

Atypical Pestivirus and Severe Respiratory Disease in Calves, Europe

To the Editor: The article by Decaro et al. (1) described an outbreak of severe respiratory disease in calves in Italy caused by an atypical bovine pestivirus. This report confirms our concern that this group of viruses is probably widespread (2) and present on >3 continents. Moreover, it demonstrates that atypical bovine pestiviruses are capable of causing disease in calves in the field and a clinical picture consistent with most bovine viral diarrhea virus (BVDV) infections that occur naturally or experimentally (3,4).

Some key issues remain unknown. The origin of the bovine pestivirus and the route of introduction into the herd are unclear, although phylogenies demonstrated a close relationship between this virus strain from Italy and atypical bovine pestiviruses from Brazil. Batches of fetal bovine serum from Brazil have repeatedly been found to be contaminated with atypical bovine pestiviruses (2,3), and there is a risk for contamination of vaccines with these viruses. Animal trade and vaccines should be considered when conducting further investigations into this outbreak.

The evolutionary relationship between the atypical and the recognized pestivirus species (1) needs to be clarified. Maximum-likelihood and Bayesian analyses of a concatenated dataset positioned atypical pestiviruses consistently in a clade sister to BVDV-1 and BVDV-2, and the larger clade was sister to pestivirus of giraffes (5). The same pattern was observed in complete genome phylogeny (1).

The term atypical is not informative, and a new name has been proposed for these bovine pestiviruses

(5). Outcomes of infections with these viruses are typical, but the viral antigens and phylogenies are unique.

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In Response: We read with interest the comment by Liu et al. (1) to our article reporting overt disease in calves caused by infection with atypical or 'Hobi'-like pestivirus (2). Although we can rule out that vaccination was the source of infection because only killed vaccines were administered on the farm, the most recent findings about this emerging group of viruses deserves further discussion regarding their possible taxonomical, diagnostic, and prophylactic implications.

The association of 'Hobi'-like pestivirus with clinical disease in cattle was confirmed by reports of experimental and natural infections (3,4). A cytopathogenic/noncytopathogenic 'Hobi'-like virus pair was isolated from a diseased heifer, demonstrating that the new group of viruses includes 2 biotypes already known for bovine viral diarrheal viruses 1 (BVDV-1) and 2 (BVDV-2) (5).

Although the clinical presentation might mimic that of extant BVDV-1/BVDV-2, distinctive features were also evident in the reported cases (1,4). At the antigenic and phylogenetic levels, 'Hobi'-like strains showed distinct differences from the other bovine pestiviruses: they were at least as different from BVDV-1/2 as are border disease virus and classical swine fever virus (6; N. Decaro et al., unpub. data). The antigenic and genetic uniqueness of 'Hobi'-like viruses will likely lead to the definition of a new species within genus *Pestivirus*, but how this species should be designated remains unclear.

Some scientists have tentatively proposed to name the virus bovine viral diarrhoea 3, but others believe this nomenclature would be problematic from regulatory and scientific standpoints (J. Ridpath, pers. comm.). Molecular assays standardized for BVDV-1/2 might not be able to detect ‘Hobi’-like strains because of the presence of mismatches in the oligonucleotide binding regions (7). Prophylactic measures should take into account the circulation of ‘Hobi’-like pestiviruses in cattle herds. Whether commercial BVDV vaccines are effective against the emerging pestivirus is unknown, and requires future *in vivo* cross-protection studies.

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Bartonella spp.
Bacteremia and
Rheumatic
Symptoms in
Patients from Lyme
Disease–endemic
Region

To the Editor: We believe the recent article by Maggi et al. (1) contains serious flaws in content and underlying message, including a poorly defined study population, lack of appropriate controls, improper use of the term bacteremia, and incongruent laboratory findings. Selection criteria were vague: the authors state only that participants were a “biased” collection of “patients selected by a rheumatologist,” with no control population included for comparison. The diagnosis of Lyme disease and other previously diagnosed conditions was solely by self-report. Although blood samples were collected from every participant, the authors apparently neglected to perform standardized testing for *Borrelia burgdorferi* or other conditions.

The term “bacteremia” signifies presence of viable bacteria in the bloodstream, which is not substantiated solely by a positive PCR result. True bacteremia was documented in only 1.7% of participants from whom a viable *Bartonella* species isolate was cultured, rather than the purported 41.1% of participants.

Surprisingly, many participants whose PCR results were positive for *Bartonella* spp. had no serologic evidence of infection (e.g., 82.5% of samples that had positive PCR results for *Bartonella henselae* were not seroreactive). Although anergy has been reported, samples from most immunocompetent and immunocompromised patients infected with *Bartonella* spp. are seroreactive (2–4), calling into question the authors’ findings. Furthermore, 24% of samples that were positive by PCR revealed no identifiable *Bartonella* spp. by DNA sequencing; these participants should have been excluded from analysis.

Maggi et al. hypothesize that *Bartonella* spp. infection is causally related to a variety of chronic ailments. In fact, there was no association within the study population between positive *Bartonella* spp. PCR results and chronic illness, self-reported Lyme disease, or even a prior diagnosis of bartonellosis.

Efforts to define the clinical and public health importance of *Bartonella* spp. require scientific rigor. The above issues challenge the validity of the study, and results should be interpreted with caution.

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