

therapies and prophylactics. Bovine spongiform encephalopathy (BSE), first identified in the UK and then throughout Europe, is the prototype trans-species transmissible prion disease, having affected cattle, humans, ungulates, and felids naturally, and multiple other species experimentally. Chronic wasting disease (CWD) is an endemic prion disease of deer and elk distinguished from BSE by its unprecedented horizontal transmissibility among cervid hosts. Thus far, CWD has not been shown to cross species barriers in nature, although several experimental inoculation studies have resulted in trans-species transmission. The CWD species barriers are fortunate, as the facile prion shedding and resultant environmental contamination would constitute a major economic and public health threat. Mounting evidence indicates that primary structure homology alone does not comprise the prion species barrier. First, the primary sequence of bovine and white tail deer prion protein is very well-conserved. Additionally, the secondary structure of the misfolded protein is suspected to be a β -sheet rich configuration in all species. Thus, tertiary structure and the quaternary arrangement of the amyloid fibrils are attractive molecular explanations for the species barrier. Functional demonstration of the mechanism(s) resulting in the species barriers is the principal question addressed in this research.

Materials and Methods

Most studies of the effects of primary or tertiary prion protein structures on trans-species prion transmission have relied upon animal bioassays, making the influence of prion protein structure vs host co-factors (e.g. trafficking and innate immune interactions) difficult to dissect. Here, we use real-time quaking-induced conversion (RT-QuIC), which relies on

the conversion of recombinant PrPC (rPrPC) by an infectious seed and detection with an amyloid-binding dye, to investigate the propensity for and the kinetics of trans-species prion conversion. This system makes it possible to investigate the molecular mechanism of trans-species transmission, which may be able to be exploited for the development of therapeutics, prevention measures, and risk assessment paradigms. To assess trans-species conversion in the RT-QuIC system, we compared CWD and BSE prions, as well as feline CWD (fCWD) and feline spongiform encephalopathy (FSE). Each prion was seeded into each host recombinant PrP (full-length rPrP of white-tailed deer, bovine or feline).

Results

We demonstrated that fCWD is a more efficient seed for feline rPrP than for white-tailed deer rPrP, which suggests adaptation to the new host. Conversely, FSE maintained sufficient BSE characteristics to more efficiently convert bovine rPrP than feline rPrP. Additionally, human rPrP was competent for conversion by CWD and fCWD. This insinuates that, at the level of protein:protein interactions, the barrier preventing transmission of CWD to humans is more similar to BSE than previously estimated.

Significance

These studies will contribute uniquely to efforts to use simplified, in vitro assays to understand the mechanism of prion conversion and species barriers. Until the species barrier is defined, it is impossible to predict transmission, the risk to humans and other hosts, or the efficacy of potential therapeutics or prophylactics for prion disease.

Serum neutralizing antibody concentrations against viral bovine respiratory pathogens in nursing beef calves

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Introduction

Nursing calf bovine respiratory disease (BRD) is a problem for some herds, and the timing of maternal antibody decline may be related to risk for calves to develop BRD. Limited information is available on the distribution of serum maternal

antibody titers among calves within and between cow-calf herds. Understanding how maternal antibody concentrations vary within and between herds may help us understand what puts nursing (preweaned) calves at risk for BRD. The objective of this study was to test the effect of calf age and farm on the magnitude of serum neutralizing antibody (SNA) titers

against viral causes of BRD in nursing calves among herds in a similar geographic location.

Materials and Methods

A convenience sample of 5 cow-calf herds with ≥ 30 calves aged ≥ 30 days located in South-Central Nebraska was selected for study. Calves had not been vaccinated at time of sampling; dams in 3 out of the 5 herds had been vaccinated with MLV viral BRD vaccine in the previous 13 months, and the dams from the remaining 2 herds had not received viral BRD vaccine in the previous 13 months. Blood was collected from calves at a single point in time for each herd. Serum was analyzed for SNA against BRSV, BVDV and BHV-1. Titers were expressed as the logarithm, base 2, of the reciprocal of highest dilution with a positive reaction. Ordinal logistic regression and linear regression were used to model the relationship between farm and calf age on antibody titer. Statistical significance was defined at $\alpha \leq 0.05$.

Results

Serological data were obtained from 168 calves from 5 cow-calf herds. The mean calf age was 61.1 days (median 62.5 days; range 23 to 91 days). The mean age of calves differed by farm. The results from ordinal logistic regression models and linear regression were in good agreement. By either modeling method, farm and age of calf were significantly associated with titers to BRSV and BVDV. Accounting for the

age of the calves, the geometric mean BRSV and BVDV titers differed by farm. Accounting for farm, BRSV titers decreased by 50% for every 35 additional days of calf age, and BVDV titers decreased by 50% for every 20 additional days of calf age. There was a significant interaction between farm and age of calf on titers to BHV-1 such that the rate of decline in BHV-1 antibody titers with increasing age depended on the farm.

Significance

Although serological titers are ordinal rather than continuous in nature, the conclusions from the statistical analysis were the same whether we used ordinal logistic regression or linear regression. By either method of analysis, we found significant differences between farms in age-adjusted titer values. That is, adjusting for the age distribution of the calves, farms differed in geometric mean SNA titers. On all farms, older calves had significantly lower antibody titers to BRSV and BVDV, probably representing a decay of maternal antibodies. The rate of age-related BHV-1 antibody decline differed by farm. These results suggest that age-adjusted SNA titers to viral respiratory pathogens vary across herds. Differences in SNA titers by farm may represent differences in calf age distribution, differences in vaccination history, or exposure to wild-type virus. Veterinary practitioners should not assume that herds in a particular geographic region have equivalent SNA titers, even after accounting for calf age, and they should expect decreasing SNA titers as nursing calves age.