Introduction and History of Foot-and-Mouth Disease Virus

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1 Introduction .................................. 2
2 The Virus ................................... 3
3 Serotypes .................................... 3
4 Genotypes ................................... 4
5 The World Reference Laboratory .............. 4
6 Transmission and Spread of FMDV ............. 5
7 Other Viruses Causing Vesicular Lesions .......... 6
8 Vaccination .................................. 6

References ....................................... 7

Abstract Foot-and-mouth disease (FMD) has been recognized as a significant epidemic disease threatening the cattle industry since the sixteenth century, and in the late nineteenth century it was shown by Loeffler and Frosch to be caused by a submicroscopic, filterable transmissible agent, smaller than any known bacteria. The agent causing FMD was thus the first virus of vertebrates to be discovered, soon after the discovery of tobacco mosaic virus of plants. It was not until 1920 that a convenient animal model for the study of FMD virus was established by Waldmann and Pape, using guinea-pigs, and with the later development of in vitro cell culture systems for the virus, the chemical and physical properties of FMD virus were elucidated during the remainder of the twentieth century, culminating in 1989 with a complete description of the three-dimensional structure of the virion. FMD virus is classified as a species in the Aphthovirus genus of the family Picornaviridae. The virus is acid labile, and the genome RNA contains a characteristic tract of polyC located about 360 nucleotides from the 5' terminus. Seven main serotypes exist throughout the world, as well as numerous subtypes. The World Reference Laboratory for FMD is located at Pirbright, Surrey, UK and undertakes surveillance of FMD epidemics by serotyping as well as by genotyping isolates of the virus. A major epidemic of FMD occurred in the UK in 2001 and was caused by a virulent strain of FMD virus with
Foot-and-mouth disease (FMD) is of great antiquity, and written records date back to a description of the disease by a monk, Hieronymous Fracastorius, who in 1546 described an epidemic which occurred in cattle near Verona, Italy. The disease became notorious as a perennial threat to the cattle industry over subsequent centuries, but it was not until the late nineteenth century that the pathogenic agent was discovered by two former pupils of Robert Koch, who were responding to a commission set up by the German government to discover the cause. Friedrich Loeffler and Paul Frosch worked originally in Greisswald but moved the project in 1909 to the island of Insel Rheims, in the Baltic Sea, where it was felt that work on FMD could be carried out without danger to livestock on the German mainland. The commission on FMD had been set up with the aim of producing a vaccine to prevent the disease, and Loeffler and Frosch took lymph fluid from vesicles caused by FMD and proceeded to filter the material through bacteria-proof filter candles in the hope that the infectious material would be retained, leaving behind an anti-toxin which could be used to confer passive immunity to healthy animals.

They were amazed when inoculated calves developed characteristic disease symptoms, and they were able to show that something had passed through the filter candles which was able to multiply in the infected animals. Loeffler and Frosch published their findings in four separate documents and a summary between 17 April 1897 and 12 August 1898, which were sent to the Minister of Culture. In the first report they stated, “Even the trial results show reliably that a bacterium which grows on a conventional substrate cannot be the etiological agent in FMD”. The second report claimed that immunization against FMD was possible, and in the third report they concluded that the FMD agent “was small enough to pass through the pores of a filter which is impermeable to the tiniest known bacteria, so small, that even the best modern immersion system renders the agent unidentifiable under our microscope”, which constituted the first description of a virus disease of animals (Loeffler and Frosch 1897, 1898). This was after D.I. Ivanovski had shown that the agent of tobacco mosaic disease would pass through a bacteria-proof filter candle,(Ivanovski 1892) but before Beijerinck devel-