The Forgotten Viruses: Cause for Clinical Concern?

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Bovine practitioners deal with viral diseases on a daily basis. These agents are well recognized as the primary pathogens in many practice situations. Although many viral agents have been isolated from cattle, those affecting the respiratory tract, bovine herpesvirus-1, and to a lesser extent, bovine respiratory syncytial virus, are generally considered to be the most economically important and the targets of prophylactic and research efforts. Economic losses due to bovine virus-diarrhea virus associated reproductive disease and, more recently with high mortality subsequent to acute infection, have received much attention. The purpose of this brief review is to consider some of the other viral agents that have been isolated from cattle by highlighting recent research in the context of clinical concerns for the practitioner and client.

DNA Viruses

Parvovirus

Bovine parvovirus, a small, non enveloped, single stranded DNA virus that is stable in the environment, was first isolated from the intestines of calves in 1959. Subsequent epidemiologic studies conducted in several countries in the 1960's and 1970's indicated that the prevalence of infection ranged from 46-86% of cattle tested. The species specificity of parvoviruses makes it unlikely that this seroconversion was the result of detection of cross-reacting antibodies. Fecal/oral and vertical transmission modes of transmission have been documented. Similar to parvoviruses in other species, bovine parvoviruses can cause enteric disease, especially in young calves. Parvoviruses have been associated with reproductive failure, including repeat breeding and embryonic death; however, a recent study found bovine parvovirus in only 2 of 948 bovine abortions in which viral agents were implicated. Although a recent survey indicates that the virus is still widespread in at least some cattle populations in North American, currently, the clinical significance of this virus is questionable.

Adenovirus

Bovine adenoviruses are non-enveloped double stranded DNA viruses that are highly stable outside the host and were first isolated in the late 1950's. Seroepidemiologic studies have indicated worldwide prevalence of infection. There is temporal and geographic variation in the prevalence of specific serotypes. Until recently 9 serotypes of bovine adenovirus were recognized. They have been associated with respiratory and enteric disease, as well as "weak calf syndrome", but have been generally considered as secondary pathogens. In the late 1980's, serotype 10 was isolated in New Zealand. This serotype has been directly associated with a distinctive hemorrhagic enterocolitis in adolescent (5-10 month old) calves in New Zealand, and recently, in Europe. To date there are no published reports of this syndrome in North American cattle.

Herpesviruses

Malignant Catarrhal Fever Virus

A gammaherpesvirus was first isolated from bovine cases of wildebeest-associated malignant catarrhal fever in Africa in the 1960's. It has since been named acephaline herpesvirus -1 (AHV-1). Although a gammaherpesvirus has yet to be cultured from cattle with so-called sheep-associated MCF (SA-MCF) in North America and other parts of the world, recent work using DNA from infected lymphoblastoid cells has confirmed the suspected high degree of genetic homology between AHV-1 and the agent that causes SA-MCF. It is possible with polymerase chain reaction to differentiate the 2 closely related gamma herpesviruses. Using a competitive ELISA it has recently been shown that virtually 100% of sheep tested had antibodies to the herpesvirus that causes SA-MCF. The epidemiology of the infection in sheep and the means and timing of transmission to cattle remains to be resolved. Although it has been thought that the virus is transmitted vertically, or in the neonatal period from ewes to lambs, the application of the PCR and ELISA suggests that young lambs are infected but that the infection is latent, or that lambs might not be susceptible early in life. Clinically, MCF in cattle is a sporadic disease with multisystemic signs and lesions. It has been thought to be invariably fatal; however, recent studies indicate that

some cattle with SA-MCF may develop chronic disease or partial to complete clinical recovery.

Encephalitic herpesviruses

In addition of respiratory and reproductive disease, bovine herpesviruses have has been associated with encephalitis in cattle since at least 1962 when the first encephalitic bovine herpesvirus was isolated in Australia. CNS disease can occur as a result of infection with isolates of BHV-1, especially in young calves. More frequently, however it is the result of infection with neurotropic isolates of BHV that are distinct genetically and antigenically from isolates of BHV-1 that cause respiratory and reproductive diseases. These include BHV-1.3 and BHV-5. Although the epidemiology and prevalence of these encephalitic herpesviruses is currently poorly understood they should be included in the list of differential diagnoses for CNS disease in cattle. The documentation of antigenic differences among these viruses also raises, as yet untested, concerns regarding crossprotection and vaccine efficacy.

RNA Viruses

Vesicular Stomatitis Virus

Vesicular stomatitis virus (VSV) is an enveloped single stranded RNA virus that is highly susceptible to lipid solvents and disinfectants. As documented in recent outbreaks in North America, vesicular disease caused by VSV infection in cattle (and swine) is of regulatory concern because it is clinically indistinguishable from foot and mouth disease. The means of viral transmission from one animal to another has remained controversial for more than 70 years, with both abrasions and insects being implicated. A recent epidemiologic study in Costa Rican dairy farms suggested that the occurrence of clinical VS on a farm was most dependent on factors relating to vector transmission. While clinical concerns with VS infection in cattle may be minimal the economic implications can be an important consideration in the recognition of infection.

Bovine Coronavirus

Bovine coronavirus is an enveloped single stranded RNA virus, that has been associated, since the early 1970's, with diarrhea in young calves . The stability of the virus in the environment is not known. The role of BCV in so-called "winter dysentery" of adult cattle and, relatedly, of winter dysentery in the epidemiology of calfhood diarrhea has been debated since the isolation of BCV. Recent studies suggest that in closed herds, where the introduction of new BCVs is minimized, that respiratory tract infections are important in BCV transmission from cows to calves and that crossprotection occurs after heterologous infection. Moreover, it has been shown that, while some antigenic and biologic diversity exists among BCV isolates from calf diarrhea and winter dysentery, that this variation was not related to the clinical source of the isolate. Another area of controversy has been the role of BCV in respiratory disease. Although past and recent studies have demonstrated shedding of BCV from cattle with respiratory disease, definitive studies similar to those in swine characterizing respiratory and enteric coronaviruses have yet to be done. Recently, coronaviruses antigenically related to BCV were isolated from wild ruminants with diarrhea and it has been suggested that these viruses may be transmissible to cattle. BCV continues to be a cause for clinical concern in respiratory and enteric disease in young and adult cattle.

Bovine Immunodeficiency Virus / Bovine Leukemia Virus

Bovine immunodeficiency virus (BIV) and bovine leukemia virus (BLV) are enveloped single stranded RNA viruses in the family *Retroviridae*. BIV, also known as bovine lentivirus, was accidentally isolated in the early 1970's from leukocytes from a cow with persistent lymphocytosis that was part of a study on BLV. BIV was "forgotten" until the advent of closely related HIV infections in humans. Several serological surveys indicate a world-wide low to moderate prevalence of infection. There is a particularly high, as yet unexplained, prevalence of BIV infection in dairy cattle in Mississippi. BIV apparently often occurs as a co-infection with bovine leukemia virus, but can occur independently. The relationship between these 2 viruses in disease expression in cattle is unresolved. Recent studies indicate that BIV is present in leukocytes in blood, milk and semen. Both retroviruses may be transmitted in milk to calves, and by injection needles, surgical instruments and rectal exam gloves. Similar to HIV in humans, experimental inoculation of cattle with BIV results in subclinical lymphocytosis, lymphadenopathy, and functional deficits in leukocytes; however, there are as yet no data documenting clinical immunosuppression similar to HIV in humans, although some circumstantial evidence suggests that chronic BIV infections mediate increased susceptibility to other diseases. It has been recently proposed that BIV is the etiologic agent in bovine paraplegic syndrome, a debilitating disease of unknown origin. BIV is closely related to, but distinct from, Jembrana Disease Virus, another bovine lentivirus that causes an acute, often fatal, syndrome in cattle in Bali, raising questions about how viral and host genetics may affect virulence and pathogenesis. BLV continues to be a cause for concern due to production losses associated with chronic infection resultant persistent lymphocytosis. Although there is increasing interest in determining the prevalence of BIV

infection and disease associations, especially in the case of unexplained chronic illness in cattle, there is as yet little definitive evidence to raise clinical concerns.

Bluetongue virus

Bluetongue virus (BTV) is a non-enveloped double stranded RNA virus in the family *Reoviridae*. There are more than 20 recognized serotypes of this arbovirus that is transmitted primarily by biting midges (*Culicoides spp).* Although fetal deformities can result from in utero infection with BTV, in most instances, BTV is a subclincal infection in cattle. Studies conducted in the late 1960's and '70's suggested this virus can cause persistent infection, similar to bovine virus diarrhea virus. This prompted strict controls on exportation of livestock from BTV endemic countries. Although most researchers currently believe that persistence is not a feature of BTV infection in cattle, regulatory concerns persist. Most recent work in BTV biology has been aimed at determining how genetic and phenotypic differences in the vector ("vector competence") impact the epidemiology of BTV infection, and in the area of diagnostic test evaluation. **Although cattle are generally considered a reservoir host for BTV, the virus will continue to be a concern for bovine practitioners from the perspective of regulatory medicine and because of its role in non-tariff trade barriers.**

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