Commentary

Bovine Viral Diarrhea in Brazil: Current Status and Future Perspectives

Matheus Nunes Weber[1], Simone Silveira[1], André Felipe Streck[1], Luís Gustavo Corbellini[2], Cláudio Wageck Canal[1]*

[1]Laboratório de Virologia, Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil; [2]Laboratório de Epidemiologia Veterinária, Faculdade de Veterinária, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil

Abstract | Bovine viral diarrhea is a disease caused by viruses of the genus Pestivirus in cattle worldwide. Herein, we present the current status of the disease in Brazil showing its nation-wide distribution. In Brazil, BVDV-1, BVDV-2 and 'HoBi'-like viruses are frequently reported whereas BVDV-2 has a higher frequency when compared with other continents. It is important to reinforce that currently Brazil has no official control program for BVDV. The significance of cattle production losses or the potential implementations of commercial barrier by other countries can possibly reason the placement of governmental veterinary measures in the near future.

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***Correspondence** | Cláudio Wageck Canal, Universidade Federal do Rio Grande do Sul (UFRGS), Brazil; **E-mail** | claudio.canal@ufrgs.br
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Introduction

The genus *Pestivirus* of the family *Flaviviridae* consists of three recognized species that can infect cattle: *Bovine viral diarrhea virus 1* (BVDV-1), BVDV-2 and *Border disease virus* (BDV) (Simmonds et al., 2011). Moreover, an atypical group of pestiviruses, initially detected in fetal calf serum from Brazilian origin (Schirrmeier et al., 2004) and putatively named 'HoBi'-like virus or BVDV-3 (Liu et al., 2009) has also been associated with clinical disease in cattle (Decaro et al., 2011; Weber et al., 2014a). These species were further subdivided in subtypes, with BVDV-1 displaying at least 17 subtypes (1a to 1q) (Deng et al., 2012; Vilcek et al., 2001), BVDV-2 presenting three subtypes (2a to 2c) (Flores et al., 2002; Jenckel et al., 2014; Tajima et al., 2001) and BDV presenting seven genotypes (Becher et al., 2003; Giammarioli et al., 2011).

Pestivirus infections in cattle may cause acute or persistent infection. Acute infections generally are subclinical but when present, signs include diarrhea, fever, leukopenia, ocular and nasal discharge. Most acute infections, in animals with non-compromised immune systems, are cleared within 14 to 21 days. Persistent infection is established when a virus, belonging to the non-cytopathic biotype, crosses the placenta and infects a non-immunocompetent fetuses. The persistently infected (PI) calves resulting from this infection may show retarded growth and congenital defects or appear normal. PI calves excrete virus throughout their lives, spreading the infection in or between herds. Many PI calves die in the first two years of life from mucosal disease (MD) or secondary infections, probably as a consequence of virus-induced immune depression (MacLachlan and Dubovi, 2011). The MD occurs when cattle are infected with both non-cytopathic and cytopathic viral biotypes that are antigenically homologous (Baker, 1995; Pocock et al., 1987).

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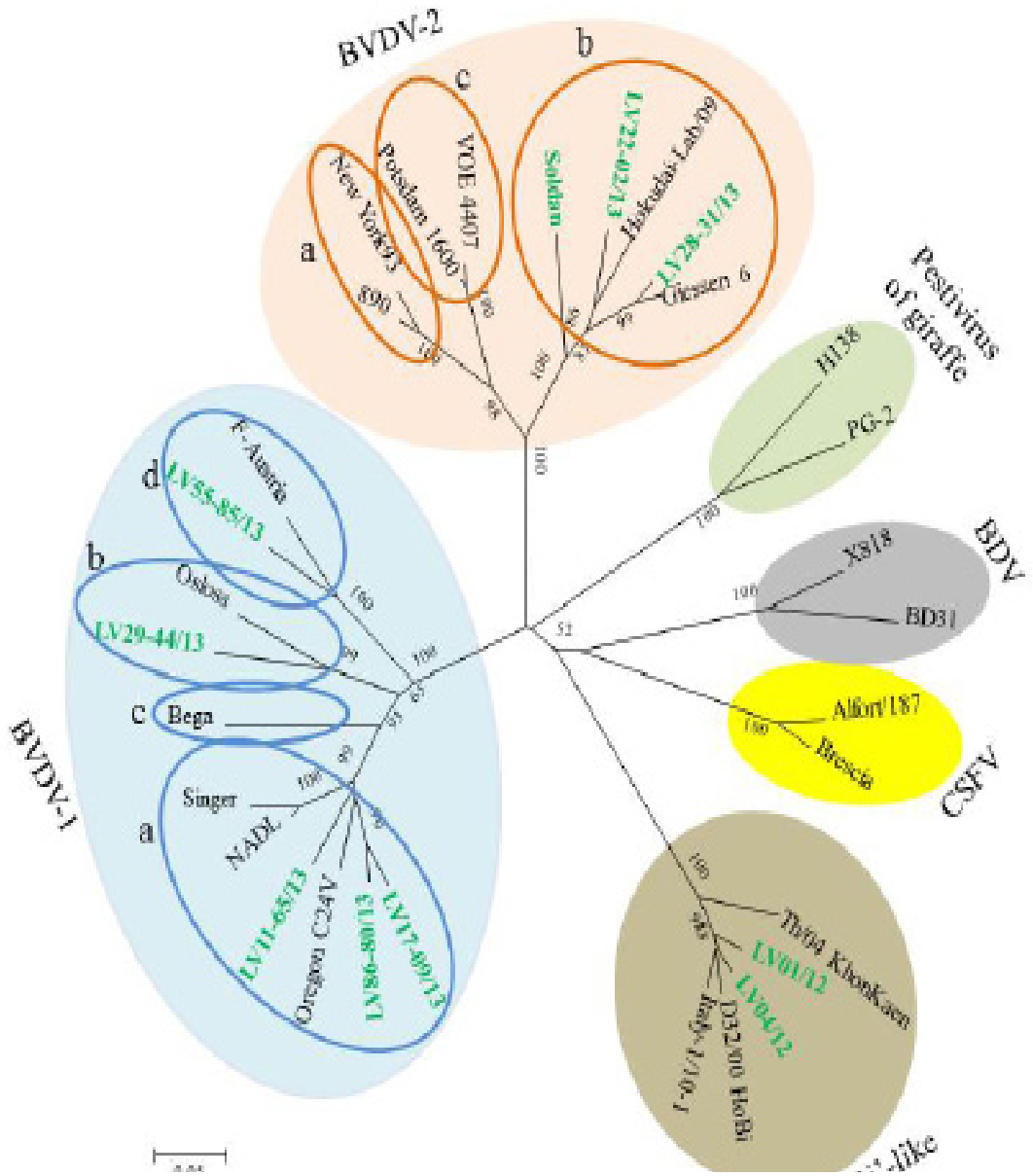

Figure 1: *Phylogenetic tree of fragments of N terminal autoprotease (N^{pro}) (363 bp) representing the pestivirus species and subtypes detected in Brazil. Sequences from Brazil and representative and reference pestivirus strains were analyzed by the neighbor-joining method and the Kimura 2-parameter model and constructed with MEGA6 (Tamura et al., 2013). Bootstrap (1,000 replicates) values >50 are indicated at the internal nodes. Brazilian isolates are highlighted in green. The length of each pair of branches represents the distance between sequence pairs in the rectangular tree. The scale bar represents the percentage of nucleotide differences in the rectangular tree. Genbank accession numbers: BVDV-1: NADL (AJ133738.1), Singer (AF145364.1), Oregon C24V (AF091605.1), LV11-65/13 (KM217386.1), LV17-09/13 (KM217388.1), LV86-80/13 (KM217398.1), Osloss (M96687.1), LV29-44/13 (KM217391.1), Bega (AF049221.2), F-Austria (AF287284.1), LV55-85/13 (KM217395.1); BVDV-2: 890 (U18059.1), New York93 (AF502399.1), Giessen 6 (AF144470.1), Soldan (AY735495.1), LV22-02/13 (KM217400.1), LV28-31/13 (KM217401.1), Hokudai-Lab/09 (AB567658.1), Potsdam 1600 (HG426491.1), VOE 4407 (HG426495.1); HoBi: D32/00_HoBi (AB871953.1) Italy-1/10-1 (HQ231763.1), LV01/12 (KC465392.1), LV04/12 (KC465395.1), Th/04 KhonKaen (FJ040215.1); BDV: X818 (NC_003679.1), BD31 (U70263.1); CSFV: Alfort/187 (X87939.1), Brescia (M31768.1); Pestivirus of giraffe: H138 (NC_003678.1), PG-2 (KJ660072.1).*

Brazil has the major commercial cattle population in the world with about 211 million of animals (USDA-FAS, 2014). The control of the foot and mouth disease (FMD) was the main focus of the Federal Veterinary Office during years. Currently, Brazil is classified as FMD free zone with vaccination in almost all the entire territory, and the last occurrence was an isolate case in 2006 (MAPA, 2014; OIE, 2014). Since then, diseases caused by pestiviruses and herpesviruses in cattle will become one of the major virus disease targeted for controlling due to production performance loses in cattle herds.

Current Status

Several reports have shown the presence of the BVDV infection in Brazil since the late 60s. The first report was a description of a gastroenteric disease with clinical and pathological features resembling mucosal disease (Correa et al., 1968). Since then, several serological studies were conducted demonstrating the wide distribution of infection in Brazilian cattle ranging from 22-67% of the animals and 43-90% of the herds (Almeida et al., 2013; Canal et al., 1998; Poletto et al., 2004; Quincozes et al., 2007; Thompson et al., 2006). The percentage of seropositive animals varies according to the locality and the type of exploration, and the implication of other animal species in the epidemiology of BVDV in Brazil is not currently known due the lack of reports.

About the genetic diversity, BVDV-1, BVDV-2 and 'HoBi'-like viruses have been frequently reported in Brazil (Bianchi et al., 2011; Canal et al., 1998; Cortez et al., 2006; Flores et al., 2000; Otonel et al., 2014; Stalder et al., 2005; Weber et al., 2014a, 2014b, 2013) (Figure 1). Bianchi et al. (2011) and Weber et al. (2014b) reported that BVDV-1 and BVDV-2 are almost equally distributed, with frequencies of 40-57% for BVDV-1 and 42-45% for BVDV-2. Apparently, these frequencies of BVDV-2 are similar from that described in Chile (Pizarro-Lucero et al., 2006) but higher when compared with the ones reported in North America (Kim et al., 2009; Ridpath et al., 2010), Europe (Arias et al., 2003; Barros et al., 2006; Jackova et al., 2008; Stalder et al., 2005; Strong et al., 2013; Tajima et al., 2001; Vilcek et al., 2001), Asia (Deng et al., 2012; Nagai et al., 2008; Xue et al., 2010; Yang et al., 2007) and Australia (Mahony et al., 2005; Ridpath et al., 2010). The genetic diversity of Brazilian pestiviruses associated with the high prevalence of BVDV-2 specially reinforce the need of the knowledge of the circulating pestiviruses due to reports of the failure of commonly used molecular detection techniques (Schirrmeier et al., 2004; Weber et al., 2014a) and significant antigenic changes at the species and subtype levels that were demonstrated by cross-neutralization (Bachofen et al., 2008; Bianchi et al., 2011; Pizarro-Lucero et al., 2006; Ridpath et al., 2010). The BDV was never reported in South America despite a case of a sheep with neurological disorder in South Brazil that was detect as positive in immunohistochemistry, but the genotyping was not performed (Pescador et al., 2004).

In Brazil, only vaccines containing inactivated BVDV-1 or BVDV-1 and BVDV-2 are licensed, despite the knowledge that live vaccines are more efficient. Most of these vaccines are polyvalent and contain also antigens of *Bovine herpesvirus type 1*, *Bovine respiratory syncytial virus* and *Bovine parainflenza-3 virus*. The use is still incipient and is performed unevenly in different regions and in different production systems (Flores et al., 2005). Moreover, Vogel et al. (Vogel et al., 2002) tested the efficacy of commercial vaccines against Brazilian isolates and verified the production of low to moderate antibody titers and no fetal protection. Since then, new vaccines were licensed but similar works were not performed yet.

Perspectives

The knowledge about BVDV infection in Brazil grew in the last years due the increasing number of laboratories involved in diagnosis and research. The ease of communication and collaboration between laboratories, the availability of quality reagents for the diagnosis and the growing interest of the vaccine industry have contributed to this growth. Anti-infection measures have been adopted by voluntary initiative, without any official interference. However, the emergence of health measures account to BVDV infection in other countries may emerge the need of the role of the official veterinary service in Brazil due to the implementation of possible health restrictions on products of cattle origin in international trade in the near future.

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