1. INTRODUCTION

Bovine viral diarrhoea virus (BVDV) infection is endemic in most cattle-producing countries throughout the world, inflicting significant economic losses. Since many if not most BVDV isolates are well adapted to cattle, the virus causes a stealthy infection and many acute (i.e. transient) infections go unnoticed provided that the virulence of the strain is low and that there are no complicating conditions. However, since BVDV virulence may vary and infection is accompanied by transient immunosuppression there is a complex of diseases attributable to acute BVDV infections, ranging from respiratory and enteric conditions to lethal haemorrhagic disease (Baker, 1995). The highest losses caused by BVDV infections occur as a result of its interference with reproductive functions. Depending on the time of infection, there may be a significant reduction of conception rates, an increased number of abortions, malformations, stillbirths or birth of persistently infected (PI) calves. The latter are immunotolerant to the persisting virus and they constantly shed large amounts of virus. PI cattle are the key to the spread of BVDV and consequently they play a pivotal role in any control or eradication programme. Many PI animals die of mucosal disease (MD) or other complications at an early age, but others may survive for many years serving as a source for virus transmission. The repeated cycle of PI animals being born, infecting susceptible animals in early pregnancy, leaving the herd for different reasons, e.g. sale or death, birth of new PI calves etc is typical for endemic BVDV infections. In herds of limited size, the infection is often eliminated without intervention (so called self clearance), provided the virus is not reintroduced. However, other herds will remain infected for long periods of time if no measures to eradicate the virus are taken.

BVDV is a small enveloped, single stranded RNA virus of the genus pestivirus in the family Flaviviridae. In contrast to classical swine fever virus, a closely related pestivirus, BVDV displays a broader genetic and antigenetic diversity. Before the description of severe hemorrhagic disease in young cattle (Rebhun et al. 1989), only one genotype of BVDV was known. However, from such cases a noncytopathic (ncp) BVDV was isolated that showed marked genetic and antigenetic differences when compared to the BVDV so far known. Consequently the terms BVDV genotype 1
(old) and 2 (new) were introduced (Ridpath et al. 1994), and later the genotypes were assigned the taxonomic status of species. BVDV-1 is the predominant species in Europe, with only a few percent of BVDV-2 present (Tajima et al. 2001).

For a long time it was thought that systematic control of BVDV was impossible due to a lack of reliable and inexpensive diagnostic tools and the ubiquitous occurrence of the virus. In addition the actual damage caused by the infection was for a long period underestimated and a systematic control was not thought to be necessary. However, the true magnitude of the infection-related damage appeared gradually with growing insights into the pathogenesis and frequency of the different clinical manifestations of the infection. Today there are a number of calculations and estimations on the economical impact of BVDV infections available, and cost benefit analyses demonstrate the advantage of systematic control measures (Moennig et al. 2005a). In parallel, high-performance laboratory diagnostic tools and improvement of vaccines and vaccination protocols became available, thus allowing the development and implementation of strategies for a systematic BVDV control that include vaccination as an option.

In the context of BVDV control it is helpful to distinguish between non-systematic and systematic approaches. The former have been used predominantly beginning with the availability of the first vaccines. After the pivotal role of PI cattle for the perpetuation of BVDV infection had been recognised, the removal of these animals from infected herds became another control option. However, as long as vaccination and/or test and removal strategies are being used exclusively on a herd basis without systematic follow-up or monitoring of the outcome, they can only be described as non-systematic. In contrast, systematic control implies a goal-oriented reduction in the incidence and prevalence of BVDV infections, typically implemented on a regional or national level (Lindberg & Houe 2005; Moennig et al. 2005a). Monitoring and evaluation of control progress are essential elements of these strategies (Houe et al. 2006).

2. NON SYSTEMATIC CONTROL - VACCINATION

With the description of the first BVDV vaccine (Coggins et al. 1961), early tools for the control of BVDV infections were available. In the decades to follow, a large number of vaccines and vaccination protocols were developed. Vaccines were either modified live viruses (MLV) or inactivated preparations. They were used either alone or in combination with other cattle vaccines. For a long time, the purpose of vaccination was the prevention of acute clinical disease in herds. The crucial issue of breaking the infectious cycle by preventing the generation of new PI animals was long neglected or not even addressed. Only in the 1990ies the importance of intrauterine protection as a primary goal of vaccination became clear.

In many countries vaccination is widely used and many different vaccines are available. However, there is no indication that vaccination alone has ever resulted in a decline of BVDV prevalence.

With growing knowledge concerning the pathobiology of BVDV infections, the important role of PI animals for the perpetuation of the infectious cycle became apparent. Consequently strategies were developed for the identification and elimination of these virus carriers. On a herd level, the test and removal strategy proved beneficial for herd health and prevention of BVDV associated losses. However, without being in the context of a larger goal-oriented systematic control effort, the reduction of infectious pressure in herds was only effective as long as no re-introduction of the virus occurred.

In summary, non-systematic control efforts may well result in improved animal health and prevent BVDV associated losses. However, their efficacy is mostly restricted to the herd level, usually for a limited time period, and no decrease of the overall BVDV prevalence can be expected.
3. SYSTEMATIC CONTROL

The first systematic control/eradication schemes were developed in Scandinavian countries in the early 1990ies. Due to a restrictive attitude from authorities in these countries to cattle vaccines in general, vaccination was no option. In most cases, the cattle industry took the initiative and the activity was later strongly supported by the competent authorities. One key factor for success was the information and motivation of all stakeholders prior to the start of the control programmes (Lindberg & Alenius 1999). In retrospect, these programmes have been very successful with several countries now being free or almost free of BVDV (Sandvik, 2004). Later some other European countries or regions followed the Scandinavian example by implementing similar control regimes for the control of BVDV (Rossmanith et al. 2001).

There is general consensus that the identification and removal of PI animals as well as the prevention of new infections with BVDV are key elements of any systematic BVDV control. Due to local conditions, a variation of the Scandinavian strategies may be introduced for the first phase of a general BVDV control programme, i.e. systematic vaccination as an additional tool.

3.1 Systematic control without vaccination

There is general agreement that the main technical elements of systematic BVDV control programmes can be summarized as follows.

Initial test for classification of herd status:

- implementation of additional biosecurity measures, e.g. movement restrictions for cattle from infected herds,
- follow up tests for identification and removal of individual infected animals in infected herds,
- continued monitoring of supposedly free herds to confirm a free status and/or for rapid detection of any new infections.

In a non-vaccination environment a herd diagnosis can be performed by assessing the serological situation, i.e. a diagnosis is based on testing samples from selected individuals representing groups of susceptible animals in a herd. The goal is to detect the presence or absence of antibodies against BVDV. Usually there is no need to test every single animal. The diagnosis can be based on testing several animals individually or by pooling samples (blood or milk) from several animals before testing. The following tests have proven to be suitable for herd level diagnosis:

- detection of antibodies in bulk milk,
- detection of antibodies in individual or pooled serum samples from young stock or in pooled samples (of milk or serum) from primiparous cows,
- virus detection in bulk milk (usually by polymerase chain reaction).

The sensitivity of using antibody levels in bulk milk to predict the presence of PI animals is close to 1 in herds not vaccinating for BVDV, whereas the specificity is much lower. The reason for an occasional false negative test (low sensitivity) result is most obvious in herds with a very recent introduction of infection when only a few animals have seroconverted. A repeated bulk milk test a few months later will solve this problem (Houe et al. 2006). The bulk milk PCR for the detection of
lactating PI cows is an inexpensive test in case an infected herd has to be cleared from PI animals. This test has to be combined with individual tests to be applied for the non-lactating part of the herd (Bendfeldt et al. 2005).

The first systematic programmes aimed at eradicating BVDV without the use of vaccines were launched in 1993-1994 in Denmark, Finland, Norway and Sweden. Despite different preconditions in terms of legal support, and with initial prevalences of herds with PI animals varying from <1% in Finland to 50% in Denmark it has taken all countries approximately 10 years to reach their final phases. First to reach eradication will most likely be Norway (Nyberg et al. 2004; Voss, 2004; Hult and Lindberg, 2005; Rikula et al. 2005).

In Austria, the outline of the scheme has followed that of the Scandinavian forerunners, and after seven years as a regional project (involving the Lower Austria region), the scheme was extended to the entire country in 2004. Today, approximately 30% of the targeted herds in Austria are certified as being free from BVDV (Rossmanith et al. 2005).

Systematic control efforts have also been implemented to a varying extent in other parts of Europe, such as on the Shetland Islands where BVDV has been eradicated (Synge et al. 1999), and in Brittany in France (Joly et al. 2005), in The Netherlands (Moen et al. 2005) and in Germany (Moennig et al. 2005b). Time-limited, project type control efforts have also been implemented in the Rome area, and in the Lecco and Como regions of Italy (Ferrari et al. 1999; Luzzago et al. 2004). Although vaccines are available in all these countries, all programmes except for the one in Germany, are based on non-vaccination approaches. It should be noted that the only approaches that have been successful in reducing the impact of BVDV infections at a larger scale are those that put emphasis on biosecurity in general, and control of direct animal contacts in particular with or without the complementary use of vaccines.

3.2 Systematic control with vaccination

Under circumstances where the Scandinavian approach of eradication BVDV might not be applicable for several reasons, systematic vaccination after removal of PI cattle is an option in order to minimize the risk of re-introduction of the virus into cleared herds. In Germany, voluntary control schemes combining test and removal of PI cattle and vaccination were devised about 15 years ago and they were applied according to a Federal guideline on a voluntary basis. Late 2004, BVDV became a notifiable infection, and regulatory statutes are currently being drafted and will most likely come into effect late 2006. Then BVDV control will change from a voluntary to a compulsory approach. Several BVDV vaccines are on the market including modified live preparations, and vaccination had always been used country-wide in non-systematic BVDV control. This situation requires an approach to testing of herds that differs from countries where vaccination is banned, since bulk milk samples are not necessarily indicative for the status of the herds.

The programme comprises the following elements:

- initial test for classification of herd status, identification and removal of PI animals,
- follow up tests for identification and removal of PI calves born within the first 12 months after clearance of infected herds,
- systematic vaccination using a vaccine and protocol with a proven record to protect pregnant animals against foetal infection,
- continued monitoring to confirm a free status,
- general and individual biosecurity measures, e.g. test certificate for an individual animal before movement.
Since vaccination might interfere with bulk milk testing, initial screening of herds depends on the epidemiological situation. In vaccinated herds, a few animals older than 6 months should be kept unvaccinated so that they can work as sentinel animals for indicating the infection pressure in the herd, if any (Pillars & Grooms, 2002; Moennig et al. 2005a). In non-vaccinated herds an initial bulk milk sample can be used to test for BVDV-specific antibodies. If any of the samples is positive, the herd is tested for PI animals. There are several options to identify PI animals: in dairy herds, bulk milk samples can be investigated by PCR. In positive cases, the PI animals will be identified by additional testing of individuals. The offspring of PI cows is by definition PI and will be removed as well. The rest of the herd can be tested either using individual or pooled blood samples or ear notch samples that will be analysed using antigen capture ELISA (individual samples) or PCR (pooled samples).

When all PI animals have been removed, systematic vaccination, preferably a two-step protocol, is implemented. Depending on the epidemiological situation vaccination can be mandatory or banned. In areas with a high density of cattle, intense trade, sub-optimal control of biosecurity and a high prevalence of BVDV, systematic vaccination should be used until the incidence of PI cattle has reached a low level. In areas with a low BVDV prevalence vaccination should be banned because the risk of re-introduction of BVDV into free herds is likely to be low. Two steps vaccination is recommended provided a licensed modified live vaccine is available (Eicken et al. 2004; Moennig et al. 2005b). First vaccination is done using an inactivated vaccine and four weeks later a booster vaccination is applied using a modified live vaccine. This protocol ensures a long-lasting immune response and a comprehensive foetal protection (Frey et al. 2002; Oguzoglu et al. 2002). It has never been observed that live vaccine virus is shed when used in the context of two-step vaccination, i.e. where modified live vaccines are only used on animals that had been primed with a first vaccination using inactivated preparations. In any case the primary goal of vaccination is to obtain broadest and most enduring foetal protection possible. Animals are being vaccinated at the latest eight weeks before their first pregnancy. A group of young animals older than 6 months is kept unvaccinated and monitored for BVDV antibodies to confirm that there is no new introduction of infection.

Continued monitoring is an essential element of the program, and herds are being tested serologically using bulk milk samples in non-vaccinated herds or spot tests of unvaccinated young stock in herds that apply systematic vaccination.

4. CONCLUSION

In December 2002, a thematic network on BVDV control in Europe was formed, after being granted funding from the EU Commission’s 5th framework (www.bvdv-control.org). With few exceptions, all older EU member states are in the network, as are Norway and Switzerland. Of the Member States that joined in 2003, Slovakia and Slovenia are represented. Among its various tasks, the network has gathered information on how BVDV control activities are carried out within the EU and in the other participating countries. From the enquiries performed within the network, it can be seen that in most parts of Europe, BVDV control is at current non-systematic and by vaccination. Of the countries that use vaccines, the UK, Ireland and The Netherlands only have killed vaccines licensed. The Scandinavian countries, Austria and Slovenia provide an exception to the general picture as they have no vaccines licensed. As mentioned earlier these countries, except for Slovenia, have large regional or national systematic eradication schemes in place where vaccines are not employed. The current European situation with respect to BVDV control was summarised at the Second European Symposium on BVD Control organised by the thematic network in Porto, October 20-22, 2004. It can be expected that the work of the thematic network and the results of the Porto meeting will add momentum to European efforts to control BVDV.
Despite its severe economic impact, BVDV is not yet listed as a disease with implications for trade within the OIE framework. This is most probably due to its worldwide ubiquitous spread and a former lack of convincing concepts for control or even eradication in a systematic manner. However, this situation is changing after several countries have succeeded in clearing BVDV infections from their cattle populations. Based on quantification of economic losses and on a decade of research on clearing and maintaining herds free from BVDV, the Scandinavian countries announced in the early 1990ies that they were attempting to eradicate BVDV. It has taken these countries about 10 years to reach the final phase of the eradication or even achieve their goal of freedom from BVDV, thereby proving that general control of the virus is possible. Encouraged by this success, other European countries or regions are reconsidering their policy concerning BVDV control. With several countries free from BVDV and others being in the process of controlling the disease, the significance of the infection for international trade needs to be re-assessed.

5. SUMMARY

Bovine viral diarrhoea virus (BVDV) infections cause one of the most important endemic diseases of cattle. During the first four decades after the first description of the infection in 1946, it was thought that - due to high and ubiquitous prevalence - control of BVDV is futile if not impossible. Vaccination using modified live and inactivated preparations and test and slaughter in selected risk groups were the only tools to limit the damage inflicted by BVDV infections on a herd basis. However, these unsystematic control efforts have not led to any reduction of the overall BVDV prevalence. With the development of reliable and inexpensive tools for the detection of BVDV and virus-specific antibodies it became feasible to monitor herds at reasonable costs for their BVDV status and to trace persistently infected (PI) cattle. In the early 1990ies several European countries have initiated regional and national systematic control and eradication campaigns. In Scandinavia, these programmes were carried out without the use of vaccination. The programmes have been very successful and to date these countries are practically free of BVDV. In other European regions, similar programmes have been implemented, both with and without the use of vaccines. Essential elements of both approaches were:

- initial testing of herds to determine their BVDV infection status,
- removal of PI animals and,
- introduction of biosecurity measures including movement restrictions for infected animals in order to avoid reinfection of cleared herds.

In programmes that allow the use of vaccines, all female cattle of a herd are systematically vaccinated as an additional biosecurity measure after removal of PI cattle. In these programmes, the main purpose of vaccination is the prevention of re-introduction of virus into cleared herds. Effective foetal protection as a result of vaccination is essential. Monitoring of herds in regular intervals is vital part of both policies.

6. KEY WORDS

Bovine viral diarrhoea, control, eradication, vaccination.

7. RESUME

Les infections dues au virus de la diarrhée virale bovine (BVDV) sont à l’origine de l’une des maladies endémiques des bovins les plus importantes. Pendant les quarante années qui ont suivi la première description de l’infection en 1946, il était communément admis, du fait de sa prévalence élevée et ubiquiste, que la prévention du BVDV était vaine, voire impossible. L’utilisation de vaccins vivants modifiés, et de vaccins inactivés, le dépistage et l’abattage de groupes à risques
étaient les seuls moyens de limiter les dégâts initiés par les infections à BVDV à l’échelle du troupeau. Toutefois, ces tentatives de prévention peu méthodiques n’ont abouti à aucune réduction de la prévalence générale du BVDV. La mise au point d’outils fiables et peu coûteux pour la détection du BVDV et des anticorps spécifiques du virus a permis de surveiller le statut des élevages vis-à-vis du BVDV pour un coût raisonnable, et de dépister les bovins infestés persistants (IPI). Au début des années 90, plusieurs pays Européens ont développé des programmes régionaux et nationaux de prévention et d’éradication. En Scandinavie, ces programmes ont été mis en œuvre sans aucune vaccination. Ces programmes ont été couronnés de succès, et, à ce jour, ces pays ne sont pratiquement plus touchés par le BVDV. Dans d’autres régions d’Europe, des programmes similaires ont été mis en place, avec ou sans utilisation de vaccins. Les éléments essentiels des deux approches ont été :

- le dépistage préliminaire des troupeaux pour déterminer leur statut vis-à-vis du BVDV,
- la réforme des animaux IPI et,
- l’introduction de mesures de biosécurité incluant la restriction du déplacement des animaux infectés de façon à éviter la réinfection des troupeaux assainis.

Dans les programmes autorisant l’utilisation des vaccins, toutes les femelles d’un troupeau sont systématiquement vaccinées, comme mesure supplémentaire de biosécurité après retrait des bovins IPI. Dans ces programmes, l’objectif principal de la vaccination est de prévenir la réintroduction du virus dans les troupeaux assainis. Une protection fœtale effective à la suite de la vaccination est essentielle. Une surveillance des troupeaux à intervalles réguliers est l’élément fondamental de ces deux approches.

8. MOTS CLES

Diarrhée virale bovine, prévention, éradication, vaccination.

9. ZUSAMMENFASSUNG


- Feststellung des BVDV-Herdenstatus,
- Entfernung der PI Tiere aus der Herde und,
• Einführung strikter Hygienemaßnahmen einschließlich der Verhängung von Verbringungsverboten für infizierte Tiere, um die Reinfektion saniertener Herden zu vermeiden.


10. SCHLÜSSELWÖRTER

Bovine Virusdiarrhoe, Bekämpfung, Eradikation, Impfung.

11. REFERENCES


