SYMPOSIUM: CALFHOOD DISEASES AND IMMUNIZATION PROGRAMS

Probable Role of Viruses in Calfhood Diseases

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ABSTRACT

Bovine enteroviruses, bovine viral diarrhea virus, rotavirus (formerly called reovirus-like agent), coronavirus-like agent, bovine adenovirus, and bovine parainfluenza-3 virus have been isolated from calves suffering from neonatal disease. The experimental disease produced by these viruses is not necessarily severe or fatal, but under farm and ranch conditions, each probably serves as an added stress factor that contributes significantly to mortality from neonatal disease. After initial losses following the introduction of a virus into a herd, the subsequent losses will be limited because the cow will produce antibodies to protect the fetus during gestation. Antibodies will also be concentrated in colostrum to protect the calf at birth. However, colostrum must be fed immediately after birth, before the calf becomes infected.

INTRODUCTION

A number of infectious agents, both viral and bacterial, are in the tissues and gastrointestinal tract of calves suffering from neonatal disease. However, disease in newborn calves is complex, and sometimes direct relationship between the disease in the field and agents isolated is difficult to prove. Many times, when healthy, naturally born, colostrum-fed calves that are held in a laboratory environment are exposed to agents isolated from newborn calves that are dying on the farm, only a very mild disease develops, and sometimes no clinical disease develops. Environmental temperatures, nutrition, and sanitary conditions are controlled in laboratory experiments, and these observations suggest neonatal disease is a mixed infection, exacerbated or intensified by the stress of adverse temperatures, high humidity, poor sanitation, and marginal or improper

nutrition.

The value of colostrum for protecting the calf from many infectious agents common to a normal herd is well known (1, 2, 25). In experimental work calves may be fed colostrum before exposure, deprived of colostrum until after exposure or deprived of colostrum for the entire experiment. When exposure to an infectious agent isolated from a sick calf does not produce disease in colostrum-fed calves on experiment, it may suggest the agent crossed the placental barrier, infection taking place before birth causing the calf to be born weak, prolonging the time between birth and colostrum feeding, or that the agent may be in the environment, infection taking place immediately at birth before colostrum feeding.

Colibacillosis, caused by particular strains of *E. coli*, is an important factor in neonatal disease today, as it was when Theobald Smith elucidated certain aspects of the disease (24). However, not all neonatal disease can be attributed to *E. coli*. In this paper, we will consider some of the viruses associated with neonatal disease and suggest possible methods of control.

REVIEW OF VIRAL AGENTS ASSOCIATED WITH CALFHOOD DISEASE

Bovine Enteroviruses

A virus of the size and characteristics of a bovine enterovirus, with the same resistance to heat and certain chemicals, was found in the lungs and other tissues of 2- and 3-day-old dairy calves affected with acute fatal scours (4, 17).

The acute fatal disease could be reproduced by exposing colostrum-deprived calves to aerosol inhalation of a filtrate of tissues containing the virus. These calves also carried a natural intestinal flora of *E. coli*. However, only those colostrum-deprived calves experimentally exposed to a filtrate containing virus developed the acute fatal disease. This virus, and the lesion produced, were also in the lungs of apparently

healthy dairy cattle in the same area which were sent to slaughter. Colostrum-deprived calves exposed to a filtrate of such lung tissue also developed the acute fatal disease.

The natural protective value of colostrum was shown readily in the experimental disease. However, the prevalence of the disease on the farms was difficult to explain because all calves born under natural conditions and kept for replacement either were allowed colostrum from the dam or were fed colostrum by nursing bottle. A study of time in feeding colostrum in relation to experimental exposure revealed that colostrum had to be fed before experimental exposure if it were to protect the calf. Feeding colostrum within 30 min after exposure failed to protect the calf, and the acute fatal disease developed.

Assistance in getting colostrum to the calf immediately after birth resulted in favorable reduction in the incidence of scours on the farms (17). Inasmuch as the reservoir for the virus was in the lungs of apparently normal cattle, there was a probable natural aerosol of the virus in the atmosphere into which the calf was born. The conclusion, therefore, was that exposure began as soon as the calf began to breath, and infection was fought by feeding colostrum as soon as the calf was delivered.

Eight serotypes of bovine enteroviruses can cross the placental barrier and infect the fetus. Stillborn calves or aborted fetuses infected with these viruses responded to the infection with the production of antibodies (10). The significance of bovine enteroviruses in the role of stillbirths and abortions has not been investigated adequately. Recently, an enterovirus was isolated from a calf that died within 1 day of birth. Antibodies to this virus were shown in the precolostral serum samples from three other calves in this herd. These antibodies indicated that this virus also can cross the placental barrier and infect the calf before birth.

Bovine Viral Diarrhea Virus

Bovine viral diarrhea virus (BVD) is a pathogen that can cross the placental barrier of susceptible cattle and cause infection at any stage of gestation (7, 14, 23). The disease in calves which develops after an intrauterine infection depends on the stage of gestation when the fetus is infected. If the fetus is infected during the first trimester, it may die or brain damage may result in underdevelopment or hypoplasia of the cerebellum. Calves that develop an intrauterine infection during the second half of gestation also may be born weak and scouring (14).

The immune system of the fetus is functional at 6 mo gestation (7). Consequently, if the fetus is infected with BVD during the last trimester, it will produce antibodies and be resistant to disease produced by BVD. Some evidence shows that infection with certain strains of BVD during the last trimester results in BVD-immune healthy calves that stay healthy (3, 19). However, there are many strains of BVD; more susceptible pregnant cows should be infected during the last trimester with different strains of BVD before this practice can be recommended.

Bovine viral diarrhea virus also can infect newborn calves (14, 15). When susceptible neonatal calves are exposed to BVD, they develop pyrexia, leucopenia, and varying degrees of scours. Nasal and lacrimal exudate also may develop. Under conditions of isolation in experimental exposures, neonatal calves usually recover. However, BVD is an immunosuppressant, and infected calves exposed to microbiological flora of the herd may develop a more severe disease that results in death (12, 22).

Rotavirus

Mebus found a virus-like agent by electron microscopy in the fluid fecal material from scouring calves (20). This agent was first called reovirus-like but now is called rotavirus because of similarity in appearance to a gear wheel (5, 11). The virus does not grow readily in cell culture and, therefore, has not been isolated and propagated for characterization extensively. Serological surveys to determine the incidence of the disease have not been undertaken, but the virus is believed to be widespread in the United States. It has been isolated in Canada (21) and England (27).

Filtrates of feces containing the virus will reproduce the disease in hysterectomy-derived, colostrum-deprived calves when introduced into the duodenum by means of a cannula or in natural-born, colostrum-deprived calves when fed orally.

The incubation period of the experimental

disease appears to be about 24 h. The epithelial cells of the intestine slough to some degree, and infected cells can be shown by staining the feces with fluorescein-stained specific antibody.

Disease caused by this virus appears to be associated with calves less than 1 wk of age. If the virus has been in the herd, colostrum feeding before exposure appears to prevent appearance of disease. There is no proof of an intrauterine infection; the agent causing the infection probably is introduced orally before or concurrent with colostrum feeding.

Coronavirus-like Agent

By electron microscopy, Stair found a coronavirus-like agent in the feces of scouring calves (26). This agent is called coronavirus-like because, like the viruses of infectious bronchitis of chickens and transmissible gastroenteritis of swine, there is what appears to be a corona around the virion. Calves from 1 to 3 wk of age are more likely to be infected with the coronavirus-like agent, but unlike the reovirus-like agent, colostrum feeding does not protect the calf completely. Workers believe that the virus and colostral antibody become disassociated as digestion takes place and the material moves through the intestine. The cornavirus-like agent can be identified by staining frozen sections of the spiral colon with fluorescein-conjugated specific antibody.

The coronavirus-like agent does not grow readily in cell culture; therefore, virus has not been isolated extensively from different herds nor have epizootiological studies been undertaken to determine by serological means the extent and incidence of the virus in the cattle population.

Bovine Adenovirus

A disease of neonatal calves in Idaho and Montana, "weak-calf syndrome," has been described (6). This is a complex disease in which the stresses of cold wet climate and marginal nutrition have a bearing on the severity of the disease. However, two viruses, BVD and a bovine adenovirus subgroup II, have been isolated from the tissues of calves affected with this disease (8, 16, 18).

The results from experimental inoculation of calves with the bovine adenovirus indicate that the virus is a pathogen that produces subcutaneous hemorrhages over the hock, polyarthritis, and arteritis (9, 18). These lesions also are in some calves affected with "weak-calf syndrome," but the virus is not fatal for experimentally infected calves nor does it produce diarrhea.

Parainfluenza-3 Virus

Parainfluenza-3 virus (PI-3) is widespread in the cattle population; practically no herd has escaped infection from this virus. Generally, it is associated with respiratory disease and particularly is associated with feedlot problems. However, examination of the serum from stillborn calves has shown that some animals have antibodies for PI-3; these antibodies indicate an intrauterine infection (10).

We have not proved yet that PI-3 infection can cause stillbirths, but any viral infection of the fetus is undesirable.

DISCUSSION

Vaccines are available for BVD, rotavirus, the coronavirus-like agent, and PI-3. All are live-virus vaccines. Recommended use and effectiveness of any of the vaccines for cow-calf operation depend on an accurate diagnosis in each particular herd and the severity and nature of the disease problem. Most mature cattle are immune to PI-3; their antibodies should protect the fetus from an intrauterine infection, and the colostrum should protect the newborn calf. However, intrauterine PI-3 infections apparently do occur, and fetal death may result (10).

Because of the danger of intrauterine infections in the first half of gestation, commercially available BVD vaccines usually are not recommended in cow-calf operations; but if BVD is a problem, animals should be immunized before they are bred. Vaccination of the replacement animals at weaning and again before breeding should produce sufficient antibodies to protect the calf from an intrauterine infection and provide antibodies in the colostrum.

Killed-BVD vaccines have been prepared and are effective (19), but they have not been produced commercially. They are being used for cow-calf operation and appear to be effective against neonatal disease, but the studies will have to be continued before definite trends can be determined. The immune status of the

animal should be determined before it is bred; this is the time to use BVD and PI-3 vaccines to help boost antibody titers.

Viruses do not produce necessarily a frank clinical disease or an acute fatal disease in newborn calves used in experimental infection experiments. Why then do so many newborn calves from which these viruses have been isolated die? I believe that virus infections cause added stress, mild debilitation, and suppression of part or all of the cellular system that provides immunity to the calf against the infectious agents that are always in the environment of the cattle population.

As virological techniques improve, better cell culturing systems evolve, and more investigators take up the problem, other viruses likely will be isolated from neonatal disease of calves. But this isolation does not imply new and complex management procedures. From our present understanding of the nature of viral infections within a herd, we cannot assume that only the sick calves have been exposed. The question arises as to what factors have tipped the balance in favor of the healthy calf. Probably no single factor alone can shift the balance in favor of the healthy calf. When a virus gains entry into a herd, results of good management practices such as good nutrition for the dam and calf and clean dry calving and calf-rearing areas may be disappointing. However, many viral infections are self-limiting in that mature animals do not die but have either overt disease or inapparent infection and recover and begin to produce antibodies against the agent in question. These antibodies will prevent an intrauterine infection and concentrated in the colostrum will protect the calf at birth if the colostrum is fed before the calf is infected heavily.

Good management and sanitation will keep exposure of the calf to a minimum, and proper feeding of the calf will cause a minimum of stress for the gastrointestinal tract. Proper nutrition for the dam will allow her to produce the optimum quantity and quality of colostrum. The most important factor of management which tips the balance in favor of the healthy calf is the herdsman with the cow at time of parturition and his assistance and aid to the calf in feeding colostrum immediately. Colostrum should be fed at least 2 to 3 days to give the calf benefit of antibodies and nutrients.

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