertain the vaccination history of the herd, and asked for details of any history of disease signs suggestive of rinderpest.

Temperatures should not be taken, except in suspicious cases; it is likely that the temperature of animals will be elevated by factors such as the disturbance of handling and standing in the sun.

Any indications of rinderpest activity, in the past or present, should be investigated by specialised diagnostic teams with access to laboratory facilities.

Full records of examinations must be kept. These will form the basis for controlling the quality of the field surveillance work, and the information on herd structure will be valuable for planning future surveillance, as well as for other livestock development programmes.

The following information should be recorded at the herd level:

- code number for herd
- name of owner
- address and location of the herd
- species
- other species in contact with herd
- date of visit
- identification of surveillance team
- herd size
- management system: dairy/meat/dual purpose; settled/nomadic/trader; grazing (common/enclosed/zero)
- vaccination history (dates, policy, etc.)
- disease history (especially signs suggestive of rinderpest).

A form to record this information should be designed. The details of the design will vary from country to country. However, a prototype design as a basis for adaptation is shown in Figure 3.

A prototype form design for recording herd structure and clinical signs is shown in Figure 4. The details on age and sex are very important in controlling the quality of the work of surveillance teams. It would soon become apparent if one team were finding herd age structures different from the other teams. Similarly, it is important to record clinical signs, even if they are attributed to causes other than rinderpest. An unusually low or an unusually high prevalence of clinical signs might cast doubt on the work of a surveillance team. Adherence to a standard design for this form would facilitate the development of standard computer programs for rapid assessment of the results of clinical surveillance.

If any clinical signs are detected, the animals affected should be marked with long-lasting paint or dye, and prompt attention from a mobile diagnostic unit with access to laboratory facilities should be sought. To refute the clinical diagnosis of possible rinderpest would normally require:

- no evidence of rinderpest virus in samples taken from the affected animals and subjected to the antigen detection procedures defined by the OIE (6)

Rinderpest surveillance: herd data

<table><tr><td>District</td></tr><tr><td>Place name</td></tr><tr><td>Map reference</td></tr><tr><td>Date</td></tr><tr><td>Team reference</td></tr></table>	District	Place name	Map reference	Date	Team reference	<table><tr><td>Herd reference</td></tr><tr><td>Name of owner</td></tr><tr><td>Address or contact</td></tr></table>	Herd reference	Name of owner	Address or contact										
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<table><tr><td>Species</td></tr><tr><td>Breed</td></tr><tr><td>No. in herd</td></tr><tr><td>Other species in contact</td></tr></table>	Species	Breed	No. in herd	Other species in contact	<table><tr><td>Production</td></tr><tr><td>Dairy</td></tr><tr><td>Meat</td></tr><tr><td>Dual purpose</td></tr></table>	Production	Dairy	Meat	Dual purpose	<table><tr><td>Movement</td></tr><tr><td>Settled</td></tr><tr><td>Nomadic</td></tr><tr><td>Trader</td></tr></table>	Movement	Settled	Nomadic	Trader	<table><tr><td>Grazing</td></tr><tr><td>Common</td></tr><tr><td>Enclosed</td></tr><tr><td>Zero</td></tr></table>	Grazing	Common	Enclosed	Zero
Species																			
Breed																			
No. in herd																			
Other species in contact																			
Production																			
Dairy																			
Meat																			
Dual purpose																			
Movement																			
Settled																			
Nomadic																			
Trader																			
Grazing																			
Common																			
Enclosed																			
Zero																			
Herd vaccination history: report approximate dates, source of vaccine, and vaccination policy, e.g. 'Animals less than 18 months'. If vaccination certificates are available, quote reference. Indicate ear punch, brands, etc.																			
History of clinical signs of rinderpest-like disease (reported by owner)																			
Summary of findings from clinical examination of herd																			

Fig. 3
Prototype form for recording herd data

- no evidence of seroconversion of in-contact unvaccinated animals using the antibody detection procedures defined by the OIE (6); and
- the identification of a reasonable alternative cause for the clinical signs.

In the absence of positive confirmation or refutation of the clinical diagnosis of rinderpest, the population concerned should be kept isolated and under close observation for as long as is necessary to reach a definite conclusion. A number of other diseases, especially peste des petits ruminants, have clinical signs similar to those of rinderpest. Methods of differential diagnosis are reviewed in the OIE recommendations (6).

Serological surveillance for rinderpest

General considerations

Serological surveillance involves collecting blood from animals, separating the serum and testing it for the presence of antibody. The advantage of this process compared to clinical surveillance is that the antibody is a permanent sign following an infection, while clinical signs may only be present for a few days, or may be absent altogether. For a given disease situation, the prevalence of seropositive animals will be much higher than the prevalence of clinical signs, and therefore easier to detect.

The antibody detection systems available at present cannot distinguish between the antibody developed after rinderpest vaccination, maternal antibody from an immune dam, and the antibody following natural infection. Therefore, serological surveillance is only a useful means of detecting rinderpest infection in animals which have not been vaccinated, and which do not have maternal antibody.

There are four possible reasons for an animal giving a positive reaction to a rinderpest antibody detection test, as follows:

- the animal may have been naturally infected with rinderpest virus
- the animal may have been vaccinated
- the animal may have maternal antibody acquired from an immune dam, or
- there may have been a non-specific reaction.

The objective of serological surveillance for rinderpest is to search for evidence of seroconversion following natural infection. If serosurveillance is being conducted in a population that has been vaccinated or in which the disease has been present, then some animals will be expected to have antibody as a result of vaccination or maternal immunity. The serosurveillance must be restricted to animals born after the cessation of vaccination, and which are too old to have

maternal antibody (more than one year old). This part of the population is considered eligible for serosurveillance.

Even within the eligible animals, finding an animal with rinderpest antibody does not in itself prove that the animal seroconverted after natural infection. The age could have been estimated wrongly, the animal might have been vaccinated despite the official cessation of vaccination, or there could be a non-specific test reaction. The results of a serosurveillance programme in Tanzania, and possible reasons for a small number of seropositive animals are described by Loretu (5).

If seropositive eligible animals are found, there should be follow-up investigations, including the following:

- re-testing the seropositive animals to eliminate the possibility of false-positive reaction
- interviewing the owner to find out if the animals had been vaccinated, or introduced from another area (in the latter case, trace-back investigation would be required)
- intensive clinical surveillance to search for signs of disease (field and laboratory antigen detection systems should be used to investigate any suspicion of disease)
- intensive and sequential serological sampling in the area, to estimate the prevalence of seropositive animals (the animals tested in the follow-up surveillance should be marked, so that they can be re-tested after some weeks: this would produce direct evidence of seroconversion, which would be expected to occur if infection were present).

It is recognised that such investigations may present special difficulties under conditions of migratory or nomadic animal husbandry. However, a high standard of investigation is required to demonstrate that a population is free from infection. If it were not possible to explain the presence of seropositive animals in the population, then it would be difficult to accept that the population was indeed free of infection. Therefore, when serosurveillance is being conducted in such populations, it is important that arrangements are in place to support any follow-up investigation that may be necessary.

Sampling procedures

The design of the sampling procedure for serological surveillance is required to give a 95% probability of detecting serological evidence of rinderpest infection if antibodies are present at a prevalence of 1% of herds in any stratum of the susceptible livestock population. This is exactly the same standard as is applied to clinical surveillance, and therefore the sampling procedure for the selection of herds and the number of herds to be sampled is identical.

Since the procedures leading to a country or region being declared free from rinderpest infection permit an overlap of the clinical and serological surveillance phases, the same herds could be used for both clinical and serological examinations during the year of overlap.

In contrast to the clinical examinations, there is no point in applying serological tests to all animals in sampled herds. Serological testing should be restricted to animals which are too young to have been included in the last vaccination round, and too old (more than one year of age) to have any residual maternal antibody. These are termed eligible animals for the purposes of serological testing. If vaccination has only recently been discontinued, the eligible animals will fall into quite a narrow age band. In general it would be unwise to assume that an animal without an ear punch or other vaccination mark had not been vaccinated.

If the recommendations of the OIE (6) are interpreted strictly, there is no allowance for any possibility of failing to detect rinderpest antibody within sampled herds. Therefore, it would either be necessary to test all eligible animals with a procedure of 100% sensitivity, which would be impractical and uneconomic; or to accept some probability of failing to detect seroconverted animals, and to compensate for this by increasing the number of herds sampled.

To calculate the number of herds to be sampled to compensate for the possibility of failing to detect a positive herd requires the concept of 'detectable prevalence'. If the true prevalence of positive herds were 0.01 (1%), but the herd testing procedure produced a 0.95 (95%) probability of detecting a positive herd (herd test sensitivity), then only 95% of the positive herds would be detectable. Thus, the detectable prevalence of positive herds would be the product of the true prevalence and the detection probability (herd test sensitivity). In this example, the detectable prevalence would

be $0.01 \times 0.95 = 0.0095$ (0.95%). The number of herds to be sampled should be calculated from this detectable prevalence, rather than the minimum prevalence required by the standard. From Table I, 299 herds have to be sampled to produce 95% probability of detecting 1% prevalence in an infinite number of herds. If the detectable prevalence were 0.95%, the number of herds to be tested would increase to 314.

This modest increase in the number of herds sampled compensates for a 5% probability of failing to detect a positive herd. It also means that a sample of eligible animals have to be tested, rather than the entire population. This could result in a considerable reduction in the overall costs of the serosurveillance programme, while still meeting the OIE standards.

The same logic can be applied to consider herd test sensitivities other than 95%. Table II shows the numbers of herds and eligible animals to be tested to achieve 95% probability of detecting 1% herd prevalence, for different herd sizes and herd test sensitivities, for an infinite population of herds.

The required sample sizes in Table II show some irregularity in progression, because prevalence is not continuous. For example, it is impossible to have a prevalence of exactly 5% in a population of 30 animals: this would suggest 1.5 positive animals. For the purposes of sample size calculation, therefore, the prevalence is rounded down to the next lower

Table II
Numbers of herds and eligible animals to be tested for 95% probability of detecting 1% prevalence of positive herds with a within-herd prevalence of 5%

Eligible	Number of animals in herd					
	Infected	Sampled				
10	1	10	10	10	8	6
20	1	20	19	19	16	11
30	1	30	29	28	23	16
40	2	40	31	28	20	12
50	2	50	39	34	25	15
75	3	75	47	40	28	16
100	5	100	45	37	24	13
200	10	200	51	41	26	14
500	20	500	56	43	27	14
Infinite	Infinite	N/A	59	45	28	14
Probability of detecting an infected herd if the specified number of animals are sampled		100%	95%	90%	75%	50%
Detectable prevalence		1.00%	0.95%	0.90%	0.75%	0.50%
Number of herds to be sampled		299	314	332	398	598
Probability of detecting infection		95%	95%	95%	95%	95%

N/A: not applicable

whole number of cases: one in this example. This conservative procedure ensures that the OIE standards are met, or exceeded, for any size of population.

Table II also shows that judicious balancing of herd test sensitivity and the number of herds sampled can result in considerable reduction in the overall number of serum samples to be tested. For example, if the typical size of a village herd were 500 cattle, to achieve a herd test sensitivity of 95% would require a sample of 56 eligible animals from each village. The overall number of samples would be 314 villages multiplied by 56 sera, producing a total of 17,584 sera to be tested. If the detection probability were reduced to 75%, the overall number would be 398 villages multiplied by 27 sera, producing a total of 10,746 samples. It is emphasised that, despite the reduced number of samples, the overall detection probability would be exactly the same.

Further reduction in the overall number of samples could be achieved by reducing the herd test sensitivity to 50%. This would require a sample of only 14 eligible animals from each village. However, the costs of the field work would increase because of the larger number of villages to be visited: it might be considered wasteful for a team to travel to a village to collect only 14 serum samples.

Surveillance to prove area freedom does not require the same level of confidence at the herd level as would be required to prove the freedom of a particular herd. A lack of sensitivity at individual herd level can be compensated for by increasing the number of herds sampled. If the average cost per herd visit and the average cost per test are known, then it is possible to alter the number of herds sampled and the number of samples per herd in such a way as to minimise the overall cost of the survey, while still maintaining the desired level of confidence.

If only a few animals per herd are tested, the overall cost of the survey tends to be high because a large number of herds must be visited. As more animals per herd are tested, the probability of detecting the disease in a herd increases, and consequently – while still keeping the same overall probability of detecting disease in the survey – the number of herds that need to be tested decreases. As the number of animals tested in each herd increases, the cost of the survey decreases, but at a slower and slower rate until, at some point, a minimum cost is reached. After that, increasing the number of animals tested per herd will increase the total cost of the survey. This cost curve tends to be very flat around the minimum, and so the optimum number of samples per herd does not need to be determined too precisely.

The exact required sample sizes can be translated into simple instructions for field staff. If a herd test sensitivity of 75% were chosen, field staff could be instructed to bleed a random sample of 30 eligible animals from each herd, or to bleed all

eligible animals in herds of less than 30 eligible animals. For small herds, the cost of collecting a few more samples than is strictly necessary is likely to be less than that of selecting a random sample of eligible animals.

Field procedures

The selection of random samples of eligible animals for serological testing must take place in the field. There is a practical problem in drawing a random sample of eligible animals from within a herd. Until the animals have been examined individually, it may not be possible to determine whether they are eligible for testing. Therefore the total number of eligible animals in the herd will not be known until after all the animals have been examined. It would then be necessary to handle the animals again in order to draw a random sample for serological testing.

In some situations, it might be easier and more economic to bleed all of the eligible animals at the first handling, and to select a random sample of the sera in the laboratory. This procedure would also have the advantage that in the event of seropositive unvaccinated animals being found, it would be possible to test the rest of the sera collected at the same time.

If it is decided only to bleed the required number of eligible animals, the most convenient method of selecting a random sample of n animals from a total of T eligible animals is given below.

If the total number of eligible animals is T , and the required sample size is n , write the numbers 1 to T as a list on a sheet of paper.

Select n different random numbers in the range 1 to T . A calculator that can generate random numbers in the range 0 to 1 is useful for this purpose. These random numbers are multiplied by T to produce random numbers in the range 0 to T , which should be rounded up to produce whole numbers in the range 1 to T . As each number is generated, mark that number in the list as an animal to be sampled. If the same random number appears twice, reject the second occurrence and replace it with another random number.

Assign numbers 1 to T to the eligible animals, or allow the animals to pass through a race or leave a handling pen one by one. This effectively gives the animals numbers in the range 1 to T according to the sequence in which they leave. If the sequential number is the same as one of the n random numbers, the animal should be tested.

An alternative method for random selection of animals, which might be more acceptable to field staff, is a 'ballot'. The identities of the T eligible animals are written on small pieces of paper, and n of these are selected at random after they have been mixed in a suitable container, such as a hat.

Analogous procedures could be used to select random samples of sera in the laboratory.

It is important not to use the method of testing every *n*th animal passing through the race: this is not a satisfactory randomisation technique.

The field procedures used in serological surveillance will be exactly the same as those used in clinical surveillance, except that blood samples will be taken from some animals. Suitable provision will have to be made for the handling and transportation of the samples to the laboratory. Forms similar to those used for the clinical surveillance would be appropriate. It will be necessary to include the sample reference number in the individual animal record of sampled animals.

Operational summary and schedule

An operational summary and schedule has been produced to assist with the planning of rinderpest surveillance programmes (Table III). This shows the sequence of operations, and their timing to comply with the OIE standards.

Discussion and application to other diseases

Epidemiological surveillance is essentially a risk management procedure in the eradication of rinderpest and many other diseases.

Vaccination is essential in the control of many diseases, but it can mask the existence of residual foci of infection. When the prevalence of disease has been reduced to a very low level, or even eliminated, it is necessary to discontinue vaccination in order to obtain the economic benefit of avoiding future vaccination costs. When vaccination is discontinued, the country faces a risk that the disease may still be present, and could cause serious outbreaks in the unvaccinated population. Epidemiological surveillance provides objective and quantified assessment of the probability that the disease could still be present.

It may also be necessary for the new disease status to be internationally verified for trade purposes. This can be relevant to imports, as well as exports, of livestock products. If a country has not demonstrated freedom from disease to international standards, then international trade agreements may restrict its right to control imports of livestock and their products from countries where the disease exists or might exist. The OIE standards for the declaration of freedom from

Table III
Operational summary and schedule for rinderpest surveillance leading to a declaration of ‘freedom from infection’

Year	Month(s)	Operation
0	10-12	Plan clinical surveillance: – stratify populations – define sample units – determine sample sizes – prepare surveillance data forms – assemble and train surveillance teams – select herds or points (sample units) to be sampled in Year 1
1	1	Discontinue vaccination
1	1	Declare <i>provisional freedom from rinderpest</i>
1	1-12	Implement clinical surveillance for Year 1: – examine selected sample units for clinical signs – follow up disease reports or suspicious findings – maintain files of data from surveillance teams – monitor progress and quality of field work
1	10-12	Review and planning: – review quality and results of field work in Year 1 – select herds or points (sample units) to be sampled in Year 2
2	1-12	Implement clinical surveillance for Year 2: – examine selected sample units for clinical signs – follow up disease reports or suspicious findings – maintain files of data from surveillance teams – monitor progress and quality of field work
2	10-12	Review and planning: – review quality and results of field work in Year 2 – select herds or points (sample units) to be sampled in Year 3 – plan procedures for serosampling (if required)
3	1-12	Implement surveillance for Year 3: – examine selected sample units for clinical signs – test eligible animals for antibody (if required) – follow up disease reports or suspicious findings – maintain files of data from surveillance teams – monitor progress and quality of field and laboratory work
3	10-12	Review and planning: – review field and laboratory work and results in Year 3 – apply for declaration of <i>freedom from rinderpest</i> – select sample units for serosurvey in Year 4 (if required)
4	1-12	Implement serosurveillance for Year 4 (if proving <i>freedom from infection</i>): – examine selected sample units for clinical signs – test eligible animals for antibody – follow up disease reports or suspicious findings – maintain files of data from surveillance teams – monitor progress and quality of field and laboratory work
4	10-12	Apply for declaration of <i>freedom from rinderpest infection</i>

disease allow international trading partners to have a quantified assessment of the risk that the disease could still exist in another country.

In the course of the surveillance programmes prescribed in the OIE standards, the risk that infection could remain is progressively reduced. If the probability of detection in each year of surveillance is 0.95 (95%), the probabilities of failing

to detect by the end of the first, second and third years are 0.05 (5%), 0.05^2 (0.25%) and 0.05^3 (0.0125%), respectively.

After the cessation of vaccination, the potential consequences of any remaining infection become progressively more serious as the susceptible population increases. However, epidemiological surveillance ensures that there is concomitant reduction in the risk that infection could persist.

The principles for the implementation of epidemiological surveillance described in this paper could readily be adapted to other diseases, such as foot and mouth disease and

contagious bovine pleuropneumonia. The criteria in the OIE standards for declarations of freedom from disease and infection relating to other diseases are different from those used for rinderpest, reflecting the differences in the epidemiology and diagnostic techniques. However, these standards are still based on clinical and serological surveillance, and the same considerations would apply to the practical implementation of surveillance programmes.

Guía para la vigilancia epidemiológica de la peste bovina

A.D. James

Resumen

El autor describe la aplicación práctica de programas de vigilancia epidemiológica de la peste bovina según dictan las normas de la Oficina Internacional de Epizootias (OIE). Se examinan los fundamentos de la vigilancia en lo que se refiere a las fases de control de la enfermedad, interrupción de las vacunaciones, vigilancia clínica y vigilancia serológica. Estas fases conducen a una declaración, primero provisional y luego confirmada, de ausencia de la enfermedad, y en última instancia a una declaración confirmada de ausencia de la infección. Se exponen asimismo métodos prácticos para la estratificación de poblaciones bovinas y la selección tanto de rebaños de muestra como de ejemplares para el muestro dentro de cada rebaño seleccionado. Se detallan las medidas que deben tomarse al observar la presencia de la enfermedad o detectar el menor indicio clínico o serológico de la misma. Durante la fase de vigilancia serológica, un adecuado equilibrio entre el número de rebaños y el número de ejemplares de cada rebaño que se someten a prueba permite una sensible reducción del número total de muestras que es preciso analizar. Los métodos utilizados en la vigilancia contra la peste bovina pueden adaptarse fácilmente a programas de vigilancia de otras enfermedades.

Palabras clave

Ausencia de enfermedad – Ausencia de infección – Peste bovina – Vigilancia epidemiológica.

■

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