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Biosecurity for neonatal gastrointestinal diseases

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Calves are born and raised in a wide diversity of environments and housing conditions, all of which affect the risk of neonatal enteric infectious disease. At one extreme are calves born in closed-beef cow–calf operations under low-density conditions on open range, such as in the low-rainfall areas of the Intermountain United States. This environment closely resembles the conditions in which the infectious agents and their hosts co-evolved before domestication. In this setting, the risk of introducing new strains of infectious agents is low, direct contact among calves is minimized, the opportunity for transmission by people and equipment is minimal, and fecal material is dispersed and exposed to environmental factors (i.e., insects, desiccation, and ultraviolet radiation) that inactivate most microorganisms. At the other exposure extreme, calves are raised in enclosed housing on continuous-flow, custom calf-raising operations. In this environment, calves are assembled from multiple herds and from sales channels in which the risk of heavy exposure to a variety of infectious agents is high. Calves are often in direct contact with one another, the physical space per calf is limited, and the risk of transmission by people and equipment is high. If housed, ventilation is often inadequate, resulting in a high relative humidity; fecal material is concentrated, with a high moisture content and without full exposure to direct sunlight. Vermin such as flies and rodents are often present in high numbers, and nutrition is provided by assembled feedstuffs of varying quality and nutritional value rather than from dam's milk. Between these two extremes are calves raised in individual hutches on dairies of their origin or beef calves raised in intensively managed rotational grazing systems in high-rainfall areas.

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Diarrhea is the most important disease of neonatal calves and results in the greatest economic loss due to disease in this age group in both dairy and beef calves [25]. Earlier studies conducted by the US Department of Agriculture found that enteric pathogens are associated with the death of up to 25% of the US calf crop annually [43]. More recently, a retrospective survey of dairy producers found that 52% (standard error [SE] \pm 2.6%) of total death losses in preweaned heifers were caused by diarrhea [65]. In beef calves, the percentage of calves from birth to 21 days of age dying from diarrhea was 5.5% (SE \pm 1.3%) [10]. Neonatal calf diarrhea is a complex, multifactorial condition with numerous factors, including pathogen exposure, strain variation, environmental conditions, management conditions, nutritional state, and immune status all interacting to cause loss in preweaned beef and dairy calves. Most, if not all, of these factors are related to biosecurity in beef and dairy calf-raising practices. Many are under management control, and most are not specific to a single infectious agent. Biosecurity is not a new concept in animal agriculture; rather, it is largely a redefinition of earlier ideas and practices historically considered to be good animal husbandry. This observation is evident when one notices in early veterinary textbooks the calls for cleanliness, disinfection, and isolation of herd replacements and sick animals [4].

General epidemiologic concepts

The two major thrusts of infectious disease biosecurity are (1) reducing the likelihood of introduction of an infectious agent into a group (external biosecurity) and (2) reducing the likelihood of its transmission when present (internal or within-herd biosecurity, or biocontainment). When approaching the control and prevention of neonatal enteric infections, knowledge of several general infectious disease epidemiology principles is useful. Essential information for designing a herd-specific control program for any infectious disease includes (1) the reservoir, (2) the modes of transmission and the agent characteristics related to each, (3) the incubation period, and (4) the period of communicability. The minimum incubation period (along with the infectious dose and the age of the calf) is critical because, for example, it establishes the maximum length of time a susceptible calf can be present in a critical calving facility before it could begin to contaminate the area if it were infected at birth. The most important reservoir for these enteric agents is previously or currently infected cattle, which is critical for producers to recognize when they are considering purchasing animals and when they are managing contact between different age groups within a herd.

Most of these agents transmit predominately by the fecal-oral route from the feces of infected animals to the mouths of susceptible animals, and do so efficiently. Immediate transmission occurs when infected animals are housed with susceptible animals in conditions that allow nose-to-nose contact or inhalation of aerosols produced by coughing, urinating, or defecating.

Indirect contact transmission requires that the infectious agent survive in the environment. Most agents of neonatal calf diarrhea survive well in nearly all environmental conditions, remaining in the environment where they can be transmitted indirectly by contact with contaminated feces, fomites such as equipment, or mechanical vectors such as flies. For enteric agents transmitted by indirect contact, key factors include the number of organisms shed in the feces and their survival characteristics in the environment compared with the infectious dose required to initiate infection in susceptible hosts. Information on the environmental survival characteristics of an indirectly transmitted agent is needed to determine how long that agent is likely to remain at an infectious dose once the area is contaminated with it. All of this is critical information for determining how to manage livestock flow through an existing set of facilities and to otherwise minimize disease transmission through management practices. The relationship between infecting agents and the environment is complex, involving factors such as the physical characteristics of the substrate material (e.g., feces, water, milk, manure slurry, dust), temperature, pH, water activity, and competing microorganisms. As a consequence, these relationships are not well defined for many combinations encountered in the farm environment.

With the rare exception, it is likely that most infectious enteric agents of cattle co-evolved with their bovine hosts long before their domestication thousands of years ago [51,52]. If an agent was able to survive under the free-range conditions of the wild bovine, it is likely that transmission occurs relatively easily in the environment of the intensively managed domesticated bovine of today. Indeed, these agents are shed by infected animals in numbers several logarithms higher per gram of feces than the total number required to infect the typical susceptible calf. Additionally, these agents have been shown to be extraordinarily flexible with regard to their genetic make-up and through survival of the fittest can rapidly take advantage of new environments and management systems. Consequently, intervention strategies devoted to a single control point may be successful in the short run but are likely to prove unsuccessful over the long run.

An important concept that is often overlooked, particularly in the midst of clinical disease outbreaks, is the “iceberg principle.” This concept is in effect both within and between herds. Between herds, clinical disease is normally seen in only a minority of herds, in which its occurrence implies significant, suboptimal management conditions. Within herds, generally only a small proportion of affected animals are clinically affected, with most being subclinically infected. For most diseases, both infectious and noninfectious, the ratio between clinical cases and subclinical cases is typically 1 : 5 to 1 : 20. In some circumstances, a herd can be widely infected with an agent, yet few if any clinical cases occur. Consideration of the iceberg principle helps prioritize efforts because in most outbreaks, attention is typically but erroneously focused only on individual animals displaying clinical signs. To wit, if isolation and sanitation practices are to be an important

component of a disease control strategy, the iceberg principle suggests that to be effective, such measures must be applied to all exposed animals and not just those that exhibit clinical signs.

General cleaning and disinfection considerations

Appropriate cleaning and disinfection procedures are critical to breaking fecal-oral transmission cycles of enteric agents that contaminate housing, feeding, or treatment equipment or other vectors and fomites. Because personal hygiene is crucial to stopping the transmission of these agents in the human hospital environment, it is also a critical component in the intense livestock production environment as well. This personal hygiene includes frequent, effective hand washing of sufficient duration with soap followed by an alcohol-based hand disinfectant [50], cleaning and disinfecting boots, and washing work clothes with bleach followed by hot air drying. Cleaning and disinfection procedures are not without pitfalls, however, and adherence to a sound protocol covering all of the infectious agents of concern is critical for long-term success. Procedures that do not affect a resistant agent such as *Cryptosporidia* oocysts or rotavirus may spread it from areas of high concentration across previously uncontaminated surfaces, where it can then contaminate materials such as water and feed at sufficient levels to provide an infectious dose. The most important first step is thorough cleaning to remove organic material (e.g., feces, milk film) before applying disinfectant [46]. Vigorous cleaning (scraping, scrubbing, flushing) cannot be replaced by applying disinfectants in larger quantities or with higher pressure. For any protocol or in nature, destruction of microorganisms initially follows a first-order logarithmic decay process and then slows [74]. In relation to the amount of time required to destroy one half of the initial population, approximately three time periods are required for a one-logarithmic (90%) reduction, six for a two-logarithmic (99%) reduction, nine for a three-logarithmic (99.9%) reduction, and so on. In addition to contact time, the concentration, temperature, pH, water content, water hardness, and amount of organic material present are critical variables determining the success of chemical disinfection. Importantly, the relationships between these factors are not straightforward [54]. For example, halving the concentration of formaldehyde requires a 2-fold increase in contact time to obtain similar microbial destruction, whereas halving the concentration of phenolics requires a 64-fold increase in contact time. A 10°C rise in temperature increases the activity of alcohols 30-fold, yet increases the activity of formaldehyde only 1.5-fold. Iodophors are highly active at low pH but are inactive at an alkaline pH. In general, effectively applied live steam inactivates the broadest range of microorganisms.

Sodium hypochlorite (bleach, NaOCl) at a sufficient concentration, contact time, and temperature combination is effective against the bacterial and

viral agents of neonatal enteric disease [87], but at practical levels is not effective against *Cryptosporidium* oocysts. It is readily available as 5.25% (household bleach) and 12.75% solutions, and it is cost effective and environmentally safe. Because it begins dissipating on dilution, however, the Centers for Disease Control recommends that diluted solutions should be used within 24 hours and that they should be stored in opaque containers. Sodium hypochlorite is rapidly inactivated by the presence of any appreciable organic material; for example, 1% albumin reduces its effectiveness by six logs, and increasing concentration or contact time does not recover this loss. Bacteria in biofilms are 150 to 3000 times more resistant. In solution, hypochlorous acid is the active form of the free chlorine. It is most available at a pH level of 6, dropping to 80% of the free chlorine at pH 7 and to 25% at pH 8, suggesting that the pH of disinfectant solutions should be monitored regularly as part of disinfection protocols. Below pH 6, it is more corrosive to metals, and more chlorine gas is released. Testing kits can be used to monitor free chlorine as part of disinfection protocols; however, because these kits measure both hypochlorous acid and hypochlorite ion (nonactive form), pH must also be considered. Recommended concentrations for use in human environments range from 500 ppm (1:100 dilution of 5.25% household bleach) and 10-minute contact time at room temperature to 5000 ppm (1:10 dilution of 5.25% bleach) and 1-minute contact time at room temperature, the higher concentrations being used in more critical areas. For viruses in veterinary hospitals and kennels, a recommended dilution of household bleach is 1:32, which results in a 0.175% sodium hypochlorite solution and a 10-minute contact time at room temperature [93] at pH 6 to 7.

The characteristics of environmental surfaces targeted for disinfection in the farm environment also influence the success or failure of various procedures [62]. For example, unfinished plywood retains 15-fold more microorganisms than varnished plywood, which supports 15-fold more microorganisms than plastic surfaces. On smooth, ideal surfaces physical removal of visible contamination by thorough washing with soap and water removes 99% of the microbial load (two logs). On typical housing surfaces, however, washing only removes 90% (one log). Proper disinfection removes an additional 6% to 7%, and terminal fumigation removes 1% to 2%. Disinfection after washing is an important step, particularly if the surface remains damp, because remaining bacteria can proliferate in the minimal nutrients leaching from wet wood and because washing can disperse an infectious agent from limited areas of high concentration broadly across other surfaces. The application of high-pressure sprays can aerosolize organisms, allowing dissemination to distant sites and posing a risk to operators if zoonotic organisms are present.

Gastrointestinal pathogens of concern

The most frequently recognized agents causing neonatal calf diarrhea include *Escherichia coli* (*E. coli*) spp., rotavirus, coronavirus, cryptosporidia,

coccidia, and *Salmonella* spp [1,85,96,102]. With the exception of *Salmonella* spp. and specific strains of *E. coli*, these organisms are ubiquitous and holoendemic, being present within the gastrointestinal tract of some if not most healthy, mature cattle, albeit in low concentrations and without clinical signs of infection. Because most all cattle are exposed to these agents at some point in their life if not continuously, they must therefore develop active immunity against these organisms. Undoubtedly, most animals develop active immunity to these organisms after infection by natural exposure to low infective doses shed by subclinically infected herd mates. Ideally, such infections result in the stimulation of immunity without the development of adverse or serious clinical disease. Alternatively, active immunity can also be developed by successful immunization with antigenically similar strains.

Mixed infections with these agents are a common phenomenon during calfhood. Management practices that minimize the risk of clinical disease by one organism generally reduce the risk of clinical disease by others. In a study of 59 calves younger than 3 weeks old from 12 beef and dairy herds with calf-scour problems, Moon and coworkers [61] found that “most infections were mixed and diarrheal calves from the same herd frequently had different infections.” In a survey of 490 preweaned calves from 45 calf-scour outbreaks, Reynolds et al [85] found that 29% of the clinical infections were mixed. Similarly, Snodgrass and coworkers [96] found that 21% of diarrheic calves less than 1 month old on 32 beef and dairy farms had mixed infections. Finally, in a study of 218 diarrheic calves less than 1 month old from 65 dairy herds, 25% of calves had mixed infections consisting primarily of rotavirus and *Cryptosporidium parvum* [33]. In most of these surveys, the most prevalent agent in diarrheic calves is rotavirus, the second being *C. parvum* at approximately half the prevalence of rotavirus. In surveys that included clinically normal herd mates, similar profiles of infectious agents were also found in the feces of these animals but at lower prevalences. These findings suggest that enteric pathogens of calves function more as secondary opportunists than as highly virulent primary pathogens. The occurrence of clinical disease therefore suggests that weaknesses are present in calf management and husbandry on those premises. Because nearly all of these pathogens are already present on most operations, control of enteric disease must therefore be focused on the interfaces between individual animals and groups of animals rather than on preventing their arrival on the operation, the traditional focus of most biosecurity efforts.

Numerous other pathogens have been implicated in neonatal diarrhea, including *Campylobacter* spp., *Clostridium* spp., Parvovirus, Breda virus, and bovine viral diarrhea virus; however, their importance in field outbreaks of diarrhea is currently unknown. Regardless, practices that are sufficient to control the common enteric agents likely will also control the lesser-known agents as well.

Salmonella

Subsets of *Salmonella enterica* serovars, such as *S. Typhimurium* and *S. Dublin*, are important causes of diarrhea in dairy and veal calves, whereas infections in single-suckle beef calves are infrequent. The pathophysiology of enteric salmonella infections is complex, involving inflammation and necrosis, increased fluid secretion and decreased absorption and digestion. In addition to enteric manifestations of disease, infected calves are frequently septicemic, which results in more severe clinical signs. Bacteremia is common in calves less than 1 month of age and is often manifested systemically as polyarthritis, meningitis, or uveitis. In addition to shedding the agent in their feces, calves developing septicemia often shed the agent in their urine and oronasal secretions even before the onset of clinical signs. The lack of awareness about the potential for shedding from the oronasal area is particularly dangerous because this source leads to spread through contamination of feeding and treatment utensils and hands, severely compromising internal biosecurity programs. Hardman and coworkers [38] found that in natural outbreaks of individually penned calves, approximately 60% of transmission was by direct contact, whereas 40% was by indirect routes, including aerosols, fomites, and vectors. This finding suggests that emphasis should be placed more broadly on controlling all means of transmission, including aerosols [105].

Salmonella spp. are hardy organisms that are well adapted to surviving in the environment [31]. They are able to proliferate rapidly at high ambient temperatures in waste milk, colostrum, and moist feeds. In the absence of direct sunlight or predation by other microorganisms, *Salmonella* spp. can survive in wet or dry substrates or on surfaces for years, particularly if they are protected by biological films such as dried saliva, milk, or fat. Biological films also protect organisms from the action of chemical disinfectants. In an experiment that simulated a barn floor under defecating cows, *Salmonella* spp. were shown to survive for 5.5 years [72]. These researchers also found *S. Typhimurium* in an empty slurry pit that had not been used for 4 years. Because *Salmonella* spp. that infect cattle can infect and proliferate in the intestinal tracts of most other animals in a farm environment (including other livestock, humans, domestic pets, rodents, and birds), these other species may also be involved in disease transmission. For example, allowing cats access to stored feeds has been identified as a risk factor for salmonella outbreaks [26]. Serotypes that frequently infect cattle are typically introduced into a herd by subclinical or incubating carrier animals and only occasionally in feedstuffs. Many of the other serotypes imported onto farms in purchased feedstuffs appear unable to establish viable transmission cycles between cattle, instead causing only sporadic infections.

Of special note is that *Salmonella* spp. and *C. parvum* infections in livestock present significant zoonotic disease risks to in-contact people and in turn to their contacts, particularly young children, the elderly, and the

immunocompromised. Because of these significant health risks, indirect and direct contact between susceptible individuals and livestock potentially infected with these agents should be minimized. Hands should be washed well, using soap and warm water and scrubbing for 15 seconds followed by an alcohol-based antiseptic hand rub [50] before eating or returning to the household. Inhalation of potentially contaminated dusts or aerosols, particularly those generated by cleaning procedures such as high-pressure washing, should be minimized. To reduce the likelihood of introducing these agents into the household and their transmission to susceptible humans or domestic pets, equipment, outer garments, and footwear exposed to potentially infected animals and their discharges should not be brought into the household.

Escherichia coli

As a major bacterial component of feces from warm-blooded animals, *E. coli* are ubiquitous in the environment of neonatal beef and dairy calves. All *E. coli* types can cause colisepticemia, but relatively few can cause enteric disease. Enteric *E. coli* infections are classified into several forms, including enterotoxigenic, enteropathogenic, enteroinvasive, enterohemorrhagic, and enteroadherent [53]. Enterotoxigenic *E. coli* are the most common form associated with disease in calves. The ability of enterotoxigenic *E. coli* to cause severe herd outbreaks of diarrhea in calves results from the expression of virulence factors, including adhesins (pili, fimbria) and enterotoxins. Adhesins (e.g., K99, F41, K88) are surface molecules that enable the bacteria to attach to specific receptors located on the intestinal epithelium of calves less than 3 days old. Once attached to intestinal cells via adhesins, bacterial expression of enterotoxins triggers intestinal fluid secretion in excess of absorptive capacity. In addition to enteric diseases caused by *E. coli*, systemic invasion by certain strains can result in septic shock and low-grade diarrhea. Diarrhea observed in these calves is generally thought to be due to endotoxemia secondary to bacteremia rather than production of enterotoxins.

Although not as hardy as *Salmonella* spp., *E. coli* survive well on typical farm environmental surfaces and in feces and dust protected from moisture and direct sunlight [8,58]. In experimentally inoculated cow manure or fresh slurry under common farm environmental conditions, both organisms decrease by one log in 1 to 3 weeks [42]. Depending on the surface characteristics, the numbers of organisms decline at about 0.25 log per day. Generally, the rate of decline is slower at lower humidity, but proliferation can occur on surfaces under saturated conditions with minimal organic nutrients (0.5 mg/L). Exposure to ultraviolet components in direct sunlight rapidly kills the organism [24].

Rotavirus

Rotavirus is a double-stranded, nonenveloped RNA virus. Rotaviruses are the most common cause of bovine neonatal diarrhea, the incidence of

infection often approaching 100% in herds, and up to one half of infections resulting in clinical disease. Infection usually occurs between 4 and 14 days of age, although younger and older calves can be affected [66]. Because the median infectious dose for rotaviral infections in other species is 10 infectious particles or less [36,103], the infectious dose for neonatal calves is likely similar. Viral invasion of small intestinal villus epithelium occurs through the luminal surface, resulting in cell destruction and shedding of damaged cells into the intestinal lumen. As a consequence of this infection route, the incubation period is short, and large numbers of virus particles are produced rapidly. Within 48 hours of initial infection, the virus can reach 1×10^{10} (ten billion) virus particles per gram of feces. Villous atrophy and cellular damage result in maldigestion and malabsorption. Maldigestion results from the loss of hydrolytic enzymes produced by mature villous cells. Failure to hydrolyze milk lactose results in lactose transit into the large intestine, where it acts osmotically, pulling water into the intestinal lumen. In addition to decreased enzyme activity, sodium and water transport processes are impaired, resulting in malabsorption. Some rotavirus strains are pneumotropic, replicating in the respiratory tract and transmitting via inhalation and by the fecal-oral route. Rotavirus is carried in adult cattle through non-clinical infection with intermittent fecal shedding [47]. Shedding increases coincident with later stages of gestation and for up to 4 weeks postpartum. In some management situations, this maternal shedding may account for most virus exposures to neonatal calves [28].

Being a nonenveloped RNA virus, rotavirus is relatively stable in the environment, being infectious in feces for up to 6 months at 25°C. In smears of human feces, human rotavirus was more stable at lower temperatures and at humidity extremes [59]. Infectious particles declined by 1 log in 29 days at 4°C and 93% relative humidity, in 16 days at 4°C and 13% relative humidity, in 2.2 days at 20°C and 55% relative humidity, and in 1.5 days at 37°C and 13% relative humidity. Some research suggests that bovine rotavirus may be more resistant than human rotavirus. Virus stability in water varies with water quality and temperature, ranging from being very stable in clean water at 4°C to falling 2 logs in 10 days in typical river water at 20°C [84]. As temperatures above 60°C are lethal to the virus [68], standard milk pasteurization procedures are effective against it. Rotavirus is susceptible to sufficient concentrations of sodium hypochlorite (1750 ppm) but is relatively resistant to many common disinfectants, such as chlorhexidine, under the same exposure conditions. Because as a nonenveloped virus it is not affected by soaps, washing with soap alone may actually spread the virus around on the washed surface [23].

Coronavirus

Coronavirus is an enveloped single-stranded RNA virus and is not as stable in the environment as rotavirus [27]. Serologic studies have demonstrated that the prevalence of serum antibodies to coronavirus approaches

100% in adult beef and dairy cattle. Calves are typically infected by coronavirus between 4 and 30 days of life [66]. Although they may not be the same virus strains, evidence is mounting that a respiratory form as well as the enteric form occurs [97]. Similar to rotavirus, infection results in damage to intestinal villous epithelium; however, infection by coronavirus often results in more severe disease manifestations because the degree of villous atrophy is greater and both the large and small intestines are affected. As described for rotavirus, coronavirus is carried in adult cattle through nonclinical infection and is shed in fecal matter. Because of their envelope, these viruses retain infectiousness better at lower rather than higher relative humidity [24] and are considerably more sensitive to soaps and common disinfectants than are nonenveloped viruses. This virus is more active in the colder climates and has been reported to cause winter dysentery in adult cattle [16,27]. Control of coronavirus (and rotavirus) infections in calves relies on continual presence of a protective antibody within the gut lumen, which can be achieved by allowing neonates to ingest colostrum or milk containing these specific antibodies from their dams (lactogenic immunity) [19].

Cryptosporidia

Cryptosporidium parvum is a common cause of neonatal calf diarrhea between 7 and 21 days of age, rarely causing diarrhea at less than 7 or more than 28 days of age [22]. Similar to rotavirus and coronavirus infection, the incidence of infection with cryptosporidia often approaches 100% in the first month of life, infection often occurs concurrently with rotavirus and coronavirus infections, and a respiratory form may occur. Unlike most other enteric protozoa, *Cryptosporidium* are immediately infectious when passed and can infect other susceptible hosts through direct contact. Because *Cryptosporidium* can autoinfect the original host, the infectious dose can be exceedingly small. For example, the median infectious dose for humans is only 87 oocysts [29], and some researchers suggest it is even lower for neonatal calves. Cryptosporidia infect and invade enterocytes in the distal small intestine, causing villous atrophy and fusion that result in malabsorption and maldigestion. Infected calves may shed 10^5 to 10^7 oocysts per gram of feces beginning with the onset of clinical signs. Importantly, fecal shedding can continue days after clinical signs subside. In California beef cow-calf herds, Atwill et al [7] found that higher stocking densities, longer calving periods, and wetter seasons were associated with higher fecal shedding prevalences in calves. Research findings on the adult carrier state are conflicting, because some have found that adult carrier animals are common [92], whereas others have found that few if any asymptomatic adult cattle apparently shed *Cryptosporidium parvum* in appreciable numbers [6,55]. Undoubtedly, infected calves are likely the most important reservoir for continuing the fecal-oral cycle on most farms because of the large numbers of oocysts that they excrete in close proximity to susceptible calves [22].

In the environment, cryptosporidia are extremely resistant to most veterinary disinfectants except 5% ammonia, 6% hydrogen peroxide, or 10% formalin [14,86,107]. They survive well in water, requiring 4 to 11 weeks to decline by 1 log [15]. Because the oocysts adhere in large numbers to the plastic and rubber surfaces of common calf-feeding and treatment equipment such as nipples, bottles, and buckets (E.R. Atwill, DVM, PhD, 2001, personal communication), common sanitation procedures are not likely to prevent fomite transmission by these items. A portion of the oocysts still retain their infectivity after mild freezing [30]. On the other hand, complete drying in thin, naturally infected fecal smears on wood kills the oocysts within 1 to 4 days [2]. Finally, because moist heating at 45°C for 20 minutes kills the oocysts [3], standard pasteurization procedures (e.g., 63°C for 30 minutes, 72°C for 15 seconds) are effective.

Coccidia

Eimeria bovis and *E. zurnii* are the species of coccidia most commonly associated with calf diarrhea. With a prepatent period of approximately 17 days, calves exposed to an infectious dose shortly after birth can present with bloody diarrhea and anemia by the third week of life. Diagnosis is easiest in calves with acute infections because many shed large numbers of oocysts in the feces. Chronically infected calves may only shed small to moderate numbers of oocysts in the stool, however, making diagnosis more difficult.

Risk factors related to spread of gastrointestinal pathogens

A large number of risk factors are potentially associated with the development of neonatal calf diarrhea. These factors can be categorized into those that are related to either (1) the calf, (2) the infectious agent, or (3) the environment of the calf. Recognizing the presence of specific risk factors on the premises followed by interpreting the relative significance of each factor is required for the implementation and coordination of specific biosecurity practices to mitigate the problem of enteric disease on that farm. Although Pence et al [70] do not provide any information on validation, they do provide a risk assessment-scoring sheet for neonatal diarrhea in beef herds. On most operations, the presence and importance of these risk factors change over time, sometimes quite suddenly, as sources of animals, husbandry practices, and, to a lesser degree, physical facilities often change with turnover of employees and in response to changes in economic conditions.

Risk factors associated with the calf

The presence of developmental, congenital, or heritable abnormalities in a calf can be a risk factor depending on the character, location, and degree of the defect. Certainly any abnormality that prevents a calf from

functioning normally (e.g., ambulating or obtaining adequate nutrition) can increase the chance of a severe enteric infection.

Failure of passive transfer of maternal immunity through colostrum ingestion is a major risk factor for development of neonatal diarrhea [21,56]. In the 1992 US Department of Agriculture National Dairy Heifer Evaluation Project, Wells et al [108] found that feeding a sufficient amount of colostrum soon enough after birth prevented 31% of the dairy heifer mortality that occurred in the first 21 days of life. Colostrum provides the necessary components of immunity during the time when a calf is immunonaive yet exposed to pathogens in its environment. Consumption of colostrum immunoglobulin from resident cows in a herd is likely to provide immunologic protection specific to the strains of pathogens found within that herd. Importantly, even if colostrum immunoglobulin specificity is appropriate for specific pathogens, maximum protection is ultimately dependent on the ingestion and absorption of an adequate mass of immunoglobulin by the calf. Immunoglobulin concentration varies from breed to breed, however, as well as from cow to cow within a breed. Such differences are well illustrated by the fact that the average concentration of immunoglobulin in beef cow colostrum is 2 to 3 times greater than that of dairy cow colostrum [73,106]. As expected, the most important factor involved in failure of passive transfer in dairy calves is low immunoglobulin concentration colostrum, whereas in beef calves delayed suckling is a leading cause [12]. For dairy cows, colostrum that is not from first milking, from cows that leaked milk, or from cows that weighed more than 20 lb should not be used for passive transfer [73]. In certain situations, beef calves may be provided alternate sources of colostrum, including colostrum obtained from nearby dairies. Again, it is imperative to appreciate that because the average immunoglobulin concentration of dairy cow colostrum is low compared with beef cow colostrum, an adequate volume (4 L) of appropriately selected dairy cow colostrum must be fed. In addition, one must also consider the risk of introducing novel pathogens when supplementing calves with an off-farm source of nonpasteurized colostrum. Unless properly pasteurized, dairy colostrum purchased for administration to beef calves in place of their dam's colostrum may be contaminated with infectious doses of undesirable infectious agents such as *Mycobacterium avium* subsp. *paratuberculosis* as well as the enteric agents of concern described in this article.

The nutritional status of the dam (particularly during late gestation, when the fetus is active metabolically and growing exponentially) is often of concern in relation to the immune status and health of the calf after birth [21]. The effect of nutrition and other factors such as dystocia on passive transfer in dairy cattle was recently reviewed by Quigley and Drewry [75]. There is little evidence of a direct link between gestational cow nutrition and immunoglobulin concentration of the calves [71]. The weak calf syndrome, however, has been reported in beef cattle when

prepartum cows consuming diets deficient in protein or energy (protein-energy malnutrition), either because of improper feeding practices or other factors such as severe weather events, in late gestation subsequently calve in environments in which the temperature is below the thermoneutral zone of the calf [67,69]. Therefore, it is only logical to recommend that producers provide feeds adequate in quantity and quality to meet National Research Council requirements for beef cattle and dairy cattle during gestation and lactation.

In comparison with beef calves, dairy calves are often fed milk replacer diets because the cost is lower than that of cows' milk. The composition and quality of milk replacers varies considerably, however, much to the detriment of very young calves with limited digestive capabilities. Some milk replacers contain heat-denatured, milk-origin proteins, poorly digestible vegetable-origin proteins, or nonlactose carbohydrate sources that the intestinal enzymes of neonatal calves cannot digest. Consumption of such products frequently results in inadequate nutrition, poor growth rates, and high morbidity and mortality due to enteric diseases [83]. Often the feeding recommendations for even high-quality milk replacers are designed for 60-lb calves, rather than the average 90-lb Holstein calf, placing the larger calves into a negative energy and protein balance until their starter consumption increases sufficiently. Nutrition of the neonatal calf is an active area of research, much of which has been summarized by Davis and Drackley [21], and changes in nutritional guidelines often reduce the risk of neonatal disease. In addition, excellent reviews on the relationship between neonatal digestive physiology and the different ingredients contained in milk replacers are available [37,82].

If nonsaleable milk is fed, it should be pasteurized before feeding to reduce the likelihood of transmitting these and other infectious enteric agents. A recent study found that raw milk and mixed milk replacer often contain high numbers of bacteria, ranging from 10^3 colony-forming units (CFUs)/mL for mixed milk replacer to more than 10^6 CFUs/mL for hospital milk [94]. Another study found that calves fed pasteurized waste milk perform better in terms of weight gain, mortality, morbidity, and health costs than those fed the same milk raw, even in the absence of the specific enteric agents of concern discussed in this article [45]. Pasteurization controls their milk-borne transmission as well.

Finally, the source of calves is a risk factor for enteric diseases when calves have been commingled from several sources or origins. Certainly, calves purchased from sale yards are more likely to have been exposed to higher concentrations and to a wider variety of pathogens compared with single-source calves or calves on pasture. Frequently, calves are purchased from market sources to graft onto cows that have lost their own offspring. Such purchased calves often introduce new strains of infectious agents that then spread through the herd in an outbreak fashion, making the situation considerably worse. In addition to increased exposure to pathogens, calves

transiting through sale yards are likely to be under more severe physiologic stress and more likely to have had failure of passive transfer [106]. A study of beef cow–calf herds found that purchasing such calves at less than 4 weeks of age increased the likelihood of a high-mortality diarrhea outbreak over four-fold [91].

Risk factors associated with the infectious agent

The primary risk factors associated with infectious agents that cause enteric infections include specific virulence factors, the size of the inoculum or pathogen load, and whether single or multiple infections exist.

As mentioned previously, virulence factors associated with bacteria include structural elements such as pili that allow bacteria to attach to the host, as well as bacterial products that augment bacterial cell growth, enhance host cell damage, or negate the immune response of the host. Both exotoxins and endotoxins can have adverse effects. Other virulence factors of enteric bacteria include those that enhance bacterial ability to resist antimicrobial agents through expression of drug resistance plasmids or integrons.

Virulence factors associated with enteric viruses or protozoa are less well described. Different strains or serotypes of viruses have been identified; however, most strains of a particular virus appear to act similarly. The challenge load of enteric bacteria, protozoa, and viruses from periparturient cattle is high because of the aforementioned physiologic immunosuppression [28].

When considering biosecurity or biocontainment, it is critical to realize that the size of the inoculum or the pathogen concentration (exposure dose) is a major factor in determining the degree of clinical disease and the rapidity of its onset rather than whether exposure occurs. This is especially true when considering the ubiquitous agents involved in bovine neonatal diarrhea, because none are extraordinarily virulent in their own right. It is logical to conclude that a large enough exposure dose, such as that likely to occur during outbreaks, will undoubtedly overwhelm even the best passive transfer of immunity and lead to an expanding outbreak in previously unaffected calves.

Risk factors associated with the environment of the calf

Risk factors for neonatal diarrhea associated with the environment of the calf are likely to be the most amenable to the implementation of specific biosecurity measures. Specific risk factors include the atmospheric conditions (temperature, humidity, wind chill, ventilation, air quality, and so forth); housing (individual calf hutches, enclosed group pens, dispersal on pasture); the physical environment (calving area, bedding, other animals, cleaning protocols, and so forth); stocking density; general hygiene and hygiene related to feeding practices; and miscellaneous stresses due to handling, surgery transportation, and the like.

Many of these potential risk factors are under management control. Because of the difficulty of executing rigorously designed large-scale studies with sufficient herd numbers to evaluate all potential risk factors, reasoning from biological plausibility is often the only basis for developing interventions when sufficient evidence is not available. Although some findings are conflicting, a limited number of field studies of different size and rigor do provide guidance for some of these risk factors. For example, Bendali et al [11] found that cleaning of the calving area immediately before calving was associated with an increased risk of neonatal diarrhea in beef calves compared with not cleaning it, whereas cleaning it after calving was associated with a decreased risk. They also found that greater cow cleanliness was associated with decreased risk. Based on data from the 1997 US Department of Agriculture National Beef Cow-Calf Study, Sanderson and Dargatz [88] reported that although 41% of birth-to-weaning mortality was attributable to dystocia, 11% was due to confined calving. In the 1992 US Department of Agriculture National Dairy Heifer Evaluation Project, Wells et al [108] found that separating heifers from their dams within the first 24 hours after birth prevented 16% of the dairy heifer mortality that occurred during the first 21 days of life. Quigely et al [76] found that calves administered sufficient amounts of colostrum and housed in individual calf hutches shed fewer enteric pathogens in their feces than calves left to nurse their dam and housed in an enclosed space with mechanical ventilation. Schumann et al [91] found that increased risk of neonatal diarrhea in beef calves was associated with wintering cows and primigravida heifers together, providing limited shelter to nursing pairs, and an increased percentage of poorly drained ground in the nursing area. Although the occurrence of diarrhea was not affected, Sivula et al [95] found that increased gain was associated with all-in, all-out group management of weaned dairy calves.

Sufficient ventilation is important to the health of housed calves [5,104]. Besides being critical for removal of transpired water vapor and reducing humidity, sufficient ventilation in enclosed housing also removes infectious aerosols. Reducing humidity can also reduce the survival time of aerosolized and surface-borne infectious agents. Although more important for respiratory disease, these factors in turn have an effect on the risk of enteric disease. Because salmonellosis, cryptosporidiosis, rotavirus, and coronavirus agents can be transmitted by aerosols, procedures that produce aerosols (pressure washing, housing flush systems) considerably increase the risk of transmission [9]. For example, Mohammed et al [60] found that dairy calves raised outside or in mechanically ventilated buildings were five-fold less likely to shed *Cryptosporidia parvum* oocysts than those raised in nonventilated barns.

Importance of other animate vectors

Within the calf's environment, other animal species may function as mechanical or biological vectors of enteric infectious agents, particularly if

they are present in large numbers and no control efforts are in effect. These species include domestic pets, humans, and vermin such as insects, rodents, and birds.

One of the most overlooked vectors that presents a significant disease transmission risk is the nuisance fly, particularly the house fly, *Musca domestica* [35]. During summer months before severe frosts, fly populations typically increase to high numbers around concentrated livestock operations such as dairies and calf-raising operations. Liquids such as diarrhea and milk or materials containing soluble components such as dried molasses and solid feces are attractive to nuisance flies. Because the larvae require greater than 90% humidity to develop, dampened organic calf bedding materials such as straw and sawdust provide an ideal substrate [89,90]. The ability of these insects to transmit enteric pathogens from feces is well documented [18,49]. Specific physical characteristics of flies, including mouth parts, body hairs and spines, and sticky foot pads can carry infectious agents in large numbers. Some pathogens pass through the fly digestive tract and remain viable in its feces. When feeding, the fly frequently moistens surfaces by regurgitating a “vomit drop” from its crop that contains residue, including infectious agents, from its previous meal. “Fly spots” are either such vomit drops or feces, both of which contain high numbers of infectious agents. Studies have determined that flies are attracted to diarrheic feces, that they can transmit *Cryptosporidia* in numbers higher than the minimal infectious dose for healthy humans, and that they can harbor this agent for 3 weeks after exposure [34]. Methods for controlling fly populations at different points in their life cycle have been reviewed [99]; however, it is important to point out that control methods based on chemical means alone are usually inadequate because flies readily develop resistance to such chemicals.

Rodents are also a frequently overlooked source of enteric pathogens in the farm environment. They have been implicated in the transmission of salmonellosis in dairy [98] and beef herds [44] and even in poultry flocks [20,41]. Because the feces from infected mice typically contain up to 1×10^4 salmonella per pellet [20], a single pellet may exceed the infectious dose for a susceptible calf. Current work suggests that rodents are a significant non-livestock reservoir of *Cryptosporidium*, because approximately one third of rodents of any age, even in nonlivestock ecosystems, shed *C. parvum* at an average of 1×10^3 oocysts per fecal pellet [77,101]. Importantly, significant rodent populations can be present long before their signs (e.g., rodent droppings and runways) are obvious or noticeable. Raccoons have also been reported to harbor *S. Typhimurium* [64].

Approach to minimizing risk factors related to gastrointestinal pathogens

A rational approach to management of neonatal gastrointestinal diseases of calves was first conveyed by Dr. Otto Radostits years ago [79–81] and

again more recently [78]. The main tenets include management strategies directed at decreasing exposure of calves to the pathogens, increasing non-specific and specific immunity of calves, and decreasing stresses on the calves. Others have recently summarized this approach as well [39,40,70]. Although this system provides an essential foundation for addressing biosecurity for neonatal gastrointestinal diseases, further refinement suggests the following four-point approach:

1. Mitigate exposure of calves to pathogens through environmental control, monitoring, and isolation.
2. Mitigate disease severity in calves through enhancement of calf health and immunity.
3. Mitigate disease severity in calves through management of stressors placed on calves.
4. Monitor disease status within the herd through appropriate record keeping and analysis.

Mitigate exposure of calves to pathogens through environmental control, monitoring, and isolation

Those calves that are known to be particularly susceptible, either because of age or other reasons, should be isolated from each other and the rest of the herd as much as possible. Once infected, particularly if infected clinically, such calves essentially act as biological amplifiers, amplifying a small but sufficient infectious dose into a much higher level of environmental contamination in their immediate surroundings and providing a high risk for transmission through direct contact. Because this increased environmental load likely exceeds the infectious dose threshold of individuals that were resistant to the prior environmental level, more individuals become infected, the infections are more severe because of the markedly higher dose, the environmental level increases even more, and an outbreak is underway. Evidence of such a cascade is provided in one study of herds in which calves that were born after the median calving date were twice as likely to develop diarrhea than those born before it [17]. Once started, such a cascade is much more difficult to stop as compared with preventing its initiation in the first place. Evidence that members of larger groups are at increased risk of diarrhea is contained in a study of Michigan dairies, which found that the incidence of calf diarrhea was approximately proportional to herd size [32]. This finding suggests that group sizes should be minimized as much as feasible, some researchers suggesting that the ideal group size is 50 [70].

All the common agents causing neonatal calf diarrhea are often present to some degree in the calves' environment. All of the agents are primarily transmitted by fecal-oral contact, so the collective strategy for minimizing exposure of calves to pathogens should be focused on decreasing exposure to fecal contamination. Realizing that every ranch or farm has its own

peculiarities regarding facilities and equipment, the following comments and suggestions should be read as general statements. Specific modifications should be individually designed to fit each production system.

Regarding dairy or beef herds calving in confined areas such as barns, the following biosecurity measures should be practiced to minimize pathogen exposure.

1. Remove late-gestation cows from areas heavily contaminated with feces, such as winter feed grounds, 1 month before calving to reduce hair coat carriage of enteric infectious agents shed by carrier cattle.
2. Separate cows requiring more intensive monitoring and thus, closer confinement, such as first-calf heifers or particularly valuable stock from those that do not.
3. Avoid moving cows into calving areas until immediately before delivery, or as late as practical.
4. Ensure that calving pens are sanitized and well bedded before and between successive calvings.
5. Clean the perineum and particularly the udder of cows before delivery.
6. Harvest colostrum from clean, sanitized udders into clean containers. Refrigerate it immediately or freeze in volumes no larger than a gallon if not administered to a calf promptly. Do not pool between dams.
7. Remove dairy calves immediately after birth and raise them in separate individual pens isolated from other calves and stock until they are older than 4 weeks.
8. Remove beef cow/calf pairs to a separate nursery area after bonding has occurred (approximately 24 hours after birth).

During the liquid-feeding phase from birth until weaning, dairy calves should be housed in individual pens or hutches to avoid contact with one another, and they should be isolated from other livestock, their airspace, and their effluent. Ideally, individual housing should be designed to prevent suckling and licking behaviors as well as fecal cross-contamination, so that transmission of enteric pathogens is minimized. The specifics regarding the construction and area requirements for dairy calves have been reviewed [57]. Calves should continue to be housed individually until 7 to 10 days after weaning. This separation allows calves to lose their suckling urge, avoids the stress at weaning of changing social structure and interactions, facilitates monitoring of feed intake during the weaning transition, and allows more accurate observations of fecal characteristics and general health [63].

Biosecurity of dairy or beef herds calving at pasture is approached with the following strategy.

1. Group primigravid heifers separately from cows during at least the last trimester of gestation.
2. Use designated calving grounds and calve heifers separately from cows. Such areas should not have been used by animals since the prior

year's calving season and should have been groomed shortly after the close of the calving season. It should be well drained and situated away from bottomlands, which tend to collect contaminants, particularly in any standing water.

3. Minimize the population density of cows as much as practical and reduce group size (<50 animals). Suggested areas per cow range from 1000 to 2000 square feet [79].
4. Remove beef cow/calf pairs to a separate nursery area after bonding but within 24 hours of calving. Exercise one-way flow regarding animal movement.
5. Rotate feeding areas during the calving season to avoid fecal contamination and pathogen build-up.

Calves demonstrating signs of lethargy or diarrhea should be removed from the group as soon as possible and placed into an isolation area. Recall the iceberg principle and consider its group of cows and calves and their area "contaminated," placing subsequently calving cows and new calves into a separate clean area. Treatments should be instituted based on physical signs and, if possible, laboratory data. Diagnostic procedures such as fecal cultures, fecal flotation, and viral identification strategies can be performed. These tests are especially important when infection with *Salmonella* spp. is a major rule out for diarrhea. Identification of rotavirus and coronavirus infection and cryptosporidiosis are arguably less essential for diagnostic purposes because in most outbreaks of acute undifferentiated diarrhea, calves frequently shed one, two, or all three of the agents simultaneously. Detection of an infectious agent in a herd known through laboratory testing to be previously free of it, however, indicates that there has been a breach of herd biosecurity. Recovering calves should be quarantined away from other animals until after the shedding of pathogens has decreased to minimal levels or for at least 3 weeks. Aside from *Salmonella* spp., the neonatal enteric pathogens with the longest shedding time are rotavirus and coronavirus, which some individuals may shed intermittently for life.

Purchased animals should be placed in separate quarantine areas before mixing with existing herd animals, especially if animals are purchased from public auctions, because the likelihood that these animals have been exposed to high doses of multiple pathogens is great. Explosive outbreaks of calf scours in beef herds are often associated with the prior purchase of a dairy calf from a sale yard to replace a calf lost because of dystocia or some other reason. A quarantine period of 21 days should be adequate to allow clinical identification of animals that are incubating any infection due to these enteric agents at the time of purchase. Quarantine of older animals for a similar period is justified because of the likelihood of increased shedding of enteric pathogens during periods of stress. Diagnostic procedures such as bacterial culture, viral detection by electron microscopy, and fecal flotation for parasite eggs can also be considered. Although it is

unlikely that these tests will give a significant advantage compared with clinical observation and isolation, they can determine the etiologic agents involved. Use of such tests in older animals is less beneficial, because with the exception of *Salmonella* spp., many infected older animals shed low levels of enteric viruses. Because of the potential for false-negative results, testing may lead to a false sense of security, and management practices that are more important for establishing biosecurity may not be established and maintained.

The flow of personnel and livestock flow are important components of within-herd biosecurity [39,40,70,100]. The critical first step is to establish infection control protocols, preferably with input from those who will be responsible for executing them. Routine training and monitoring of personnel to ensure that they understand infection control protocols and that they are properly executing them are critical to biosecurity success. Because some aspects of these protocols involve significant additional effort, an understanding of why the additional effort is necessary will likely result in better adherence. Personnel and equipment flow as well as livestock flow and its effluent flow should be one-way, away from the youngest, most susceptible calves toward older, more resistant animals. On farms with sufficient personnel and equipment, tasks should be divided up between those personnel who remain “clean” for such tasks as mixing and delivering liquid feed and those who are potentially contaminated by performing tasks such as picking up empty milk bottles, treating sick calves, and so on. Personnel who are potentially contaminated through working with older or sick calves and their equipment should not return to areas with susceptible calves until they have changed their outer clothes and used appropriate procedures to thoroughly disinfect their hands, boots, and equipment. Some have recommended that calves that leave young, susceptible groups, such as for hospitalization, should not return to that group for at least 3 weeks [100].

Strict control of farm visitors must be maintained because many pathogens can be carried by humans or inanimate objects such as automobiles, tractors, livestock handling equipment, or livestock feeding equipment. For both their own and the animals’ health, visitors should be discouraged from coming into contact with them or their effluent. If animal contact is necessary, visiting individuals should be provided with the means to wash their hands and footwear before and after contact. Barrier clothing should also be worn to prevent cross-contamination of separate facilities.

Mitigate disease severity in calves through enhancement of calf health and immunity

Neonatal diarrhea is a multifactorial disease process. Infection alone is not sufficient to cause disease because although almost all calves are infected shortly after birth, most do not develop clinical disease. As mentioned

previously, the single strongest factor influencing the risk of death caused by neonatal calf diarrhea is the passive immune status of the calf.

The concept of failure of passive transfer has largely been used to describe situations in which the neonate does not absorb adequate levels of colostral immunoglobulins. This concept is undoubtedly attributable to the fact that immunoglobulins are such a large constituent of colostrum and they have been thoroughly studied. It is clear, however, that colostrum is a complex fluid that in addition to immunoglobulins contains various immune cells, immunoactive substances such as cytokines, and nutritional elements. Consequently, the risk of a calf contracting an enteric pathogen is a complex equation in which serum immunoglobulin concentrations are an important factor, albeit a single one.

Low immunoglobulin-concentration colostrum with the resultant ingestion of an inadequate mass of immunoglobulin is the primary cause of failure of passive transfer in dairy calves. In a study of 900 first-milking colostrums from Holstein cows, only 29% contained sufficient IgG1 concentration to provide an appropriate mass of IgG in a 2-L volume [73]. It is currently recommended that dairy calves be fed 4 liters of dairy colostrum in the first 12 hours of life to obviate the risk of failure of passive transfer caused by a lack of adequate immunoglobulin mass. To ensure intake soon enough, esophageal feeders are often used to administer these volumes.

In contrast with dairy calves, failure of passive transfer in beef calves is less likely to be due to low colostral IgG1 concentration, but rather to a failure to physically ingest and subsequently absorb the colostral immunoglobulins. Beef calves should be provided with adequate shelter during and after calving to avoid environmental stresses that lessen the calves' drive to rise and nurse. Ideally, calving should be monitored to ensure adequate mothering, which is especially important with first-calf heifers. Calves that do not rise and successfully nurse their dam within 1 to 2 hours should be assisted with nursing, or alternatively, force-fed either their dam's colostrum or frozen dairy cow colostrum. If dairy cow colostrum is used, its low average immunoglobulin concentration must be mitigated by feeding 4 liters within the first 12 hours of life. The producer must be aware that such colostrum may also be contaminated with enteric and other infectious agents (e.g., *Mycobacterium avium* subsp. *paratuberculosis*).

Mitigate disease severity in calves through management of stressors placed on calves

Stress is defined as any adverse stimulus, event, or condition, either internal or external, that disturbs an animal's physical or neurogenic homeostasis. Although there are likely numerous biological consequences of stress, a well-documented response involves the rapid and immediate increase in corticotropin secretion by the anterior pituitary gland, followed by greatly

increased secretion of cortisol by the adrenal gland. Some of the beneficial effects of increased cortisol secretion include mobilization of labile proteins and fats from cellular stores for cellular energy needs, as well as numerous anti-inflammatory effects that aid in the resolution of inflammation. One of the more notable consequences of increased cortisol secretion, however, involves its extensive effects leading to immune suppression. In general, cortisol-induced atrophy of lymphoid tissues throughout the body leads to a significant decrease in both cellular and humoral immunity. It is this broad-ranging immune suppression that can lead to an increased incidence and severity of disease.

Common stresses incurred by neonatal calves include dystocia, crowding, exposure to environmental extremes such as heat, cold, or wet conditions, excessive or inappropriate handling, and exposure to pathogens [48]. Even the process of a normal parturition is a stressful condition as the fetal animal undergoes transition from intrauterine to extrauterine life. Fetal plasma cortisol levels double within minutes after uncomplicated parturition but typically decrease within the first days of life. The natural increase in plasma cortisol is necessary for normal pulmonary, intestinal, and brain development; pulmonary surfactant production; and preparation of liver glycogen stores for energy needs. Calves with dystocia are likely to have temporarily increased plasma cortisol levels and other significant laboratory abnormalities, including metabolic and respiratory acidosis and hypoglycemia [13]. Current studies indicate that the increased incidence of failure of passive transfer in calves with dystocia is not caused by a failure to absorb colostral immunoglobulins, but rather is due to the severe metabolic derangements that make these calves less likely to nurse in a timely fashion [106]. Alleviation of the stress of dystocia, therefore, should be directed toward correcting metabolic derangements and ensuring appropriate colostrum intake.

Exposure to environmental extremes is likely to affect calves adversely by inhibiting normal nursing behavior and producing prolonged elevations in serum cortisol levels. Both of these factors clearly have an adverse effect on the calves' immune status, so newborn calves should be placed in sheltered environments that are free from wind and moisture and extremes of heat or cold. Providing calves with dry bedding is a critical factor in preventing problems associated with cold temperatures [69]; however, these shelters must be managed appropriately to minimize the concentration of enteric pathogens within them.

Crowding and mishandling of calves should be minimized to lessen the effect of neurogenic stress. Although limited research in this area has been undertaken in calves, it is logical to assume that calves would react similarly to other mammals in such stressful situations, with resultant increased plasma cortisol levels and subsequent immune suppression. Finally, it is logical to presume that minimizing crowding will likely not only decrease the neurogenic stress of calves but also will unquestionably decrease exposure to enteric pathogens.

Monitor disease status within the herd through record keeping and analysis

With either confined or pasture calving, it is important to keep adequate records. Records are useful for determining the timing of animal movement and for identifying the epidemiologic factors associated with sick animals as well as recording what diagnostic tests were performed, when and what treatments were administered, and their results. Particularly on larger operations, complete records maintained in a computerized database are crucial for initially determining what risk factors are associated with a neonatal diarrhea problem and then for monitoring the success of interventions.

Biosecurity, as it relates to neonatal gastrointestinal disease, should be approached as a fluid concept. Adequate records markedly enhance a producer's and a veterinarian's ability to regularly evaluate and revise neonatal disease control and prevention protocols in response to changing conditions, actual risks, and new knowledge and tools for dealing with neonatal enteric disease.

Summary

Infectious diarrhea is an important cause of neonatal calf morbidity and mortality that results in significant economic losses in the beef and dairy industries. Although numerous risk factors related to the occurrence of neonatal diarrhea have been identified, they can all be categorized into those that are related to the calf, the pathogens involved, or the environment of the calf. The immune status of calves, specifically the level of passively acquired immunity through colostrum, is the major risk factor related to the calf and the occurrence of diarrhea. Although numerous pathogens have been implicated in the occurrence of neonatal diarrhea, only a relatively limited number are commonly involved. Most should be viewed as secondary opportunists rather than primary pathogens, because none are extraordinarily virulent, and with the exception of *Salmonella* spp., most are present within the gastrointestinal tract of many healthy, mature cattle. Important risk factors related to pathogens involved in neonatal calf diarrhea involve the size of the inoculum and the occurrence of multiple infections. Finally, when considering the environment and housing conditions in which beef and dairy calves may reside, it is clear that tremendous variations exist. Despite these variations, the risk factors associated with the environment of the calf are also those that are the most amenable to the implementation of general environmental control and monitoring strategies as well as specific biosecurity measures.

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