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Cryptosporidium parvum infection in cattle: are current perceptions accurate?

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The perception that cattle are major reservoirs for *Cryptosporidium parvum* infections in humans and that *C. parvum* is a major cause of diarrhea and production loss in cattle might not reflect the whole situation. Numerous management factors influence the epidemiological and clinical picture associated with *C. parvum* infections in cattle. Whereas *C. parvum* is highly prevalent in young dairy calves and confined beef calves, it occurs rarely in calves on range and in adult cattle. In well-managed herds, clinical disease due to *C. parvum* is also rare. Therefore, *C. parvum* infections in cattle might not be as important as current perceptions would indicate.

Cryptosporidium parvum transmission: cattle to humans or humans to cattle?

It is a widely held perception that cattle are the most important reservoir for outbreaks of *Cryptosporidium parvum* infection in humans [1]. However, is this perception accurate? It is well established that *C. parvum* is a zoonotic parasite, and reports of *C. parvum* transmission by way of direct contact between infected calves and humans demonstrate this zoonotic potential [2]. Epidemiological studies also indicate direct contact with farm animals is associated with an increased risk of *C. parvum* infection in humans [3]. As a result, people who handle cattle frequently, such as dairy farm workers, have higher rates of infection and exposure to *C. parvum* than those who do not have contact with cattle [4,5]. Although only a small segment of the population in the developed world has direct contact with cattle, this potential for zoonotic transmission has resulted in cattle being implicated as sources for both sporadic and waterborne outbreaks of cryptosporidiosis in the general population. However, cattle have never been conclusively proven to be the source of a waterborne outbreak of cryptosporidiosis in humans. In North America, for example, the human specific *Cryptosporidium hominis* and not *C. parvum* has in fact been responsible for nearly all drinking water outbreaks of cryptosporidiosis in humans, and all outbreaks have been associated with failure of the water treatment facility or an absence of adequate water treatment [6]. Therefore, cattle have probably been unfairly implicated in outbreaks of cryptosporidiosis in humans.

Molecular characterization studies have shown that two species of *Cryptosporidium* are responsible for 97% of *Cryptosporidium* infections in immunocompetent humans and 80% of infections in immunocompromised individuals [7]. Currently, these species are known as *C. hominis*, which is specific for humans, and *C. parvum*, which has a wide host range, including cattle. These species are morphologically identical, and could not be differentiated before the development of molecular techniques. Thus, the development and use of molecular techniques to investigate waterborne outbreaks of disease have revealed that cattle can be unfairly implicated in waterborne outbreaks of cryptosporidiosis. For example, in the report detailing the infamous Milwaukee outbreak of cryptosporidiosis in 1993, cattle were listed as a potential source for the outbreak [8]. However, recent molecular analysis of samples obtained during the outbreak revealed that *C. hominis* was the infectious agent and cattle were not associated with the outbreak [9]. Although the development of molecular techniques has been extremely valuable, the subsequent changes to *Cryptosporidium* nomenclature might have also led to cattle being unfairly implicated as sources for outbreaks of cryptosporidiosis in humans owing to confusion with respect to *C. parvum* transmission cycles. Prior to *C. hominis* being given species designation it was referred to as the *C. parvum* 'human genotype' with the current *C. parvum* species being referred to as the *C. parvum* 'bovine genotype' [10]. Based on the conclusions made from recent studies, the use of these genotype designations (human and bovine) might have created the impression that *C. parvum* infections in humans (previously the *C. parvum* 'bovine genotype') undoubtedly have a zoonotic origin, with cattle being the source [11,12]. However, simply identifying *C. parvum* instead of *C. hominis* in human clinical samples or in environmental samples does not prove that zoonotic transmission has occurred or that cattle are the source. Humans are very capable of transmitting *C. parvum* to other humans, as demonstrated in swimming pool outbreaks where *C. parvum* has been

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identified [13]. Therefore, when *C. parvum* is identified in sporadic cases or waterborne outbreaks of human cryptosporidiosis it indicates a wide range of potential sources, including humans or human sewage, as well as cattle, other livestock or wildlife.

Additional confusion regarding the transmission cycle of *C. parvum* could stem from recent studies that have identified the occurrence of sub-genotypes within *C. parvum* [14,15]. Although the species *C. parvum* has a wide range of hosts, certain subgenotypes of *C. parvum* appear to be restricted to humans, whereas others occur in both humans and cattle. As a result, it has been suggested recently that the occurrence of the same *C. parvum* subgenotypes in human and bovine cases of cryptosporidiosis indicates the occurrence of zoonotic transmission [11]. However, as stated above, humans are quite capable of transmitting these subgenotypes to other humans. In fact the occurrence of human specific subgenotypes of *C. parvum* provides additional evidence that cattle pose less of a risk in the transmission of *C. parvum* to the general population than currently perceived. The use of subgenotyping techniques will be valuable in future investigations of waterborne outbreaks of cryptosporidiosis in humans caused by *C. parvum*. However, it must be emphasized that for *C. parvum* subgenotypes that occur in both humans and cattle, human contamination of the water supply could be the source of infection for both humans and cattle, and simply the subsequent finding of the parasite in cattle should not result in these cattle being implicated as the source of the outbreak.

Targeting the actual reservoir

Epidemiological studies explain why cattle as a whole are not major reservoirs for *C. parvum*. Dairy calves, specifically those less than one month of age are commonly infected with the parasite. Numerous longitudinal studies demonstrate virtually 100% of dairy calves become infected with *C. parvum* at some point early in life [16–18]. Dairy calves, especially those suffering from diarrhea, can excrete 10^7 oocysts per gram of feces [19], and these calves can produce billions of oocysts during the one to two weeks in which their infections are patent. In beef calves, *C. parvum* prevalence can be high within intensively managed units [20], but the prevalence in beef calves is often lower than in dairy calves, even when raised in similar conditions [21]. Factors such as passive immunity could account for this difference as beef cows, on average, produce significantly higher concentrations of immunoglobulin in their colostrum than dairy cows [22]. Not surprisingly, in less intensively raised calves, the prevalence of *C. parvum* infection decreases [23], and calves raised on open range have a low overall prevalence of *C. parvum* infection. In North American cow–calf herds raised on open range, the overall *C. parvum* prevalence in calves is 3–6%, with a peak of 13% reported in calves less than 2 months old [24,25]. Corresponding with this decreased prevalence is also a decrease in the intensity of oocyst excretion. In contrast to dairy calves, beef calves produce far fewer oocysts per gram of feces, with the reported maximum excretion of around 8000 oocysts per gram of feces [24]. Occasionally, severe outbreaks of cryptosporidiosis can occur in beef calves (see '*C. parvum* and bovine neonatal diarrhea', below), where large numbers of oocysts are excreted. The frequency of these outbreaks, however, is not known. Nevertheless, there are marked differences between beef calves on range, confined beef calves and dairy calves with respect to *C. parvum* infection patterns, and beef calves, particularly those raised on range, pose little risk with respect to zoonotic transmission of *C. parvum*.

Adult beef and dairy cattle also pose little risk with respect to zoonotic transmission of *C. parvum* as infections are extremely rare. Following infection, calves develop lasting immunity to *C. parvum* and are resistant to secondary challenge [26]. Thus, the high prevalence of the parasite amongst young dairy calves combined with the development of immunity, probably accounts for the low prevalence of *C. parvum* in adult dairy cows. Recent studies demonstrate less than 1% of post-weaned and adult dairy cows excrete *C. parvum* oocysts in their feces [27,28]. In a recent longitudinal study, no adult dairy cows excreted *C. parvum* oocysts in their feces over a 282 day study period, despite the fact that dairy calves housed in the same barn excreted *C. parvum* oocysts [29]. The prevalence of *C. parvum* oocyst excretion is also low in adult open range beef cows, ranging from 0.6% to 7.1% in the US [25,30,31] and 1.1% in western Canada [24]. A prevalence of around 1% has also been reported in feedlot cattle (cattle in a concentrated feeding operation) in North America [30]. In both adult beef and dairy cattle, oocyst excretion is of low intensity, and it has been estimated that *C. parvum*-positive adult beef cows and feedlot cattle produce an average of 3.38 and 1396 oocysts per gram of feces, respectively [30,31]. A high *C. parvum* prevalence in adult beef cattle has been reported [32], but the intensive nature in which cattle were raised could account for the higher prevalence observed.

Further evidence that indicates most cattle are not major reservoirs for *C. parvum* infection in humans comes from a recent study that shows that many older cattle could be infected by the non-zoonotic *C. bovis* rather than *C. parvum* [33]. Therefore studies in which *C. parvum*-like oocysts have been detected in cattle should be interpreted with caution if molecular characterization has not been performed. In fact, few *Cryptosporidium* isolates have been genotyped in beef cattle. Thus, in previous epidemiological studies, such as those referred to above, oocysts of the non-zoonotic *C. bovis* or other genotypes might have been excreted. Notwithstanding the recent identification of *C. bovis*, *C. parvum* infections are rare in older calves and adult cattle, particularly those on open range. Even though adult cattle produce greater quantities of feces than do young calves, the overall *C. parvum* environmental loading capacity of adult cattle is low [31]. In a very recent study examining a watershed in Ontario, Canada in whch cattle were the major livestock present in the study area, sporadic and low levels of *Cryptosporidium* oocysts were detected [34]. The non-zoonotic *Cryptosporidium andersoni* was detected in 50% of the water samples, but *C. parvum* was found only in a single sample from a site influenced by both agriculture and urban development. Thus, cattle grazing on open range do not pose a serious risk to humans with respect to transmission of *C. parvum*

directly or indirectly through contaminated water. By contrast, confined calves, such as dairy calves, can be a significant source for *C. parvum*, although research shows dairy farms themselves might not be major sources of contamination for surface water [35]. Nevertheless, because of the intensive way they are raised, feces produced by dairy calves or confined beef calves can be easily managed to mitigate risks posed by *C. parvum* and other pathogens. For example, composting of manure deactivates *C. parvum* oocysts [36] and the practice of composting manure before spreading it on pastures should be encouraged.

C. parvum and bovine neonatal diarrhea

C. parvum often can be identified in cases of neonatal diarrhea in calves [16,20], and experimental infections demonstrate that *C. parvum* can cause clinical disease in calves [19,37]. As a result, *C. parvum* is considered to be a major cause of neonatal diarrhea in calves, which results in economic losses to cattle producers [38]. However, many cattle operations, particularly those that are well managed, have few problems with respect to neonatal diarrhea [39,40] and simply the presence of *C. parvum* in a herd is not enough to cause outbreaks of clinical disease. In fact, *C. parvum* is commonly identified in healthy calves and in herds without any diarrhea problems [16,23,41]. Unlike experimental studies, neonatal diarrhea in the field is a complex, multifactorial disease in calves that not only involves pathogen exposure, but environmental, management, and nutritional factors as well [39]. When diarrhea due to *C. parvum* does occur, it is rarely severe in well managed herds, and there is no evidence the disease has any long-term impact on growth or production in calves [16,42]. Complicating matters is the fact that in virtually every outbreak of neonatal diarrhea in calves multiple pathogens can be identified and mixed infections often occur [16,41,43]. Fortunately, these fecal–oral transmitted pathogens, including *C. parvum*, are effectively controlled through the use of good management and proper husbandry. Maintaining a closed herd, supplying clean dry bedding to calves and cows, ensuring calves receive adequate transfer of passive immunity, and reducing exposure to the pathogen through isolation of sick animals, reduced stocking density, and good general hygiene greatly reduce the incidence and severity of neonatal diarrhea [39]. Many of these management factors are associated with a reduced risk of *C. parvum* infection in calves [44,45]. Although not well characterized, outbreaks of severe cryptosporidiosis in beef calves on range are associated with the presence of puddled water in calving areas, selenium deficiencies in the dams, and the introduction of a dairy calf to the herd, thus emphasizing the importance of management in controlling cryptosporidiosis [42,46]. Therefore, although *C. parvum* is a cause of diarrhea in calves, it is only one of many pathogens that contribute to the complex etiology of bovine neonatal diarrhea.

Because good husbandry and management can be used effectively to reduce the incidence and severity of neonatal diarrhea in calves, prophylactic medications and vaccines to control cryptosporidiosis should not be necessary. Several studies have investigated the potential for vaccination to control cryptosporidiosis in calves [47,48] and studies have shown that the drug halofuginone is effective in controlling cryptosporidiosis in calves [49,50]. However, there is no evidence that cryptosporidiosis can affect overall production in calves, and in a recent study, the use of halofuginone to prevent *C. parvum* infection in calves did not result in increased weight gain [50]. Thus, the costs to the producer associated with using vaccines or medications to control cryptosporidiosis do not appear to be justified. For herds in which neonatal diarrhea is severe enough to result in increased mortality, which justifies the use of a vaccine or medication, the major deficiencies in husbandry and management inevitably associated with the operation should be addressed. Providing prophylactic drugs and vaccines to operations in which poor husbandry and bad management prevail is not a sustainable solution and is likely to be counterproductive in the long run.

Conclusion and future perspective

The prevalence, oocyst excretion intensity, clinical signs, and zoonotic potential associated with *C. parvum* infections in cattle can vary considerably from herd to herd. At this moment, the cattle that are infected with *C. parvum* throughout the world will almost exclusively be young calves, less than two months of age, and many of these calves will not be suffering clinical disease. Well managed herds have few problems with *C. parvum* or neonatal diarrhea and pose little (if any) risk with respect to environmental contamination and zoonotic transmission. On farms where neonatal diarrhea is severe enough to present a problem, *C. parvum* will most certainly be found, but so will other enteropathogens such as rotavirus, coronavirus, *E. coli*, *Salmonella* and *Eimeria*. Poor husbandry and bad management are also likely to prevail in these situations. However, much of our research concerning bovine cryptosporidiosis has focused on these herds in which neonatal diarrhea is problematic and *C. parvum* is highly prevalent. As a result, we have developed a general perception regarding *C. parvum* infections in cattle based solely on problem herds and therefore this perception is not accurate. Closed cow–calf operations on open ranges that are well managed pose little risk with respect to transmission of *C. parvum* to humans. Unfortunately, many of these operations might lose access to valuable grazing land by being included with those few farms that do present a risk. It is the more intensive operations that pose a risk of environmental contamination and zoonotic transmission, but this risk is limited to young calves and can still be mitigated by good husbandry and management practices. As research continues in this area, it is important that we also focus on well managed herds to gain a more accurate picture of the clinical and zoonotic significance of *C. parvum* infections in cattle. Furthermore, we should make an effort to commend those producers that have few problems with *C. parvum*, and other pathogens owing to their excellent management and good husbandry, and encourage other cattle producers to reach that level.

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