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Enteric viral infections in lambs or kids

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ABSTRACT

Diarrhoea in lambs and kids is often a complex, multi-factorial syndrome. Common infectious causes of diarrhoea in lambs and kids during the first month of life are of bacterial or parasite nature. However, despite appreciable improvements in management practices and prevention and treatment strategies over the last decades, diarrhoea is still a common and costly syndrome affecting newborn small ruminants. Recent advances in the diagnostics and metagenomic investigations of the enteric environment have allowed discovering a number of novel viruses, although their pathobiological properties remain largely unknown. Assessing more in depth the impact of these viruses on the health and productions of these livestock animals is necessary and requires the development of accurate diagnostic tools and updating of the diagnostic algorithms of enteric pathological conditions.

1. Introduction

Diarrhoea in lambs and kids can be defined as a complex, multi-factorial syndrome. Interactions between animal susceptibility, nutritional status, environmental factors, flock/herd management and a variety of infectious agents acting often in a synergistic mode may influence the onset and evolution of the disease. Common bacterial causes of diarrhoea in lambs and kids during the first month of life are *Escherichia coli*,*Cryptosporidium* spp., *Salmonella* spp. and *Clostridium* spp. (Tzipori et al., 1981; Holland, 1990; Uzzau et al., 2001). Rotaviruses are also often associated with enteric disease in small ruminants (Alkan et al., 2012). However, in general, the role of viruses in the syndrome still remains largely unexplored and likely overlooked. Recent advances in the diagnostics and metagenomic investigations of the enteric environment have provided clues to understand the diversity of small ruminant enteric virome. By reviewing the literature, we provide herewith an update on the enteric viruses identified in small ruminants and eventually associated with enteric disease, on the basis of either observational or experimental studies.

2. Adenoviruses

In small ruminants, adenoviruses have been associated with both enteric and respiratory signs of various severity and adenovirus-induced disease is usually referred to as pneumo-enteritis (Belak, 1990). Adenoviruses (family Adenoviridae) are non-enveloped viruses with an icosahedral nucleocapsid of 90–100 nm in size, with a double stranded DNA genome of 26–45 Kbp in length (Davison et al., 2003). Adenoviruses are genetically/antigenically highly heterogeneous and infect a broad range of vertebrate hosts (Harrach et al., 2011). Currently, the family Adenoviridae includes five genera, *Atadenovirus, Aviadenovirus, Ichtadenovirus*, *Mastadenovirus* and *Siadenovirus* (Harrach et al., 2011).

Seven distinct ovine adenovirus serotypes and two caprine adenovirus serotypes, belonging to the genera *Atadenovirus* or *Mastadenovirus* (Table 1), have been identified thus far (Lehmkuhl and Hobbs, 2008). The various types differ in their antigenic and biological properties (haemagglutination spectrum, *in vitro* cultivation, virulence) (Belak, 1990). Although adenoviruses seem to be species-specific, isolates antigenically related to bovine adenovirus type-2 or adenovirus type-7 have been reported in lambs (Belák and Pálfi, 1974; Davies and Humphreys, 1977).

Virological and serological investigations have revealed that adenoviruses are common in populations of small ruminants worldwide (Belak, 1990). Prevalence of antibodies to the various ovine adenovirus types is high (Pálfi and Belák, 1978; Adair et al., 1984; Lehmkuhl and Hobbs, 2008). Asymptomatic infections or prolonged shedding of virus after acute infection are frequent. The virus is shed with nasal secretions, faeces and/or urine. Young animals with low or no maternal immunity are more susceptible to adenovirus infection. Morbidity in a flock/herd is high, while mortality is influenced by age, adenovirus type/strain and eventual co-infections with other pathogens (Belak, 1990).

Adenovirus infection is usually observed in 2–12-week-old lambs. One week after infection, the disease starts with enteric

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Table 1
Classification/nomenclature of adenoviruses identified in small ruminants (Lehmkuhl and Hobbs, 2008).

Genus	Species	Serotypes
Atadenovirus	Ovine adenovirus D	Ovine adenovirus 7 Goat adenovirus 1
Mastadenovirus	*Ovine adenovirus A*	Ovine adenovirus 2 Ovine adenovirus 3 Ovine adenovirus 4 Ovine adenovirus 5 Bovine adenovirus 2
	Ovine adenovirus B	Ovine adenovirus 1
	Ovine adenovirus C[a]	Ovine adenovirus 6
	Caprine adenovirus A[a]	Goat adenovirus 2

[a] Not classified officially.

signs that persist for nearly one week. Respiratory signs appear 2–3 days after onset of the enteric signs and include sneezing, nasal discharge, conjunctivitis and altered breathing. Febrile response is also observed in the animals. Respiratory signs tend to persist, evolving into a chronic form. Sometimes, only respiratory sign are observed (Belak, 1990), while in other cases the enteric form is predominant (Smyth et al., 1994). Fatal hyper-acute infections may also occur in neonatal lambs (DeBey et al., 2001). The disease observed in kids is similar, with enteric and respiratory signs being described in those animals (Lehmkuhl et al., 1997, 2001; Olson et al., 2004). Encephalitis by adenovirus has been described in an adult goat (Lehmkuhl and Cutlip, 1999; Lehmkuhl et al., 2001).

Prevention of the infection is based on adoption of good hygiene measures and correct management of the flock/herd. Experimental inactivated bivalent vaccines proved to be safe and effective (Belak, 1990), although commercial vaccines are not currently available.

3. Astroviruses

Astroviruses are small round non-enveloped viruses, with a positive-sense 3′ poly-adenylated RNA of 6–7 kb in size (Mendez and Arias, 2007). Astroviruses are mostly associated with enteric infections in mammalians and avian species, although extra-intestinal localisation and disease may occur in avian species and in some mammals (Mendez and Arias, 2007; Blomström et al., 2010; Li et al., 2013).

Ovine astroviruses were first identified in the late 1970s in Scotland (Snodgrass and Gray, 1977). Small round virus-like particles were observed by electron microscopy in the faeces of lambs 4–6 weeks of age with acute diarrhoea. Virions with a typical five-to-six pointed star shape were clearly distinguishable in some samples. Faecal filtrates from a naturally infected lamb were given orally to a gnotobiotic lamb, which subsequently excreted the virus. Also, faecal filtrates of the experimentally infected lamb were given orally to two further gnotobiotic lambs, which developed diarrhoea and excreted the virus (Snodgrass and Gray, 1977). Infections in gnotobiotic lambs with the ovine astrovirus were repeated in a distinct experiment, and the infection determined mild diarrhoea after an incubation period of about 48 h. Astroviruses infect only mature villus epithelial cells and subepithelial macrophages in the small intestine, where they produce partial villus atrophy. Infected enterocytes are replaced with cuboidal cells from the crypts, and the lesion gradually heal by 5 days after infection (Snodgrass et al., 1979).

Structural analysis and genome sequencing of the ovine astrovirus prototype confirmed that the virus is part of the *Mamastrovirus* genus, Astroviridae family (Herring et al., 1981; Jonassen et al., 2001, 2003). Subsequent studies have revealed that the ovine astrovirus prototype is genetically unrelated to bovine astroviruses (Tse et al., 2011) and that genetically diverse astroviruses may infect sheep (Reuter et al., 2012a).

4. Bunyaviruses

Bunyaviruses are enveloped, spherical viruses with a diametre of approximately 80–120 nm and a genome consisting of three segments of negative-sense single-stranded RNA (large, medium and small segments). The family Bunyaviridae includes over 350 viruses, mostly transmitted by arthropods, which are divided into five genera: *Hantavirus*, *Nairovirus*, *Orthobunyavirus*, *Phlebovirus* and *Tospovirus*. Several bunyaviruses have been reported to infect small ruminants, but only a few are responsible for enteritis in these animals (Hubálek et al., 2014) (Table 2).

Nairobi sheep disease was first observed in a sheep with acute gastroenteritis in Nairobi, Kenya (Montgomery, 1917). The virus, prototype of the *Nairovirus* genus, is also known as *Ganjam virus*. Nairobi sheep disease is widespread in East Africa and India and it is transmitted by metastriate ticks, e.g. *Rhipicephalus appendiculatus* (Africa), *Haemaphysalis wellingtoni*, *Haemaphisalis intermedia* (India) (Marczinke and Nichol, 2002). The vertebrate hosts are sheep and goats, although the rat *Arvicanthis abyssinicus* may serve as a reservoir of the virus (Simpson, 1966). The disease may appear after introduction of naïve livestock into an endemic area and it is regarded as one of the most pathogenic infection in small ruminants, with mortality risk rates as high as 90%, as animals die from acute haemorrhagic fever. The disease is observed only in sheep and goats, with less severe signs in the former species, whereas other ruminants are, in general, refractory to the infection. Signs of disease usually appear 4–6 days after the tick bite and start with fever, peaking to 42 °C and persisting for 1–7 days. Diarrhoea is usually observed 1–3 days after onset of fever, characterised by watery and fetid faeces that turn haemorrhagic in the following days. Infected animals may also display depression, respiratory distress with mucopurulent nasal discharge and pulmonary oedema, myocarditis and tubular nephritis. Pregnant ewes and goats often abort and the foetuses may display developmental defects (Montgomery, 1917; Weinbren et al., 1958). Nairobi sheep disease is a notifiable disease and sporadic cases of human infection have also been reported. An attenuated vaccine is available for its control (Davies et al., 1974).

Rift Valley Fever virus (*Phlebovirus*), or *Zinga virus*, was first isolated from an epizootic of high mortality in lambs and abortion in pregnant ewes in the Great Rift Valley, Kenya, in 1930 (Daubney et al., 1931). Outbreaks of Rift Valley fever were limited to the African continent until 2000, when severe and simultaneous outbreaks of the disease occurred in Yemen and Saudi Arabia and later in Madagascar and Mayotte. The geographic expansion poses a threat to European countries (Chevalier et al., 2010), especially as *Rift Valley Fever virus* is a mosquito-borne infection, transmitted by insects of the genera *Aedes* and *Culex* (Chevalier et al., 2010). A number of vertebrate species are susceptible to *Rift Valley Fever virus* infection, including wild and domestic ruminants and rodents. While ruminants develop clinical signs, rodents, mainly rats of the genera *Arvicanthis* or *Rattus*, serve as reservoirs. Equines and pigs can also be infected, but do not display clinical signs. Fatal

Table 2
Bunyaviruses associated with enteric disease in small ruminants.

Virus	Genus	Vector	Reservoir
Nairobi sheep disease virus	*Nairovirus*	Ticks	Rats
Rift Valley fever virus	*Phlebovirus*	Mosquitoes	Rodents
Schmallenberg virus	*Orthobunyavirus*	Biting midges	Wild ruminants?