Acta virol. **27** : 371—375, 1983

DIFFERENTIAL SIGNIFICANCE OF EPIZOOTOLOGICAL FACTORS IN THE CONTROL OF FOOT-AND-MOUTH DISEASE. A BRIEF REVIEW

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Received August 15, 1982

Summary. — The discovery of respiratory tract involvement in the pathogenesis of foot-and-mouth disease (FMD) and the recognition of the role of inhaled aerosols in virus transfer opened new outlooks in the epizootology and prophylaxis of the disease. Nevertheless, FMD should be regarded for an infection transmitted by contaminated passive vectors including man and stable equipment. Transient persistence of FMD virus in the upper respiratory airways of cattle is of interest, but there is no reason to consider this for a significant hazard. Regular annual immunization with a vaccine containing the most isolated virus serotypes seems to be the best way how to prevent epizootics and panzootics.

Key words: *foot-and-mouth disease virus*; *virus transfer*; *pathogenesis*; *epizootology*; *vaccination*

The foot-and-mouth disease (FMD) has still remained world-wide the most important and for economic reasons the most meaningful animal disease. Despite of all progress, FMD is the subject of intensive research, concentrating to further improvement of its prophylaxis and aiming at its eradication. Recently, due to analytic approach, the epizootology of this virus infection has experienced certain alterations.

In the first instance the involvement of respiratory tract in the pathogenesis of FMD was discovered. In contrast to the older view that the predominantly epidermotropic FMD virus enters the body via mouth cavity and that the site of its primary attachment is the epithelium of oral mucosa, recent detailed investigations in ruminants have pointed at the essential participation of respiratory epithelium as a portal of entry. It was shown that to infect cattle — the most susceptible species for FMD virus — by oral route, about 10^5 more virus is needed than for intranasal infection (Sellers 1972; Terpstra 1972). In swine — probably for anatomical reasons — the portal of entry is limited to alimentary tract only; hence swine may be less susceptible to FMD virus infection than cattle. In respect to this, the virus-containing aerosol formed in the inhaled air has recently been recognized to represent the source of infection (Sellers, Parker 1972; Sellers *et al.*, 1973). The exhalation of aerosol causes a high accumulation of virus in the stable air. In addition, the usual high relative humidity of the stable-atmosphere contributes to a stability of the agent. It can be assumed that the virus-enriched aerosol in the stable air substantially facilitates the quick infestment of all livestock (nearly 100% morbidity).

Persons handling the FMD-infected animals also inhale the virus via respiratory tract. The agent can be temporarily isolated from the naso-pharyngeal washings. Even a man to man transfer by aerosol was observed. When the tested person had been staying first in the infected environment and then in another room, the virus was isolated from nasopharyngeal washing of the addressed person (Sellers *et al.*, 1970; Sellers *et al.*, 1971). This interesting finding of the appearance of FMD virus in the respiratory tract of extremely exposed persons is certainly of higher theoretical than practical importance, but confirms the role of virus-containing aerosols in the direct transfer of FMD.

The virus-containing aerosol is important not only for direct contact infection, but it may represent an indirect transmission factor in the spread of infection either from stable to stable or from herd to herd and under certain conditions also for larger distances (Barlow 1972; Barlow and Donald 1973). It seems that FMD virus-containing aerosols from sick animals may be blown by the wind more than 100 km away. Investigations on the stability of FMD virus in aerosol droplets showed that the virulence had remained unchanged at temperature of 20 °C and relative humidity of 60% (Donaldson and Ferris 1975). The virus is more stable in aerosols composed of larger droplets ($\geqq$ 6 µm) than in those containing smaller droplets as the former reveal numerous virus aggregates. During the night in absence of UV-radiation, the virus survives in humid atmosphere for many hours. The uptake of infected aerosols to susceptible animals is accomplished by inhalation or licking, whereas stabled animals are less endangered by wind than those in the meadow. At lower relative air humidity the virus is sooner inactivated. Aerogenic transfer is therefore rare in hot and dry tropical countries. On the other hand, conditions favouring the virus survival in aerosols better co-incide at the seashore (Donaldson *et al.*, 1982; Gloster *et al.*, 1982). The transfer of FMD for a far distance to oversea, occasionally observed in the time of autumn windstormes, may be better explained this way than by the earlier supposed transfer via planctone.

FMD represents a typical indirectly transmitted infection: as evidenced by the history of fighting FMD epizooties, direct contact have always been of limited significance. The newly discovered transfer of the virus via aerosols and/or contaminated dust blown away by wind seems to be a less effective mode of spread among other indirect transmission factors already known for a longer period of time. It would be over the scope of this brief report to discuss the manyfold passive vectors (Röhrer and Olechnowitz 1980). They are known since long and influence considerably the measures to fight the disease. Minimal quantities of the agent mechanically adhering to vectors or suspended in them coming into direct or indirect contact with susceptible animals are essential for the spread of infection. The easy transmissibility of FMD virus is the reason of its high infectivity exceeding many other viruses. The high attachment efficiency, invasibility and reproduction capacity of FMD virus can explain the explosive secondary outbreaks. Because the infected animals secrete and excrete great amounts of the virus before or at the onset of clinical symptoms, objects of all kind present in the stable — including clothing of the animal attendance and of other persons which came in contact with them — as well as working kits of all kind, transportation vehicles and sewage may be contaminated and can transfer the agent from the stable before the herd has been declared infectious. A very special problem is the handling of milk and its transport. Along with unanimated vectors also living passive vectors should be taken in account, namely domestic animals in the farm not susceptible to the agent as poultry and probably other birds as well. It remains unclear to which extent the migration of birds could be responsible for passive transfer of FMD virus to far distances (Murton 1964; Sard 1978). As the migration of birds and the occurrence of outbreaks do not coincide, such a possibility finds no support. The notion repeatedly mentioned in English literature that migrant birds introduced FMD to British Islands which had previously been free of the infection should be reconsidered because during either World Wars the islands remained devoid of any epizootic although the continent was heavily infested. To explain the occasional occurrence of FMD on British Islands and in other regions for long time free of FMD one must take in account the introduction of virus by personal traffic; it cannot be stressed enough that the main vector of FMD virus is the man. Nearly each secondary outbreak is on his responsibility. In addition to the personnel in the stable and/or of the farm, occasional visitors may contribute as well. Man carries the virus over on his clothing, skin, hair etc.; all this can happen before the epizootics has been recognized. Theoretically, it may be assumed that the source of infection from infected person was the vesicle fluid from the mouth mucosa or from the interdigital skin area. However, man suffer rarely from overt FMD. Even subjects who were in continuous contact with the virus for occupational reasons become ill only exceptionally either after exposition to high virus doses or because of their high susceptibility. Such persons rather undergo inapparent infection which develops in a certain percentage as indicated by appearance of specific serum antibodies. It must be anticipated that persons exposed to continuous inhalation of virus-containing aerosols acquire inapparent infection (Röhrer and Olechnowitz, 1980).

The described data clearly reveal the manyfold variability of transfer opportunities and in turn point to the difficulties which should be overcome by the epizootologist tracing the reservoir of the primary outbreak. The possible role of virus carriers, in addition to indirect vectors, has been repeatedly discussed in this respect. The problem had emerged already in the beginning of FMD research because of its enormous epizootologic significance, but recently it has been regarded for only a theoretical question, because continuous virus shedding was not in accordance with the results of ad hoc designed trials. These investigations had repeatedly shown that already a few days after bursting of vesicles no virus transfer can occur upon contact with acutely sick animals. This is in accordance with the experience that quarantine of infested farms can be cancelled 21 days after healing of lesions without any danger of virus spread. However, a thorough final disinfection is inevitable to interrupt the possible persistence of dried virus attached to dirt particles. To avoid late shedding, careful removal is obligatory of claws always participating in pathogenetic process. In the cornified layer between epidermis and the rest of horny substance virus particles may accumulate; being shed during the growth of the claws (Brandt 1928; Brandt 1958) they simulate persistent infection. Recent discussion on persistent virus shedding in FMD was evoked, however, by other findings. Not far ago, FMD virus has been recovered from nasopharyngeal washings at least in a certain percentage of convalescent ruminants: within several weeks or even months after recovery the number of virus carriers decreased (Bekkum *et al.*, 1959; Burrows 1966; Burrows 1967; Sutmoller and Gaggero 1965; Sutmoller *et al.*, 1968). The main site of persistence was the pharyngeal mucosa, tonsils and dorsal gingiva (Graves *et al.*, 1971). Of cardinal epizootologic importance is the finding that the persistently shed FMD virus has gained properties different from the wild type virus (Kaaden *et al.*, 1970). The recovered virus is non-infectious for highly susceptible cattle (Weyhe 1966). It shows antigenic differences when compared to wild type virus by complement fixation and lower replication efficiency in cell culture. The role of bovine enterovirus, often occurring in the nasopharynx of cattle, in the persistence of FMD virus is unclear. Phenotypic mixing of bovine enterovirus with the RNA of FMD virus has been reported (Sutmoller *et al.*, 1971); this allows the FMD virus RNA to enter cells displaying receptors for bovine enterovirous. Interestingly, in such cases FMD virus can be isolated from the blood devoid of specific antibodies. More detail investigations on the relationship between bovine enterovirus and FMD virus are lacking.

The results of transient FMD virus persistence in convalescent cattle rised great interest among veterinarians especially in countries which have remained spared of infection either due to their geographical position or to the efficient control measures against virus spread. Such countries recently ask a certificate from the country of origin testifying that the imported cattle underwent testing for FMD virus presence. This demand — at first glan ce exaggerated — can be understood facing the great risk threatening unprotected domestic cattle in recipient countries. Based on the experience accumulated during many decades in several countries, however, there is no reason to believe that neglecting the virus carriership would cause a significant hazard (Röhrer 1967). No support is available for assumption that persistent shedders are responsible for repeated outbreaks of FMD in infection-free periods. No data confirm the persistence in and shedding form carriers of the virulent FMD strains. In first instance, out of manyfold associations, the mechanical transfer of the agent by vectors is most striking. To interrupt this chain is the cardinal task in fighting against FMD. This demand was fulfilled at best, if all herds of cattle were regularly annually immunized with a vaccine, currently produced with respect to the antigeni drift and virulence of the virus. In last ten years, this experience was made in most European countries.

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