1. Foot-and-Mouth Disease

Foot-and-mouth disease (FMD) is an acute, highly contagious viral infection of cloven-hoofed domestic animals and wildlife, easily transmitted by direct and indirect contact as well as by aerosol. The disease has not only significantly inhibited livestock industries in infected countries but has also resulted in widespread international trade restrictions against animals and products originating in such countries. An outbreak of FMD in Canada would be a national disaster.

1.1 Etiology

FMD virus is a member of the *Picornaviridae* family of RNA viruses. There are seven immunologically and serologically distinct types of FMD virus (A, O, C, Southern African Territories (SAT1, SAT2, SAT3), and Asia 1) with many strains. There is no cross protection between different serotypes, and cross protection is limited within serotypes.

1.2 Susceptible Species

FMD has a wide host range in both domestic and wild cloven-hoofed animals including cattle, swine, sheep, goats, deer, elk, antelope, bison, and water buffalo. Elephants are also susceptible. Llamas and alpacas have a high natural resistance to infection. Some will develop mild clinical signs following direct contact with infected cattle, but will not transmit FMD to other camelids under field conditions. Horses are also resistant.

Experimentally, other species including mice, rats, guinea pigs, rabbits, embryonating chicken eggs, and chickens may be infected, but they are not implicated in the spread of FMD.

1.3 Global Distribution

FMD is present in many areas of the world, with the exception of countries in North and Central America (north of Panama), Australia, New Zealand, Chile, and the European Union (EU). In North America, FMD was last reported in 1929 (USA), 1952 (Canada) and 1954 (Mexico). The EU adopted a non-vaccination policy in 1991 when the disease was brought under control. Recent, acute outbreaks in Taiwan (1997, 2000), Japan (2000), Korea (2000, 2002), South Africa (2000), Argentina (2001), and Europe (2001) have alerted FMD-free countries of the need for permanent FMD awareness. This is due to the continuing FMD threat through illegal imports and global movement.

A copy of the OIE list of FMD-free countries is available at http://www.oie.int/eng/info/en_fmd.htm, and those countries recognized by CFIA as FMD-free are listed at http://www.inspection.gc.ca/ english/ anima/ heasan/ fad/ fmd/ freexe.shtml.

1.4 Epidemiology

FMD is highly contagious. It can spread over great distances through direct contact between infected and susceptible animals, and through indirect contact with contaminated animal products (meat, raw milk, hides), feed, bedding, and inanimate objects (fomites). Large amounts of virus

will be present in tissues, excretions, and secretions (including milk, blood, semen, urine and faeces) shortly before the onset of clinical signs in cattle and pigs, and one or two days before the appearance of clinical signs in sheep. Mechanical transfer of infected meat or bones by dogs, foxes or birds is possible. In Canada's 1952 outbreak, a second nidus of infection in April was attributed to contaminated meat bones that were held in a freezer but later carried off by dogs.

Humans can carry the virus on hands, under fingernails, on clothes, on footwear, and on agricultural equipment and machinery. The virus may be introduced from fomites through the skin or mucous membranes by brushes, surgical instruments or orally by ingestion of contaminated feed. Mechanical transmission by insects has never been shown experimentally.

Pigs are important amplifiers of the virus (e.g. on average, one pig may excrete as much virus as 1000 to 3000 cattle, depending on the virus strain).

Concentrations of pigs can generate virus aerosols (plumes) over considerable distances, if environmental conditions are suitable. Airborne survival is favoured by cooler weather and a relative humidity of 60%. The 1981 isolation of FMD virus on the Isle of Wight was attributed to airborne spread over the English Channel (250 kilometres (km)). Prior to this, it was generally accepted that the maximum aerosol spread over land was 10 km. Although they can be dramatic, plumes are usually not important in the spread of the disease.

In the absence of plumes, airborne transmission from cattle and sheep could not be shown experimentally to occur over distances in excess of about 3 km. Simulation studies in Australia demonstrated that the domestic threat of wind-borne spread is low. Similarly, Canada does not have the environmental conditions to promote aerosol spread in large areas of the west. A study has been commissioned by Environment Canada to identify where weather conditions would be favourable to FMD spread.

Pigs are primarily infected by ingestion of infected feed. Cattle are largely infected by inhalation of infected aerosols; this is due to their much larger respiratory tidal volume. Pigs are also relatively resistant to infection by inhalation. Sheep are considered a maintenance host, exhibiting few clinical signs in spite of being infected and shedding virus. The role of sheep in disease outcomes was particularly dramatic during the 2001 UK outbreak of FMD.

1.4.1 Incubation Period

For regulatory purposes, the *OIE Terrestrial Animal Health Code* 2005 cites a standard incubation period of 14 days. The EU Directive 2003/85/EC cites 21 days for incubation in sheep and goats, prior to the onset of clinical signs. In field outbreaks, the incubation period may vary from 2 to 14 days (cattle 3 to 5; pigs 4 to 9) depending on infection dose, strain of virus and susceptibility of the host. In naive animals, it can be as short as 24 hours. Twenty-one days is accepted for animals with a certain degree of immunity; these are cases where the field virus eventually overpowers the immune system. These longer incubation periods are seen in endemic situations or where vaccination is practised.

Spread between farms is characterized by longer incubation, while spread within a farm is more rapid (as short as two days). Logically, one would expect a smaller infectious dose from "between farm" infection than "within farm" infection, hence the longer incubation in cases of between farm infection.

Note: For tracing purposes, during an outbreak in a susceptible animal population (e.g. in Canada), the incubation period may be regarded as 7 +/- 4 days, depending on the individual outbreak circumstances.

1.4.2 Persistence in the Environment

The persistence of FMD virus under various conditions in the environment and in animal products is well documented. Sunlight has little effect on the virus, but desiccation does have an impact. Thus, it is important that disinfected premises be dried out prior to repopulating. (Refer to re-stocking in paragraph 3.8. of this document.) Virus survival times are as follows:

- 26 to 200 days in soil, sacking or straw, depending on climate
- 35 days on cardboard, wood or metal contaminated with blood
- 398 days on fat-contaminated wood
- 48 hours in experimental animal confinement rooms
- up to 2 weeks on wool
- 4 weeks on cow hair
- 14 days in dry manure (8 days in moist manure)
- 34 to 42 days at 12^{o} to 22^{o}C in liquid manure
- 21 days in wash water from pens

FMD virus is most sensitive to changes in pH, and is most stable at pH 7.4 to pH 7.6, but it can survive at pH 6.7 to pH 9.5 at refrigeration temperature (≤40^{o}C). It is readily inactivated at pH values less than 5 or greater than 10.

FMD virus survives almost indefinitely at freezing temperatures. Semen and embryos (unless treated according to the International Embryo Transfer Society protocol) can retain the FMD virus. Destruction of most strains occurs with heating to 56^{o}C for 30 minutes. Temperature conditions for FMD virus destruction in animal products are provided in Appendix 3.

1.4.3 Persistent Carriers

A carrier is an animal from which the virus can be isolated more than 28 days after infection. Ruminants may become carriers, with the virus persisting in the pharynx and dorsal soft palate for up to five years in African buffalo, three years in cattle, nine months in sheep and four months in goats. This carrier state exists in spite of circulating antibodies of natural *or* vaccine origin. It is estimated that the majority (50% to 80%)[6] of cattle will become carriers, regardless of their vaccination status. Pigs do not develop a carrier state.

Field experience has shown that carriers can cause new outbreaks (e.g. SAT2 FMD strain in African buffalo to cattle), but experiments have been unable to reproduce virus transmission from carriers to susceptible animals. This absence of transmission may be because carriers shed much less virus than viremic animals, and the virus may not be accessible (wrapped in mucus). In spite of the absence of experimental research in this area, the potential presence of live FMD virus in vaccinated ruminants has a critical influence on international trade and the debate over vaccine use.

1.4.4 Modes of Introduction and Transmission

FMD can spread directly through the movement of infected animals, indirectly by contaminated animal products or fomites, and by aerosol. A study of over 880 primary outbreaks reported

around the world between 1870 and 1993 shows the relative importance of these transmission methods in initiating an outbreak:

- 66% from meat products
- 22% from airborne sources
- 6% from livestock importations
- 4% from fomites
- 3% from contaminated vaccines (not an issue with the antigens held by the North American FMD vaccine bank)

It is interesting to note that no outbreaks were attributed to the movement of international travellers, except through transporting contaminated fomites or meat products.

Despite the various means of potential transmission, once FMD is introduced into a country, the primary means of spread is directly through movement of infected sub-clinical animals prior to recognition of the disease and by contaminated fomites. Probably 95% of outbreaks are the result of direct contact between infected and susceptible animals.

1.5 Pathogenesis

FMD virus enters the susceptible animal by inhalation (cattle) or ingestion (swine). The virus replicates in the pharynx, spreads through the blood and lymph nodes, which then disseminate the virus to body fluids and epithelial tissues. Following virus replication, vesicles and clinical signs appear, antibody production begins and viremia ends, with a decline in virus titre in tissues and fluids and healing of vesicles. FMD virus has been found in milk and semen up to four days before clinical signs appear. However, most virus is shed at the onset of clinical expression, except in sheep, which may spread the virus one or two days before clinical signs occur.

1.6 Diagnosis

The World Organisation for Animal Health's Terrestrial Animal Health Code defines the occurrence of FMD virus infection as follows:

i) Isolation of the live virus from an animal or product of that animal;

ii) Detection of viral antigen or genome from (an) animal(s) showing clinical signs, or confirmation of an epidemiological link to a confirmed or suspected outbreak of FMD;

iii) Detection of antibodies to non-structural proteins of FMD virus in (an) animal(s) that are not a consequence of vaccination and either clinical signs or epidemiological link to known or suspect outbreak.

FMD diagnosis is based on history, clinical signs, lesions, and laboratory tests. In Canada, control measures may be instituted based on suspicion of the disease, high-risk sample submission, presumptive diagnosis or confirmed diagnosis, depending on the situation at hand.

The North American Animal Health Committee – Control Program for foot-and-mouth disease emergency program, formerly the North American Foot-and-Mouth Vaccine Bank (NAFMDVB),

has defined presumptive and confirmed diagnosis as a basis for communication between countries.

A *presumptive diagnosis* is defined as follows:

1. A CFIA diagnostician has investigated an outbreak; and
2. Has found clinical signs consistent with the disease (a vesicular disease in a known susceptible species) and other epidemiological information also points to the disease; and
3. Samples have been sent to the National Centre for Foreign Animal Diseases (NC-FAD) under the highest priority; and
4. The country has taken action to contain the disease; and
5. In some cases, the country has chosen to eradicate.

A *confirmed diagnosis* is defined as follows:

1. For the index case, viral antigen to one or more of the serotypes of FMD has been identified by the double antibody sandwich ELISA in samples from one or more animals showing clinical signs consistent with FMD or epidemiologically linked to a confirmed or suspected outbreak of FMD, or giving cause for suspicion of previous association or contact with FMD; or
2. The virus has been isolated and identified by NC-FAD; or
3. Antibodies to structural or non structural proteins to FMDV, specific to one or more of the serotypes of FMD that are not a consequence of vaccination; or residual maternal antibodies have been identified in one or more animals with either epidemiological links to a confirmed or suspected outbreak of FMD, or showing clinical signs consistent with recent infection with FMDV or viral ribonucleic acid (RNA) to structural or non structural genes of FMDV.

A confirmed FMD diagnosis will trigger international reporting. The virus must also be sent to the World Reference Laboratory (WRL) for FMD in Pirbright, United Kingdom (UK). Submission to the WRL is important for the determination of the genomic relationship of the "newly isolated" virus relative to other viruses at the WRL. This information is essential for the molecular epidemiology and will also provide indications to the NAFMDVB administrators if the available concentrated antigen(s) are likely to protect against the "new" virus. If not, other vaccine arrangements can be initiated.

Appendix 5 and 6, respectively, refer to epidemiological sampling of herds undergoing depopulation and surveillance sampling during and after an outbreak to establish FMD freedom.

1.6.1 Clinical Signs

Clinical signs in cattle are as follows: salivation, depression, anorexia, and lameness caused by the presence of painful vesicles in the epithelium of the lips, tongue, gums, nostrils, coronary bands, interdigital space, and teats. Fever and decreased milk production usually precede the appearance of vesicles. The vesicles rupture, leaving large denuded areas that may become secondarily infected. Location and severity of lesions may vary with the strain of virus involved. Zebu cattle breeds show milder clinical signs.

Clinical signs and lesions in pigs, sheep, and goats are similar to those in cattle, but milder, especially in sheep and goats. Lameness is the predominant sign in these species. Detailed clinical descriptions for domestic species can be found in reference texts.

1.6.2 Aging of Lesions

Efforts should be made to find the oldest lesions in the herd, and backdate the time of introduction. Aging of lesions is undertaken to determine the date of entry of the virus into the herd. As a guide, unruptured vesicles are 0 to 2 days old; newly ruptured vesicles with epithelial remnants are 1 to 3 days; ruptured vesicles without epithelium or fibrous healing are 3 to 10 days and open lesions with marked fibrous tissues are 7 days or more.

1.6.3 Mortality/Morbidity

The morbidity rate of FMD can be 100%. Mortality in adults is low (5%); but in suckling pigs and lambs, it may approach 75%. Deaths are generally associated with cardiac lesions.

1.6.4 Laboratory Diagnosis

Laboratory tests include the following:

- Double Antibody Sandwich (DAS) ELISA for detection of antigens in epithelial tissue; and/or
- virus isolation and/or detection of specific genetic material by polymerase chain reaction.

Susceptible animals may be inoculated to determine the species tropism. Laboratory tests are essential to differentiate FMD from other vesicular diseases.

Appendix 1 provides a summary of diagnostic procedures at the NC-FAD along with a flowchart for vesicular diseases. Pre-clinical detection of FMD is possible with conventional reverse transcriptase PCR (RT-PCR) or real-time (kinetic) RT-PCR, which will be used after the index case.

1.6.5 Differential Diagnosis

AUSVETPLAN provides a comprehensive list of diseases where signs or lesions are similar to FMD:

- Exotic viral diseases: swine vesicular disease, bluetongue, vesicular stomatitis, rinderpest, peste des petits ruminants, vesicular exanthema
- Endemic infectious diseases: mucosal disease (BVD), contagious ecthyma (ORF), infectious bovine rhinotracheitis/infectious pustular vulvovaginitis, bovine papular stomatitis, malignant catarrhal fever, bovine ulcerative mammalitis, pseudocowpox, dermatophilosis infection
- Dermatitis: scalding, contact dermatitis, photosensitisation
- Phytophotodermatitis: contact with certain plants containing furocoumarins (especially Umbelliferae parsnips, celery, parsley)
- Trauma/Lameness: laminitis, hoof abscess, foot rot, bad floors, new concrete, mud

1.7 Natural Resistance and Immunity

1.7.1 Innate and Passive Immunity

In endemic countries, zebu breeds (*Bos indicus*) exhibit milder clinical signs than introduced European breeds (*Bos taurus*), but both transmit infection. However, resistant species can become infected and transmit the virus. Young animals are usually more susceptible to FMD than adults, unless protected by passive colostral immunity.

1.7.2 Active immunity

Active immunity is conferred by natural infection or vaccination. Cross-protection between strains of FMD virus is variable within the same serotype, and none occurs between different serotypes. Animals can be infected by multiple serotypes and super infected by new FMD strains or serotypes.

1.7.3 Vaccination

Inactivated FMD vaccines have been successfully used in many parts of the world to control and at times eradicate FMD. However, improperly inactivated vaccines have led to the spread of the disease. Therefore, it is necessary to acquire quality vaccines that have been safety tested before being used. A vaccine will stimulate a predominantly humoral immune response and, in cattle, offer good protection against live virus challenge using the antigenically related strain of FMD virus. There is no cross-protection between the seven serotypes. Even within each serotype, there may only be partial cross immunity, as strains have distinct antigenic characteristics. This is particularly true of serotype A.

To achieve maximum advantage from a FMD vaccine, the virus strain used to produce the vaccine must share as many antigenic characteristics with the outbreak strain as possible. Resistance to clinical disease induced by these vaccines wanes rapidly after four to six months, so vaccination must be repeated at intervals to maintain an acceptable protection level.

In the past, North American veterinary authorities had a negative attitude toward FMD vaccination. However, in recent years, environmental and animal welfare groups have expressed concern regarding the traditional approach to eradicating FMD: disposal of carcasses through slaughter. Given the high quality, reasonably priced vaccines that are now available, emergency vaccination has become a viable alternative. Concurrent with this development, the OIE has modernized the guidelines for using vaccines, thus making emergency vaccination more appealing.

1.8 Public Health

Humans can become infected through skin wounds or the mouth lining by handling infected livestock, contacting the virus in the laboratory or drinking infected milk. Infection does not occur through eating meat. These rare infections are temporary and mild, and FMD is not considered a public health problem. Wearing protective facemasks (e.g. N 99) will reduce the probability of infection and disease spread.

More frequently, humans are afflicted with Hand, Foot and Mouth Disease, a vesicular disease caused by Coxsackie virus A16, which is not related to FMD (Picornavirus) in animals.

1.9 Bio-Security

In Canada, veterinarians attending the foreign animal disease training sign a document stating that they will not have contact with susceptible species for five working days. The World Reference Laboratory for FMD and the Lelystad laboratory in The Netherlands are practicing a 72-hour rule. During an FMD outbreak, a delicate balance must be maintained between enforcing long down times following contact with infected species and bio-security concerns. Recent work with types O/UK/35/2001 and O/TAW/97 has shown that the disease was not transmitted to swine when first responders washed their hands or showered and donned clean outerwear (Amass et al, 2003 & 2004) before handling animals. These findings are in contrast to those of Sellers et al, 1970 where showering did not prevent transmission following activities far exceeding what would be expected during a routine veterinary examination.