RINDERPEST

AETIOLOGY

Classification of the causative agent

Rinderpest (RP) is caused by a negative-strand RNA virus of the *Morbillivirus* genus within the family *Paramyxoviridae*. The virus existed as a single serotype, so that all strains cross-protect fully and are only differentiated by molecular characterisation. The most commonly used vaccine, a cell culture-attenuated rinderpest virus (RPV), was derived from an early African isolate, but was effective throughout Africa, the Middle East, and Asia.

Note that the official name of the virus was changed in 2016 to *Rinderpest morbillivirus*, and some references to the virus may use this name.

Resistance to physical and chemical action

Temperature:	Half life of the virus at 56°C is approximately 5 minutes and approximately 3.5 minutes at 60°C
pH:	Stable between pH 4.0 and 10.0
Disinfectants/chemicals:	Susceptible to lipid solvents and most common disinfectants (phenol, cresol, β-propiolactone, sodium hydroxide 2%/24 hours used at a rate of 1 litre/m^2)
Survival:	Quickly inactivated in environment as RPV is sensitive to light, drying and ultraviolet radiation. Survives in shaded pastures and buildings for at least 48 hours. Can remain viable for long periods in chilled or frozen tissues

EPIDEMIOLOGY

Between 2002 and 2011 there were no reported field cases of rinderpest. The eradication campaign concluded in 2011 with the international declaration of global freedom from rinderpest.

This status is based on three pillars: absence of significant risk of infection of both domestic and wildlife populations; completion of the pathway defined by the OIE for recognition of national rinderpest freedom by all OIE-Member and non-Member Countries; the cessation of all rinderpest vaccinations throughout the world

In immuno-naïve populations, RP presents itself as an epidemic with high morbidity and mortality rates (up to 100%). In these classic instances of disease, highly transmissible, virulent RPV strains dominate. In endemic areas, milder RPV strains emerged and survivor host populations may have adapted; disease was found principally in younger animals with waning maternal immunity. Domestic cattle played an important role in maintenance of RPV while, in the wild, African buffalo seemed to hold a central role, though sylvatic survival of the virus was limited.

Although the disease has been eradicated, stocks of the virus continue to exist in laboratories worldwide. The next step is to reduce the number of such holding facilities to a reasonable minimum, in order to decrease the risk of accidental or deliberate release.

Thus, rinderpest remains as a notifiable disease

Hosts

- In the field: affects artiodactyls
  - high morbidity and mortality among domestic cattle, water buffalo (*Bubalus bubalis*) and yak (*Bos grunniens*); European cattle (*Bos primigenius taurus*) more susceptible than zebu breeds (*Bos primigenius indicus*)

    - some wild ruminants are highly susceptible: African buffalo (*Syncerus caffer*), giraffe (*Giraffa cameloparadalis*), eland (*Taurotragus oryx*), kudu (*Tragelaphus strepsiceros* and *T. imberbis*), wildebeest (*Connochaetes* sp.) and various antelopes
    - sheep and goats can be infected but rarely show clinical signs and are epidemiologically unimportant
- Asian pigs seem more susceptible than African and European pigs
- Wild swine: bush pigs (*Potamochoerus porcus*) and warthog (*Phacochoerus africanus*)
- Dogs can seroconvert upon consuming infected meat and become resistant to infection with canine distemper virus
- Rinderpest can infect Camelids, especially in endemic areas but did so rarely; these are dead-end hosts and do not transmit the virus

Transmission

- By direct or close indirect contact between infected and susceptible animals
- Airborne transmission is limited and only possible under specific circumstances and short distances
- RPV is sensitive to heat and direct sunlight but can survive for at least 48 hours in infected pastures or barns; fomites are a viable but uncommon means of transmission
- No evidence of vertical transmission
- Introduction of RPV into free areas is almost always by means of infected animals

Sources of virus

- Shedding of virus begins 1–2 days before pyrexia in ocular and nasal secretions, and at later times in saliva, urine and faeces
    - blood and all tissues are infectious before the appearance of clinical signs
- During periods of clinical disease, high levels of RPV can be found in expired air, nasal and ocular discharges, saliva, faeces, semen, vaginal discharges, urine and milk
- Infection is via the epithelium of the upper or lower respiratory tract
- No carrier state

Occurrence

The Food and Agriculture Organization of the United Nations (FAO), in close association with the OIE, launched a Global Rinderpest Eradication Program (GREP) in 1994, calling for eradication of the virus by the year 2010.

The last known rinderpest outbreak in the world was reported in 2001 (Kenya). By the end of 2010, FAO was confident that all rinderpest virus (except for those conserved in laboratories) had been proven to be extinct. GREP can claim responsibility for assisting the veterinary services of countries historically affected by rinderpest in taking action to eliminate the infection, halt vaccination, and develop evidence of the absence of the rinderpest virus and infection. Activities included clinical disease research, serological surveillance sampling, contingency planning and laboratory support.

Historically, the virus was widely distributed in Asia, with regular incursions into Europe. The virus was introduced into Africa towards the end of the 19th century where it caused a devastating pandemic. Full genome sequence analysis has shown that all known rinderpest isolates fall into one of four phylogenetic lineages, one covering Asian isolates, one covering African isolates and one each for the main vaccine viruses and their virulent parents.

RPV was found throughout the African continent, although was eradicated in South Africa and most of North Africa at a relatively early stage, with almost all isolates coming from a broad belt of sub-Saharan countries.

The Asian lineage was recorded in Afghanistan, India, Iran, Iraq, Korea (Rep. of), Kuwait, Lebanon, Oman, Pakistan, Russia, Saudi Arabia, Turkey, Sri Lanka and Yemen and it is assumed that RPV outbreaks in other countries were caused by viruses of the same lineage. The last Asian country to be infected with the virus, Pakistan, declared freedom from rinderpest in 2003.

For more detailed information on the occurrence of this disease worldwide, see the OIE *World Animal Health Information Database* (WAHID) Interface [http://www.oie.int/wahis/public.php?page=home]

Facilities holding RPV containing material

For the immediate future, existing collections of virulent and attenuated rinderpest viruses will remain under sequestration in research and approved vaccine manufacturing laboratories. To guard against the accidental release of virus from laboratory sources, FAO and the OIE are collaborating in establishing the principle of international oversight and regulation of facilities holding rinderpest virus based on minimizing the number of repositories. Countries holding RPV containing material are expected to perform sequencing and destruction or to safely move them to an OIE-FAO approved holding facility.

Annual reports on RPV containing material should be submitted to the OIE by the end of November each year by the Veterinary Authority of a Member Country hosting an institution or institutions holding RPV containing material. A separate report, drawn up in accordance with the available model, should be produced for each institution. A final report should be submitted to the OIE for each institution when all materials have been destroyed and no new activities are foreseen for the future.

DIAGNOSIS

Classical rinderpest resulting from contact exposure has an incubation period of 3–15 days, dependent on the virus strain and the degree of exposure.

For the purposes of the OIE *Terrestrial Animal Health Code*, the incubation period for rinderpest is 21 days.

Clinical diagnosis

Clinical signs of rinderpest have not been seen since 2001. A milder form of the disease, with the potential to regain classical characteristics, used to occur in association with endemic situations in East Africa.

Classical acute or epizootic form

- Clinical disease is characterized by an acute febrile attack within which prodromal and erosive phases can be distinguished
- Prodromal period (time between onset of fever and first appearance of oral lesions) lasts on average 3 days
  - affected animals develop a pyrexia of between 40°C and 41.5°C together with partial anorexia, depression, reduction of rumination, constipation, lowered milk production, increase of respiratory and cardiac rate, congestion of visible mucosa, slight serous to mucopurulent ocular and nasal discharges, and drying of the muzzle
- Erosive phase with development of necrotic mouth lesions
  - at height of fever: flecks of necrotic epithelium appear on the lower lip and gum and in rapid succession may appear on the upper gum and dental pad, on the underside of the tongue, on the cheeks and cheek papillae and on the hard palate; erosions or blunting of the cheek papillae
  - necrotic foci can fuse to form larger patches; material works loose giving rise to shallow, nonhaemorrhagic mucosal erosions
- Gastrointestinal signs appear when the fever drops or about 1–2 days after the onset of mouth lesions
  - diarrhoea is usually copious and watery at first; later may contain mucus, blood and shreds of epithelium; accompanied, in severe cases, by tenesmus
- Diarrhoea or dysentery leads to dehydration, abdominal pain, abdominal respiration, and weakness
- In terminal stages of the illness, animals may become recumbent for 24–48 hours prior to death; death usually occurs 6–12 days following onset of fever
- Deaths will occur but mortality rate will be variable; may be expected to rise as the virus gains progressive access to large numbers of susceptible animals
  - depending on the strain of RPV, initial mortality rates may be as low as 10–20% or in the order of 90% in highly susceptible animals. Animals in areas with endemic peste des petits ruminants (PPR) may show resistance to RPV and lower mortality
- Some animals die while showing severe necrotic lesions, high fever and diarrhoea, others after a sharp fall in body temperature, often to subnormal values
- In rare cases, clinical signs regress by day 10 and recovery occurs by day 20–25

Peracute form

- No prodromal signs except high fever (>40–42°C), sometimes congested mucous membranes, and death within 2–3 days
- This form occurs in highly susceptible young and newborn animals

Mild subacute or endemic form

- Clinical signs limited to one or more of the classic signs
- Usually no associated diarrhoea
- May show a slight, serous, ocular or nasal secretion
- Fever: variable, short-lived (3–4 days) and not very high (38–40°C)
- No actual depression; animals may continue to graze, water and trek
- Low or no mortality, except in highly susceptible species (buffalo, giraffe, eland, and lesser kudu)
    - in these wild species: fever, nasal discharge, typical erosive stomatitis, gastroenteritis, and death

Atypical form

- Irregular pyrexia and mild or no diarrhoea
    - fever may remit slightly in the middle of the erosive period, and
    - 2–3 days later, return rapidly to normal accompanied by a quick resolution of the mouth lesions, a halt to the diarrhoea and an uncomplicated convalescence
- The lymphotropic nature of RPV leads to immunosuppression and favours recrudescence of latent infections and/or increased susceptibility to other infectious agents

Sheep and goats

- Variable signs; some pyrexia, anorexia and minor ocular discharge
- Sometimes diarrhoea
- Asian RPV strains can be transmitted to cattle by contact with infected small ruminants

Pigs

- Swine in Asia more commonly affected
- Pyrexia, anorexia and prostration
- Erosions of buccal mucosa 1–2 days after fever and diarrhoea at 2–3 days
- Diarrhoea may last a week leading to dehydration and possible death

Lesions

- Either areas of necrosis and erosions, or congestion and haemorrhage in the mouth, intestines and upper respiratory tracts
- Highly engorged or grey discoloration of abomasum (epithelial necrosis of mucous membrane); pyloric region severely affected and shows congestion, petechiation and oedema of the submucosa
- Rumen, reticulum and omasum usually unaffected; necrotic plaques are occasionally encountered on the pillars of the rumen
- Enlarged and oedematous lymph nodes
- White necrotic foci in Peyer's patches; lymphoid necrosis and sloughing leaves the supporting architecture engorged or blackened
- Linear engorgement and blackening of the crests of the folds of the mecum, colon and rectum ('Zebra striping')
- Typically the carcass of the dead animal is dehydrated, emaciated and soiled
- Histologically, evidence of lymphoid and epithelial necrosis accompanied by viral associated syncytia and intracytoplasmic inclusions
- In milder form of rinderpest, most domestic animals escape development of erosions
    - some may develop slight congestion of mucous membranes and small, focal areas of raised, whitish epithelial necrosis may be found on the lower gum (no larger than a pin head); possibly a few eroded cheek papillae
- In milder form of rinderpest in wild animals
    - African buffaloes infected with milder RPV have demonstrated enlarged peripheral lymph nodes, plaque-like keratinized skin lesions and keratoconjunctivitis

- Lesser kudus were similarly affected with blindness due to severe keratoconjunctivitis but no diarrhoea
- Eland also showed necrosis and erosions of the buccal mucosa together with dehydration and emaciation

Differential diagnosis

Cattle

- Bovine viral diarrhoea/mucosal disease
- Malignant catarrhal fever
- Infectious bovine rhinotracheitis
- Foot and mouth disease
- Papular stomatitis
- Jembrana disease
- Vesicular stomatitis
- Contagious bovine pleuropneumonia
- Theileriosis (East Coast fever)
- Salmonellosis
- Necrobacillosis
- Paratuberculosis
- Arsenic poisoning

Small ruminants

- Peste des petits ruminants
- Nairobi sheep disease
- Contagious caprine pleuropneumonia
- Pasteurellosis

Swine

- *Campylobacter* spp.
- *Brachyspira hyodyesntereiae*
- Salmonellosis

Laboratory diagnosis

Samples

- Animals showing a pyrexia are probably viraemic and usually the best source of blood for detecting or isolating virus; take blood from several pyrexic animals
  - sterile whole blood preserved in heparin (10 IU/ml) or EDTA (0.5 mg/ml) and transferred to laboratory on ice (but not frozen); do not use glycerol as preservative transport media as it inactivates RPV
  - blood for serum, although antibodies are unlikely to be detected until the mucosal phase
- Spleen, prescapular or mesenteric lymph nodes of dead animals chilled to sub-zero temperatures for virus isolation
- Full set of tissue samples is advised in 10% neutral buffered formalin for histopathology and immunohistochemistry
  - base of the tongue, retropharyngeal lymph node and third eyelid are suitable tissues
- Ocular and nasal secretions of infected animals during either the prodromal or the erosive phase

Procedures

NB: Because of the restrictions on the distribution of RPV-containing materials, positive control virus or viral antigen are not generally available for these tests.

Identification of the agent

Virus detection and identification using the reverse-transcription polymerase chain reaction (*RT-PCR*)

- This is the method of choice for sensitivity and specificity
- Reverse-transcription real-time PCR (RT-qPCR) is the most sensitive, though traditional RT-PCR can also be used
- Viral RNA can be purified from
  - spleen (not ideal due to its high blood content)
  - lymph node and tonsil (ideal)
  - peripheral blood lymphocytes (PBLs)
  - swabs from eyes or mouth lesions (contingent)
  - whole blood
- Suitable oligonucleotide primers, and basic protocols, are given in the *Terrestrial Manual* chapter on Rinderpest
- The World Reference Laboratory in the United Kingdom (UK), which is also an OIE Reference Laboratory for rinderpest and other morbillivirus diseases, and the OIE Reference Laboratory in France (see OIE website: http://www.oie.int/eng/OIE/organisation/en_listeLR.htm), can advise on use of these techniques for field sample analysis

Virus isolation

- RPV virus can be cultured from the leukocyte fraction of whole blood (heparin or EDTA) or uncoagulated blood
- Virus can also be isolated from samples of the spleen, prescapular or mesenteric lymph nodes of dead animals
  - 20% suspensions (w/v) of lymph node or spleen may be used
- Virus isolation is best carried out on cells expressing the morbillivirus receptor (SLAM). Vero-SLAM lines exist; the B95a lymphoblastoid cell line expresses SLAM and is a sensitive host for RPV

Antigen detection by agar gel immunodiffusion

- Test is neither highly sensitive nor highly specific however is robust and adaptable to field conditions
- Conducted in Petri dishes or on glass microscope slides covered with agar
- Rinderpest hyperimmune rabbit serum should be placed in the central well; control positive antigen is placed in alternate peripheral wells (in the absence of RPV antigen as a positive control, use PPRV, e.g. a preparation of PPRV vaccine virus); negative control antigen is placed in well four
- Reaction area should be inspected from 2 hours onwards for the appearance of clean, sharp lines of precipitation between the wells forming a line of identity with the controls
- Tests should be discarded after 24 hours if no result has been obtained
- Positive results from small ruminants should be treated as having been derived from a case of peste des petits ruminants (PPR) although further testing is recommended given the lack of specificity of this test

Identification of virus-specific antibodies

The competitive enzyme-linked immunosorbent assay

- Due to restrictions on the distribution of the RPV antigen used in this ELISA, it is no longer available

Virus neutralization

- NB Since this test requires the manipulation of live vaccine virus, the VNT can currently only be undertaken in FAO and OIE approved high security laboratories with specific permission to carry out the procedure
- Antibodies are detectable in serum of infected animals at 8-14 days post infection
- The presence of any detectable antibody in the lowest (usually 1:10) final serum dilution is considered to indicate previous infection with rinderpest virus

For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.1.19 Rinderpest in the latest edition of the OIE *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Diagnostic Techniques".

PREVENTION AND CONTROL

Sanitary prophylaxis

- Humane slaughter and disposal of sick and in-contact animals
  - destruction of cadavers; these should be burned or buried
- Strict quarantine and control of animal movements
- Effective cleaning and disinfection of contaminated areas of all premises with lipid solvent solutions of high or low pH and disinfectants as described above; includes physical perimeters, equipment and clothing
- Vaccination against rinderpest is now prohibited
- Fresh meat (which has undergone normal pH changes) and hides pose little risk but for purposes of trade, please refer to the appropriate Chapter and corresponding Articles in the OIE *Terrestrial Animal Health Code*

Medical prophylaxis

- Due to success of GREP, vaccination for rinderpest has been supplanted by surveillance in domestic and wild animals; the later acting as sentinels due to higher susceptibility
  - vaccination of small ruminants with rinderpest vaccine to protect against peste de petits ruminants (PPR) is now prohibited but an effective homologous PPR vaccine is now available to control this disease in small ruminants
- In order to prepare for the possibility of a rinderpest virus release, under the terms of the international sequestration agreement, FAO and OIE, in collaboration with member countries, have developed a strategic plan for the post-eradication era that includes:
  - International contingency plan
  - Designation of a minimum number of Reference Centres/Reference Laboratories
  - Creation of emergency vaccine repositories to maintain preparedness.

CONTROL

Contingency planning

The great success of GREP led the world to a post-eradication era, in which surveillance of livestock and control measures regarding RPV repositories are fundamental. Thus, the creation of national contingency plans that are similar in their procedures represents the necessary next step.

FAO has made available a template to assist in the preparation of RPV national contingency plans in which each step has suggested measures to be adopted.

For more detailed information regarding vaccines, please refer to Chapter 3.1.19 Rinderpest in the latest edition of the *OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* under the heading "Requirements for Vaccines".

For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE *Terrestrial Animal Health Code*.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Scientific and Technical Department (scientific.dept@oie.int). Last updated January 2020