Veterinary Microbiology 167 (2013) 135–144

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

Equine rotaviruses—Current understanding and continuing challenges

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ARTICLE INFO

Article history:
Received 3 January 2013
Received in revised form 4 July 2013
Accepted 7 July 2013

Keywords:
Equine rotavirus
Foal
Diarrhoea
Virus
Review

ABSTRACT

Equine rotaviruses were first detected in foals over 30 years ago and remain a major cause of infectious diarrhoea in foals. During this time, there has been substantial progress in the development of sensitive methods to detect rotaviruses in foals, enabling surveillance of the genotypes present in various horse populations. However, there has been limited epidemiological investigation into the significance of these circulating genotypes, their correlation with disease and the use of vaccination in these animal populations. Our knowledge of the pathogenesis of rotavirus infection in foals is based on a limited number of studies on a small number of foals and, therefore, most of our understanding in this area has been extrapolated from studies in other species. Questions such as the concentrations of rotavirus particles shed in the faeces of infected foals, both with and without diarrhoea, and factors determining the presence or absence of clinical disease remain to be investigated, as does the relative and absolute efficacy of currently available vaccines. The answer to these questions may help direct research into the development of more effective control measures.

1. Introduction

Rotaviruses were first observed in the faeces of a foal with diarrhoea in 1975 in Great Britain (Flewett et al., 1975). They had been detected previously in faeces from a vervet monkey in 1958, but it was not until rotaviruses were recognised as a major cause of neonatal diarrhoea in calves in 1969 and children in 1973 that significant research into this pathogen in other species commenced (Bishop and Davidson, 1973; Malherbe and Strickla, 1967; Mebus et al., 1969). Initially referred to as a reovirus-like agent, the name rotavirus was later adopted from the Latin "rota" (wheel), because of the wheel-like appearance of virions by electron microscopy (EM) (Fig. 1) (Flewett et al., 1974).

Rotaviruses are the most prevalent viral pathogens identified in the faeces of foals with diarrhoea. The frequency of detection of rotaviruses in clinical cases varies from 20 to 77% and they appear to be endemic in most, if not all, horse populations (Browning et al., 1991c; Conner and Darlington, 1980; Dwyer et al., 1990; Netherwood et al., 1996). Diarrhoea in young foals is a labour intensive disease that is costly to manage. An inactivated maternal vaccine has been available commercially since the mid 1990s, but despite this rotaviruses are still a major cause of diarrhoea in foals.

2. Rotavirus classification

Rotaviruses belong to the family Reoviridae, subfamily Sedoreovirinae, genus Rotavirus (Carstens, 2010). They are icosahedral, non-enveloped viruses that have a segmented,

Abbreviations: G, glycoprotein; P, protease sensitive protein; EM, electron microscopy; ELISA, enzyme-linked immunosorbent assay; PCR, polymerase chain reaction; RT-PCR, reverse transcription polymerase chain reaction; RT-LAMP, reverse transcription loop-mediated isothermal amplification; TLPs, triple-layered particles; DLPs, double-layered particles; SLPs, single-layered particles; BLS, *Brucella* spp. lumazine synthase.

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http://dx.doi.org/10.1016/j.vetmic.2013.07.010

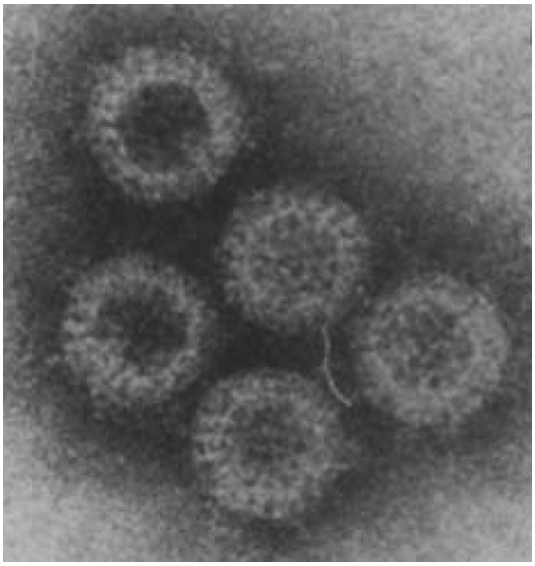

Fig. 1. Rotavirus particles as seen by negatively stained electron microscopy.
From Rodger et al. (1980).

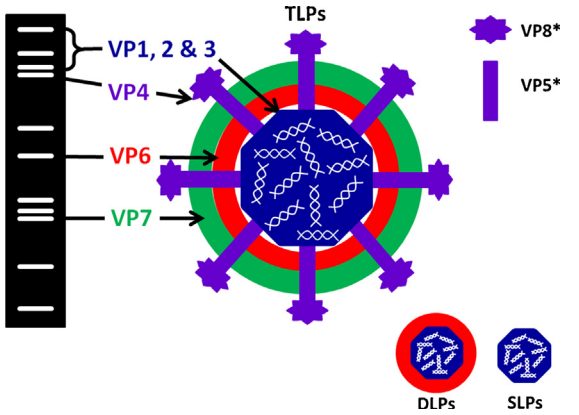

Fig. 2. Schematic representation of the equine rotavirus genomic electrophoretic pattern and the virion morphology including triple-layered particles (TLPs), double-layered particles (DLPs) and single-layered particles (SLPs).

double stranded RNA genome (Newman et al., 1975; Welch and Thompson, 1973). The genome consists of 11 segments (Rodger et al., 1975) encoding six virion proteins (VP1-4, 6 & 7) and six non-structural proteins (NSP 1-6). The eleventh gene segment codes for both NSP5 and NSP6.

The virions have a triple capsid (Labbé et al., 1991; Rothnagel et al., 1994). The outer capsid is composed of the glycoprotein VP7, with spikes composed of VP4, the intermediate capsid is formed by VP6, and the inner capsid is enclosed by VP2 and contains VP1 and VP3 (Fig. 2). When visualised by EM, the infectious triple-layered particles (TLPs) have a diameter of 100 nm. Double-layered particles (DLPs) that have lost the outer capsid are 70 nm in diameter, and the less frequently identified single-layered particles (SLPs) have only the inner core remaining (Ciarlet and Estes, 2003). Neither DLPs nor SLPs are infectious. Loss of the outer capsid is promoted by chelation of Ca^{2+}.

The intermediate capsid protein VP6 is used to classify rotaviruses into groups A–H (Matthijnssens et al., 2012b). Group A rotaviruses are the major cause of diarrhoea in humans and animals. Group B rotaviruses have been detected in calves, lambs, piglets and humans and group C rotaviruses in calves, piglets and humans (Ghosh et al., 2007; Medici et al., 2011; Park et al., 2011; Theil et al., 1995). Only group A rotaviruses have been detected in horses (Browning et al., 1991c; Dwyer, 2007).

The VP7 glycoprotein in the outer capsid is the major neutralisation antigen. It is encoded by the ninth genomic segment and is used to classify group A rotaviruses into G types, 27 of which are currently recognised (Matthijnssens et al., 2011). There are 6 G types reported in equine rotaviruses (Browning et al., 1991a, d; Hoshino et al., 1983a,b; Imagawa et al., 1994; Isa et al., 1996).

The protease sensitive VP4 is a minor neutralisation antigen encoded by the fourth genomic segment, and determines the P type. There are 35 different P types currently recognised (Matthijnssens et al., 2011), 6 in equine rotaviruses (Garaicoechea et al., 2011; Hardy et al., 1993; Isa and Snodgrass, 1994; Isa et al., 1996; Taniguchi et al., 1994). VP4 is also associated with haemagglutination, infectivity and virus attachment. Infectivity is enhanced by proteolytic cleavage of VP4 into two fragments, VP5* and VP8*, by trypsin in the small intestine (Graham and Estes, 1980).

Initially, the classification of rotaviruses into G types required cross-neutralisation assays with panels of hyper-immune sera (Hoshino et al., 1984; Kalica et al., 1981; Offit and Blavat, 1986). Classification into P types was more complex and generally required either P type specific monoclonal antibodies or the generation of reassortant viruses with identical G serotype genes but distinct P type genes. Serotyping has been largely replaced by genotyping (Gentsch et al., 1992; Gouvea et al., 1990). The nucleotide sequence of the VP7 gene correlates closely with G serotype designations. As VP4 is the minor neutralisation antigen, it is difficult to raise P serotype specific antibodies, making P serotyping much more demanding. As a result, fewer P serotypes have been definitively characterised, and P genotyping has been much more commonly used in epidemiological studies. When known, the P serotype is denoted by a number, while the P genotype is denoted by a number within square brackets.

A uniform scheme for the nomenclature of group A rotaviruses based on full genome sequencing has been adopted by the Rotavirus Classification Working Group. The nomenclature is shown in Table 1 (Matthijnssens et al., 2008). Full genome comparisons suggest that rotaviruses are generally host specific and that interspecies genomic reassortment is uncommon.

3. Epidemiology and aetiology

Equine rotaviruses are ubiquitous in horse populations. The evidence for the widespread nature of rotavirus infection includes the high prevalence of rotavirus antibodies in adult horses (Conner and Darlington, 1980;