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Vesicular Diseases in Livestock with Special Reference to Foot and Mouth Disease

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Many vesicular diseases are caused by viruses due to their epitheliotropic nature, which are characterized by formation of vesicles. Vesicles are found on oral mucosa, on the feet, and on the mammary glands of females. They lead to more morbidity but less mortality cases but rather lead to production and thereby economic losses to the farmers. Among vesicular disease FMD is one of the extremely contagious, acute viral disease, mainly of all cloven footed domestic animals (Coetzer et al., 1994), and also occur in wild animals characterized by fever, vesicular lesions and erosions of epithelial cells of mouth, tongue, nares, muzzle, feet and mammary glands (Jamal and Belsham, 2013). This disease leads to myocarditis in young animals, thereby early mortality in calves. It is OIE listed "A" disease because of its economic impact and was the first animal virus to be recognized.

Keywords: Vesicular diseases, Foot and Mouth disease, Virus, Livestock, Oral mucosa.

FMD is caused by *Aphthovirus* grouped under family *Picornaviridae* which is a small (27-28 nm) non-enveloped ss RNA + senseviruswith icosahedral symmetry (Belsham, 1993).This virus as an etiological agent for FMD was first demonstrated by Loeffler and Frosch in 1897. FMD virus shows 7 Serotypes namely O, A, C, Asia-1, SAT-1, 2 and 3 and with multiple subtypes further in these (Bachrach, 1968).The serotypes A, O, C and Asia 1 are prevalent in India with the order of prevalence as O>Asia1>A~C. These serotypes do not show any cross protection among themselves(Leforban and Sumption, 2010).The serotypes A and O were discovered by Valle and Carre (1922), serotype C by Wailmann and Trautwein (1926) and at last the 7th serotype Asia 1 was discovered in Pakistan from buffaloes in 1954 (Brooksby JB, Rogers, 1957). The incubation period of this virus is 2 to 14 days (OIE, 2012).

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Host range

Animals like cattle, buffaloes, sheep, goat, pigs, deer, elephant, llama, alpaca, antelope, hedgehogs, porcupines, kangaroos, guinea- pigs and camels are susceptible. Suckling mice are most susceptible to FMD infection (<14 days old). Horse, donkey, mule, camel are found to be resistant. Many strains show jumping behavior, as many strains infecting the cattle are also seen in deer and wild pigs also (OIE, 2012; Jubb *et al*., 2007; McGavin and Zachary, 2012; Vegad and Katiyar, 2005).

Economic importance

Mortality is higher in young calves, lambs and piglets around 20% -50% and low in adult animals (1-5%), while in susceptible cloven footed animals morbidity is nearer to 100% that's why leads to production losses.

Transmission (OIE, 2012; Vegad and Katiyar, 2005**)**

i. By direct contact between susceptible and infected animals.
ii. Direct contact of susceptible animals with contaminated inanimate objects like clothing, foot wears and vehicles etc.
iii. Intake of infected milk.
iv. Inhalation of infectious aerosols contaminated with virus.
v. As FMD virus can be transmitted through airborne route, can spread to long distances. Pigs are most important source for this spread. (Sellers and Parker, 1969; Donaldson and Ferris, 1980; Alexandersen *et al*., 2002a). This virus can spread up to 300 kilometer through air (Gloster *et al*., 1981, 1982; Donaldson *et al*., 1982a, b; Sorensen *et al*., 2000, 2001).
vi. Virus can come through infected saliva, faeces and urine to the environment and can infect the susceptible population.
vii. There is rare evidence that carrier animals can be the source of infection. This virus usually localizes in oropharynx and persists for 6 months. So, usually the carrier state can remain for 6 months to 3 years in cattle and it is of shorter duration in sheep, goats (6 months) and buffaloes. While pigs do not act as carriers (Hedger and Stubbins, 1971; Alexandersen *et al*., 2002b).

Higher concentration of virus can be observed in other tissues without the presence of any visible lesions (Burrows *et al*., 1981; Zhang & Alexandersen, 2004; Arzt *et al*., 2011).

Clinical signs and gross lesions

The severity of clinical signs depends upon stain of virus, species of the animal, age, breed and individual immune response of the animals. The mortality rate in this disease is less (up to 5%) but high in young calves, piglets and lambs (up to 50%), While, the morbidity can reach up to 100%. Large amount of virus is seen in vesicular fluid but less evidence of virus in faeces (Hyslop, 1965; Scott *et al*., 1966; Parker, 1971; Garland, 1974).

Worldwide Distribution of different serotypes of FMD virus

Region	FMD Serotype
Europe and South America	O, A, C
Asia	O, A and Asia-1
Africa	SAT -1, SAT-2 and SAT-3
Southern Africa	SAT-3
Middle East	O, A, Asia-1, SAT-1

Cattle

High fever (104p -106p F), sudden fall in milk yield, stomatitis which leads to anorexia and long ropy strings of saliva hanging with smacking of lips and tongue which is quite characteristic of this disease (Vegad and Katiyar, 2005).Vesicles on buccal mucosa, dental pad and tongue, when these rupture leads to painful mastication in animals. Vesicles are also seen in feet, mainly in the clefts and coronet which leads to lameness. Vesicle on mammary gland, vulva can lead to mastitis and metritis respectively (OIE, 2012; Jubb *et al*., 2007).Vesicular lesions can extend up to rumen, reticulum, omasum and abomasum. These diseases can lead to abortion in pregnant animals. In calves no vesicular lesions are seen rather extra epithelial lesions are seen in heart i.e. Tigroid heart (necrotizing myocarditis) and acute gastroenteritis which are more dangerous and lead to acute mortality (OIE, 2012; McGavin and Zachary, 2012).This virus can lead to endocrine damage in recovered animals so led to rough coat with long hairs and thereby thermoregulation is affected. These animals with affected thermoregulation are called as **panters**. Animals mostly show recovery within 2 weeks after infection (OIE, 2012; Vegad and Katiyar, 2005**)**.The presence of vesicular lesions on epithelial surfaces can later on lead to secondary bacterial infection and can cause more general complications.

Sheep and goats

Sheep and goats can show pyrexia, oral lesions and lameness but of milder degree. Agalactia is one of the important feature seen in sheep and goats. But in sheep and goats clinical signs are milder and are not much evident as compared to other animals (Donaldson and Sellers, 2000; Alexandersen et al., 2002c; Hughes et al., 2002).

Swine

Fever, hoof lesions on coronary band and inter-digital space are more painful and severe than any other species leads to lameness, oral lesions are not common but snout vesicles are seen. The

S.no.	Species	Acting as host
1.	Goats and sheep's	Maintenance host
2.	Pigs	Amplifier host
3.	cattle	Indicator host

piglets show frequent mortality (Jubb et al., 2007; McGavin and Zachary, 2012).

Microscopic lesions

The epithelial cells become swollen, rounded and loosen shows pyknotic changes in nuclei and acidophilic cytoplasm. The inflammatory exudate get collected between loosen cells. These cells undergo liquifactive changes later on. In some places cells may be denude. The vesicular fluid contains degenerated epithelial cells, erythrocytes and leucocytes (Vegad and Katiyar, 2005; OIE, 2012; McGavin and Zachary, 2012).

Diagnosis

(OIE, 2012; Vegad and Katiyar, 2005)

I. On the basis of history and clinical signs
II. Serological tests: CFT, AGPT, FAT
III. Sandwich ELISA or typing ELISA, RIA, Micro-SNT
IV. Molecular tests: RT-PCR,
V. Nucleic acid hybridization
VI. Nucleic acid sequencing
VII. In-situ hybridization

ELISA is capable to detect viral antigen and its serotypes that's why often preferred over CFT. For virus isolation calf thyroid cells and BHK-21 cell line are used. Virus neutralization test or ELISA are main prescribed tests according to OIE while CFT is used as an alternate test for viral identification (OIE, 2012; Vegad and Katiyar, 2005).

Differential Diagnosis (OIE, 2012)

Vesicular stomatitis, swine vesicular disease and vesicular exanthema of swine are very difficult to distinguish from FMD clinically. So, it is very important to differentiate these diseases from FMD.

Vesicular stomatitis

It is a vesicular disease caused by *Vesiculovirus* member of family *Rhabdoviridae* having two serotypes namely, *New Jersey and Indiana.* It is mainly an acute disease of horse but also have importance in cattle and pigs which is transmitted by vectors Sandflies, Blackflies, Seasonal outbreaks, direct contact with infected animals and contaminated objects. This virus leads to formation of vesicles on mouth, feet, snout and udder. Resemble FMD and not seen in sheep's and goats.

Incubation period of this virus is 3 to 5 days. This virus leads to fever and vesicles formation that resemble FMD lesions. Vesicles rupture to cause profuse salivation and anorexia but recovery may occur within 3-4 days. Most severe signs are seen in Horses, with oral lesions, drooling, champing, mouth rubbing, lameness, and coronary band lesions. In Cattle and pigs vesicular lesions in oral cavity, mammary gland, coronary band, and inter-digital region are seen. Which leads to salivation, lameness and recover within 2 weeks. Gross and histopathological lesions are just similar to FMD.

Pathogenesis
(Alexandersen *et al*., 2003; Arzt *et al*., 2011, Sastry and Rao; 2001**)**
↓
Virus through droplets / ingestion entered into the body
↓
Replication in pharynx or respiratory tract
↓
Invades the epithelial cells and produce degenerative and inflammatory changes
↓
Accumulation of fluid and fibrin leads to the separation of cells
↓
Ballooning degeneration, followed by liquifactive necrosis
↓
Leads to vesicle formation mainly in cells of *stratum spinosum* (middle layer)
↓
Leucocytic infiltration occurs
↓
Virus spread to lymph nodes
↓
Virus through blood spread to other body parts (mucus membranes, vulva, heart, udder and GIT etc.)

Vesicular stomatitis vs. FMD

Vesicular stomatitis less contagious.	FMD more contagious.
Vesicular stomatitis lesions generally found in one area of the body	Can involve many parts of the body.

Comparative overview of different vesicular diseases in livestock (OIE, 2012; Sastry and Rao; 2001)

	Foot and mouth disease	Vesicular stomatitis	Swine vesicular diseases	Vesicular exanthema
Agent	*Aphthovirus*	*Vesiculovirus*	*Enterovirus*	*Calcivirus*
Hosts	Cattle, pig, sheep, guinea pigs, man, wild animals but not in horse	Almost in all animals including horse	Pigs mainly	Pigs and horse
Transmission	Aerosol, direct, indirect, ingestion	insects	Contaminated meat consumption	Uncooked pork ingestion and garbage ingestion
Lesions	Vesicular lesions in mucus membranes and lesions in heart	Vesicular lesions without lesions in heart	Lesions like FMD	Lesions like FMD
Morbidity and mortality	Morbidity 100% while mortality <1%	Morbidity up to 90% while mortality is low	Both mortality and morbidity are low	Morbidity varies up to 100% while mortality is low
Samples to be collected	Esophageal pharyngeal fluid (cattle) or throat swab (pigs), serum and blood in proper preservatives and tissues in 10% formalin.	Vesicular fluid collection aseptically and frozen	Vesicular fluid collection	Vesicular fluid collection, serum and unclotted blood

Swine vesicular disease virus/Porcine enterovirus infection (OIE, 2012)

It is a contagious disease of pigs characterized by fever, vesicular lesions and is caused by *Enterovirus* member of family *Picornaviridae*. This disease is transmitted by direct or indirect contact with infected animals or feces and contaminated environment, ingestion of contaminated pork, virus excreted from nasal or mouth secretions. It is mainly a disease of pigs with high morbidity but can lead up to 10% mortality in piglets. This disease also resemble with FMD but less severe than FMD. Post-infection protective antibodies are produced in this infection. This virus leads to fever (104p -105p F), vesicles and erosions on snout, mammary glands, coronary band, and inter-digital areas. Vesicles on the coronary band of the claws especially at the heel are almost characteristic which leads to lameness.

Vesicular exanthema of swine (OIE, 2012)

It is an acute, febrile contagious viral disease of swine characterized by formation of vesicles on the snout, around the mouth and on the feet. It is very difficult to distinguish this disease clinically from foot and mouth disease, vesicular stomatitis and swine vesicular disease.This disease is caused by *Calicivirus*.Although it is a mild disease with low mortality rate but in affected pigs, heavy weight loss can occur. Leads to abortion in pregnant sows and lactating sow become dry.

This disease is often transmitted by direct contact, oro-nasal and lachrymal secretions, urine, faeces, insemination, blood transfer feeding of raw or insufficiently cooked meat. Vesicular lesions occur on the snout, around the mouth and on the feet, accompanied by fever, variable anorexia and malaise. Vesicles can also be seen on the udder and teats of nursing sows. A vesicle on rupture leads to erosive areas. Morbidity is around 100% with no significant mortality.

FMD v/s other similar diseases

i. Rinderpest: It is systemic disease with high mortality, severe leucopenia, necrotic and ulcerative stomatitis, and absence of vesicles, only small greyish-white punctate present, and diarrhea.

ii. MCF: Shows necrotic stomatitis, kerato-conjunctivitis, head and eye form, lesions most prominent on muzzle.

iii. Bluetongue: Foot lesions (coronitis and

Some other diseases to be distinguished from FMD:

S.no.	Species	Disease
1.	Swine	Vesicular stomatitis, Swine vesicular disease, Vesicular exanthema of swine
2.	Cattle	Rinderpest, IBR, BVD, MCF, Bluetongue
3.	Sheep	Bluetongue, contagious ecthyma

laminitis) without vesicles.

iv. BVD: Severe diarrhea, erosive oral lesions and high mortality.

v. Foot rot: Foot lesions present causing lameness but vesicles absent.

Prevention and control (OIE, 2012)

i. Provide sanitary conditions to the animals.

ii. Quarantine measures are to be followed.

iii. Slaughter and stamping out policy is taken care of if necessary.

iv. The free movement of animals in herd should not be allowed.

v. The carcass, beddings and infected materials should be disposed of very cautiously.

vi. This virus can be inactivated at temperature more than 50 ^{O}C and at a pH 9. Many chemical disinfectants like sodium hydroxide (2%), sodium carbonate (0.2%) and sodium hypochlorite (3%) are quite effective.

vii. Since 2003 onwards, Project Directorate on FMD, ICAR and Government of India harmonized the strains used for vaccine production in India. The serotypes O (Vaccine strain O IND R2/75), A (Vaccine strain A IND 40/00) and Asia 1 (Vaccine strain IND 63/72) were used for vaccine. The serotype C strain was discontinued since October 2003.

CONCLUSION

FMD is one of the most contagious animal disease which leads to huge economic losses. FMD virus is having wide host range, can spread by different means and having many serotypes (7). All these factors often increasing the chances of mutation in this virus and can lead to development of new variants. Nowadays, the zoonotic significance of this disease is also posing a threat to public. So, it is foremost step to eradicate or control this disease very critically and cautiously.

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