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Understanding the transmission of foot-and-mouth disease virus at different scales

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Foot-and-mouth disease (FMD) is highly infectious, but despite the large quantities of FMD virus released into the environment and the extreme susceptibility of host species to infection, transmission is not always predictable. Whereas virus spread in endemic settings is characterised by frequent direct and indirect animal contacts, incursions into FMD-free countries may be seeded by low-probability events such as fomite or wind-borne aerosol routes. There remains a void between data generated from small-scale experimental studies and our ability to reliably reconstruct transmission routes at different scales between farms, countries and regions. This review outlines recent transmission studies in susceptible host species, and considers new approaches that integrate virus genomics and epidemiological data to recreate and understand the spread of FMD.

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Characteristics of foot-and-mouth disease

Foot-and mouth disease (FMD) affects cloven-hoofed animals (including cattle, sheep, goats and pigs), and is caused by an RNA virus (FMDV) in the family Picornaviridae. Characteristically, vesicles develop, especially in epithelia around the mouth, feet and mammary glands. Case-fatality is usually low except in young stock, but productivity losses and costs associated with control can be substantial [1]. The disease is highly contagious, and the potential for infection of different domesticated and wildlife hosts, not all of which show obvious signs of disease, is a further challenge to control [2]. FMDV exists as seven discrete serotypes, and the disease mainly occurs in Africa and Asia, with global distribution mirroring poverty and livestock density [3•]. New virus strains evolve and emerge regularly and give rise to successive waves of infection, which sometimes spill over into FMD-free regions. Vaccination with killed vaccines is used on a large scale but the immunity induced is short lived and is serotype and sometimes strain specific [4•].

During acute infection, transmission is facilitated by virus shedding from ruptured vesicles and in bodily excretions and secretions, including breath, milk and semen [5] (Figure 1). Susceptible ruminants can be infected by very low doses of inhaled virus through direct contact with the breath of other acutely infected animals, or indirectly by resuspension of aerosols from contaminated materials. Pigs are relatively resistant to FMDV infection via inhalation routes [5]. Other routes of infection such as ingestion or through abrasions require a higher dose of virus. Depending on conditions, FMDV can survive for days to months in the environment and in various animal products including meat [6]. There is a rapid immune response to infection associated with FMDV clearance, but some ruminant hosts continue to harbour virus, becoming carriers with low and declining levels of FMDV in specific nasopharyngeal epithelial sites [7] and associated lymphoid tissues [8].

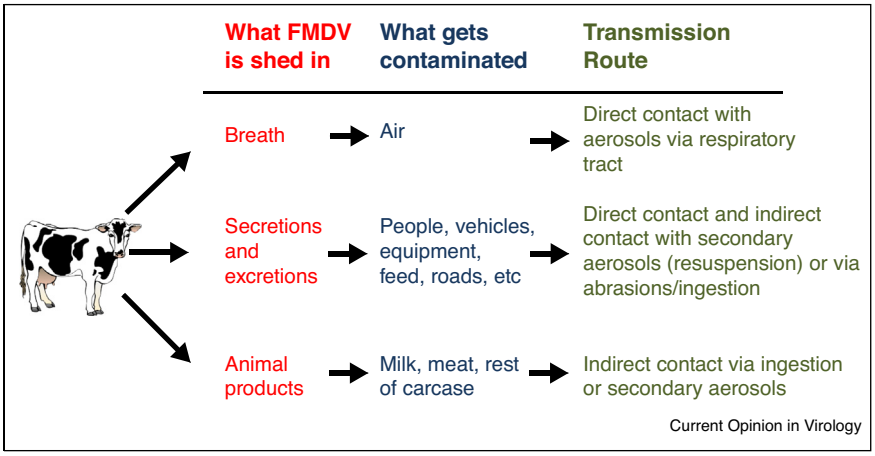
In the absence of obvious epidemiological links between infected animals, FMDV incursions into FMD-free countries must often be explained by low-probability events. This gives rise to the reputation of FMD as one of the most infectious diseases. A classic example was the long distance wind-borne spread of FMD to the Isle of Wight in the South of England in 1981 from a pig farm on the North French coast [9]. This contrasts with disease circulation within epidemics, or in and between countries where FMD is endemic, where spread occurs most readily via more predictable routes due to direct contact between animals and via traded animal products.

A challenge is to understand, quantify and model the multiplicity of different transmission routes possible for FMD at different scales in order to predict the disease's spread and the likely impact of control measures.

Experimental studies of transmission

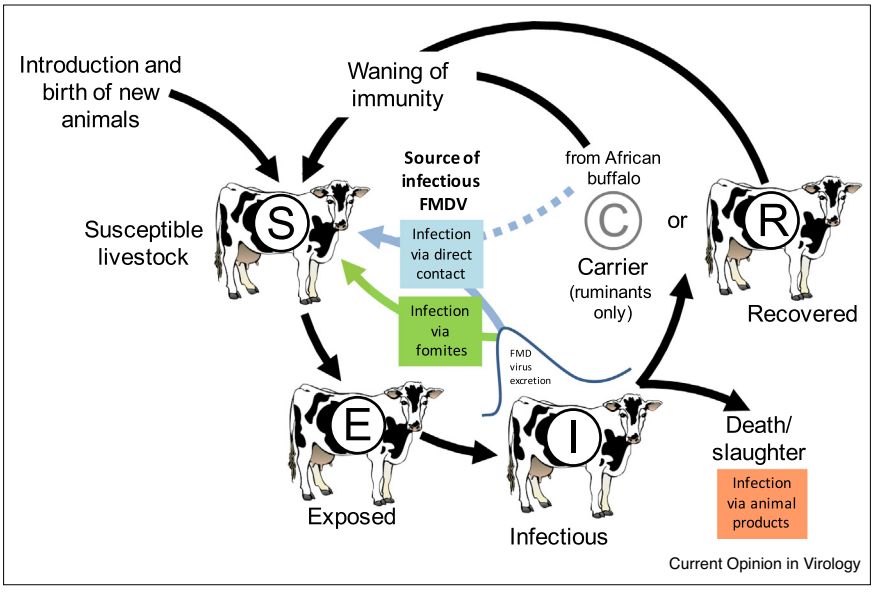
Experimental studies under controlled conditions have contributed enormously to our understanding of the pathogenesis and transmission dynamics of FMD (Figure 2), including sites of virus replication and persistence, incubation and shedding periods, minimum infectious doses by various routes, the nature and impact of the

Figure 1



Principal routes by which infectious FMD virus can be spread between susceptible animals (reviewed in [5]).

Figure 2



A simple S (susceptible), E (exposed) I (infected) and R (recovered) model describing cycles of FMDV replication and transmission in livestock. Susceptible animals can be infected via direct contact with infectious animals, through ingestion of infected animal products, via exposure to inanimate objects contaminated with FMDV (fomites), or through ingestion/aerosol contact with infected animal products. The period of infectiousness broadly correlates with the expression of clinical signs, although precise timing of these events has been observed to vary in experimental studies with different host species, infection models and FMDV serotypes.

immune response and differences between host species [5,10,11,12•]. It is important to recognise that these studies predominately focus on experimental infection in cattle, and consequently, transmission studies for other domesticated hosts (pigs, small ruminants and Asian buffalo) are under-represented in the literature. Furthermore, controlled studies with dangerous pathogens in animals are constrained by ethical, biosecurity, capacity and cost considerations. Small-scale studies lack the power to quantify low probability transmission routes, such as from fomites, contaminated feed or carriers. Thus, it is often difficult to quantify the force of infection arising from different transmission opportunities that may occur in the field and hence to recognise those of most importance under different circumstances.

A common difficulty for experimental studies is reconciling the need to design challenge models that reflect real-life