PicoRNAviridae

The Family **Picornaviridae** includes a large number of viruses. The family is so named because the viruses are small in size and contain RNA.

Enterovirus

- Porcine encephalomyelitis
- Swine vesicular disease
- Avian encephalomyelitis
- Avian nephritis
- Duck hepatitis
- Turkey viral hepatitis

Aphthovirus

- Foot-and-mouth Disease (Aphthous fever)

FOOT-AND-MOUTH DISEASE

(Commonly k.a. : **Aphthous Fever**)

Foot-and-mouth disease (FMD) is an extremely contagious, acute viral disease of **all cloven-footed / cloved-hoofed animals** *(feet divided into 2 parts)*, characterized by fever and vesicular eruption in the mouth and on the feet and teats (udder). It is rarely fatal except in very young animals.

However, because of the speed with which it spreads, the trade sanctions imposed on countries in which it occurs, and the loss in production by affected animals, FMD is one of the world's most important animal diseases. Government of India has also launched a FMD Control program (FMD-CP) for control of this.

CAUSE / ETIOLOGY

The disease is caused by an aphthovirus, which is a non-enveloped, single stranded RNA (**ssRNA**) virus, with strong epitheliotropic features. The disease occurs in cloven-hoofed animals, the most important being **Cattle, Sheep, Goats, and Pigs**.

Wild cloven-hoofed animals, including deer, antelope, wild boar/ pigs, camel, wild buffalo, bison, elephant, yak, llama and giraffe are also susceptible to natural infection.

The virus occurs in seven principal antigenic types. These are designated in the international nomenclature as O, A, C, SAT 1, SAT 2, SAT 3, and Asia 1 ('O' from the department of Oise; 'A' from Allemagne, 'C' from a revised classification; and SAT 1, SAT 2 and SAT 3 from South African Territories).

Out of 7 types, namely, **O, A, and Asia 1 are prevalent in India**. In cattle, type O is the predominant type, followed by Asia 1.

SPREAD

- Infection is spread mainly by the air-borne route.
- Direct contact between infected and susceptible animals, especially by inhalation of infectious aerosols.
- Direct contact of susceptible animals with fomites (hands, footwear, clothing, vehicles, etc.). The virus may be transported on the shoes or clothing of humans, in or on the bodies of migratory birds or animals, and in such products as raw hides, milk, bedding, and forage (i.e., fodder).
- Ingestion of contaminated milk (by calves)
- Consumption (primarily by pigs) of untreated contaminated meat products (swill feeding).

An important feature is Extreme Infectiousness of the virus, and the ease with which it is carried. Recovered cattle can carry the virus for periods of up to 2 years, and recovered sheep may carry it for up to 6 months.

Morbidity may approach 100%. Mortality in general is low in adult animals (1–5%) but higher in young calves, lambs and piglets (20% or higher).

PATHOGENESIS

Incubation period is as short as **2-3 days** in close contact and as long as **10-14 days** from windborne infection. Virus is usually acquired by inhalation via air-borne route.

After entry, the primary viral replication occurs in the pharynx or respiratory tract. Once infection gains access into the bloodstream (viraemia), the virus is widely disseminated throughout the body, **probably in mononuclear cells**, and produces lesions, chiefly in epithelial tissues. Almost 24 hrs after infection, virus begins replicating and virus is excreted in high quantities in expired air, in all secretions including milk, and from ruptured vesicles.

Gross lesions often develop at pressure points ,in areas subjected to mechanical trauma, or unusual physiological conditions, such as the epithelium of the mouth and feet, and to a lesser extent, the teats.

The specific effects are **limited to the epithelium at the site of predilection,** particularly the skin epithelium of mucosa, feets and teats. The lesion begins as a localized **"balloon degeneration"** of cells in the middle of the **stratum spinosum** of the epithelium. The inter-cellular prickles are lost, and the epithelial cells become round and detached from one another. Their cytoplasm takes an intensely eosinophilic stain, and their nuclei are pyknotic.

Oedematous fluid containing bits of fibrin accumulates between the cells and separates them. Neutrophils infiltrate the epithelium at this stage. **Liquefactive necrosis** and accumulation of serum and leukocytes produce vesicles.

The **VESICLES are roofed over by the compressed stratum corneum, lucidum, and granulosum, and extend down to the basal layer,** which usually remains in place over the heavily congested dermis.

These small vesicles (aphthae) coalesce to form large vesicles (**bullae**), which cause large areas of epithelium to be easily shed or rubbed off. Loss of epithelium is most common on the dorsal surface of the anterior two-thirds of the bovine tongue, leaving a raw, red surface that oozes blood.

The pain from this denuded area explains the severe anorexia.

In young animals, the virus reaches myocardial muscle cells, usually causing hyaline degeneration and necrosis of cardiac muscle cells leading to **necrotizing myocarditis** (Tigroid heart necrosis).

SIGNS

In typical field cases in cattle, the onset begins by a sudden fall in milk yield and a high fever (104° - 106° F), Shivering, accompanied by severe dejection and anorexia, followed by the appearance of an **acute painful stomatitis**. The signs are directly related to the lesions.

Viral effects in the oral mucosa produce excess salivation (hanging in long ropy strings - drooling) and make eating painful and animal refuses food and water.

Vesicles and bullae (1-2 cm in diameter) appear on the **buccal mucosa**, and on the **dental pad and the tongue**. These rupture within 24 hours, leaving a **raw painful surface**. **Smacking (opening and closing) of the lips and tongue, Grinding of the teeth, Drooling Saliva** is characteristic.

Along with the oral lesions, vesicles also appear on the **feet**, particularly in the clefts & on the coronet, Claws & Coronary bands subsequently the erosive painful lesions causing stamping or kicking of the feet. Rupture of the vesicles causes acute discomfort and produces **Lameness**. The animal is often recumbent, with a marked, painful swelling of the coronet.

Vesicles may occur on the teats, the vulva, and the conjunctiva. When the teats orifice is involved, severe mastitis often follows.

Secondary bacterial infection may interfere with healing.

Young calves and lambs are more susceptible than adults, and during outbreaks, heavy mortality may occur in them as a result of **severe myocardial damage**, even when typical vesicular lesions are absent in the mouth and feet.

(Sequel remarks) *(consequence)* Important sequel to the FMD infection are

1. **Abortion and subsequent infertility are common sequels.**
2. **Very rapid loss of condition and fall in milk yield occur during the acute period**.
3. A sequel to FMD in cattle, probably due to **endocrine damage**, is a chronic syndrome of Dyspnoea, Loss of heat control '**panters**' ; lack of heat tolerance (panting);, overgrowth of **HAIRS**, and Anaemia

LESIONS

The specific lesions in their early stages are microscopic, and are **limited to the epithelium at the site of predilection**. The lesion begins as a localized "**balloon degeneration**" of cells in the middle of the **stratum spinosum** of the epithelium

In cattle, the distribution of vesicular lesions is characteristic.

Vesicles or blisters in mucosa over the **lips, dorsum of the tongue, and hard & soft palate**, dental pad, gums, cheek are severely involved, and also over nostrils & muzzle.

Lesions occur in the skin and ear, the **coronary band adjacent to the inter-digital space**, teats, udder, snout of pigs, corium of dewclaws and interdigital spaces

The conjunctiva may be affected

Erosions in Forestomach **lined by squamous epithelium** , on the **Rumen Pillars** at post mortem is seen and sometimes in reticulum, omasum too. Mucosa of the abomasum and small intestine may show **punctate haemorrhages**, or diffuse Oedema. The mucosa of the large intestine may be hyperaemic and blue-red.

Small epidermal vesicles may also occur in grossly normal skin of the **brisket, abdomen, hock, and perineum**.

The small vesicles (aphthae) over affected areas may coalesce to form large vesicles (**bullae**), causing larger areas of epithelial erosions and bleeding wounds. Loss of epithelium is most common on the dorsal surface of the anterior two-thirds of the bovine tongue, leaving a raw, red surface that oozes blood.

Gray or yellow streaking in the heart from degeneration and necrosis of the myocardium in young animals of all species ('tiger heart')

Lesions in the myocardium are most common in the fatal disease in very young calves or lambs, but also occur in pigs and young goats. The lesions observed in the **wall and septum of the left ventricle**, and seldom in the atria, appear as small, **Greyish-Yellow streaks** of irregular size, which give the myocardium a STRIPED appearance - so-called "**tiger heart**". Microscopically, hyaline degeneration and necrosis of muscle fibres are accompanied by an intense lymphocytic, occasionally neutrophilic, infiltration.

In the skeletal muscles, lesions similar to those in the myocardium may be observed. Sharply defined areas of necrosis are seen grossly as **grey foci** of various sizes, and microscopically, necrosis of muscle bundles is associated with intense leukocytic infiltration.

ZOONOTIC IMPORTANCE

Disease is zoonotic; In humans, disease is usually mild and limited to appearance of vesicles on the hands, feet, and oral mucosa.

DIAGNOSIS

In differential diagnosis of FMD, it is necessary to consider all the **clinically indistinguishable** Vesicular Diseases first, like:

- Vesicular stomatitis
- Swine vesicular disease
- Vesicular exanthema of swine

FMD has to be differentiated from other diseases, presenting nearly similar lesions:

- Rinderpest (globally eradicated)
- Bovine viral diarrhoea and Mucosal disease
- Infectious bovine rhinotracheitis
- Bluetongue
- Epizootic haemorrhagic disease
- Bovine mammillitis
- Bovine papular stomatitis; Contagious ecthyma
- Malignant catarrhal fever

Samples to be collected for Lab Diagnosis

- ✓ Epithelium from an unruptured or recently ruptured vesicle or vesicular fluid
- ✓ Epithelial samples should be placed in a transport medium which maintains a pH of 7.2–7.6 and kept cool.
- ✓ Where collecting epithelial samples is not possible, blood and/or oesophageal–pharyngeal fluid samples taken by probang cup in ruminants

or throat swabs from pigs provide an alternative source of virus. Probang samples should be refrigerated or frozen immediately after collection

- ✓ Myocardial tissue or blood can be submitted from **fatal cases**, but vesicles are again preferable if present

Laboratory Tests:

1. Reverse-transcription polymerase chain reaction (RT-PCR)
2. Virus isolation: by inoculation of primary bovine (calf) thyroid cells or lamb kidney cells.
3. Antigen detection ELISA – using monoclonal antibody or polyclonal antisera-based assays; used to detect and type FMD viral antigen
4. Complement fixation test – less specific and sensitive than ELISA;

SEROLOGICAL TESTS for FMD are performed in support of four main purposes namely:

1. to certify individual animals prior to import or export (i.e. for trade)
2. to confirm suspected cases of FMD
3. to estimate the prevalence of infection or to substantiate its absence
4. to demonstrate the efficacy of vaccination.

Virus Neutralisation Test The quantitative VN microtest for FMD antibody is performed using cell lines in flat-bottomed tissue-culture grade microtitre plates

Solid-Phase Competition ELISA : used for the detection of antibodies against each of the seven serotypes of FMDV. In place of guinea-pig or rabbit antisera, suitable Monoclonal Antibodies (MAbs) can also be used to detect antigens coated to ELISA plates either directly or after capture by MAbs.

Liquid-phase blocking ELISA: Antigens are prepared from selected strains of FMDV grown on monolayers of BHK-21 cells , identify only coated strains