Control and eradication of viral diseases of ruminants

Lasse Olavi Nuotio
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Abbreviations and definitions

Abbreviations

AGID agar gel immunodiffusion
BHV bovine herpes virus
BLV bovine leukemia virus
BTM bulk-tank milk
BVD bovine viral diarrhoea, also BVD/MD
BVDV bovine viral diarrhoea virus
CAEV caprine arthritis encephalitis virus
CNS central nervous system
cp cytopathic form of BVD virus
CPE cytopathic effect
DNA deoxyribonucleic acid
Decision (in context of EU legislation) Decision of the Commission of the European community
EBL enzootic bovine leukosis
EIA enzyme immunoassay
ELISA enzyme-linked immunosorbent assay
IACS Integrated Administration and Control System (EU-implemented)
IBR infectious bovine rhinotracheitis, also IBR/IPV
ID$_{50}$ infectious dose for half (50%) of target population
IgM immunoglobulin of type M
IPV infectious pustular vulvovaginitis
LD$_{50}$ lethal dose for half (50%) of target population
LR latency-related
LSA lymphosarcoma
MD mucosal disease
MV maedi–visna of sheep
MVV maedi–visna virus
ncp noncytopathic form of BVD virus
PCR polymerase chain reaction
PI persistently infected, used especially in reference to BVD
PL persistent lymphocytosis
RNA ribonucleic acid
RT reverse transcriptase
se sensitivity of a diagnostic test
SIR model Susceptible–Infective–Recovered compartmental model
SN serum neutralization, alternative (inexact) abbreviation for VN
sp specificity of a diagnostic test
SRLV small ruminant lentivirus
VN virus neutralization test
Definitions

**Basic reproduction ratio, $R_0$:** the number of secondary cases generated by one primary case in a totally susceptible population of defined density.

**Explant culture:** tissue transferred from the body and placed in a culture medium for growth.

**Heuristic:** relating to or using a general formulation that serves to guide investigation, or pertaining to the use of the general knowledge gained by experience.

From Putt et al. (1988):

*Infectivity* is the measure of the ability of the disease agent to establish itself in the host. The term can be used qualitatively (e.g. low, medium or high), or it can be quantified using a statistic like infectious dose 50, or ID$_{50}$. This refers to the individual dose or numbers of the agent required to infect half (50%) of a specified population in controlled conditions. It often is expensive or not feasible to determine the actual ID$_{50}$ and the infectivity is expressed using the tissue culture ID$_{50}$ or TCID$_{50}$ as the dimension. Another gauge for infectivity could be the within-herd basic reproduction ratio.

*Virulence* is a measure of the severity of the disease caused by the agent. In a strict sense it is a laboratory term, used to measure the ability of the agent to produce disease under controlled conditions, and often quantified by a statistic known as lethal dose 50, or LD$_{50}$. This means the individual dose or numbers of the agent required to kill half (50%) of a specified susceptible population in controlled conditions.

*Pathogenicity* is an epidemiological term used to describe the ability of an agent of known virulence to produce disease in a range of hosts under a range of environmental conditions.

From Swinton (2002):

**Latent period:** The time from infection to when the individual is infectious to others. Also referred to as the “presheding period”.

**Incubation period:** The time that elapses between infection and the appearance of symptoms of a disease.
Abstract

The monitoring and control of infectious animal diseases, limiting or prevention of their spread and efforts towards their eventual eradication are central tasks of the veterinary civil service. In addition to the cost-effectiveness of prophylaxis over disease and treatment, the animal welfare aspect is also involved. The purpose of this work is to review, describe and assess the available control measures against selected viral infections or diseases of domestic ruminants.

The selected infections or diseases are bovine viral diarrhoea/mucosal disease (BVD), infectious bovine rhinotracheitis/infectious pustular vulvovaginitis (IBR), enzootic bovine leukosis (EBL) and maedi–visna (MV) of sheep. Each is recognized as a significant disease of domestic animals. Decisive control and eradication measures are necessarily based on the biological, veterinary and diagnostic characteristics of the afflictions, as well as on their epidemiology in terms of the intrinsic determinants of the hosts, host–agent relationships and sources and transmission of the infection, and occurrence of these infections or diseases. This information is compiled and presented in the first part of the thesis with special reference to available or possible control and eradication measures. These measures and programmes against the four afflictions employed in major cattle and sheep producing countries in individuals and herds and on national and international levels are outlined and assessed briefly.

In the descriptive part of the thesis the domestic and EU legislation that forms the official framework for disease control and eradication are outlined. The development in the situation concerning these four infections or diseases is described from the early records to date. The first recorded entries of the occurrence of BVD and EBL in Finland date back to the 1960s, those of IBR to the beginning of the 1970s and of MV to the beginning of the 1980s. Large-scale surveillance and health monitoring among dairy, suckler-cow and beef herds and sheep flocks, starting during the first half of the 1990s, enabled the estimation of actual prevalences of these infections and diseases. A common feature of the occurrence of these infections or diseases is that none has had a prevalence of more than an estimated few percent before 1990, and a maximum of 1% since then. This has formed a very favourable starting point for the nation-wide control and eradication measures. The voluntary control programmes or schemes, as well as the official control and eradication measures are described. The successful eradication of IBR and EBL in 1994 and 1996, respectively, and the significant reduction in the occurrences of BVD and MV from 1990 to date, are reported in detail.

The efficacies of the official control and eradication measures and of the actions of the voluntary control programmes or schemes are analyzed further, making use of a heuristic formulation for the infection reproduction number (R), i.e. the number of secondary cases produced by one infective animal. The influence of the measures is resolved into the three components of R: the probability of transmission, frequency of infectious contacts and length of the infectious period, and the impact of the measures on each component is graded on a three-step scale.
The conclusion is drawn that the official measures complemented by voluntary actions for control and eradication have for the most part been adequate. The significance of financial compensation from the state for the costs incurred in the control of notifiable diseases is noted. In the case of BVD the decisive measures for final eradication have only been available since 2004 and their impact will be seen in the next few years. The role of continued surveillance and health monitoring for both overseeing the situation with BVD and MV, and maintaining an IBR and EBL-free status is emphasized.
List of original publications

The present thesis is based on the following original studies, referred to in the text by the Roman numerals I to V


The original articles I, II, IV and V have been reproduced with kind permission from Elsevier.
1 Introduction

Determined disease control in Finland has led to the situation where there are, at least for the present, few important infectious diseases in domestic production animals. Many of the OIE A- and B-list diseases of ruminants have either never been detected in Finland or not for a long time. None of the bovine diseases present, namely paratuberculosis, babesiosis, cysticercosis and malignant catarrhal fever, has a significant prevalence (MMM, 2004). Of the bovine diseases or infections in the OIE other diseases list, salmonellosis, bovine viral diarrhoea, cryptosporidiosis and toxoplasmosis, and infections caused by *Campylobacter jejuni/coli*, *verocytoxigenic Escherichia coli* and *Listeria monocytogenes* have been recorded, but the prevalence of each is either low or insignificant. However, respiratory infections, especially in young animals, caused by bovine respiratory syncytial, corona and parainfluenza viruses are prevalent. The only OIE B-list diseases of sheep and goats possibly present are maedi–visna and scrapie, and of the other diseases listed only infections by *L. monocytogenes*. All three are encountered only occasionally, if at all (MMM, 2004).

The monitoring and control of infectious animal diseases, limiting or prevention of their spread and efforts towards their eventual eradication are central tasks of the veterinary civil service. The cost-effectiveness of disease prevention compared to that of disease and treatment is appreciated on both herd and national economy levels. This is reflected by existing animal health and national food quality programmes, and the comprehensive national and EU legislation concerning infectious animal diseases. The logic of animal disease control has been tabulated by Willeberg (2005, modified):

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Goals</th>
<th>Strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endemic</td>
<td>Determine and reduce occurrence</td>
<td>Control agent</td>
</tr>
<tr>
<td></td>
<td>Prevent spread</td>
<td>Identify and control risk factors</td>
</tr>
<tr>
<td></td>
<td>Reduce impact</td>
<td>Improve resistance</td>
</tr>
<tr>
<td>Sporadic or epidemic</td>
<td>Determine occurrence</td>
<td>Surveillance</td>
</tr>
<tr>
<td></td>
<td>Prevent spread</td>
<td>Strategic vaccination</td>
</tr>
<tr>
<td></td>
<td>Eradicate</td>
<td>Quarantine, movement control, zoning</td>
</tr>
<tr>
<td>Free</td>
<td>Assess and reduce risk of (re)introduction</td>
<td>Contingency plans</td>
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<tr>
<td></td>
<td>Preparedness</td>
<td>Risk mitigation</td>
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<td></td>
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<td>Documenting freedom</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Surveillance</td>
</tr>
</tbody>
</table>
This dissertation will not further explore the economic aspects of disease control and eradication. While acknowledging the realities of the agricultural industry the stand is taken that the prevention of unnecessary pain and suffering of animals has an intrinsic value beyond mere counting of costs. The EU directive 98/58/EC laid down general rules for the “protection of animals of all species kept for the production of food, wool, skin or fur or for other farming purposes”. These rules are reflected in the “Five Freedoms”, as adopted by the Farm Animal Welfare Council and quoted in the EU Animal Health and Welfare Internet site (EU, 2005). The third of the five is “Freedom from pain, injury and disease – prevention or rapid treatment”. Furthermore, the reformed common agricultural policy (CAP), which will be introduced in the EU during 2005−2009, will contain as a key element a ‘single farm payment’ system. This system is closely linked to compliance with rules on animal welfare, among others.

The best way to prevent the occurrence of a disease is to eradicate it and to ensure subsequent freedom of the disease with sufficient control measures. In many cases this is an option only with outbreaks of economically devastating diseases or human life threatening zoonoses, such as foot-and-mouth disease or rabies. The eradication of endemic and prevalent diseases that produce only mild or inapparent symptoms may be considered impractical if not impossible, especially if the suggested control measures are deemed unreasonably exacting or otherwise extreme.

The objectives of this thesis are first to examine the biological, veterinary and especially the epidemiological characteristics described in the literature of four viral infections or diseases of domestic ruminants: bovine viral diarrhoea/mucosal disease (BVD/MD), infectious bovine rhinotracheitis/infectious pustular vulvovaginitis (IBR/IPV), enzootic bovine leukosis (EBL), and maedi–visna (MV) of sheep. This background information is compiled with special reference to the possible or available control measures both on individual, herd, and country-wide levels. The available information of the actual control measures applied especially in member states of the European Union and the Scandinavian countries is also reviewed and the measures assessed briefly.

Secondly, the objective is to review the legal framework for the disease control activities, and to describe in detail the control, eradication and surveillance measures applied in Finland. BVD/MD falls in Finland into the “Endemic”, MV into the “Sporadic” while IBR/IPV and EBL fall into the “Free” category of Willeberg (2005, above). The development in the situation of the four infections or diseases from the sixties to date, as a result of applying these measures, is described thoroughly.

Thirdly, the efficacies of the control and eradication measures applied in Finland are assessed employing a heuristic formulation of a central theoretical concept of infectious disease epidemiology, the infection reproduction ratio (R), i.e. the number of secondary cases produced by an infective animal. The three components of the formulation are the probability of transmission, the frequency of infectious contacts and the length of the infectious period, and the impact of the measures on each component is graded on a three-step scale.
2 Review of the literature

2.1 Description of the diseases

2.1.1 Bovine viral diarrhoea/Mucosal disease (BVD/MD)

Aetiology

Bovine viral diarrhoea/mucosal disease, BVD/MD or BVD for short, is caused by a pestivirus in the *Flaviviridae* family. The genome of the virus (BVDV) is a single-stranded, positive sense ribonucleic acid molecule of approximately 12 500 nucleotides. The virion core is icosahedral and the spherical enveloped virus particle is 40–60 nm in diameter (Donis, 1995; ICTV, 2003). BVDV occurs in noncytopathogenic (ncp) and cytopathogenic (cp) forms (Corapi et al., 1988). These terms do not refer to the virulence of the virus in the field but to the effect of the strains on cell culture. However, these two types behave differently in the host animal. Ncp strains produce viremia and are excreted by the animal while cp types do not produce viremia or infect the foetus and are poorly excreted (Lambot et al., 1998). Two antigenically distinct genotypes, 1 and 2, have been recognized; both may occur in ncp and cp forms (Ridpath et al., 1994). However, the genotyping itself was based on the 5’ untranslated region, which does not code for structural proteins. Genome characterization studies have shown extensive antigenic and genetic diversity among BVDV type 1 strains, and subtypes or genetic clusters 1a through 1d have been described (Vilcek et al., 2005; Baule et al., 2001). Mucosal disease results from a process in persistently infected (PI) animals whereby the persisting ncp strain mutates to cp, or there is a recombination of the ncp strain with an exogenous superinfecting cp strain (Kummerer et al., 2000, Tautz et al., 1998). BVDV is closely related to classical swine fever and border disease of sheep viruses. However, it has been pointed out (Edwards and Paton, 1995) that the virological nomenclature of pestiviruses based on the host species is increasingly unsatisfactory.

*Intrinsic determinants of the agent*

**Infectivity** The order of magnitude of the infectious dose is some 2000 TCID$_{50}$ by the intranasal and 1–2 TCID$_{50}$ by the subcutaneous route (Cook et al., 1990). A dose similar to the subcutaneous dose was also sufficient intramuscularly (Antonis et al., 2004). Thus, it appears that the TCID$_{50}$ and the ID$_{50}$ do not differ if the animals are exposed parenterally. Judging from the slow or limited spread of the transient infection within a herd, the contact infectivity is qualitatively at most of a medium level.

**Virulence** An acute infection LD$_{50}$ has not been reported for BVDV. The infection in adults frequently runs a subclinical course, while young animals are more prone to develop actual symptoms. Genotype 2 is considered more virulent than genotype 1. For example, the thrombocytopenic strains responsible for the hemorrhagic syndrome observed in Northern America are of genotype 2 (Odeon et al., 1999,
Ellis et al., 1998). However, Goens (2002) pointed out that genotype 2 has been present for a long time and in other parts of the world where severe acute BVD is rare, or has not been reported. The mucosal disease displays a higher level of virulence of BVDV: the condition is invariably lethal (Baker, 1995).

**Pathogenicity**  
BVDV is able to infect a wide range of both domestic and wild ungulate species (Lindberg, 2002; Løken, 1995).

**Persistence**  
If a foetus is infected by ncp-BVDV before it develops immunocompetence (during the first trimester of gestation), tolerance can ensue and the virus can persist in the animal (PI animal) for life (Done, 1980). The persistence is associated with the failure of ncp-BVDV to induce type I interferon in comparison to cp strains, and not because the uterus is refractory to the cp form of the virus (Charleston et al., 2001).

**Pathogenesis and the clinical picture**

The acute transient BVDV infection lasts 2–3 weeks. The infection causes leukopenia and thrombocytopenia, and impairs the cellular immunity functions (Corapi et al., 1989; Bruschke et al., 1997). BVD in young animals is characterized by fever, inappetence, respiratory symptoms and diarrhoea (Tråven et al., 1991). The infection in susceptible adult cows is in most cases subclinical or there is only a temporary dip in the milk production. Acute forms of the disease associated with high mortality, often with hemorrhagic syndrome, have also been described (Pellerin et al., 1994; Ridpath et al., 2005). BVDV can cross the placenta and infect foetuses of all ages (Lindberg, 2002). Infection during the first 4 months of foetal development may, in addition to the development of a PI foetus, cause embryonic resorption, abortion and intrauterine growth retardation. Congenital malformations of the eye and CNS can result from infections that occur between the fourth and sixth months of foetal development. Mummification, premature birth, stillbirth, and the birth of weak calves are also possible outcomes of foetal infection (McGowan and Kirkland, 1995; Fray et al., 2000). The PI animals shed the virus continuously in all secretions and excretions (Brock et al., 1991); they can show impaired growth and lack of thriftiness but can also appear clinically normal. PI cows can conceive and give birth to calves that will also be PI animals (Baker, 1987). In adult bulls the infection can have an effect on semen quality and the infection can be transmitted via the semen collected during the infection. The mucosal disease of PI animals appears between 6 months and 2 years of age. In the acute form it is characterized by fever, anorexia, extensive mucosal erosions throughout the alimentary canal, profuse diarrhoea and wasting, and death within 3 weeks (Baker, 1995). Chronic MD can also present dermatological lesions and laminitis and the animal may survive for several months (Lindberg, 2002).
Diagnostic aspects

There are no pathognomonic clinical signs of infection with BVDV in cattle. With the distinct exception of classical MD, especially adult animals frequently show no signs at all or the signs are very unclear (Lindberg, 2002). Diagnostic investigations must therefore rely on laboratory-based detection of the virus or virus-induced immune response in submitted samples. The methods are the same for both genotypes 1 and 2.

Detection of virus or viral components

Three methods for detecting BVDV can be distinguished. The virus may be propagated in cell culture (Brock, 1995; OIE, 2004) or BVDV antigens can be demonstrated either immunohistochemically in organ samples using specific antibodies (Haines et al., 1992, Grooms and Keilen, 2002), or with ELISAs employing immobilized capture antibody and a detector antibody conjugated to a signal system (Kramps et al., 1999). The major viral antigens detected this way are referred to as E" (previously E0 or gp48) and NS2-3 (previously p80/p125) (Sandvik, 2005). A third alternative is direct detection of viral RNA using molecular tools, such as reverse transcription–polymerase chain reaction (RT-PCR; Weinstock et al., 2001; Mahlum et al., 2002). RT-PCR should be targeted at the highly conserved 5′ untranslated region of the genome to ensure that all relevant genetic subgroups are detected (Sandvik, 2005). Multiplex assays have also been developed where both genotypes of the virus can be determined simultaneously (Gilbert et al., 1999). However, genotyping the virus to diagnose BVD is of little relevance (Goens, 2002). Isolated strains or amplified parts of the viral genome can further be sequenced and the sequence information used for epidemiological and eradication purposes (Ståhl et al., 2005). Confirmation of the mucosal disease diagnosis requires demonstration of the cp type of BVDV. Ideally, the presence of both cp and ncp types should be shown.

Detection of an immune response against BVDV

Cellular immunity, measured as the proliferation of peripheral blood monocytes (“lymphocyte proliferation assay”), has been described (Larsson and Fossum, 1992). However, most studies of the immune response to BVDV have focused on humoral immunity. The major antigens against which the antibodies are produced are referred to as E1 and E2 (Sandvik, 1999). The antibodies produced by an immunocompetent animal can be detected from 2–3 weeks to years after an acute infection. A broad variety of serological tests has been adopted for BVDV serology. The reference assay has for a long time been the virus neutralization (VN) test (Edwards, 1990), which primarily detects antibodies against E2 (Sandvik, 2005). While sensitive and specific, it requires careful standardization and monitoring of the cell culture and media used, and is not optimal for examining a few occasional samples. Enzyme immunoassays, such as ELISAs, offer a rapid, robust and a high-throughput method not only for serum but also for bulk-tank milk samples.
from non-vaccinated dairy herds (Niskanen et al., 1989, Niskanen, 1993), making it suitable for large-scale screening. The most common ELISAs apply the indirect approach, where the immobilized antigen is used to trap the specific antibodies, which are then detected using species-specific anti-antibodies conjugated to some signal system. Other serological tests used include immunodiffusion in agar gel, complement fixation, indirect immunofluorescence and Western blotting (Sandvik, 1999). Seronegativity combined with isolation of cp BVDV is the best confirmation of MD, while seronegativity combined with isolation of ncp BVDV is the best confirmation of a persistent BVDV infection (Goens, 2002).

Performance of diagnostic tests suitable for screening

In testing 1000 field serum samples, the BVDV antigen ELISA of Kramps et al. (1999) showed 99% specificity and 98% sensitivity relative to the VN test. The manufacturer of a commercial kit for detecting BVDV quotes figures of 100% for both se and sp (HerdChek, IDEXX Corp. USA). The single-tube single-enzyme RT-PCR assay (Weinstock et al., 2001) was shown to be a sensitive and specific test for the detection of BVDV in bovine serum pooled in lots of up to 100 samples. The manufacturer of a commercial kit for detecting antibodies against BVDV quotes figures of 100% se and 98.2% sp for serum samples relative to the VN test, and 95.2% se and 100% sp for milk samples relative to serum (SVANOVA BVDV-Ab, Svanova Biotech AB Sweden).

2.1.2 Infectious bovine rhinotracheitis/Infectious pustular vulvovaginitis (IBR/IPV)

Aetiology

IBR/IPV, or IBR for short, is caused by bovine herpesvirus 1 (BHV-1) in the genus *Varicellovirus* of the subfamily *Alphaherpesvirinae*, which belongs to the *Herpesviridae* family. The genome of the virus is linear double-stranded DNA of approximately 125 300 base pairs. The virion core is an icosapentahedral nucleocapsid, 100 nm in diameter and composed of 162 capsomers; the pleomorphic enveloped virus particle is about 150–200 nm in diameter (ICTV, 2004a). Only a single serotype of BHV-1 is recognized, but subtypes of it are distinguished on the basis of restriction enzyme cleavage patterns of the viral DNA (Metzler et al., 1985). These types are referred to as 1.1 (respiratory subtype) and 1.2 (respiratory and genital subtype). The subtype 1.2 has been further classified with molecular tools into 2a and 2b. The former encephalitic subtype 1.3 has been reclassified as a distinct herpesvirus, designated as BHV-5 (Roizman et al., 1992).

Intrinsic determinants of the agent

Infectivity  Intranasally, a dose of $10^{7.7}$ TCID$_{50}$ was sufficient to infect cattle in age groups 2 and 5 weeks, and 6 and 18 months (Msolla et al., 1983). Straub (1987)
determined that the intranasal infective dose was 3.2 TCID\textsubscript{50} for a virulent strain, while 32 TCID\textsubscript{50}/dose of AI semen were not sufficient to infect any of 44 inseminated dams (Goffaux et al., 1976). However, Turin et al. (1999) estimated that the minimal dose to infect a cow by AI was 32 infectious viral particles.

**Virulence** The LD\textsubscript{50} of BHV-1 infection has not been reported. Morbidity to the infection approaches 100% and mortality may reach 10%, particularly if complications occur. The subtype 1 is generally considered more virulent than subtype 2 (Edwards et al., 1991), but the virulence of BHV-1.1 and BHV-1.2 in genital infections of bulls has not been compared (Vogel et al., 2004).

**Pathogenicity** While BHV-1 causes infections predominantly in domestic and wild cattle (OIE, 2004), it has occasionally been isolated from cases of vaginitis and balanitis in swine and from aborted equine fetuses (Murphy et al., 1999).

**Persistence** The virus proceeds from the primary mucosal lesion by neuronal axonal transport in a naked nucleocapsid form to the nearest ganglion, usually trigeminal or sacral (dorsal root), and the viral DNA either causes a cytopathic infection or establishes a persisting latent infection (Jones, 1998). A wide variety of stimuli, such as stress, transport, parturition and treatment with glucocorticoids may reactivate the infection and lead to secretion of the virus. The mechanisms of latency and reactivation have been extensively studied, but the details are not yet fully understood (Inman et al., 2002). It has been shown that only a small region of the viral genome, referred to as “latency-related” (LR), is transcriptionally active in latently infected neurons (Turin et al., 1999). The LR gene products may even promote neuronal survival by inhibiting programmed cell death (Ciacci-Zanella et al., 1999), thereby also sustaining the infection in the cell.

**Pathogenesis and the clinical picture**

An uncomplicated acute respiratory or genital infection lasts for 5–10 days. BHV-1 causes leukopenia and a lack or diminished number of macrophage-granulocytes, MHC class II antigen presenting cells, as well as reduced cytokine secretion in the lung and regional lymphoid tissue (Tikoo et al., 1995). Other effects of the infection that induce immunosuppression include down-regulation of the expression of MHC class I molecules on the surface of infected cells and interference with the protective function of CD8\textsuperscript{+} cytotoxic T lymphocytes (Turin et al., 1999). The animals mount a vigorous humoral response that lasts for over 5 years (Chow, 1972). However, the immune response is not able to eliminate the persistent infection. Maternal antibodies can interfere with the development of an active antibody response to antigen, but do not necessarily prevent virus replication and the establishment of a latent infection (Lemaire et al., 1995). This can result in seronegative latent carriers of the virus, which has been demonstrated experimentally (Lemaire et al., 2000). The infection in adults is frequently mild or runs a subclinical course. The clinical signs of the respiratory form (IBR) include a serous progressing to a mucopurulent nasal discharge, conjunctivitis which may be accompanied by corneal opacity, salivation, inflamed nares (“red nose”), fever, and a lack of appetite (Wyler
et al., 1989). In uncomplicated IBR infections, most lesions are restricted to the upper respiratory tract and trachea. BHV-1 infection is an important component of the upper respiratory tract infection referred to as “shipping fever” or bovine respiratory complex (Tikoo et al., 1995). The genital form (IPV), pustular vulvovaginitis in cows and pustular balanoposthitis in bulls, is characterised by a mild to purulent vaginal discharge and necrotic lesions in vaginal or preputial mucosae. Other manifestations of BHV-1 infection include abortion, endometritis and a systemic disease affecting the visceral organs in young calves (Wyler et al., 1989).

Diagnostic aspects

Subclinical infection or mild respiratory signs do not readily suggest an infection by BHV-1, as it must be differentiated from several other viral respiratory processes, such as infection with respiratory syncytial or coronavirus. However, fulminant IBR or IPV does produce more distinguishable symptoms that, in connection with pathological and epidemiological signs, can arouse distinct suspicion. Laboratory examination is required to make a definite diagnosis.

Detection of virus or viral components

Four methods for detecting BHV-1 can be distinguished. The virus may be propagated in cell culture using, for example, primary or secondary bovine kidney, lung or testis cells, or established cell lines such as the Madin-Darby kidney cell line (OIE, 2004), and demonstrated in the culture with neutralizing monoclonal antibody, by immunofluorescence or the immunoperoxidase test. BHV-1 antigens can be demonstrated either in swab smears with direct or indirect fluorescent antibody tests or immunohistochemically, or in tissue samples by immunofluorescence (Edwards et al., 1983). The viral antigen can also be detected with ELISAs employing immobilized capture antibody and a detector antibody conjugated to a signal system (Collins et al., 1988). The fourth alternative is direct detection of viral DNA using molecular tools, such as DNA–DNA hybridization or the polymerase chain reaction (PCR). The latter has been used in the detection of viral DNA in infected semen samples (van Engelenburg et al., 1993), but it is not yet an internationally recognized diagnostic tool (OIE, 2004).

Detection of an immune response against BHV-1

Tests for cell-mediated immunity include tests for delayed type hypersensitivity, leukocyte migration factor and granulocyte migration inhibition factor in the presence of BHV-1 antigen (Deptula, 1994). Interleukin-2 production has also been used to measure the cell-mediated immune response to BHV-1 (Miller-Edge and Splitter, 1986).

Tests for humoral immunity: A variety of tests have been used to detect antibodies against BHV-1 both in serum and in milk. Virus neutralization tests are performed
with many modifications; these refer to the virus strain, the cell culture or line used, and to actual procedural variations. The test is sensitive and specific but requires careful standardization. ELISAs offer a feasible alternative to VN and many versions have been described (Kramps et al., 1993). Indirect ELISA is the most common, but as yet there are no standard procedures for ELISAs (OIE, 2004). ELISAs can also be used to detect antibodies in bulk-tank milk. A third alternative to testing samples for antibodies against BHV-1 is the indirect fluorescent antibody test (Wellemens and Leunen, 1973, referred to in OIE, 2004).

Performance of diagnostic tests suitable for screening

In a comparative ring test among European laboratories using a set of reference sera and sera and milk samples from experimentally-infected and vaccinated animals, the sensitivity and specificity of VN for sera was 93% and 96%, that of indirect ELISA 87% and 99%, and of glycoprotein E (gE) specific ELISA 72% and 92%, all respectively (Kramps et al., 2004). The gE ELISA is the only test able to distinguish between infected and vaccinated animals. The indirect ELISA showed a sensitivity of 98% and a specificity of 93% for milk samples while the corresponding figures for gE ELISA were 58% and 88% (Kramps et al., 2004). The manufacturer of a commercial kit for detecting antibodies against BHV-1 (SVANOVA IBR-Ab, Svanova Biotech AB Sweden) quotes figures 100% se and 92% sp for serum samples relative to VN, and 92.8% se and 100% sp for milk samples relative to serum.

2.1.3 Enzootic bovine leukosis (EBL)

Aetiology

The epidemiological cause of EBL is bovine leukosis virus (BLV), an oncogenic deltaretrovirus in the Retroviridae family. The genome of the virus consists of two identical single-stranded RNA subunits of 8 714 nucleotides associated with several structural proteins, such as nucleo- and nucleocapsid proteins, and enzymes including reverse transcriptase. The actual length of the RNA molecule may slightly vary depending on the strain. The virion core is icosahedral and the enveloped virus particle is 100–120 nm in diameter (ICTV, 2004b). The genus Deltaretrovirus also includes primate and human T-lymphotropic viruses (ICTV, 2002).

Intrinsic determinants of the agent

Infectivity  Studies on BLV infectivity have used the number of infected cells rather than of virus particles as the dose. Thus, 2000–20 000 BLV-infected lymphocytes, given intravenously, transmitted the agent to susceptible calves (Klintevall et al., 1997). In a separate study, 12% of steers receiving 10 000 lymphocytes and 62% of steers receiving 50 000 lymphocytes subcutaneously acquired BLV infection (Buxton and Schultz, 1984). Gatei et al. (1989) determined that a low dose of 200 infected bovine B-lymphocytes given intravenously in diluted whole blood was enough to
start the infection in sheep. A dose of $3.9 \times 10^9$ and $3.9 \times 10^8$ lymphocytes given as a rectal inoculation of infected bovine blood to cows and sheep, respectively, started the infection in all animals (Henry et al., 1987). On the other hand, leucocyte-free semen from BLV-infected bulls, given intraperitoneally, did not infect any of the challenged sheep (Kaja and Olson, 1982).

**Virulence**  Actual LD$_{50}$ estimates for the slow infection have not been reported. A large proportion of the infected animals remain asymptomatic. Some 30–70% of infected cattle develop persistent lymphocytosis (PL), and only 0.1–10% develop lymphosarcomas (LSA). The latter condition is usually fatal (OIE, 2004).

**Pathogenicity**  BLV is the agent of chronic lymphatic leukaemia/lymphoma in cows, sheep and goats. Infection without neoplastic transformation has also been observed in capybaras and water buffalos, and can experimentally be obtained in pigs, rabbits, rats, cats, dogs, deer and some primates (Burny et al., 1980).

**Persistence**  After entry into the host cell (predominantly B-lymphocyte) the virion-associated reverse transcriptase generates a double-stranded DNA copy of the viral RNA, and the proviral DNA is then integrated into the host chromosome. The process involves the long terminal repeat (LTR) sequences that flank the viral genome (Fine and Sodrosky, 2000). The proviral DNA can also exist in both unintegrated linear and circular forms in the cell (Reyes and Cockerell, 1996). The latency ensues from blocking the expression of the provirus on the transcriptional level, but the actual molecular mechanisms are still incompletely understood. Once integrated, the proviral DNA stays in the chromosome for the life of the cell. The silencing of the provirus is also important in the long-term persistence of infection (Tajima et al., 2003).

**Pathogenesis and the clinical picture**

Cattle may be infected at any age, including the embryonic state. The incubation time to clinical signs (LSA) is typically >3 years. In addition to PL, a polyclonal expansion of IgM+, CD5+ B cells, the BLV infection may also lead to persistent B-cell lymphopenia (Beyer et al., 2002). Progression to PL in BLV-infected cattle was shown to correlate with CD4+ T cell dysfunction in response to BLV antigens (Orlik and Splitter, 1996) and to require a genetic predisposition (Ferrer, 1979). It has been demonstrated that bovine major histocompatibility (bovine lymphocyte antigen, or BoLA) types correlate with the risk of infection as well as the development of PL and LSA (Stear et al., 1988), and that BoLA alleles conferring resistance or susceptibility may vary according to breed (Bernoco and Lewin, 1989; Hopkins and DiGiacomo, 1997).

PL is considered as a benign lymphoproliferative condition, characterized by lymphocyte counts above 7 500 cells/mm$^3$ (Timoney et al., 1988). The presence of integrated provirus in a few specific sites is one of the factors that can promote differentiation from the non-neoplastic to the neoplastic condition (Kettmann et al., 1980). The virus is a C-type oncovirus and does not encode viral oncogenes (v- onc$^-$) (Timoney et al., 1988). It carries a transactivating gene, tax, which is required for
replication and can transactivate several cellular genes whose expression could lead to transformation (Twizere et al., 2000). Furthermore, one of the gene products (G4) encoded by the so-called region X at the 3' end of the genome has shown oncogenic potential (Kerkhofs et al., 1998). The details of the monoclonal neoplastic transformation of B cells are still incompletely known. In LSA, lymph nodes and a wide range of tissues are infiltrated by neoplastic cells. Organs frequently involved are the abomasum, right auricle of the heart, spleen, intestine, liver, kidney, omasum, lung, spinal cord and uterus (OIE, 2004). Cattle with PL frequently show no clinical signs, whereas the signs associated with LSA will depend on the site of the tumors, and may include digestive disturbances, emaciation, general debility, and sometimes neurological manifestations. Cattle with LSA almost invariably die, either suddenly or within months after the onset of clinical signs (OIE, 2004).

**Diagnostic aspects**

Animals with PL can usually be detected only from samples tested in the laboratory either haematologically (Bendixen, 1965) or serologically. LSA-associated digestive disturbances, weight loss, lameness, or even dark blood in the faeces due to tumorous abomasal ulcers are not pathognomonic. However, animals with LSA frequently have enlarged and firm superficial lymph nodes and uterine and pelvic node tumors that may be detected by rectal palpation. These signs, as well as tumor masses in intestinal organs encountered in meat inspection, may arouse more distinct suspicion. However, definite diagnosis of LSA requires histopathological examination of the neoplastic tissue, and serological testing for antibodies against BLV.

**Detection of the virus and viral components**

There are basically two methods to demonstrate the presence of the agent. The virus may be isolated by separating the mononuclear cells from blood, incubating them either with or without foetal bovine lung cells, and testing for capsid p24 and envelope gp51 antigens in the culture supernatant (OIE, 2004). The BLV may also be detected as the provirus using PCR or nested PCR, followed by gel electrophoresis and staining (Rola and Kuzmak, 2002). The latter is considered to be the most rapid and sensitive method (Beier et al., 1998; OIE, 2004).

**Detection of immune response against BLV**

Tests for cell-mediated immunity are not in routine use in BLV infection diagnostics. Changes in immune functions with several tests measuring neutrophil functions and mononuclear cell subset analysis in animals experimentally infected with BLV have been studied by Flaming et al. (1997), among others.

Tests for humoral immunity: The antibodies most readily detected are those directed towards the envelope glycoprotein gp51 and capsid protein p24. The two most common serologic tests are or have been AGID and indirect or blocking
ELISAs; both are prescribed tests for international trade (OIE, 2004). The indirect ELISAs can be used for both serum and milk samples. International (OIE) standard sera are available for calibration of the ELISA assays.

**Performance of diagnostic tests suitable for screening**

Choi et al. (2002) assessed the diagnostic sensitivity and specificity of commercial agarose immunodiffusion (AGID) and the antibody capture enzyme immuno-sorbent assay (EIA) for the detection of antibodies against BLV, using Western blotting as the standard. The two tests failed to detect 39% and 35%, respectively, of the animals determined positive by the Western blot test. There are also other reports (e.g. Trono et al., 2001; Dolz and Moreno, 1999) suggesting that screening with AGID or some EIAs is not sufficient to identify all positive animals. Reichel et al. (1998) tested five ELISA kits with a set of well-defined sera (including reference sera from OIE) and compared the results with those obtained with AGID and the electrophoretic immunoblotting (EIB) test. The performance of the ELISAs ranged from 88 to 99% correct classification. The ELISA tests detected about 10% more reactors than the combined AGID and EIB tests. A commercial test (CHEKIT-Leucotest, Dr. Bommevi AG, Switzerland) for antibodies in bulk-tank milk showed 97% sensitivity but only 44% specificity in relation to AGID, after the sensitivity and specificity of the latter was accounted for (Sargeant et al., 1997b). The manufacturer of another commercial kit for detecting antibodies against BLV gp51 (SVANOVA BLV-gp51-Ab, Svanova Biotech AB Sweden) quotes figures of 100% se and 93.4% sp for serum samples relative to AGID. The test is claimed to detect the standardized international reference serum E4 at a dilution of 1/40 000 in milk.

### 2.1.4 Maedi–visna (MV) of sheep

**Aetiology**

Maedi (respiratory), visna (nervous system, wasting), and arthritic forms of the disease are caused by a retrovirus in the *Lentivirinae* subfamily of the *Retroviridae*. The genome of the virus (MVV) consists of two copies of viral RNA associated with one (p7) of the structural *gag* gene proteins. The length of the RNA molecule depends somewhat on the strain; the EMBL databank strains vary between 9189 and 9225 nucleotides (EMBL, 2005). The virion core is a cylindrical nucleocapsid, and the enveloped virus particle is approximately 100 nm in diameter (Clements and Zink, 1996; ICTV, 2004c). MVV is genetically closely related to caprine arthritis-encephalitis virus (CAEV), and together these two are often referred to as small ruminant lentiviruses (SRLV) (Blacklaws et al., 2004), or occasionally as ovine lentiviruses (OvLV) (Clements and Zink, 1996). It has even been suggested (Valas et al., 1997) that North American and French caprine arthritis-encephalitis viruses have emerged from ovine maedi–visna viruses and that sheep to goat transmission of SRLV is frequent (Shah et al., 2004).
Intrinsic determinants of the agent

Infectivity  The ID$_{50}$ of colostrum or milk has not been reported, but the minimal infectious dose has been determined as 10 TCID$_{50}$ via the trachea and 10$^7$ TCID$_{50}$ via the intranasal route (Torsteinsdottir et al., 2003). Lairmore et al. (1986) infected five newborn lambs intratracheally with 10$^4$ – 3.1 × 10$^6$ TCID$_{50}$ of OvLV; each developed interstitial pneumonia by 4 weeks of age.

Virulence  The LD$_{50}$ for the slow infection has not been reported. The virus may be carried for the life of the animal without any clinical signs, but if they appear the condition is eventually fatal. The mortality may reach 20–30% in newly-infected animals (Sigurdsson et al., 1952). There is some indication of breed predisposition to the clinical illness (Timoney et al., 1988; Straub, 2004).

Pathogenicity  The host range of MVV is sheep and goats, although there is some serological evidence of SRLV infection in wild ruminants, moufflon, ibex and chamois, which are related to sheep and goats (Morin et al., 2002).

Persistence  After entry into the host cell the virion-associated reverse transcriptase generates a double-stranded DNA copy of the viral RNA. The virion-associated integrase then integrates the proviral DNA into the host chromosome; the long terminal repeat sequences that flank the viral DNA genome have a function in the process (Clements and Zink, 1996; Fine and Sodrosky, 2000). Once integrated the viral DNA stays in the chromosome for the life of the cell. The long term persistence of the virus, in addition to the latency inside the cells, involves antigenic variation, probably due to mutations especially in the highly variable region of the env gene (Andrésdóttir et al., 2002).

Pathogenesis and the clinical picture

The major host cells of MVV are cells of the monocyte-macrophage lineage (Gendelman et al., 1986). The incubation time can be several months to years until clinical signs appear (Houwers et al., 1987; OIE, 2004). Considerable virus replication takes place in the first few weeks after infection, and during this acute phase the virus spreads throughout the host. Primary sites of viral replication include the lymph nodes, spleen and bone marrow (Clements and Zink, 1996). Infected monocytes mature into macrophages in the organs (lung, brain, joints), and the differentiation of the cells also activates viral gene expression (Gendelman et al., 1986). However, the lack of a permissive system for virus replication in tissue cells and the fact that terminally differentiated (short-lived) macrophages are the only infected cells in tissue suggest a constant viral source. Gendelman et al. (1985) identified clusters of infected macrophage precursors in bone marrow as such a source. Viral gene expression in tissue macrophages results in the development of an intense inflammatory response. The nature of the inflammatory reaction in each site is similar, consisting of an interstitial, mononuclear cell reaction, sometimes with large aggregates of lymphoid cells and follicle formation (OIE, 2004). The interstitial pneumonia in lungs is characterised by thickened, often fibrotic...
interalveolar septa and peribronchial infiltrates of lymphocytes and macrophages (Georgsson and Palsson, 1971). A large proportion of the infected animals develop an indurative mastitis and infected macrophages enter the milk from the inflamed mammary gland. In the brain there are intense perivascular inflammatory cuffs, diffuse infiltrates of lymphocytes and macrophages, frequently accompanied by demyelination (Petursson et al., 1976). Affected joints have hyperplastic synovial membranes with accumulation of plasma cells and macrophages in the subsynovial soft tissue. Advanced cases may show carpal bursitis, mineralization of the soft tissues and erosion of the joint cartilage (Clements and Zink, 1996). Kidneys may also show vasculitis.

The gross pathological findings in maedi are usually restricted to the lungs, which are consolidated and do not collapse when the thoracic cavity is opened, and to the associated lymph nodes. The lungs and lymph nodes increase in weight (up to 2–3 times the normal weight) (OIE, 2004). Apart from neurogenic muscular atrophy, visna does not produce gross pathological signs. Major clinical signs of maedi include a dry cough, expiratory dyspnea, emaciation in spite of good feed intake, and strain-dependent mastitis and/or arthritis. The clinical course may last 3–8 months but the condition is eventually fatal. The major clinical signs of visna include weakness of the hind legs, progressing to complete paralysis. Sometimes other central nervous system disorders (ataxia, muscle tremors) are present. The clinical course may last several years, with periods of remission (Straub, 2004, Murphy et al., 1999). Arthritic processes are frequently seen in association with both maedi and visna, but a polyarthritis of especially the carpal and tarsal joints may also be the main presentation of the disorder (Cutlip et al., 1985). Variable degrees of all three forms may be seen naturally in the same animals (Timoney et al., 1988).

**Diagnostic aspects**

The onset of clinical signs is insidious and in both maedi and visna is seldom detected in sheep less than 3 years of age. Weight loss and dyspnea in the early stages of maedi are not pathognomonic. The shepherds in Iceland are reported to have differentiated between “wota”, i.e. watery maedi and “purra”, i.e. dry maedi by lifting sick sheep by their hind legs. In cases of adenomatosis a copious amount of watery nasal discharge flows out of the nostrils, while in cases of dry maedi no nasal discharge is seen (Straub, 2004). Visna is also hard to detect before signs of paralysis of the hind legs set in. The arthritic processes can also have a diffuse aetiology. Definite diagnosis, especially in the early stages of the diseases, requires confirmation in the laboratory.

**Detection of the virus or viral components**

The virus may be isolated from leucocytes of live animals by culturing the cells together with indicator cells, such as sheep choroid plexus cells, and observing the development of the cytopathic effect (CPE; OIE, 2004). The presence of viral anti-
gen in CPE areas can be demonstrated, for instance, by immunolabelling. The virus may also be isolated from necropsy tissues (lung, synovial membranes, etc.) by making explant cultures and demonstrating the virus in the CPE areas, as above. The virus particles may also be detected in the CPE areas by electron microscopy, or indirectly by the reverse transcriptase assay. Adherent macrophage cultures can be established from lung-rinse material and virus production tested as described above (OIE, 2004). The virus may furthermore be demonstrated with nucleic acid recognition methods such as PCR, either directly from the proviral state or, combined with reverse transcriptase polymerisation, from viral RNA. The amplification is then followed by Southern blotting and in situ hybridization (Leroux et al., 1997; Extramiana et al., 2002). The latter techniques are especially useful in determining the infection status of animals that cannot be definitely diagnosed by serology, e.g. due to late seroconversion (Knowles, 1997).

Detection of an immune response against MVV

Even though cell-mediated immunity is invoked by the infection, tests for this type of immune response are generally not used in MVV infection diagnostics (OIE, 2004).

Test for humoral immunity: The establishment of a positive antibody status is sufficient for the identification of virus carriers (OIE, 2004). The two viral antigens of major importance in routine serology are envelope glycoprotein gp135 and core protein p28, although other proteins such as envelope protein p90 (Fevereiro et al., 1999) can also be used in the assays. The assays now commonly used are agar gel immunodiffusion (AGID) and whole-virus antigen ELISA (Houwers and Schaake, 1987). Both are prescribed tests for international trade (OIE, 2004). Other tests used mainly in specialized laboratories are Western immunoblotting and immunoprecipitation. The milk antibody assay may also be appropriate if ewes are being milked.

Performance of diagnostic tests suitable for screening

The PCR-based methods to detect viral RNA or proviral DNA generally have a high analytical sensitivity, at least in the pre-seroconversion phase of the infection (de Andrés et al., 2005). However, the complexity of many of these assays limits their value in large scale studies or in less than fully-equipped laboratories. Extramiana et al. (2002) have reported a simple PCR method, the se and sp of which are as good as or better than those of serological methods. Both the AGID and whole-virus ELISA suffer from the variable quality and high production cost of the viral antigen used, and the sensitivity of AGID is considered insufficient as a gold standard for the serology of SLRV infections (Saman et al., 1999). The reported se of 29 AGID tests for SRLV antibodies, relative to ELISA, was on average 65.3% (de Andrés et al., 2005). More sensitive and stable ELISA assays employing monoclonal antibodies (Houwers and Schaake, 1987) or recombinant viral proteins and peptides (Kwang and Torres, 1994; Saman et al., 1999) have been developed. Saman et al.
(1999) reported a sensitivity of 99.4% and specificity of 99.3% relative to immuno-
(Western) blotting. A sensitive competitive-inhibition ELISA developed for the
diagnosis of CAEV infections has also been successfully applied to the diagnosis of
MVV infections (Herrman et al., 2003). The authors quote 98.6% se and 96.9% sp
for their test in relation to immunoprecipitation. Commercial test kits for detect-
ing antibodies against MVV are available (for example ELISA Maedi–Visna/CAEV,
Pourquier Institute, France), but exact se or sp figures have not been reported for
the kit. The ELISA techniques are also applicable to antibodies in milk, but a lower
sensitivity would be expected, since the levels of lentivirus antibodies in milk are
substantially lower than in serum (Knowles et al., 1994).

2.2 Comparative epidemiological aspects of the diseases

2.2.1 Occurrence of the infection/disease

BVD

BVD is present in most cattle-raising countries of the world (Lindberg, 2002). The
OIE Handistatus statistics for Europe (Handistatus, 2004a) disclose that the infec-
tion is present in each country that has sent in a report, with the exception of
Iceland. Based on the detection of antibodies against BVDV either in BTM or in
sera of individual animals, the prevalence of infected herds in individual countries
most often ranges from 70% to 100% (Edwards et al., 1987; Niskanen et al., 1991;
Braun et al., 1997). The prevalence of herds with PI animals has ranged from 15%
to 45% (Houe, 1995; Frey et al., 1996). The Scandinavian countries are an excep-
tion; after ten years of control and eradication programmes the seroprevalence
among herds in each country is below 10% (Valle et al., 2005; Hult and Lindberg,

IBR

The infection appears prevalent in most cattle-raising countries (Straub, 2001). The
OIE Handistatus statistics for Europe (Handistatus, 2004b) disclose that the infec-
tion is present in the majority of the countries that have sent in a report, with
the exception of Iceland and the EU Member States to which the additional guar-
antees for IBR apply (Austria, Denmark, Finland, Germany and Sweden; Decision
2004/558/EC). Switzerland is also considered to be free of infection (Ackermann
and Engels, 2005), although the Handistatus statistics claim that it was positive in
2004.

In Europe the prevalences before control and eradication campaigns have been de-
scribed as variable to high, or in some cases quantitatively; e.g. 62–65% in Belgium,
13–79% in Hungary, 62–85% in Italy, 40% in the Netherlands in dairy cattle, and 20–
38% in Poland (Ackermann and Engels, 2005; Boelaert et al., 2000; Tekes et al., 1999).
Bulk-tank milk surveys in England and Wales revealed that 69% of dairy herds had an-
tibodies against BHV-1 (Paton et al., 1998), while in the Netherlands the correspond-
ing figure was 84% (van Wuijckhuise et al., 1998). Of the Scandinavian countries, additional guarantees apply to Denmark and Sweden. Norway has been recognized as free of IBR since 1994 (Anon., 2003) and Sweden since 1998 (Danielsson, 2003).

**EBL**

Serological surveys have revealed that BLV infection is widely disseminated throughout the world, with high prevalence rates in North and South America, Africa, Asia and Australia (Hopkins and DiGiacomo, 1997). In Europe, official EBL-free status has been established for 14 EU Member States, and for several regions of Italy (Decision 2004/320/EC). According to the OIE Handistatus statistics (Handistatus, 2004c), the last reported occurrence of EBL was at least 7 years before the report from 2004 in 4 countries (Andorra, Cyprus, Czech Republic and Georgia). Nationwide surveys of EBL seroprevalence in other European countries are not in the public domain. The herd-level seroprevalence in the US has been estimated as 85–90% (Wells et al., 1998), which is similar to that occurring, for example, in Argentina (Trono et al., 2001). Of the Scandinavian countries, Denmark and Sweden are officially free of EBL, while in Norway the last seropositive cow was detected in a small dairy herd in 2002 (Anon, 2003).

**MV**

MV occurs worldwide, with the exception of Iceland (Pålsson, 1985), New Zealand and Australia (Greenwood et al., 1995). Some of the other European countries besides Iceland may be considered free according to the OIE definition (<1% of herds infected with 99% probability) (quoted by Peterhans et al., 2004). However, the OIE Handistatus statistics (Handistatus, 2004d) claim that there are 11 countries among the 42 listed where the disease has never been reported; in four of these the disease is not even notifiable. Only few studies have reported actual country-level prevalences of maedi–visna among sheep flocks. The slightly outdated report of Simard and Morley (1991) quotes a figure of 63% from 286 flocks in Canada having at least one seropositive animal, with a mean prevalence of 12% within flocks, while Kita et al. (1990) report that all of the 18 flocks of sheep tested in Poland were infected, with a range of within-flock serological prevalence from 1.2% to 45.9%. More recently, Schaller et al. (2000) found only 9% from 226 flocks of breeding associations in Switzerland to be antibody-positive for maedi–visna virus. Of the Scandinavian countries, 35 MVV antibody positive sheep flocks were found in Norway in 2002 (Anon, 2003). Occasional sheep health control serum samples were positive for MVV antibodies both in 2002 and 2003 in Denmark (Veterinaerinstitut, 2004) and in Sweden (Jordbruksvärket, 2004).

### 2.2.2 Intrinsic determinants of the hosts

The intrinsic determinants of the hosts, pertinent to development the diseases, are compiled from Radostits et al. (2000), Murphy et al. (1999) and Timoney et al.

2.2.3 Host–agent relationship

Data pertinent to the host – disease agent relationship are compiled from Radostits et al. (2000), Murphy et al. (1999) and Timoney et al. (1988) for all the diseases, and further from Polak and Zmudzinski (2000), Houe (1999) and Brownlie et al. (1987) concerning BVD, from Thiry et al. (2005), Hage et al. (2003), and Tikoo et al. (1995) concerning IBR, from Monti and Frankena (2005), Licursi et al. (2002), Willems et al. (1993), and Mammerickx et al. (1987) concerning EBL, and from Pepin et al. (1998), Clements and Zink (1996) and Bird et al. (1993) concerning MV, and are presented in Table 2.

Table 1  Intrinsic determinants of the hosts pertinent to the development of the diseases

<table>
<thead>
<tr>
<th>Determinants</th>
<th>BVD</th>
<th>IBR</th>
<th>EBL</th>
<th>MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect of age on susceptibility¹</td>
<td>N</td>
<td>Y, 1²</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Association of age with severity of disease¹</td>
<td>Y, 2</td>
<td>Y, 2</td>
<td>A, 3</td>
<td>A, 3</td>
</tr>
<tr>
<td>Typical age of clinical manifestation, years</td>
<td>1–3</td>
<td>0,5–3</td>
<td>4–8</td>
<td>&gt;2</td>
</tr>
<tr>
<td>Breed predisposition²</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Effect of gender on susceptibility¹</td>
<td>N</td>
<td>F, 1</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Effect of gender on clinical manifestation¹</td>
<td>N</td>
<td>F, 1</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Impact of gestation or parturition on propagation of disease³</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Effect of immunological status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of maternal immunity, months</td>
<td>3–9³</td>
<td>2–4</td>
<td>1–3</td>
<td>3–6</td>
</tr>
<tr>
<td>Immunity after infection, years</td>
<td>&gt;3</td>
<td>&gt;3</td>
<td>–4</td>
<td>–</td>
</tr>
<tr>
<td>Protection afforded by vaccination²</td>
<td>1</td>
<td>2</td>
<td>U</td>
<td>–</td>
</tr>
</tbody>
</table>

1 young (Y)/adult (A), or male (M)/female (F). If predisposition exists, the more affected age or gender is indicated. N = no predisposition
2 scale: 3, major; 2, significant; 1, minor or incomplete; 0, insignificant or non-existent; U, possible but significance unknown
3 non-PI animals
4 information not available or not relevant
2.2.4 Sources and transmission of the disease agents

The sources of the agent during infection and the principal means of transmission are compiled from Lindberg (2003), Rossmanith et al. (2001), Bitsch et al. (2000), Lindberg and Alenius (1999) and Kommisrud et al. (1996) concerning BVD, from Turin et al. (1999), Mars et al. (1999), and Vonk Noordegraaf et al. (1998) concerning IBR, from Meas et al. (2002), Hopkins and DiGiacomo (1997), Sargeant et al. (1997a) and Johnson and Kaneene (1991) concerning EBL, and from Peterhans et al. (2004), Blacklaws et al. (2004), and Preziuso et al. (2004) concerning MV, and are presented in Table 3.

2.2.5 Extrinsic determinants of the diseases

The major extrinsic determinants, pertinent to development the diseases, are climate, soils and man (Putt et al., 1988). The first two can interact in a variety of ways and affect the environment of the host and possible vectors. Climates that necessitate indoor housing during the winter months predispose the closely-confined animals to spreading of the agents, especially via the respiratory route. This has been experimentally demonstrated for BVDV and BHV-1 (Mars et al., 1999), and observed for MVV (Blacklaws et al., 2004). Temperate or cold climates may also enhance the survival of the agent in the environment. The possibility of vector trans-
<table>
<thead>
<tr>
<th>Sources and transmission</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BVD$^1$</td>
</tr>
<tr>
<td>Sources</td>
<td></td>
</tr>
<tr>
<td>Main or major sources</td>
<td>Secretions/serum</td>
</tr>
<tr>
<td>In blood</td>
<td></td>
</tr>
<tr>
<td>Minor sources</td>
<td>Excretions</td>
</tr>
<tr>
<td>Vertical transmission</td>
<td></td>
</tr>
<tr>
<td>Germ line</td>
<td>0</td>
</tr>
<tr>
<td>Intrauterine or transplacental</td>
<td>3</td>
</tr>
<tr>
<td>Horizontal transmission</td>
<td></td>
</tr>
<tr>
<td>Live animal trading</td>
<td>3</td>
</tr>
<tr>
<td>Direct contact between animals</td>
<td></td>
</tr>
<tr>
<td>Ingestion of colostrum or milk</td>
<td>0/2$^2$</td>
</tr>
<tr>
<td>Respiratory or oral route</td>
<td>3</td>
</tr>
<tr>
<td>Venereal</td>
<td>0</td>
</tr>
<tr>
<td>Indirect contact between animals</td>
<td></td>
</tr>
<tr>
<td>Embryo transfer</td>
<td>1</td>
</tr>
<tr>
<td>Environmental (e.g. pastures)</td>
<td>2</td>
</tr>
<tr>
<td>Invertebrate vector</td>
<td>0</td>
</tr>
<tr>
<td>Airborne</td>
<td>U</td>
</tr>
<tr>
<td>Fomites</td>
<td>1</td>
</tr>
<tr>
<td>Iatrogenic or other human</td>
<td></td>
</tr>
<tr>
<td>Through animal products (serum, semen)</td>
<td>1/2$^2$</td>
</tr>
<tr>
<td>Mechanical (needles, rectal palpation)</td>
<td>0</td>
</tr>
<tr>
<td>Other domestic or wild species as reservoir</td>
<td>U</td>
</tr>
</tbody>
</table>

1 scale: 3, major; 2, significant; 1, minor or occasional; 0, insignificant; U, possible but significance unknown
2 transiently infected/PI animal
mission is only associated with BLV (Johnson and Kaneene, 1991); however, this is probably only a minor or insignificant route (Hopkins and DiGiacomo, 1997).

The determinants due to man include the extensive trade of animals and products of animal origin, providing opportunities for the agents to spread. This is shown especially unequivocally with MV (Straub, 2004). On the other hand, the use of vaccines and drugs and the implementation of control measures and eradication programmes seek to counter the inadvertent spread and proliferation of the infections.

Information on other infections or diseases as specific extrinsic determinants to advance the present diseases is scarce. The cp-type BVDV superinfection is required to produce the mucosal disease in PI animals infected with ncp-BVDV (Kummerer et al., 2000). Coinfection with bovine respiratory syncytial virus (BRSV) and ncp-BVDV produced a synergistic depression on alveolar macrophage functions (Liu et al., 1999). A novel bovine lymphotropic herpesvirus (Rovnak et al., 1998) and bovine immunodeficiency virus (BIV, Meas et al., 2002) appeared to be possible cofactors for BLV infection. MVV replication was enhanced in sheep coinfected with sheep pulmonary adenomatosis virus (Dawson et al., 1990).

2.3 Control and prevention measures against the diseases

2.3.1 Individual and herd levels

Measures applied to control and limit the spread of the infections and diseases on a low level are compiled from Greiser-Wilke et al. (2003) and Lindberg and Alenius (1999) concerning BVD, from Hage et al. (2003), van Schaik et al. (2002), Graat et al. (2001) and Vonk Noordegraaf et al. (1998) concerning IBR, from Pence et al. (2004), Danielsson (2003) and Hopkins and DiGiacomo (1997) concerning EBL, and from Knight (2004), Houwers et al. (1987) and Cutlip and Lehmkuhl (1986) concerning MV, and are presented in Table 4.

2.2.2 Regional and national levels

Measures applied to control and limit the spread of the infections and diseases on medium level are compiled from OIE statistics (Handistatus, 2004a), Sandvik (2004), Lindberg (2003), and Bitsch et al. (2000) concerning BVD, from OIE statistics (Handistatus, 2004b), Vonk Noordegraaf et al. (2004), Holzhauer et al. (2003) and Pospisil et al. (1996) concerning IBR, from OIE statistics (Handistatus, 2004c), Danielsson (2003), Hayes and Burton (1998), DiGiacomo (1992) and Gottschau et al. (1990) concerning EBL, and from OIE statistics (Handistatus, 2004d), Peterhans et al. (2004), Houwers et al. (1987) and Biront and Deluyker (1985) concerning MV, and are presented in Table 5.
2.3.3 International (EU) level

The European Union subsidizes animal disease eradication and monitoring programmes that aim at eliminating endemic diseases in, and preventing the spread of exotic diseases into the community. The diseases covered include IBR in AI and embryo units and other types of enterprise, EBL and MV (EU, 2005). The measures in the programmes include a wide range of activities such as vaccination, testing of animals, compensation for slaughtering or culling, and treatment. The EU legislation pertinent to BVD, IBR, EBL and MV are reviewed below, in subchapter 4.1.2.

<table>
<thead>
<tr>
<th>Control measures</th>
<th>Diseases</th>
<th>BVD</th>
<th>IBR</th>
<th>EBL</th>
<th>MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>On individual level</td>
<td>Vaccination</td>
<td>Vaccination of both seronegative and seropositive animals</td>
<td>Use of disposable/sterile instruments</td>
<td>Separation of offspring from infected dam</td>
<td>Separation of infected animals from non-infected</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Separation of offspring from infected dam</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No feeding of milk or colostrum from EBL-suspected herd or herd of unknown status, unless pasteurized</td>
<td></td>
<td></td>
</tr>
<tr>
<td>On herd (flock) level</td>
<td>Testing of animals for PI-status, positive culled</td>
<td>All animals &gt;6 mo of age tested for antibodies seropositive separated or culled, seronegative tested repeatedly every 3 mo, or All animals vaccinated repeatedly; calves reared in isolation and tested at least twice, seronegative stock raised in separation or All animals removed premises cleaned and disinfected and restocked with IBR-free herd</td>
<td>Elimination of all BLV-antibody or antigen positive cattle, or at least isolation of seropositives</td>
<td>Slaughtering entire flock or Slaughtering seropositive animals and their progeny</td>
<td>Regular testing of all animals in the flock or Restrictions on contacts to uncertified flocks, or animals quarantined until shown seronegative</td>
</tr>
<tr>
<td></td>
<td>No purchase of antibody-positive pregnant dams</td>
<td></td>
<td>Testing herd additions retesting after 60 d</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Herd certificates updated with annual retesting</td>
<td></td>
<td>Annual testing of the herd for BLV antibodies and check of herd records</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No contacts with un-certified animals (no common pastures, visits to exhibitions, etc)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4 Infection or disease control measures on individual and herd levels
The OIE Terrestrial Animal Health Code (web version: OIE, 2005) sets conditions for qualification for and maintenance of country and region freedom from IBR and EBL, as well as requirements for the import of live animals with respect to IBR, EBL and MV. The requirements extend to the import of semen with respect to IBR and EBL. The conditions are presented in Table 6.
<table>
<thead>
<tr>
<th>OIE Terrestrial code</th>
<th>Diseases</th>
<th>BVD</th>
<th>IBR</th>
<th>EBL</th>
<th>MV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualification</td>
<td>Not specified</td>
<td>Disease or suspicion of it notifiable</td>
<td>All LSA-like tumors reported to veterinary authority, and examined in competent laboratory</td>
<td>If LSA confirmed or can not be ruled out, the herds of origin are traced and all cattle over 2 yr of age tested</td>
<td>Not specified</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No animal vaccinated against IBR/IPV for at least 3 yr</td>
<td></td>
<td>At least 99.8% of herds qualified as free</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>At least 99.8% of herds qualified as free</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maintenance</td>
<td>Not specified</td>
<td>Annual survey with sufficient sample to reveal &gt;0.2% prevalence with 99% confidence</td>
<td>Annual survey with sufficient sample to reveal &gt;0.2% prevalence with 99% confidence</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Requirements for import</td>
<td>Not specified</td>
<td>Imported animals show no clinical signs of IBR/IPV on day of shipment and Come from an IBR/IPV free herd or Were kept in quarantine station for the 30 d prior to shipment, and tested negative twice with an interval of at least 21 d</td>
<td>Imported animals come from a herd in which: No clinical or pathological evidence or positive EBL test result within preceding 2 yr and All animals &gt;2 yr of age tested negative twice during preceding year, at an interval of at least 4 mo The imported animals tested negative for EBL within 30 d prior to shipment</td>
<td>Imported animals showed no clinical signs on day of shipment and Animals &gt;1 yr of age tested negative for MV during the 30 d prior to shipment Animals come from flocks where MV was not diagnosed during preceding 3 yr and which had had no additions from flocks of inferior status during the same period</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Or if destined to not qualified herd: Showed no clinical signs and were vaccinated with inactivated vaccine 1–6 mo prior to shipment Imported fresh and frozen semen from a donor bull in an IBR/IPV free herd Frozen semen: the bull kept in isolation for period of collection and 30 d after, and tested negative at least 21 d after the collection</td>
<td>Imported semen from a donor bull in an EBL-free herd The bull tested negative for EBL twice, at least 30 d before and 90 d after semen collection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
2.4 Attempts to eradicate the diseases, essential measures and perceived problems in eradication

2.4.1 BVD

The only country-wide control and eradication schemes for BVD have been launched in Scandinavia. These programmes, initiated in the early 1990s, have reduced the BVD prevalence in each country below 10%, but the struggle with the “tail” of the occurrence will probably take longer than once expected. However, the Shetland Islands (UK) did initiate a BVD control scheme simultaneously with the Scandinavian countries in 1994, and by January 1997 the last scheduled young stock tests were negative, indicating that the islands had been successfully cleared of BVD. Unfortunately, a dam carrying a PI foetus was introduced to the islands in 1998, which resulted in 21 new infected herds and meant that a new round of BVDV clearance had to be started (Sandvik, 2004). Regionwide eradication programmes have been initiated, for instance, in Lower Austria (Rossmanith et al., 2001), German Lower Saxony (Greiser-Wilke et al., 2003), the Rome province of Italy (Ferrari et al., 1999), the Bretagne area of France (Joly et al., 2005), the Netherlands (Mars et al., 2005) and Slovenia (Grom and Barlic-Maganja., 1999). The BVD prevalences in each case have been substantially reduced from the original levels.

The Lower Austrian programme, initiated in 1996, was designed according to the Swedish programme (Alenius et al., 1997), highlighting the central role of the identification and elimination of PI animals (Rossmanith et al., 2001). An important risk factor for BVDV transmission in Austrian local conditions is communal grazing, where susceptible pregnant cattle from several herds may be mixed with unrecognized PI animals. The programme is based on four principles: 1) information and education for all groups involved, 2) dividing the herds into presumably non-infected and infected, 3) the protection of non-infected herds and 4) systematic disease clearance in infected herds (Rossmanith et al., 2005). An Austrian federal law was laid down in 2004 committing all herd owners to eradicate BVDV according to the Scandinavian scheme (Anon., 2004).

A Federal guideline for the control of BVD was issued in Germany in 2000 (Moen nig and Greiser-Wilke, 2003) and some Federal States have even provided additional regulations concerning compensation for PI animals and additional costs. For example, German Lower Saxony (Niedersachsen), where the seroprevalence of BVDV infection is high, has a programme with the following main points (Greiser-Wilke et al., 2003):

(1) Voluntary participation;

(2) Identification of PI animals by testing all stock <3 years of age in the participating herds twice (at least 14 days apart) for the antigen, and culling those positive in both tests;

(3) Systematic vaccination of female offspring;

(4) Applied biosecurity measures, including trade only with herds of equivalent status.
In a defined area of the Rome province of Italy a programme to eradicate BVD was launched in 1997 (Ferrari et al., 1999). The programme makes use of the serum samples collected biannually from every bovine animal >1 year of age as part of brucellosis and leucosis eradication programmes. The voluntary BVD eradication programme is based on three measures:

1. Immediate removal and slaughter of PI animals;
2. Movement control by submitting blood samples of newly introduced animals to serological and virological investigations;
3. Serological and virological control of all animals sold to other reproduction units if the herd has not yet acquired BVD-free status.

Vaccines are used in the programme only if specifically requested by the herd owners.

The Scandinavian programmes have several common features. A strict non-vaccination policy is observed in each, which allows identification of infected herds in large-scale screenings based on the detection of antibodies. In outline the eradication programmes are comprised of four steps (Sandvik, 2004; Greiser-Wilke et al., 2003):

1. Pinpointing the infected herds by repeated nationwide surveys of herds. Dairy herds are monitored through BTM sample testing. Alternatively, sera from a limited number of animals representing all epidemiological groups of the herd are tested for antibodies against BVDV (“spot testing”).
2. Certification and monitoring of non-infected herds; certifications updated regularly by retesting.
3. Virus clearance of infected herds, using high BVDV antibody levels in ELISA tests as an indication of an active infection, and individually testing all animals >2–3 month of age, or milk of primiparous cows and sera of young stock in suspected herds, for antibodies. Virus isolation is performed from each animal displaying a low level of antibodies, and all positive animals are culled. Follow-up testing of the herd has to be performed at regular intervals until all calves at six months of age are seronegative.
4. Establishing prophylactic measures and biosecurity guidelines to prevent re-infection.

The Slovenian programme (Grom and Barlic-Maganja, 1999) focuses on breeding selection herds, breeding herds for young bulls, the herds of origin of these bulls and AI stations. The programme is based on blood-sampling from entire herds. This labour-intensive approach is considered to be the only method giving reliable information on the seroprevalence of BVDV infection within each herd, and enabling immediate identification of PI animals among the seronegative ones. Bovine breeding herds in Slovenia have never been vaccinated against BVDV infection.
Essential measures and perceived problems in eradication

**Essential measures** Regular testing of all herds, locating the herds most likely to have an active infection and removing PI animals from them, and strict control of livestock trade associated with the risk of PI animals. Moennig et al. (2005) propose that the removal of PI animals, monitoring of the health status in combination with systematic vaccination might be an alternative acceptable in Europe outside of Scandinavia.

**Perceived problems** Insufficient sensitivity of antigen-ELISA tests to detect PI animals, especially in the presence of maternal antibodies (Rossmanith et al., 2001). Furthermore, the sensitivity of the tests to detect the virus in the semen of acutely-infected bulls is not satisfactory (Sandvik, 2005). The current vaccines are not marker vaccines and do not convey solid protection to the foetus (Grooms, 2004).

2.4.2 IBR

IBR has successfully been eradicated from several European countries or regions (Austria, Denmark, Norway, Sweden and Switzerland, and the province of Bolzano in Italy; Decision 2004/558/EC). In each case, eradication was based on the testing of animals for antibodies against BHV-1, culling or separating the seropositive animals from the seronegative ones and subsequent restocking with only seronegative stock. Vaccination was not employed in these countries. This rigorous “selection” approach is considered unfeasible in many other European countries (Belgium, Hungary, the Netherlands, and the province of Veneto in Italy) where the prevalence of the infection is high. The latter countries or regions are basing their IBR control on large-scale vaccination with marker vaccines. In Germany a few states are applying the “selection” approach, while the majority are vaccinating. Regional voluntary eradication programmes have also been launched in France and the Republic of Ireland (Brownlie, 2005).

The control and eradication scheme of Belgium has been divided into three phases. The first consisted mainly of voluntary vaccination, classification of the herds and evaluation of virus spread; this phase was completed in 1999–2000 (Vanopdenbosch and Kerkhofs, 2004). The second, current phase includes compulsory vaccination, culling or vaccination of infected animals and strict control of transfers. The objectives of this phase are the ending of virus spread, and eventual ending of vaccination. The third phase will include qualification of herds after the end of vaccination, compulsory culling of infected animals, and strict zoosanitary measures and control of stock movement. Transition to phase three will be based on the results of yearly random sampling and serology (Limbourg et al., 2002).

Tanyi and Varga (1992) presented guidelines for the eradication of IBR in Hungary. They considered three courses of action: the separation and vaccination of infected animals in herds, eradication by generation shift and eradication by total herd replacement. Regional voluntary programmes are active in Hungary at present (Brownlie, 2005).
In the province of Veneto, Italy, it is recommended that the herds are first classified into two categories on the basis of the seropositivity level. Vaccination with a live marker vaccine is to be used only in herds having a high seropositivity, while the “test and remove” concept should be used in the (majority of) low seropositivity herds (Nardelli et al., 1999).

In the Netherlands the best strategy on the basis of data available so far, together with a model study, consists of three measures (Franken, 2004):

(1) Obligatory vaccination with a live marker vaccine according to a programme, the vaccinations being recorded by the animal health service. Herds complying with or fitting in a given set of conditions may receive financial compensation;

(2) Elimination of the last gE positive (infected) animals;

(3) Completion of the vaccination programme (estimated to be in 2005).

Essential measures and perceived problems in eradication

Essential measures  A live marker (gene-deleted) vaccine and a diagnostic test to differentiate between vaccinated and infected animals in countries or regions of high prevalence; the separation and eventual culling of seropositive animals; strict control on external contacts between herds.

Perceived problems  Failure to easily detect seronegative latent carriers (Lemaire et al., 2000) could pose a threat to IBR-free herds and AI centres. The tests for antibodies against BHV-1 in BTM samples will only detect herds in which the BHV-1 prevalence is greater than 10% (Hartman et al., 1997) or 20% (OIE, 2004), so that BTM-negative herds need some confirmatory test of their infection status. In countries where the majority of dairy herds are already free or BTM-negative this means considerable expenditure.

2.4.3 EBL

Enzootic bovine leukemia has successfully been eradicated from several European Union countries: Belgium, Denmark, Germany, Spain, France, Ireland, Luxembourg, the Netherlands, Austria, Sweden and the United Kingdom, and many regions or provinces of Italy (Decision 2004/320/EC). Jazbec et al. (1985) reported the eradication of EBL from Slovenia.

The identification of infected animals either by haematological or serological methods, employing biosecurity measures such as raising young calves with colostrum and milk from only seronegative dams, and eventual culling of the seropositive animals, have formed the common approach in Europe, as well as in New York State of the United States (Brunner et al., 1997), Australia (Ross and Kirkland, 1993)
and New Zealand (Hayes and Burton, 1998). DiGiacomo (1992) reviewed and dis-
cussed the three successful approaches to eradicate BLV on the herd level: test and
slaughter, test and segregate, and test and implement corrective management. The test and segregate approach has been used more frequently in North America
than the other approaches (Shettigara et al., 1989; DiGiacomo, 1992). The respec-
tive advantages and disadvantages of these approaches, and the efficiency in erad-
icking the infection are:

- **Test and Slaughter:** The infection will be eliminated in months, whatever the
  initial prevalence. The approach can be exceedingly expensive if the initial
  prevalence is high. Reports of using this approach describe a reduction of prev-
  alence from 11% to 4% in 6 months in 222 herds (Maas-Inderwiesen et al.,
  1978), and from 10% to 2% in 12 months in 32 herds (Burki et al., 1983).

- **Test and Segregate:** Segregating the seropositive and seronegative stock into
  separate premises or locations will keep the latter free of infection (Kaja et
  al., 1884; Weber et al., 1987). Separating the two groups but housing them in
  the same premises may prevent the infection from spreading to the seronega-
  tive group, but evidence for eventual eradication of the infection is inconclu-
  sive (Johnson et al., 1985). Animals from the seropositive group will not be re-
  moved prematurely but by natural attrition, which may take several years.

- **Test and Implement Corrective Management:** The approach includes both sur-
  veillance (testing) and measures to prevent the transmission of the virus. Rup-
  panner et al. (1983) reported a reduction from 50% to 14% seroprevalence
  while Sprecher et al. (1991) were able to significantly decrease the seropreva-
  lence in all age cohorts, e.g. in the 181 days to parturition cohort from 44% to
  17% within three years. In both studies the measures focused on the preven-
  tion of transfer of blood (lymphocytes) between cattle. In this approach there
  is no need to invest in separate housing, or to prematurely cull animals, but it
  requires a long-term commitment with repeated testing and vigilant mainten-
  ance of the altered management.

**Essential measures and perceived problems in eradication**

**Essential measures** Elimination of BLV-seropositive animals from the herd with at
least three consecutive tests for all animals, 3–6 months apart, and strict avoidance
of blood (lymphocyte) contacts between animals.

**Perceived problems** The tests for antibodies against BLV in BTM will only detect
herds in which the BLV prevalence is greater than 5% (Klintevall et al., 1991; Hayes
and Burton, 1998). In large herds the prevalence may well remain below 5%. The
length of the time from infection to seroconversion (57 d, 95% CI 49–75 d) may
complicate the assessment of the time and route of transmission.
2.4.4 MV

Iceland is the only European country that has definitely eradicated the disease (Pálsson, 1985). However, according to the OIE Handistatus statistics (Handistatus, 2004d) the last reported clinical case of MV, for example in Ireland, had been in 1986. An eradication programme had been carried out in this country in the 1970s and early 1980s (Guven, 1985). However, Ireland is not free of CAEV according to the OIE statistics.

Control and eradication programmes for lentivirus infections have been established or attempted in many other European countries: Belgium (Biront and Deluyker, 1985), Denmark (Hoff-Jørgensen, 1985), France (Remond et al., 1985), the Netherlands (Houwers et al., 1987), Norway (Krogsrud, 1985; Dyrehelsetilsynet, 2003), Sweden (SVA, 2003) and Switzerland (Scheer-Czekhowski et al., 2000). Similar programmes or procedures are also active in North America (Knight, 2004; Menzies and Simard, 2001; Williams-Fulton and Simard, 1989). There are four common features to most of these programmes:

– Serological testing of all animals over 6 months of age;

– Segregating or culling of the seropositive animals and their progeny, or, in case the proportion of seropositive animals in the flock is high, stamping out the entire herd;

– All animals over 6 months of age are tested at 6 to 12-months intervals, and the seropositive animals removed. This testing is repeated until no new seropositive animals are detected in two annual tests;

– All replacement animals for the free herd must originate only from similar free herds – or the animals must be quarantined and shown to be seronegative with sufficient testing.

Variations in the general scheme include delivery by Caesarean section or isolation at birth of the progeny from seropositive dams and heat-treating or pasteurizing of the dam’s colostrum and milk (Houwers et al., 1987). Restrictions are imposed on contacts with other herds on pasture or in animal shows, and the Norwegian programme (Krogsrud, 1985) also has explicit restrictions on ram circle activity. Most programmes require regular follow-up testing even after attaining the free status, either of all animals or a representative sample of them.

Essential measures and perceived problems in eradication

Essential measures  So far the only really effective measure for eradication on a national scale has been decisive stamping out in the Icelandic manner. The culling of seropositive animals and their progeny in a repeated testing scheme has been shown to be effective in clearing individual herds of the infection.
**Perceived problems**  Estimates for the mean time from infection to seroconversion range from weeks to several months, and some animals may remain seronegative (Sihvonen, 1981; Pepin et al., 1998). Some seropositive ewes may even become seronegative shortly after lambing as a result of depleting circulating antibody through the colostrum (Knight, 2004). The clearing of herds under control schemes which depend essentially on detecting seroconverted animals may hence be impeded.
3 Aims of the study

The aims of the present thesis were to:

1 compile and review information presented in the literature concerning
   • the aetiology and pathogenesis of four significant viral infections and diseases of domestic ruminants (I, III–V)
   • the epidemiological aspects or features of these infections and diseases (I–V)
   • the control and prevention measures applied against these infections and diseases (I–V)
   • the attempts to eradicate these infections and diseases (I–V),

2 describe
   • the legal and official framework for control of the four infections and diseases in Finland (II–V)
   • the measures applied to control and eradicate these infections and diseases from Finland (I–V)
   • the development in the situation of these infections and diseases in Finland (I–V)

3 assess the efficacy of the measures applied in Finland employing the concept of the reproduction ratio of infections (R).
The Finnish approach to control and prevention

4.1 Framework and measures

4.1.1 Pertinent domestic and EU legislation

General

The Animal Diseases Act (55/1980) with its later amendments (809/1992, 424/1994, 1193/1996, 491/1997, 1000/1997, 398/1998, 804/1999 and 1000/1999), and the Animal Diseases Decree (601/1980) laid down on basis of the Act, with its later amendment (117/1998), provide the general framework for the control and prevention of all animal diseases. The classification of specific diseases according to their communicability, severity and other characteristics is given in Decision 1346/1995 of the Ministry of Agriculture and Forestry (MAF). This decision has been amended three times (532/1997, 136/1998 and 200/2004). The domestic legislation concerning control of animal diseases in intra-community trade and trade with third countries (foremost MAF Decrees 1338/96 and 655/2003, and decisions 572/95 and 1548/94, with their later amendments) are harmonized with the respective EU legislation. To complement the official measures to prevent the import of animal diseases through trade the Association for Animal Disease Prevention (ETT ry) has issued standing instructions for import of animals, semen and embryos (ETT, 2004). Observing the instructions of this private association is voluntary, but the ETT member slaughterhouses, dairies, and egg packaging plants do not accept animals or products from animals imported in contravention of or neglecting the instructions. The “Domestic legislation” chapters below deal with the disease-specific statutes and other legislation such as overall health-control programmes in which the diseases are referred to. Although laid down in the disease-specific decrees and circulars, the actual control programmes and schemes are presented separately.

BVD

Domestic legislation  Prior to May 2004 there was no specific domestic legislation for BVD. A new decree was laid down in 2004 to control this disease (MAF 2/EEO/2004). The decree elevated the status of BVD to notifiable and cases of BDV must be reported monthly to the Department of Food and Health (earlier Veterinary and Food) of the MAF. The new decree enables decisive actions to limit the spread of the infection. Specifically, a suspected or confirmed BVD-positive herd is placed under restrictive measures that include mandatory reporting of the infection to the associated dairy and slaughterhouse, and to visitors whose entrance to the animal shed is unavoidable. Protective clothing and footwear must be provided to these visitors. Further, all the animals on the farm must be listed and accounted for, moving of the animals to or from the farm except to slaughter is prohibited, and contact with other cattle, sheep or goat farms must be prevented. The essential measure to eliminate the infection is culling all of the PI animals and their progeny less than 3 months of age, and subsequent follow-up between 4 and
12 months after the PI animals have been culled. Pending application by the owner of a PI animal, the authorities can order its slaughter at the partial expense of the state. Inspection visits, the taking of appropriate samples by the veterinarian and examination of the samples, pursuant to the decree, are also recompensed by the state. The district veterinarian is obliged to conduct an epidemiological investigation to identify the source of the infection and to trace the contact herds where the infection may have spread. The contact herds are also placed under restrictive measures if deemed appropriate, and the BVD situation is assessed. If goats, sheep or pigs are also kept on the farm the district veterinarian decides on the testing of these animals. The restrictive measures are withdrawn only either after the initial suspicion is shown to be unfounded, or the follow-up after culling of the PI animals has proved that there is no more active infection in the herd, or 30 days have passed after slaughter of all cattle and disinfection of the premises.

The MAF circular 3/93, laying down the health requirements for bovine semen, necessitated that bull calves to be sold to rearing stations and their herds of origin must be tested for antibodies against BVDV. The calves had to be retested at the rearing station and as bulls at the AI station at least once a year for BVDV antibodies, with negative results. If a bull seroconverted while in the station the semen taken since the last seronegative result could not be used. The MAF decree 6/EEO/2004 replaced circular 3/93. The requirements have been preserved except that if a bull seroconverts while in the station the semen taken since the last seronegative result can be used if it is tested for BVDV, with negative results.

**EU legislation** EU legislation does not contain BVD-specific directives or regulations. Directive 2003/43/EEC, the fourth amendment to Directive 88/407/EC especially with respect to the animal health requirements applicable to intra-Community trade and imports of semen of bovine animals, requires that the donor bulls be tested for both BVD virus antigen and antibodies against BVDV before and during the quarantine preceding movement to AI centres. The condition for entering the AI centre is that if seroconversion occurs during the quarantine the animals that are still seronegative are kept in quarantine until no seroconversions occur in the group for a period of three weeks. Seropositive animals are allowed entry to the AI centre. When in the centre, all the seronegative animals must be tested once a year for antibodies against BVDV. Should an animal seroconvert, every ejaculate of that animal collected since the last negative test shall either be discarded or tested for BVD virus antigen with negative results.

**IBR**

**Domestic legislation** The control measures for IBR were laid down in the MAF circular 1/93. The disease is notifiable according to MAF decision 426/1993 and cases of IBR must be reported without delay to the Department of Food and Health (earlier Veterinary and Food) of the ministry. If IBR infection is suspected in a herd, all bovine animals of the herd must be tested for antibodies against BHV-1. A suspected or serologically confirmed IBR antibody-positive herd is placed under restrictive measures that include the following:
- Seropositive and clinically ill animals must be isolated to the extent possible from the other animals and kept indoors;

- Bovine animals can only be transported from the farm for slaughter;

- Delivery of bovine semen from the herd and the use of animals for natural mating are prohibited;

- After the seropositive animals have been culled the stalls and appliances must be cleaned and disinfected with disinfectants that are active against viruses;

- Unnecessary visits to the animal shed must be avoided and the use of protective clothing and footwear in the shed is mandatory.

No restrictions are imposed on the use of milk or its delivery to the dairy.

The restrictive measures can also be based on results from the annual bulk-tank milk surveillance. Pending application by the owner and the recommendation of the district veterinarian, the authorities can order the slaughter of seropositive animals at the partial expense of the state. The clinical examination of the entire herd and taking of the appropriate samples by the veterinarian, pursuant to the decree, are also recompensed by the state. The municipal veterinarian is obliged to conduct an epidemiological investigation to map the spread of the infection, according to instructions from the district veterinarian. The restrictive measures are only withdrawn after seropositive animals have been culled and the other animals tested negative twice, one month after the culling and then four months after the first test, at the earliest. If goats, sheep or pigs are also kept on the farm the district veterinarian decides on the testing of these animals.

The compulsory health control program (MAF 16/EEO/1997) for deer farms requires that all the deer over 6 months of age on farms that sell animals must be examined once for antibodies against BHV. Seropositive animals must be isolated and the veterinary authorities decide how they are dealt with.

The Veterinary Department letter 1104/143 (1981) concerning health monitoring programme for AI bulls stipulated that an AI bull had to be tested for antibodies against BHV-1 before entering the AI station, and before sending it from the station to slaughter. The MAF circular 3/93 replacing 1104/143 and laying down the health requirements for bovine semen necessitated that bull calves to be sold to rearing stations and their herds of origin must be tested for antibodies against IBR/IPV. The calves had to be retested at the rearing station and as bulls at the AI station at least once a year for IBR antibodies, with negative results. If a bull seroconverted while in the station the semen taken since the last seronegative result could not be used. The MAF decree 6/EEO/2004 replaced circular 3/93, but the requirements have been preserved. The MAF circular 1/94, laying down the health requirements for bovine embryos, requires that the herd of origin of the donor animal must have been free of IBR/IPV for the previous 6 months.
EU legislation  Annex E (II) to Directive 64/432/EEC, last amended in 1997 (Directive 97/12/EC), lists IBR among the diseases for which national control programmes may be approved and additional guarantees requested. IBR is also a disease for which the control and eradication programmes in both AI and embryo units and other types of enterprise may receive a financial contribution from the Community (latest Decision 2004/450/EC, Annex I Part A). Finland has since 1994 been one of the IBR-free countries to which the additional guarantees for IBR apply (latest Decision 2004/558/EC, Annex II). The guarantees include:

- Bovine animals for breeding and production, originating from countries or regions to which the guarantees do not apply, and destined to Finland, must come from a holding on which no clinical or pathological evidence of IBR has been recorded for the past 12 months;

- they must have been isolated for 30 days immediately prior to movement and all bovine animals in the same facility must have remained free of clinical signs of IBR during that period;

- they and other bovine animals of the isolation facility must be tested with negative results for antibodies against BHV-1 not earlier than 21 days after their arrival at the isolation facility; and

- they must not have been vaccinated against IBR. Bovine animals for slaughter must be transported directly to the slaughterhouse.

Directive 2003/43/EC, the fifth amendment to Directive 88/407/EC laying down the animal health requirements applicable to intra-Community trade and imports of semen of bovine animals, requires that the donor bulls be tested for antibodies against BHV-1 (whole virus) both before the quarantine if the animals do not come from an IBR-free herd, and during the quarantine with negative results. If any animals test positive during the quarantine, these animals shall be removed immediately from the quarantine station and the other animals in the group retested no less than 21 days after the removal of the positive animals, with negative results. The bulls are to be tested at least once a year for antibodies against BHV-1 (whole virus) with negative results. If the result is positive the animal must be isolated and the semen collected since the last negative test may not be subject to intra-community trade. Decision 94/113/EC, amending Directive 89/556/EEC on animal health conditions governing intra-Community trade in and importation from third countries of bovine embryos, requires that the donor animal must come from a herd in which no animal has shown signs of IBR/IPV during the previous 12 months.

EBL

Domestic legislation  The earliest government decision concerning the control of EBL was given in 1966 (MAF 242/1966). This decision outlined the haematological screening of herds based on leukocyte counts (Bendixen, 1965). Subsequent MAF circulars (168/1976, 173/1979 and 183/1980) refined and expanded upon the control measures. The current MAF circular 2/1993 contains a programme
(part 8) for attaining herd-level freedom from EBL. This part was removed in 1997 (MAF15/EEO/97) when mainland Finland was officially declared free of EBL. EBL is a notifiable animal disease according to MAF decision 426/93 and cases of EBL must be reported without delay to the Department of Food and Health (earlier Veterinary and Food) of the ministry.

The current measures are as follows: if a bovine animal is suspected of having EBL based on clinical symptoms (e.g. tumorous external lymph nodes) or pathological or meat inspection findings (e.g. lymphoid tumors in several organs), histological and serological samples must be taken and examined in the National Veterinary and Food Research Institute. The herd of origin (as a suspected leukotic herd) is placed under restrictive measures by the official municipal veterinarian. Restrictions can also be imposed on a herd on the basis of the annual bulk-tank milk surveillance results. Serum samples from all bovine animals of the herd are examined for antibodies against BLV immediately and again after three months at the earliest. All bovine animals over two years old are also examined clinically. If all results turn out negative the restrictions are withdrawn. If seropositive animals are found, the restrictions are maintained until all such animals are slaughtered and the other animals are found to be seronegative in samples taken no sooner than three months after the last slaughter. Pending application by the owner and the recommendation of the district veterinarian, the authorities can order the slaughter of seropositive animals at the partial expense of the state. The clinical examination of animals suspected of leukemia and the taking of appropriate samples by the veterinarian, pursuant to the Circular, are also recompensed by the state. The restrictions are only withdrawn when all animals are seronegative. The municipal and district veterinarians are obliged to conduct a further epidemiological investigation to map the spread of the infection. If sheep are also kept on the farm the district veterinarian decides on the testing of these animals.

The Veterinary Department letter 1104/143 (1981) concerning health monitoring programme for AI bulls stipulated that an AI bull had to be tested for antibodies against BLV before entering the AI station, and before sending it from the station to slaughter. The MAF circular 3/93, replacing 1104/143 and laying down the health requirements for bovine semen, necessitated that bull calves to be sold to rearing stations and their herds of origin must be tested for antibodies against BLV. The calves had to be retested at the rearing station and as bulls at the AI station at least once a year for BLV antibodies, with negative results. If a bull seroconverted while in the station the semen taken since the last seronegative result could not be used. The MAF decree 6/EEO/2004 replaced circular 3/93, but the requirements have been preserved. The circular 1/94 of MAF, laying down the health requirements for bovine embryos, requires that the herd of origin of the donor animal must have been free of EBL for the previous 3 years, or otherwise shown to be free of the disease.

and the minimum criteria that the national plans for the eradication of EBL should satisfy to receive a financial contribution from the Community were established in Directive 78/52/EEC. Mainland Finland has since 1996 been officially free of EBL (latest Decision 2004/320/EC, Annex V).

Decision 98/372/EC concerning the animal health conditions for imports of live bovine animals from certain European countries requires that the herds of origin of the animals to be imported must be EBL-free as defined by Annex 5 to the Decision and tested for antibodies against BLV within a month before import, with negative results. Animals intended for meat production or to be transported directly to slaughter must come from herds included in national programmes for the eradication of EBL. Directive 2003/43/EEC, the fifth amendment to Directive 88/407/EC laying down the animal health requirements applicable to intra-Community trade and imports of semen of bovine animals, requires that the donor bulls to be quarantined before entry to the AI station must come from an officially EBL-free herd, or produced by dams tested for antibodies against BLV with negative results. The bulls must be tested within 28 days preceding the quarantine, and at least once a year in the AI centre for antibodies against BLV with negative results. If the test result of a bull while in the AI station is positive the animal must be isolated and the semen collected since the last negative test may not be subject to intra-community trade. Decisions 94/113/EC and 2005/217/EC, amending Directive 89/556/EEC on animal health conditions governing intra-Community trade in and importation from third countries of bovine embryos, requires that the donor animal must come from a herd that is EBL-free, or from a herd that is not EBL-free but for which certification has been obtained that there have been no clinical cases of EBL during the previous three years.

MV

Domestic legislation  Maedi–visna in sheep and caprine arthritis encephalitis (CAE) in goats are notifiable animal diseases according to the MAF decision 1346/1995, and cases of MV and CAE must be reported without delay to the Department of Food and Health (earlier Veterinary and Food) of the ministry. The current decree on the control of MV and CAE was given in 2001 (MAF 15/EEO/2001). This decree replaced MAF decision 1/EEO/1999 on the subject.

The current measures are as follows: if there are reasonable grounds to suspect that sheep of a flock have MV the municipal veterinarian places official restrictive measures on the flock and takes samples to confirm the diagnosis. The restrictive measures prohibit the movement of the animals to or from the farm except to slaughter, and delivery of sheep-based products to other sheep or goat farms requires permission from the district veterinarian. If the diagnosis is confirmed, blood samples are taken from all sheep over 1 year of age and tested for antibodies against MVV. The district veterinarian is obliged to conduct an epidemiological investigation to trace the source of the infection and those contact herds where the infection may have spread further. The official restrictive measures are also imposed on all suspected contact herds and all sheep over 1 year of age in each are tested for antibodies against MVV. Costs from sampling and laboratory
examinations are defrayed by the state. The restrictive measures are withdrawn only if the diagnosis is not confirmed in the laboratory examination of the samples, if all infected (seropositive) animals and their progeny are culled and the other sheep over 1 year of age test negative for antibodies against MVV in two subsequent samplings, 5–7 months and 12–16 months after the first sampling, or if at least 14 days have passed after the slaughter of all sheep and goats and disinfection of the premises.

**EU legislation** Directive 91/68/EEC defining the animal health conditions governing intra-Community trade in ovine and caprine animals requires that animals for breeding must have been obtained from a holding and must only have been in contact with animals from such a holding in which MV has not been clinically diagnosed in the previous three years. This period shall be reduced to 12 months in the animals infected with MV have been slaughtered and the remaining animals react negatively in two subsequent tests for antibodies against MVV. Health guarantees provided for the herds by approved control programmes also meet the requirements for trade. Directive 91/68/EEC lists MV in Annex B III as one of the diseases for which national control programmes can receive financial contribution from the Community, according to Decision 90/424/EC. Directive 92/65/EEC, laying down animal health requirements governing the trade in and imports into the Community of, for instance, semen of sheep, requires that the animals used for the collection of semen fulfil the criteria laid down in Directive 91/68/EEC for animals intended for breeding.

### 4.1.2 Control programmes

#### BVD

A voluntary BVD control program was launched by the Veterinary and Food Department of MAF in 1994. The programme included both dairy and beef herds, and was based on formal affiliation to the programme and meticulous recording of animal-related events in the herd by the owner. The herds were tested twice with 4–12 month intervals either using BTM or individual sera as samples, and classified either as BVD-free I or II class herds, or BVD herds. Herds in BVD-free class I had neither antibodies against BVDV nor showed any indication of infection. Animals in herds classified as BVD-free class II had antibodies against BVDV but there was no indication of active infection in the herd. BVD herds contained animals positive in the virus isolation test (PI animals). The programme contained detailed instructions concerning the regular serological follow-up of the herds, the trade of animals between herds, visits of animals to exhibitions and measures to eradicate the active infection from BVD herds.

The voluntary control programme launched in 1994 expired at the end of 2004. The new decree (MAF 2/EEO/2004) provided a reviewed voluntary BVD health control scheme for cattle herds. The control scheme is recommended especially for farms that actively sell animals for breeding, or that have joined an embryo-ring operation. The new scheme, like the old control programme, is based on regular testing of the herds for antibodies against BVDV, and the commitment of the herd owners
to comply with the requirements of the scheme; however, the classification of herds has been removed. The new scheme sets new time limits for the regular retesting of the herds. After the first two tests for antibodies against BVDV with a 7 to 18-month interval the herd has to be retested with an interval of at most 24 months. The annual BTM surveillance testing is accepted for the purposes of the scheme. The scheme is also more explicit with regard to embryo transfer and artificial insemination than the old control programme. The semen used in a herd that has joined the control scheme must come from an officially approved AI centre, and the embryos from the same herd or from another herd in the scheme. If this is not the case the dam that has conceived must be examined for antibodies against BVDV at the earliest 4 weeks but at most 12 weeks after the insemination or embryo transfer. If the dam seroconverts it must be isolated before parturition. The offspring must also be isolated and examined for BVDV as soon as possible. The stipulations for trade and contact with other herds such as visits to exhibitions have mainly been preserved from the old programme. The municipal veterinarian is obliged to issue a health certificate to herds both in the scheme and not in the scheme provided that the conditions of the voluntary scheme have been observed.

In addition to the official control programme, a voluntary control or “sanitation” programme for dairy herds found to have antibodies against BVDV in BTM was set up by the VALIO dairies cooperative in 1994. The sanitation agreement between the farmer and the associated dairy required that all the bovine animals >3 months of age in the herd were tested to identify the seronegative PI-animals. If found they were slaughtered and about a year later 3 to 15-month-old animals were tested. The latter included those that were too young to be tested in the first round. The costs of sampling and laboratory examinations were defrayed by the associated dairy; however, the owner took care of the expenses due to slaughtering the PI animals. The farmer further agreed to obtain new animals for the herd only from known BVD-negative herds. The Association for Animal Disease Prevention (ETT ry) took over the administration of the sanitation programme in 2000. The programme was eventually replaced by the decree MAF 2/EEO/2004.

**IBR**

The MAF circular 1/93 laying down the control measures for IBR does not include further control programmes or schemes.

**EBL**

The MAF circular 2/93 laying down the control measures for EBL contained a programme that set standards by which a herd could be declared and remain free of EBL. The programme was voluntary except for herds selling bulls to AI stations or exporting live animals into the European Community. A cattle owner could join the programme through written agreement with the municipal veterinarian. Adhering to the programme required detailed accounting of the animals’ identification, dates of birth, slaughtering or cause of death, selling to or buying from other herds, and copies of health certificates.
Achieving the EBL-free status required that:

- All bovine animals >24 months old and those <24 months old and introduced to the herd from herds of unknown EBL-status were tested twice at 4–12 month intervals for antibodies against BLV. A BTM sample in dairy herds could be used for testing, but the animals not contributing to BTM (dry cows, those treated e.g. with antibiotics, heifers and bulls) must have been sampled individually.

- All the results were negative and no clinical signs of EBL or BLV infection had been detected for the previous two years.

- If an animal was introduced from a herd of unknown EBL status it must have been tested for antibodies against BLV within 30 days prior to the intended transfer with negative results. The transferred animal must have been kept in isolation for at least 4 months and then retested for BLV infection. If the introduction took place between the first two tests of the entire herd, then the second testing could be done at the earliest 4 months after the introduction of new animals.

- If a new herd was composed entirely of animals from certified EBL-free herds, the district veterinarian could approve its EBL-free status on this basis. However, the herd must have been tested for antibodies against BLV 4–6 months after the approval, with negative results.

The municipal veterinarian was obliged to issue a health certificate to a herd fulfilling the criteria above.

Maintaining the EBL-free status required that:

- All the animals >24 months old in an EBL-free herd must have been tested for antibodies against BLV every third year. As above, a BTM sample in dairy herds could be used for testing but animals not contributing to the BTM must have been sampled individually.

- New animals introduced to an EBL-free herd must without additional testing have come from a certified EBL-free herd. If an animal came from a herd of unknown EBL status it must have been >24 months old and tested for BLV infection within 30 days prior to the intended transfer, with negative results. The transferred animal must have been kept in isolation for at least 4 months and retested. The transfer of animals <24 months old needed permission from the district veterinarian.

The programme contained further stipulations and conditions for visits to animal exhibitions and other happenings, for contact with animals of other herds on pasture, and AI and embryo transfer activities. However, this programme for herd-level EBL-freedom (part 8) of the circular was removed in 1997 (MAF decision 15/EEO/97) when mainland Finland was declared officially free of EBL.
The first control programme for MV, approved by the MAF, was launched in 1995. This programme was voluntary. The current decree on the control of MV (MAF 15/EEO/2001) also contains a health control programme (part 9) which is compulsory for flocks with more than 20 ewes. The new programme is only slightly revised from the previous voluntary programme. The MV control programme takes into account the slowly progressing nature of the disease necessitating constant clinical and serological monitoring of the health status of the flocks. Joining the programme, having the scheduled serological tests done on the flock and observing the other conditions of the programme enable the sheep farmer to obtain a stepwise rising health status and eventually the official MV-free status for his flock. All the sheep in the flock must be listed and accounted for, and animals that are tested for MV must have some form of individual identification, e.g. an ear tag. The list of animals >12 months of age must contain the following information: breed, gender, identification number, date of birth, pedigree, date of slaughter or date and cause of death. Detailed data on all purchases, selling or movements of animals, and contact information on the buyers or sellers must also be available. The programme furthermore contains detailed instructions for acquiring new animals from other herds and contact with other herds, e.g. through animal exhibitions. Costs from examination of all of the samples as well as those incurred from compulsory sampling are defrayed by the state; however, the owner has to cover those incurred from voluntary sampling. The control programme is schematically presented in Figure 1.

4.2 Development in the disease situation

4.2.1 General

Prior to 1990 the monitoring of domestic animals for viral diseases mainly consisted of annual statistics compiled from the results of samples sent in to the central veterinary laboratory because of mandatory testing of specific animals or animal groups, to be examined for a particular viral infection or disease, or to determine the cause of death of an animal. The latter frequently also included virological examinations. While these statistics do in a very general way reflect the viral disease situation, no actual prevalence studies with proper random sampling were conducted. Screening of bulk-tank milk samples of dairy herds for antibodies against selected viral disease agents, introduced in 1990, began to significantly improve knowledge of the actual occurrence of the bovine infections or diseases BVD, IBR and EBL. A reasonably comprehensive annual serological survey for antibodies against the MV virus among sheep breeding flocks, started in 1994, gave corresponding cross-sectional information on the occurrence of MV in Finland.

4.2.2 Materials and methods

The results of the virus neutralization tests, haematological, serological and bulk-tank milk surveillance examinations (I–V) were extracted from annual statistics
Figure 1 MV control programme for sheep. Reprinted from V, p 216, with permission from Elsevier.

compiled by the Finnish National Veterinary Institute (since 1994 the National Veterinary and Food Research Institute EELA). Official meat inspection data (IV) were compiled from the annual statistics of the Veterinary Department of MAF. Detailed information of applied control and eradication measures were obtained from the archives of the State Provincial Office of Southern Finland (III). The insemination
statistics of the herds (III) were obtained from the registers of ProAgria Agricultural Data Processing Centre Ltd, Vantaa Finland, with permission from the herd owners. The individual groups of animals from which the haematological or serological samples were taken, are identified in the descriptions of the developments in the disease situation below.

The haematological method (IV) consisted of counting the leukocytes of a blood sample in a counting chamber and applying the classification key of Bendixen (1965) to the results. The serological methods consisted of in-house virus neutralization tests (BVD prior to 1990, III) and in-house (IV) or commercial agar gel immunodiffusion (AGID) assays (V). Commercial enzyme immunoassays (EIA or ELISA) were used to examine the serum and bulk-tank milk samples since 1990 (I–IV). Microplate readers were used to measure the optical densities of the kit test plate wells and associated software to process and interpret the raw data. The presence of BVD virus in serum samples was determined by culturing in bovine turbinate cells (I) or using the immunoperoxidase method (II). Details of the tests and Information of the vendors of the commercial kits can be found in the original publications.

4.2.3 Situation according to health monitoring

BVD (I, II)

Rislakki (1961) mentioned that antibodies against viral diarrhoea virus had also been tested for in samples taken to study the occurrence of para-influenza in cattle, but had not been found. However, Estola (1964) noted this disease in his review on animal virus diseases in Finland, and claimed a low level of occurrence. Positive findings from serological testing for antibodies against BVDV were occasionally reported in the annual statistics of the National Veterinary Institute (Table 7). The samples came from individual animals and information on the numbers of herds they represented is no longer available. However, the small numbers of samples examined in most years before 1987 indicate that the number of herds must have been only a small fraction of the total.

IBR (III)

Monitoring for IBR among specific groups of animals started in 1965 (Table 7). The tested animals consisted mainly of heifers to be exported, live animals imported to Finland, and animals with a respiratory infection for which a definite diagnosis was considered necessary. Compared to the numbers of samples examined for BVD the annual numbers for IBR show a moderate increase. The average number of samples examined was 68 in 1965–1973 (range 4–159), 661 in 1974–1985 (range 335–890), and 2126 in 1986–1989 (range 523–2947). The samples came from individual animals and information on the numbers of herds they represented is no longer available. Even between 1986 and 1989 the average number of samples represented only some 0.15% of the contemporary cattle population and the fraction of herds they came from was most likely of the same order of magnitude.
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<td>0/3</td>
</tr>
<tr>
<td>1981</td>
<td>0/44</td>
<td>0/718</td>
<td>76/10 062</td>
<td>3/102</td>
</tr>
<tr>
<td>1982</td>
<td>1/12</td>
<td>0/660</td>
<td>68/10 694</td>
<td>–</td>
</tr>
<tr>
<td>1983</td>
<td>10/66</td>
<td>0/776</td>
<td>58/9 642</td>
<td>–</td>
</tr>
<tr>
<td>1984</td>
<td>0/307</td>
<td>0/890</td>
<td>28/8 795</td>
<td>–</td>
</tr>
<tr>
<td>1985</td>
<td>0/40</td>
<td>0/734</td>
<td>27/9 951</td>
<td>0/140</td>
</tr>
<tr>
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<td>0/161</td>
<td>0/2 947</td>
<td>12/9 052</td>
<td>0/108</td>
</tr>
<tr>
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<td>0/1176</td>
<td>0/2 872</td>
<td>11/9 049</td>
<td>0/2</td>
</tr>
<tr>
<td>1988</td>
<td>24/1 699</td>
<td>0/2 352</td>
<td>14/7 163</td>
<td>0/7</td>
</tr>
<tr>
<td>1989</td>
<td>7/509</td>
<td>0/1 014</td>
<td>7/8 237</td>
<td>0/207</td>
</tr>
<tr>
<td>1990</td>
<td>199/521</td>
<td>3/2 920</td>
<td>18/7 839</td>
<td>0/291</td>
</tr>
<tr>
<td>1991</td>
<td>208/4 698</td>
<td>97/6 624</td>
<td>28/7 373</td>
<td>0/120</td>
</tr>
<tr>
<td>1992</td>
<td>221/6 135</td>
<td>1/7 496</td>
<td>26/8 490</td>
<td>–</td>
</tr>
<tr>
<td>1993</td>
<td>141/5 465</td>
<td>0/4 954</td>
<td>24/7 139</td>
<td>–</td>
</tr>
<tr>
<td>1994</td>
<td>2 832/16 524</td>
<td>0/5 237</td>
<td>7/9 604</td>
<td>46/12 931</td>
</tr>
<tr>
<td>1995</td>
<td>936/9 480</td>
<td>0/3 078</td>
<td>13/7 326</td>
<td>12/10 362</td>
</tr>
<tr>
<td>1996</td>
<td>196/4 100</td>
<td>0/2 343</td>
<td>4/6 139</td>
<td>8/14 118</td>
</tr>
<tr>
<td>1997</td>
<td>303/2 841</td>
<td>0/2 903</td>
<td>2/4 723</td>
<td>0/14 095</td>
</tr>
<tr>
<td>1998</td>
<td>330/2 323</td>
<td>0/2 125</td>
<td>0/4 616</td>
<td>0/10 802</td>
</tr>
<tr>
<td>1999</td>
<td>494/2 565</td>
<td>0/2 298</td>
<td>0/3 278</td>
<td>0/10 312</td>
</tr>
<tr>
<td>2000</td>
<td>447/3 913</td>
<td>0/2 688</td>
<td>0/2 781</td>
<td>0/6 769</td>
</tr>
<tr>
<td>2001</td>
<td>491/3 620</td>
<td>0/2 132</td>
<td>0/2 095</td>
<td>1/12 427</td>
</tr>
<tr>
<td>2002</td>
<td>98/2 898</td>
<td>0/2 020</td>
<td>0/2 230</td>
<td>1/16 783</td>
</tr>
<tr>
<td>2003</td>
<td>22/3 150</td>
<td>0/2 313</td>
<td>0/2 296</td>
<td>0/16 602</td>
</tr>
<tr>
<td>2004</td>
<td>312/3 588</td>
<td>0/1 790</td>
<td>0/1 977</td>
<td>0/16 356</td>
</tr>
</tbody>
</table>

¹ no. positive/no. tested
² no record available
³ before 1979 hematological and since then serological results
The infection was encountered for the first time in December 1970, when the serum of an AI bull showing signs of respiratory infection tested positive for antibodies against BHV-1. On closer (and partly confirmatory) testing in 1971, nine of its station mates were also found to have antibodies against the virus. Between 1972 and 1989 the antibodies were not encountered in health monitoring (Table 7), but in 1990 calves with signs of respiratory infection in a large herd turned out to be seropositive against BHV-1. This herd was also positive in the first BTM surveillance in the same year. The total number of herds with BHV-1 infection in the subsequent investigation and BTM surveillance in 1991 was five and the total number of seropositive animals in these herds was 90. Health monitoring from 1992 onwards has not revealed any new seropositive herds. Strict control measures in 1991 eliminated the infection from all but one herd. The last BHV-1 infected herd was entirely stamped out in 1994.

**EBL (IV)**

Berger and Henriksson (1966) were the first to note the presence of EBL in Finland and the need for control measures against it. Compared to BVD and IBR the health monitoring for BLV infection or manifest EBL has been more intense since that year. Information on the occurrence of the infection or disease was based on meat inspection statistics and haematological testing between 1966 and 1978 and subsequent serological monitoring since 1979 (Table 7). The haematologically positive PL animals were those classified into Bendixen group III (Bendixen, 1961). The haematologically or serologically tested samples were drawn from three groups of animals: i) herds suspected of leukosis on clinical or meat inspection grounds, herds of origin of bull calves intended for AI service and herds sold at auction (on average 80–85% of the samples); ii) heifers exported to the Soviet Union (15–20%); and iii) occasionally the AI bulls (1–2%). The average number of leukotic animals found in meat inspection/100,000 animals at slaughter between 1968 and 1978 was 11 (range 3–19). The average proportion of positive haematological results between 1966 and 1978 was 1.4%. A decreasing trend was apparent in the proportions of positive serological results from 0.8% in 1979 to 0.04% in 1997. In addition to confirmatory testing for meat inspection findings, the samples came from individual animals and information on the numbers of herds they represented is no longer available. The monitoring results have been negative since 1997.

**MV (V)**

The first record of samples being tested for antibodies against MVV is from 1976, according to the annual statistics of the National Veterinary Institute (Table 7). A small number of samples were tested annually in 1976–1981, and then again in 1985–1991. The testing was associated mainly with the conditions of import and specific diagnostic purposes. The first positive results in the health monitoring came from samples of three imported sheep in 1981. Since the (re)detection of MV infection in Finland in 1994 the health monitoring of sheep for MV has been considerably increased (Table 7).
4.2.4 Situation based on annual BTM surveillance data (I–IV)

The first BTM surveillance for antibodies against specific viruses took place in 1990. In that year the random sample of dairy herds examined covered about one-fourth of all dairy herds. Since 1992 a laboratory sample of BTM has been obtained from virtually every dairy herd in the country. The laboratory samples have been examined for IBR and EBL since 1990. In 1992 a random sample of 5 024 of the 37 923 laboratory BTM samples collected in the same year were tested for BVD. Since 1993 all of the BTM laboratory samples have also been tested for BVD. The numbers of laboratory samples examined and the results as herd level seroprevalence for BVD, and numbers of IBR and EBL positive BTM samples between 1990 and 2004 are presented in Table 8. The numbers are compiled from the annual animal disease statistics of the National Veterinary and Food Research Institute, EELA (previously National Veterinary Institute).

Table 8 Annual dairy herd BTM surveillance data, 1990–2004

<table>
<thead>
<tr>
<th>Year</th>
<th>BTM no. tested</th>
<th>Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>BVD % positive</td>
</tr>
<tr>
<td>1990</td>
<td>9 879</td>
<td>–¹</td>
</tr>
<tr>
<td>1991</td>
<td>36 889</td>
<td>–</td>
</tr>
<tr>
<td>1992</td>
<td>5 024/37 923²</td>
<td>0.80</td>
</tr>
<tr>
<td>1993</td>
<td>34 115</td>
<td>0.96</td>
</tr>
<tr>
<td>1994</td>
<td>34 169</td>
<td>0.99</td>
</tr>
<tr>
<td>1995</td>
<td>32 588</td>
<td>0.66</td>
</tr>
<tr>
<td>1996</td>
<td>30 569</td>
<td>0.37</td>
</tr>
<tr>
<td>1997</td>
<td>28 577</td>
<td>0.42</td>
</tr>
<tr>
<td>1998</td>
<td>26 934</td>
<td>0.37</td>
</tr>
<tr>
<td>1999</td>
<td>24 872</td>
<td>0.36</td>
</tr>
<tr>
<td>2000</td>
<td>22 698</td>
<td>0.45</td>
</tr>
<tr>
<td>2001</td>
<td>21 040</td>
<td>0.24</td>
</tr>
<tr>
<td>2002</td>
<td>19 870</td>
<td>0.29</td>
</tr>
<tr>
<td>2003</td>
<td>18 519</td>
<td>0.15</td>
</tr>
<tr>
<td>2004</td>
<td>17 300</td>
<td>0.23</td>
</tr>
</tbody>
</table>

¹ not tested
² no. tested for BVD/no. tested for IBR and EBL
Individual serum samples of beef and suckler-cow herds were obtained on farm premises in 1993–1994, and at slaughter since 1995. From 2003 the sampling has been targeted especially at suckler-cow herds using the type of production data in the central bovine register (Rikula and Joutsenlahti, 2004). The numbers of samples examined and the numbers of positive results for BVD, IBR and EBL are presented in Table 9. The results are shown as absolute numbers to avoid the impression that they are actual prevalences. However, the targeted sampling in 2003–2004 has covered >90% of the approximately 1300 suckler-cow herds so that an estimate for herd-level prevalence is reasonably accurate. This estimate is 0.4% for 2003 and 0.15% for 2004.

### Table 9  Annual beef cattle and suckler-cow herd surveillance data, 1993–2004

<table>
<thead>
<tr>
<th>Year</th>
<th>No. samples tested</th>
<th>BVD no. positive</th>
<th>IBR no. positive</th>
<th>EBL no. positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993</td>
<td>3 248</td>
<td>54</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1994</td>
<td>12 764</td>
<td>64</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1995</td>
<td>2 544</td>
<td>40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1996</td>
<td>2 839</td>
<td>24</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1997</td>
<td>2 845</td>
<td>18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1998</td>
<td>2 758</td>
<td>21</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1999</td>
<td>2 920</td>
<td>24</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2000</td>
<td>2 899</td>
<td>17</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2001</td>
<td>2 996</td>
<td>10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2002</td>
<td>2 816</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2003</td>
<td>6 753¹</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2004</td>
<td>4 248</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

¹ sampling targeted to suckler-cow herds in 2003–2004

### 4.2.5 Situation based on annual beef and suckler-cow herd surveillance data, 1993–2004 (I–IV)

Further information on the occurrence of the infections or diseases BVD, which can be considered endemic, and MV, which can still claim a sporadic occurrence in Finland, is presented in Table 10. Except for the first three years, 1994 to 1996, the annual numbers of cattle herds with PI animals show no clear trend. Compari-
son of the data in Tables 8 and 10 indicates that the annual incidence risk of PI herds in Finland agrees well with the range of 0.02–0.03 cited by Lindberg (2002). The numbers of sheep flocks tested for MV between 1994 and 2004 represented roughly one-third of sheep farms according to the main production sector data (TIKE, 2005); it was 29.1% in 2001 and 37.0% in 2002. The main production sector sheep farms form approximately a half of all of the sheep farms receiving agricultural subsidies according to the IACS register data (TIKE, 2005).

Table 10  Number of BVD PI herds and MV status of sheep flocks, 1994–2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Cattle</th>
<th>Sheep flocks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of BVD PI herds</td>
<td>no. of BVD PI herds</td>
</tr>
<tr>
<td>1994</td>
<td>27</td>
<td>545</td>
</tr>
<tr>
<td>1995</td>
<td>13</td>
<td>431</td>
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<td>1996</td>
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<td>507</td>
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<td>1997</td>
<td>1</td>
<td>430</td>
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<td>1998</td>
<td>6</td>
<td>340</td>
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<td>1999</td>
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<td>2</td>
<td>320</td>
</tr>
<tr>
<td>2003</td>
<td>0</td>
<td>307</td>
</tr>
<tr>
<td>2004</td>
<td>2</td>
<td>275</td>
</tr>
</tbody>
</table>
5 Discussion

5.1 Assessment of the measures applied in Finland

5.1.1 General approach in assessment

An overall appreciation of the efficiency of the control and eradication measures can be gained by the actual results, i.e., development of the infection or disease situation. The combined efficacy of the measures could in theory be tested quantitatively for each affliction by comparing the observed developments to a hypothetical situation of “no control measures applied,” with some appropriate statistical procedure. However, this zero-control situation is not available, and the approach needs to be an essentially qualitative assessment based on compiling the existing information.

A central factor in determining the disease situation is the performance of the applied diagnostic tests. The diagnostic sensitivity and specificity are essentially population parameters that describe the test performance for a given reference population (with a given distribution of covariance factors), under defined conditions (laboratory, chosen cut-off, etc). The available information of the sensitivities and specificities of the employed tests is given in the original publications and summarized above for each disease in the diagnostic test performance subsections. However, in practice the lack of proper gold-standards usually prevented a critical evaluation of the alleged performance in the actual target population and given in-house conditions. Having to resort to intra-test controls only was tolerated because it was considered that this less than optimal situation was offset by the fact that each herd and in some instances each animal was tested repeatedly.

To establish at least some transparency and structure in the assessments of the applied control measures the reproduction ratio of infections, denoted with R, sometimes (curiously) referred to as reproductive rate (e.g., Lindberg, 2002) will be employed. This term is a dimensionless multiplication factor that refers to the average number of secondary cases generated by one primary case during its infectious period (Anderson and May, 1982). A specific case of R is the basic reproduction ratio, $R_0$, which refers to the situation when one infective individual is introduced into a population consisting entirely of susceptible individuals. Although the notation $R_0$ strictly speaking relates only to the theoretical specific case, it appears customary in the literature to use this symbol to also mean the net or effective R (e.g., Halloran, 1998). $R_0$ is considered useful in evaluating different strategies or interventions for disease control (Graat and Frankena, 1997; Halloran, 1998; Lindberg and Houe, 2005). $R_0$ for a specific type of contact can be conceptualized as a composite of three components: the probability of transmission for the contact type ($\beta$), the frequency of these contacts per time unit (c), and the duration of the infectious period (D), or as a formula:

$$R_0 = \beta \times c \times D$$

Some notes or specifications of the components need to be made. Halloran (1998) reported that the transmission probability ($\beta$) depends on characteristics of the in-
fectious host, of the susceptible host, of the parasite and on the definition of the contact. The characteristics of the infectious and susceptible host are reduced in the formula into some average or typical values, which of course is a gross over-simplification. The general health or immune status of the susceptible host, for example, can have a substantial effect on the transmission probability. Characteristics of the parasite, translated into inherent transmissibility of the etiological agent (Fraser et al., 2004), are also an important strain-dependent variable, although not amenable to control. There are also further assumptions including a constant frequency of infectious contacts and uniform infectivity during the infectious period.

To be useful in assessing intervention measures the three components should be independent of each other, or at least clearly separable. However, the frequency of infectious contacts (c) depends on the presence of the infectious animal(s), i.e. on the length of the infectious period (D). Once or if the infectious animal is, for instance, culled from the herd the frequency obviously drops to zero. If some intervention in the assessments below aims in the first place to shorten D then the secondary effect on c will not be considered. The length of the infectious period, D, does have an upper limit, i.e. the length of the period in the course of natural infection. Shortening of this period is one of the important intervention measures available, especially with agents of infections that are able to establish a persistent infection. For the sake of clarity, this component could also be denoted with \( D_{\text{int}} \) in the formula.

Thurmond (2005) suggests a fourth component to the equation, namely the reduction in the number of susceptible individuals in the population, as per vaccination, but does not present an explicit way to add the component to the formula. The effect of this factor could be included either in component \( \beta \) (characteristics of the susceptible host, Halloran, 1998), or component c in the formula. Nokes and Anderson (1988) simply replace the frequency c with the number of susceptibles present. Graat and Frankena (1997) present a formula for “number of effective contacts”, or \( R_0 \), where component c is replaced with terms of classical compartmental SIR model, in the form \( S_t \times I_t \times N \) (\( S_t \) for proportion of susceptible and \( I_t \) for proportion of infectious animals at time t, and N for total host population). Reducing the absolute number or proportion of the susceptibles leads directly to a decrease in \( R_0 \). Anderson and May (1991) allow for the susceptibles with the relation \( R = R_0 \times x \), where x is the proportion of susceptible animals in the population.

The heuristic simple formula above is, as defined, valid only for one specified type of contact producing a single type of infection, or “single infected compartment” (van den Driessche and Watmough, 2002). A more general or realistic formula accounting for all major types or compartments would need a substantially more rigorous approach (Farrington et al., 2001). The assessments of the disease control measures (below, in Tables 11–14) inevitably group together more than one specifiable type of infectious contact or compartment. The levels of influence of the measures on the three components are assigned in keeping with what is understood to be the strongest and not some hardly determinable average influence. Nevertheless, given the simplifications and groupings the plain deterministic formula is considered sufficient for the present rudimentary assessment of the control measures.
A numerical value for $R_0$ is by definition the initial upper boundary value for the net reproduction ratio $R$. The simple equation can only yield very sketchy numerical estimates for $R$ (Thurmond, 2005). Models for more accurate estimating of $R_0$ may be classified roughly into three groups depending on the data required (Farrington et al., 2001). The first is to build up a mathematical expression for it using parameters describing the contact structure in the target population, while the second approach relies on the time series data of susceptibles and cases, or final epidemic size data in a defined population. The third approach is to derive expressions for $R_0$ based on quantities estimated from the endemic equilibrium of the infection, such as aggregated surveillance data or serological surveys. However, a numerical value obtained in one setting can only be generalized with considerable provisos. The overall $R_0$ can be refined to within-herd (between individual) and between-herd $R_0$, which most likely have different values for a given infection. Available numerical estimates or reasonable deductions for the reproduction ratios of the infections are presented below. The $R_0$ is frequently considered to be a threshold parameter: for $R_0 < 1$ the epidemic will eventually die out, while for $R_0 > 1$ the infection will spread. Implicit in the formulas for $R$ is that the host population should be reasonably large in number to reach a meaningful stability in the parameters, for example in the frequency of infectious contacts. This does not necessarily materialize in small herds and chance fluctuations may be the deciding factor in the course of an outbreak within such a herd.

5.1.2 Assessment of the measures in terms of reproduction ratio $R$

The assessments are in each case based on intrinsic determinants of the hosts (Table 1), host–agent relationships (Table 2), and especially on sources of the agent and means of transmission (Table 3).

**BVD**

The measures to control BVD, the components of both within-herd and between-herd $R$ they influence and their assessed thrusts are compiled in Table 11.

Numerical estimates for the basic reproduction ratio of BVD infection have been presented by Cherry et al. (1998). The within-herd $R_0$ was estimated at 2.3 without, but at 35.0 with PI animals in the herd. Lindberg and Houe (2005) present semi-quantitative estimates for the transmission probability and frequency of infectious contacts for transmission of BVDV between herds, but do not venture to combine the estimates to derive actual numerical reproduction ratios.

**IBR**

The measures to control IBR, the components of both within-herd and between-herd $R$ they influence and their assessed thrusts are compiled in Table 12.
### Table 11  Assessment of BVD control measures using the disease reproduction ratio

<table>
<thead>
<tr>
<th>Measure</th>
<th>Influence on component</th>
<th>Within herd&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Between herds&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual health monitoring and surveillance data</strong></td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Voluntary programs 1994–2004, 2005–</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culling of PI animals</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Biosecurity measures (conditions on trade and other contacts, etc)</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Conditions on AI and embryo transfer (2005–)</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Measures of the decree 2/EEO/2004</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive measures on farm</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Culling of PI animals and their progeny &lt;3 months of age</td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Restrictions on animal movements</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Biosecurity measures (mandatory reporting to stakeholders, protective clothing for visitors, etc)</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Epidemiological investigation (tracing of contact herds)</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the decree 6/EEO/2004 of MAF and Directive 2003/43/EEC (animal health requirements in respect to bovine semen)</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>c&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>D&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>1</sup> scale: 2, major; 1, minor; 0, negligible
<sup>a</sup> probability of transmission in a given contact type
<sup>b</sup> frequency of infectious contacts of the given type
<sup>c</sup> duration of the infectious period
### Table 12  Assessment of IBR control measures using the disease reproduction ratio

<table>
<thead>
<tr>
<th>Measure</th>
<th>Influence on component</th>
<th>Within herd&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Between herds&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual BTM surveillance and health monitoring data</td>
<td>β&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Classification according to decision 426/93 of MAF (immediate notification of authorities)</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the circular 1/93 of MAF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive measures on farm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of seropositive and clinically ill animals</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Restrictions on animal movements</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Restrictions on delivery of semen and use of animals for natural mating</td>
<td>β</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Biosecurity measures</td>
<td>β</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Culling of seropositive animals and serological follow-up of entire herd</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Epidemiological investigation (tracing of contact herds)</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the decree 16/EEO/1997 of MAF (Health control program for deer farms)</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the Decisions 94/113/EC and 2005/217/EC (trade and import of bovine embryos)</td>
<td>β</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Additional guarantees of the Community (Decision 2004/558/EC)</td>
<td>β</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<sup>1</sup> scale: 2, major; 1, minor; 0, negligible  
<sup>a</sup> probability of transmission in a given contact type  
<sup>b</sup> frequency of infectious contacts of the given type  
<sup>c</sup> duration of the infectious period
The within-herd $R_0$ has been estimated at 4–7 (Hage et al., 1996; 2003). Franken (2005) quotes a between-herd $R_0$ of 5.6 without vaccination, 2.6 with vaccination using dead marker vaccine, but only 1.5 with vaccination using live marker vaccine.

**EBL**

The measures to control EBL, the component(s) of both within-herd and between-herd $R$ they influence and the assessed thrusts are compiled in Table 13.

<table>
<thead>
<tr>
<th>Measure</th>
<th>Influence on component</th>
<th>Within herd$^1$</th>
<th>Between herds$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual BTM surveillance and health monitoring data</td>
<td>$\beta^a$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c^b$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D^c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Classification according to decision 426/93 of MAF (immediate notification of authorities)</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Measures of the circular 2/93 of MAF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive measures on farm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culling of the seropositive animals and serological follow-up of entire herd</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Epidemiological investigation (tracing of contact herds)</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Program for obtaining and maintaining the herd disease-free status (biosecurity)</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Measures of Decision 98/372/EC (animal health conditions for imports of live bovine animals, “additional guarantees”)</td>
<td>$\beta$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the decree 6/EEO/2004 of MAF and Directive 2003/43/EEC (animal health requirements in respect to bovine semen)</td>
<td>$\beta$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the Decisions 94/113/EC and 2005/217/EC (trade and import of bovine embryos)</td>
<td>$\beta$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

1 scale: 2, major; 1, minor; 0, negligible

$^a$ probability of transmission in a given contact type

$^b$ frequency of infectious contacts of the given type

$^c$ duration of the infectious period
No numerical estimate for within-herd $R_0$ is available, but if ingestion of colostrum and milk is a major natural route of infection, then the (natural) $R_0$ is probably not much more than the average number of calves an infected cow will have during its lifetime.

**MV**

The measures to control MV, the component(s) of both within-herd and between-herd $R$ they influence and the assessed thrusts are compiled in Table 14.

Numerical estimates for within flock $R_0$ are unavailable, but if ingestion of colostrum and milk is a major route of transmission (Peterhans et al., 2004), then the $R_0$ on pasture, just as with EBL, is probably not much more than the average number of lambs an infected ewe will have during its lifetime. However, aerosol transmission of the infection during indoor winter housing (Pålsson, 1976) may be more extensive and the $R_0$ of this type of contact probably would be higher in Finland than the former type.

### 5.2 Summary of the efficacy of applied measures and some further inferences

#### 5.2.1 BVD

The assessments in Table 11 indicate that the measures have a greater potential for the prevention of virus spread between than within herds, which makes epidemiological sense. Considering the sources of the virus and means of transmission (Table 3), there is theoretically only one effective within-herd approach, i.e. identifying and culling the PI animals, which shortens the infectious period (D). The $R_0$ for acutely-infected animals has been estimated at 2.3 (Cherry et al., 1998), but even this is probably a slight overestimate and the infection spreads very sluggishly with only transiently infected animals present in the herd (Lindberg and Houe, 2005).

The spread of infection between herds takes place mainly through the trade of PI animals or dams carrying a PI foetus, through close contact on pastures, and to some extent through infected semen or embryo transfer (Table 3). Consequently, the efficient measures include identifying and culling PI animals and strict biosecurity measures when purchasing (if at all) a pregnant dam that may have seroconverted during gestation. These measures are able to reduce component $\beta$. Restrictions on animal movements and biosecurity measures to prevent indirect transmission by people are able to reduce component $c$, and adherence to the animal health requirement with respect to semen will also have significant potential to reduce component $c$.

Before the laying down of the new decree (MAF 2/EEO/2004) the delay between actual transmission between herds and suspicion and subsequent detection of a
new PI herd was too long to effectively limit the spread within a herd. The voluntary programme launched in 1994 would have provided a tighter schedule for the control than the once-a-year BTM surveillance, at least when affiliating to the scheme, but unfortunately only a small minority of farmers affiliated to it. For example, the number of affiliated farms was 593 in 2001 (MMM, 2002), i.e. 2.8% of

<table>
<thead>
<tr>
<th>Measure</th>
<th>Influence on component</th>
<th>Within herd$^1$</th>
<th>Between herds$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual health monitoring data</td>
<td>$\beta^a$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c^b$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D^c$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Classification according to decision 1346/1995 of MAF (immediate notification of authorities)</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Voluntary control program (1995–2001) and revised program compulsory to flocks with &gt; 20 ewes, 2001–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous (repeated) serological monitoring of all animals &gt; 1 year of age</td>
<td>$\beta$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Biosecurity measures (acquiring of new animals to flock, restrictions on contacts to flocks of lower status, etc)</td>
<td>$\beta$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of the decree 15/EEO/2001 of MAF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictive measures on farm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictions on animal movement</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Culling of the seropositive animals and their progeny; serological follow-up of the flock</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Epidemiological investigation (tracing of contact flocks)</td>
<td>$\beta$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Measures of Directive 91/68/EEC (animal health conditions in trade of ovine and caprine animals)</td>
<td>$\beta$</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Measures of Directive 92/65/EEC (trade in and import to Community of semen of e.g. rams)</td>
<td>$\beta$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$c$</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$D$</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

$^1$ scale: 2, major; 1, minor; 0, negligible
$^a$ probability of transmission in a given contact type
$^b$ frequency of infectious contacts of the given type
$^c$ duration of the infectious period
the contemporary dairy herds. However, the control efforts in 1994–2003, effective between herds (Table 11), did reduce the seroprevalence of both dairy and beef BVD herds, and the number of PI herds detected annually (I, II). In fact, five out of the seven in 2000, eight out of the nine in 2001 and both of the herds with PI animals in 2004 were new findings. This indicates that PI herds, once discovered, were efficiently dealt with, but that the infection has not yet been stamped out from the population.

The restrictive measures of the new decree imposed on a suspected or confirmed BVD farm, associated with the epidemiological investigation of the contact farms (Table 11), are taken to provide the tools for the final elimination of the infection within the next few years (II). However, the comprehensive and up-to-date information in the Central Bovine Register, Bovine Transfer Register and Animal Holding Register could immensely assist the control and eradication efforts, if the most could be made of it. The sampling at slaughter targeted at suckler-cow herds, which uses data from the Central Bovine Register (Rikula and Joutsenlahti, 2004), demonstrates how highly effective a coordinated effort can be. A health-monitoring programme for the three-phase calf rearing operations would benefit not only the control of BVD but also that of much more prevalent respiratory infections caused, for instance, by respiratory syncytial (RS) virus in young stock. Adjustments in the interpretation of screening test results towards higher sensitivity at the cost of a lower specificity would probably also be advisable in the final stages of the eradication.

5.2.2 IBR

The assessments in Table 12 indicate that the measures possess more potential to prevent the spread between than within herds, rather like in case of BVD. Considering the sources of the virus and means of transmission (Table 3), there is theoretically only one effective within-herd approach, i.e. identification and removal either by separation or culling of the seropositive animals, which reduces component D. The within herd $R_0$ has been estimated at about 5 without vaccination (Hage et al., 2003; Franken 2005). However, the proportions of seropositive animals in the known IBR herds (III, Table 3) do suggest a lower reproduction ratio in the Finnish settings.

The spread of infection between herds takes place mainly through the trade of infected animals, contact on pastures, and the use of infected semen and embryos (Table 3). Culling or restricting the trade of seropositive animals can reduce the probability of transmission ($\beta$) through this route. Restrictions on animal movements and biosecurity measures to limit indirect spread can reduce the frequency of infectious contacts (component c). Adherence to the animal health requirements with respect to semen and embryos can reduce both the probability of transmission ($\beta$) and the frequency of infectious contacts (c).

Annual health monitoring and BTM surveillance, as well as meticulous epidemiological investigation were instrumental in detecting and tracing the IBR-positive herds in 1990–1991 (III). Isolation and eventual culling of seropositive and clinically
ill animals, both shortening the infectious period \((D)\), were the main measures applied. Total stamping out of one large herd did of course put an end to this source of infection. On-going measures, i.e. continued surveillance, the obligation to immediately notify the authorities, and strict control of animal health both in importing live animals and semen or embryos will be indispensable in limiting the chances of re-entry of the virus and preventing wanton spread of the infection.

The five Finnish IBR-positive herds formed three epidemiological units and AI remained the only plausible route of transmission for each unit \((III)\). Only one of the herds had purchased an infected animal but the infection had not spread within the herd. The efficacy of transmission – or between-herd \(R_0\) – through AI was estimated at a low 1 in 3000 inseminations. However, the low efficacy may be countered by the large numbers of inseminations performed annually.

The most obvious risks of (re)introducing IBR into Finland are associated with untested semen and embryos, and possibly inadvertent import of (tested) seronegative latent carrier animals. It has been considered possible that wild ruminants, especially reindeer \((Rangifer tarandus)\), could be a source of infection for cattle. A herpesvirus serologically related to BHV-1 has been isolated from two female reindeers in Finland \((Ek-Kommonen et al., 1986)\). Furthermore, neutralizing antibodies against BHV-1 have also been detected in reindeers \((Ek-Kommonen et al., 1982; Annual statistics of National Veterinary Institute 1983)\). However, none of the known IBR-positive farms was located in the proper reindeer husbandry area in Finnish Lapland, and those dairy herds located in the area have consistently been negative in BTM surveillance. Thus, the role of wild ruminants in the epidemiology of IBR in Finland remains only a theoretical possibility.

5.2.3 EBL

In keeping with BVD and IBR, the assessed measures (Table 13) have somewhat more potential to prevent the spread of BLV infection or EBL between than within herds. According to the sources of the virus and means of transmission presented in Table 3 there should be two effective measures to prevent both the within-herd and between-herd spread: isolation of the seropositive animals from the uninfected seronegatives – or preferably culling of the former, biosecurity measures to prevent the iatrogenic spread through contaminated needles, and preventing the access of herd-mates to the amniotic membranes, fluids etc. after parturition. Isolation or culling will reduce component \(D\) in within-herd spread and component \(\beta\) in the between-herd spread, since the spread of infection between herds takes place mainly through the trade of animals with PL, and possibly to some extent through contaminated semen and embryos. Biosecurity measures effectively reduce component \(c\) in the spread both between and within herds. Theoretically, heat-treatment of the dam’s colostrum and milk or feeding of the offspring only with those from seronegative cows in the herd does have a significant potential to limit the spread within a herd by reducing both \(\beta\) and \(c\). Transmission by blood-sucking insects is most likely only a highly theoretical possibility and measures to prevent it will have only a very marginal effect (if any).
Continued surveillance, immediate notification of authorities, restrictive measures on farms and epidemiological investigation to trace the contacts are considered elementary in limiting the spread of the infection between farms in the Finnish setting. In addition to these, adherence to the requirements of animal health both in importing live animals and semen or embryos will be invaluable in preventing the re-entry of the virus. The risk of (re)introducing EBL to Finnish cattle can theoretically be associated with import of untested semen and embryos. Iatrogenic import across borders via uncleaned needles, surgical appliances or dehorning devices etc. is practically impossible. Import of infected but still seronegative animals or illicit import of animals with PL must also be considered rather remote possibilities.

5.2.4 MV

The assessments in Table 14 indicate that, as above, the measures have a better potential to prevent or limit the spread of infection between flocks than within them. Considering the sources of the virus and means of transmission (Table 3), there are theoretically only a few effective within-flock approaches: heat-treating the ewes’ milk and bottle-feeding the newborn lambs (reducing $\beta$), total separation of the offspring from infected ewes (reducing $c$) and culling the infected animals (reducing $D$). However, the first two are feasible only as temporary measures, for instance, to preserve some valuable genetic stock. Repeated testing of all the animals and immediate culling of the seropositives is practically the only effective approach within flocks.

The spread of infection between flocks takes mainly place through the trade of infected animals. Consequently, the effective measures to prevent or limit between-flock spread include immediate culling of seropositive animals and adherence to the animal health conditions for intra-Community trade of ovines, which reduce the probability of transmission ($\beta$). Restrictions on animal movement from infected flock and other biosecurity measures decrease the frequency of infectious contacts ($c$). Obligation to notify the authorities immediately when the disease is even suspected, and epidemiological investigation to trace the contacts shorten the time to trace the infected animals (reducing $D$).

In Finland, infective contact with other flocks, e.g. on pasture or in exhibitions, is possible but too infrequent to be epidemiologically significant. Rams that in the breeding season visit many flocks do have the potential to spread the infection, but this is also not known to have happened in Finland. Total stamping out of infected flock is certainly even more effective than selective culling in preventing the further spread of the infection. The control program requires this if $> 10\%$ of the animals $> 1$ year old are seropositive. Seven out of the 14 infected flocks revealed in the 1994 survey or traced later were eventually stamped out. Six tried the selective culling and repeated testing approach and three eventually attained an MV-free (M3) status. Two of the remaining four flocks ended sheep production, and the other two dropped out of the programme once the restrictive measures were withdrawn ($V$). The importance of epidemiological investigation was clearly dem-
onstrated: the survey revealed eight of the fourteen flocks and the other were traced among the contact flocks.

After the clearing of the last infected flocks in 1998 (V) the infection surfaced again four years later (Table 7). This emphasizes the importance of continued monitoring of a slow and insidious disease like MV. The epidemiology of the findings in 2001 and 2002 is not yet firmly established, but preliminary results indicate that the animals had had contacts with the known MV-positive flocks (V). This accords with the observation that the isolated virus strains match with those isolated earlier (Laamanen et al., 2006).
6 Conclusions

1 The measures applied in Finland largely concur with those listed in the control measure Tables 4 and 5, with some minor and one major exception: vaccination against either BVD or IBR has never been attempted. The financial compensations for the culled animals that the farmers were or are entitled to and the fact that the control activities against notifiable diseases are mostly carried out at the government’s expense have no doubt eased the compliance with the official control procedures.

2 Occasional BVDV antibody-positive samples have been recorded in the annual statistics of the National Veterinary Institute since 1965. The Finnish approach of monitoring the BVD antibody status of a large majority of all cattle herds and systematically tracing and eliminating the animals persistently infected with BVDV was successful in reducing the seroprevalence of the infection to less than a third of what it was when the voluntary control programme was started in 1994, and even further in respect to PI herds. However, decisive progress to complete eradication will require the instruments of the new decree, in effect since May 2004.

3 It appears that IBR or BHV-1 was introduced into Finland in 1968 when importing a live AI bull to a station. The infection is considered to have spread via infected semen to a number of herds, estimated at less than 10. The large-scale BTM surveil- lances in 1990–91 revealed three IBR herds and meticulous tracing of their contact herds and testing all of the animals in them detected two further herds. Culling of the seropositive animals from the herds, restrictive measures on their animal trade and subsequent serological follow-up, and total stamping-out of one herd were sufficient in eradicating the infection from Finland without the need to resort to the use of vaccines. Continued surveillance and the obligation to notify authorities immediately will guard against unchecked spread in the case of re-entry of the infection.

4 The database of haematological and later serological health monitoring results show that EBL was introduced into the country probably before the 1960s. Between 1966 and 1997, positive results were recorded annually in the statistics of the National Veterinary Institute. Culling of the seropositive animals from the herds and restrictive measures on their animal trade were essential and sufficient measures to eradicate this infection. Continued surveillance, strict examination of suspicious pathological or meat inspection samples and the obligation to immediately notify authorities will safeguard the present disease-free situation.

5 It is probable that MV was first introduced into Finland in 1981 in imported sheep. The infection was not detected between 1982 and 1993 according to the annual statistics of the National Veterinary Institute, until a large-scale survey in 1994 and subsequent investigation revealed that the infection had insidiously already spread to 14 flocks. The stamping out of entire flocks in several cases, cull-
ing of seropositive animals and their progeny, scheduled serological testing and restrictive measures on farms were sufficient to reduce the occurrence to an undetectable level. However, the two positive serological findings in surveys carried out in 2001–2002 demonstrate that the sporadic occurrence of MV is still possible.
7 References


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