CHAPTER 9
Coccidiosis in Sheep
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9.1 INTRODUCTION

Eimeria spp. are the only intestinal coccidia of sheep. Coccidiosis can cause considerable morbidity and mortality, especially when lambs are reared in production systems that involve a high stocking rate (Hidalgo Argüello and Cordero del Campillo, 1999) [43929] [713]. Additionally, subclinical coccidiosis can affect production of infected animals (Chartier and Paraud, 2012) [42418] [247].

9.2 ETIOLOGY

Species of the genus *Eimeria* affecting sheep and goats were considered the same for many years due to the morphological similarity of their oocysts. Cross-infection studies have shown that coccidia in small ruminants are host-specific (McDougald, 1979) [40125] [1163]. Currently, 13 *Eimeria* spp. are recognized affecting sheep worldwide (Table 9.1). Two of these, *E. crandallis* and *E. ovinoidalis*, are the most pathogenic (Catchpole et al., 1976 [38330] [187]; Joachim et al., 2018) [42235] [822].

9.2.1 Morphology and Life Cycle

Morphologic characteristics of 13 ovine *Eimeria* spp. oocysts are summarized in Table 9.1, and Figures 9.1 and 9.2.

After the excretion of unsporulated oocysts in feces, sporulation can be completed under ideal conditios in 1-4 days (Table 9.2), but maybe delayed several weeks in cold weather. Oocysts are also sensitive to low humidity and temperatures above 40 ºC or below -30 ºC (Foreyt, 1990 [38906] [546]). Excystation of sporozoites occurs in intestinal lumen, and sporozoites invade intestinal cells, where they undergo 2 rounds of schizogony. One of the characteristic of ovine coccidia is that the first generation schizonts are large, approaching being macroscopic and contain thousands of merozoites. The second generation schizonts and gamonts are typically small and they are site-specific. The prepatent period depends on the *Eimeria* sp. and is 12 days or more (Table 9.3).

9.3 EPIDEMIOLOGY

9.3.1 Transmission and Epidemiology

The ingestion of sporulated oocysts from the environment is the only known mode of transmission (Gregory et al., 1983 [41892] [620]; Hassum and Menezes, 2005 [39174] [683]; Chartier and Paraud, 2012 [42418] [247]; Saratsis et al., 2013 [42063] [1495]).

Environmental contamination or oocysts excreted by adult sheep or lambs of the last season may be the initial source of infection in lambs. Later, given the high multiplication rate of the parasite in susceptible animals, lambs become the most important source of infection for younger and susceptible animals, resulting in a rapid spread of the disease (Taylor, 1995 [44189] [1683]; Gauly et al., 2004 [43923] [585]). Oocyst excretion peaks around the period of weaning,

and then excretion of oocysts declines with age of lambs, suggesting the development of a specific immune response (Hidalgo-Argüello and Cordero del Campillo, 1987 [37992] [712]; Reeg et al., 2005 [37361] [1401]).

Transmission may be favored by some management factors in indoor reared lambs such as those related with poor hygienic and overcrowded conditions; thus a high concentration of animals kept on dirty and damp bedding are more at risk than those on slatted floors or clean bedding (Taylor et al., 2007 [44694] [1688]; Saratsis et al., 2011 [42061] [1494]). The use of pens to house different age groups is also considered a risk factor. In this respect, bottle feeding of lambs can prevent infection, but transmission may occur during colostrum intake from ewes or by contamination of equipments (Hidalgo-Argüello and Cordero del Campillo, 1999 [43929] [713]). Clinical coccidiosis may also occur in extensive management systems particularly when there is a high population density and a reduction in pasture availability (de Souza et al., 2015 [41843] [348]). In this case, a marked seasonality is usually observed. In many cases, the times of greatest risk coincide with spring grazing with symptoms appearing 2 to 3 weeks after turnout. However, depending on geographical factors or different grazing routines, cases of clinical coccidiosis in lambs are also described in summer or even in autumn (Skirnisson, 2007 [45692] [1583]; Odden et al., 2017 [37570] [1263]; Macrelli et al., 2019 [45083] [1109]).

9.3.2 Immunity and Predisposing Factors

The role of passive immunity in ovine coccidiosis is controversial. Some authors consider that feeding colostrum protects lambs from coccidiosis during the first weeks of life. This is supported by studies that showed significantly increased growth rates in lambs born from hyperimmunized ewes (by inoculation with high doses of *Eimeria* spp. oocysts during pregnancy) compared with lambs born from unimmunized animals (Gregory and Chatchpole, 1989 [39073] [618]; Gregroy et al., 1989 [39072] [621]).

The susceptibility and the dynamics of oocyst excretion is clearly related to the development of specific and effective immune responses. The absence of such protective responses makes young animals more susceptible, and it is in this age group where clinical coccidiosis is most frequently observed. The onset of clinical disease varies within an age range depending mainly on the farming system and / or the immune status of each animal. The excretion dynamics of oocysts increases progressively until reaching a peak, in which some animals excrete up to 10^6 oocysts per gram of feces (opg). As results of active immunity after the exposure to the parasite, the animals acquire resistance showing a progressive reduction in oocysts excretion. However, the protective immunity is not absolute, and the animals may continue to harbor a small number of coccidia throughout their lives (Catchpole et al., 1993 [38333] [186]; Taylor, 1995 [44189] [1683]; Platzer et al., 2005 [42038] [1359]; Daugschies and Najdrowski, 2005 [43843] [333]; Zanetti Lopes et al., 2013 [43956] [1872]).

The achievement of an immune status against homologous infections, as well as the maintenance of such protection over time, may be affected by a number of factors, most of them stress related factors such as inadequate nutritional intake, weaning, dietary changes, transport, or drastic changes in climatic conditions. Other possibilities that have been considered responsible for the loss of resistance to infection are the presence of concomitant infections, the alteration of complex interactions with intercurrent digestive parasites or even due to sex-related factors. Thus, some authors reported that females are more susceptible to *Eimeria* infection than males during pregnancy, birth and lactation (Catchpole and Harris,

1989 [38332] [184]; Taylor et al., 2007 [44694] [1688]; Yakhachali and Golami, 2008 [43955] [1840]; Chartier and Paraud, 2012 [42418] [247]; Carrau et al., 2016 [42398] [175]).

9.3.3 Prevalence and Geographical Distribution

Coccidial infections in sheep are ubiquitous. Although differences in prevalence were observed in different regions, they could generally be more closely related to the factors mentioned in the previous section. Obviously, some environmental or climatological conditions may favor the accumulation of sporulated oocysts in certain periods of the year with higher humidity and higher temperatures. For this reason, the sampling period and even the characteristics of the epidemiological study such as the sample size could affect the prevalence obtained in each case. Some reviews on the epidemiology of ovine coccidiosis during the last decades have shown this worldwide distribution and wide ranges of prevalence mentioned above (Chartier and Paraud, 2012 [42418] [247]; de Souza et al., 2015 [41843] [348]; Khodakaram-Tafti and Hashemnia, 2017 [43855] [880]).

9.4 PATHOGENESIS, CLINICAL SIGNS AND LESIONS

9.4.1 Pathogenesis

The pathogenesis of coccidiosis in sheep is affected by all factors inducing changes in parasite-host interaction, such as all those considered in some previous sections. In addition, other factors related to the parasite itself, such as the predominant species or the infective dose, or factors associated with the host, such as the different genetic susceptibilities and earlier exposure to the parasite, may also be considered (Jolley and Bardsley, 2006 [39416] [837]).

Another important factor of clinical signs that characterize coccidiosis is the strong interaction of coccidia with the intestinal flora, as well as the infective dose, establishing a clear relationship between the severity of the clinical signs/mortality, and the number of sporulated oocysts ingested by the susceptible animals. The pathogenicity of *Eimeria* may also be modified if coccidiosis is associated with concomitant infections caused by parasites or even other pathogenic agents such as viruses or bacteria (Wright and Coop, 2007 [44693] [1822]; Chartier and Paraud, 2012 [42418] [247]; Bastiani et al., 2012 [43917] [87]; de Souza et al., 2015 [41843] [348]).

All species of *Eimeria* in sheep affect the small and/or large intestines except *E. gilruthi*, which is detected in the abomasum of sheep (Maratea and Miller, 2007 [41998] [1124]; Hermosilla et al., 2016 [43928] [707]); its life cycle is unknown. In general, 2 species (*E. crandallis* and *E. ovinoidalis*) affecting the distal half of intestines are considered major pathogens, while the remaining *Eimeria* spp. are thought to be of negligible importance. In any case, they are usually present leading to mixed infections (Nourollahi-Fard et al., 2016 [42018] [1252]; Joachim et al., 2018 [42235] [822]).

Damage in large intestines as a result of parasite proliferation can lead both severe hemorrhage and water reabsorption disorders. One hypthesis proposed that the fact that the species that develop their endogenous cycle in the large intestines are more pathogenic, was explained by the shorter length of this intestinal part. In addition, the rate of cellular turnover is much lower here, so that the damage caused is more difficult to compensate than in the

small intestines. Subsequent diarrhoea, dehydration, and emaciation may produce the death of the affected animals (Khodakaram-Tafti and Mansourian, 2008 43930 879). In the most severe forms, inflammation of the intestinal mucosa causes a significant loss of fluid and electrolytes as well as plasma and lacteal constituents leading to acidosis and serum electrolyte derangement (Engidaw et al., 2015 43922 494). In contrast, the *Eimeria* spp. that develop more superficially in the small intestines are usually less pathogenic. The reduction of the suface area available for absortion affects feed efficiency. In addition to all digestive disorders, an increase in plasma levels of some hormones which are associated with anorexia, such as cholecystokinin and somatostatin, has also been described (Lima, 2004 43934 1020).

9.4.2 Clinical Signs

Lambs with severe coccidiosis may die without prompt and appropriate treatment. In these cases, the mortality percentage can reach up to 10% of infected animals or more. Clinical signs may appear fairly suddenly and lambs only mildly ill the day before, may be very sick the next day. In other cases, before death occurs, some lambs may have a tucked up and open-fleeced appearence, showing fecal staining of the perineum and hindlegs, reflecting the first cases of diarrhea. The change in the fecal appearance is coincided with the first detection of oocysts, which varies according to the prepatent period of each species (Lotze, 1954 44184 1092; Taylor, 1995 44189 1683; Lima, 2004 43934 1020; Chartier and Paraud, 2012 42418 247; Khodakaram-Tafti and Hashemnia, 2017 43855 880).

Acute signs of coccidiosis include different degrees of yellow to dark watery diarrhea (with or without blood). In many cases, the feces have clumps of mucus and intestinal tissue. As a result, the lambs may be dehydrated with pale mucous membranes, and hematological evaluation shows a decrease in levels of erythrocytes, hemoglobin and iron. They will invariably be depressed but fever is not always present. When this occurs, it is usually during the early stages of the disease. Other clinical signs that have been seen in some coccidiosis outbreaks are related to abdominal pain and bloating (Lotze, 1954 44184 1092; Foreyt, 1990 38906 546; Wright and Coop, 2007 44693 1822; Khodakaram-Tafti and Mansourian, 2008 43930 879; Koçkaya and Özşensoy, 2016 43932 903).

In other cases, coccidiosis is manifested by subacute or chronic clinical forms, with less obvious clinical signs, and affecting the animals for a longer period of time. Lambs with chronic coccidiosis may have had acute severe coccidiosis earlier or may not ever have been noticed ill. The animals that develop these clinical forms of the disease have different levels of digestive disorders, which determine nutrient and electrolyte losses, as well as absorption alterations, with the consequent reduction of mineral and vitamin levels (Lima, 2004 43934 1020; Sahinduran et al. 2006 43945 1476). Poor body condition score and weight loss are often the most common findings in these cases. It is also common that the perianal regions may be dirty due to intermittent diarrhea. Recovery time can be long dependent on the severity of intestinal tissue damage, and some lambs with chronic coccidiosis may never fully recover (Lima, 2004 43934 1020; Andrews, 2013 43915 41).

In lambs with mild coccidiosis there is some degree of inappetance, a reduction in weight gain, uneven lamb size and higher food conversion ratio. Sometimes, feces are softer or non-pelleted. Subclinical coccidiosis is also considered to increase the susceptibility of animals to other infections (de la Fuente et al., 1993 38580 344; Alzieu et al., 1999 42368 36).

9.4.3 Lesions

9.4.3.1 Gross

The most important lesion is catarrhal enteritis that affects the jejunum, ileum, cecum and possibly the colon. The bowel may appear congested, edematous, thickened and have petechiae (Lotze, 1952 [39941] [1091]; Hidalgo Argüello and Cordero del Campillo, 1999 [43929] [713]; Taylor et al., 2003; [42099] [1687] Khodakaram-Tafti and Mansourian, 2008 [43930] [879]).

In lambs, coccidiosis usually results in enterocyte hyperplasia, which in addition to thickening of the intestinal wall, leads to the development of whitish 1-2 mm diameter non-pedunculate plaques/polyps or nodules (Figure 9.3, also see Figure 1.28F, **Chapter 1**), which are a coalescence of different stages of the parasite (schizonts, gamonts, oocysts). These lesions may have certain morphological characteristics and a variable distribution pattern throughout the intestine depending on the species of *Eimeria* involved, although it seems that they do not develop in *E. faurei* and *E. weybridgensis* infections (Hidalgo Argüello and Cordero del Campillo, 1999 [43929] [713]; Khodakaram-Tafti and Hashemnia, 2017 [43855] [880]).

The presence of polyps may not reflect severity of coccidiosis. In *E. bakuensis* infections, more prolific polyps can also be observed, whose pathogenic role is unknown. Similarly, in advanced cases of coccidiosis, progresive thickening, folding or corrugating to pseudoadenomatosis of the intestinal mucosa associated to numerous well-raised nodules are seen. These nodules sometimes are pedunculated reaching 0.3 to 1.5 cm in diameter and are comprised of hypertrophic crypt-villus units in which epithelial cells are infected by the parasite. For some authors, these polypoid lesions are the result of the mitotic stimulation of some parasitic stages (progamonts). When these proliferative lesions are projected towards the serosa of the intestines, they determine a lesion pattern that has been denominated cerebraliform, which could have diagnostic value in coccidiosis (Gregory et al., 1987 [43925] [623]; Taylor et al., 2003 [42099] [1687]; Khodakaram-Tafti and Mansourian, 2008 [43930] [879]; Chartier and Paraud, 2012 [42418] [247]). Lesions in abomasum are associated with macroscopic schizonts of *E. gilruthi* (Figure 1.28G**, Chapter 1**).

9.4.3.2 Microscopic

Histopathologically, lesions are associated with loss of surface epithelial cells, villous atrophy (mainly during the first asexual stages of the parasite) and crypt destruction or compensatory hyperplasia (associated with gamonts). Destruction of the mucosa may result in the presence of ulcerations. Hemorrhages and edema may also be noticed in the mucosa and submucosa. Hyperplastic reactions use to be more manifiest in older animals, and hemorrhages are more common in younger animals. Intense inflammatory cell infiltration may be noted in the hyperplastic areas. The infiltrations are generally composed of eosinophils, lymphocytes, neutrophils and macrophages. In some cases, proliferation of connective tissue is observed due to chronic inflammatory reactions. Likewise, analysis by immunohistochemical methods of cytokine and chemokines expression at the gut lesions, reveals that the most expressed mediators are the interleukin-1α and the interferon-γ. (Taylor et al., 2003 [42099] [1687]; Ozmen et al., 2012 [43939] [1295]; Chartier and Paraud, 2012 [42418] [247]).

Enteritis may vary in severity, affecting the lamina propria and even the submucosa. As a result of all these morphological alterations, the function of the epithelial cells can be compromised, at the same time as intestinal motility and intercellular signalling, triggering the clinical signs above mentioned (Gregory and Catchpole, 1987 [41893] [617]; Jolley and Bardsley,

2006 [39416] [837]).

Of the 2 most pathogenic species, *E. ovinoidalis* causes lesions in the terminal ileum, cecum and proximal colon inducing edema and thickened wall. Minimal lesions are associated with large (300 µm in diameter) first generation schizonts that develop in cells deep in the lamina propria of the terminal ileum. The second generation schizonts infect epithelial cells lining the colonic crypts, and subsequently gamonts attack the remaining crypt epithelium, leading to destruction of most of the cells, including stem cells. Various degrees of lymphocyte depletion have been observed present in the ileal lymphoid follicles in *E. ovinoidalis* infected lambs 3 weeks after infection, showing decreased follicle size and reduced staining for leukocyte common antigen (CD45) and B-cell markers (Gregory and Catchpole, 1987 [41893] [617]; Khodakaram-Tafti and Hashemnia, 2017 [43855] [880]).

Similarly, *E. crandallis* first generation large (250 µm in diameter) schizonts are located in the lamina propria of the jejunum. The development of first generation schizonts is associated with the infiltration of eosinophils and lymphocytes into the lamina propria as well as the appearance of areas of focal necrosis, destruction of crypts, and hypertrophy of the surrounding crypts. Second generation schizonts are observed within the cytoplasm of jejunal and ileal epithelial cells. The lamina propria then shows an inflammatory response associated with the development of second asexual stage of the parasite. There is resulting villous atrophy and loss of crypts. Finally, pro-gamonts are seen within epithelial cells of the crypts and villi of the small intestines and cecum, differentiating subsequently into micro-and macrogamonts. The presence of gamonts results in congestion and inflammation of the mucosa. This inflammatory response seems to be related with the presence of increased numbers of inflammatory cells (lymphocytes and macrophages) within the lamina propria. In heavy infections, the cecum and colon may be similarly affected, showing hyperplastic crypts with large enterocytes and increased number of globet cells. Under experimental conditions, lambs infected with a high number of oocysts also showed schizonts in enlarged mesenteric lymph nodes. These parasite stages presented similar characteristics to those observed at the intestinal wall (Lotze et al., 1964 [44185] [1094]; Gregory et al., 1989 [1713] [622]; Gregory and Catchpole, 1990 [41895] [619]; Taylor et al., 2003 [42099] [1687]; Taylor et al., 2007 [44694] [1688]).

9.5 DIAGNOSIS

9.5.1 Coproscopical Methods

Although oocysts can be detected by microscopic examination of diarrheic feces in heavily infected lambs, concentration methods are often necessary for the detection of oocysts (Vadlejch et al., 2011 [43952] [1726]).

Flotation methods using solutions with densities > 1.18 are useful in the detection of *Eimeria* spp. oocysts from feces. Among them, one of the most widely used is the saturated sodium chloride solution, although some authors suggest the use of sodium chloride solutions with higher specific gravity (1.27 g/mL) by adding glucose or sucrose flotation fluids to increase the sensitivity of this technique on ovine fecal samples (Cringoli et al., 2004 [43920] [307]; Cervantes-Valencia et al., 2016 [42483] [199]; Odden et al., 2018 [43937] [1262]).

Detection of large numbers of oocysts alone is not sufficient for diagnosis of clinical coccidiosis. Additional data on epidemiology (age, number affected, mortality) and clinical

signs (diarrhea in young animals) as well as post-mortem findings (thickening cecum, inflammation of the intestine or detection of different parasitic stages in scrapings of the intestinal mucosa) can aid diagnosis. Likewise, this diagnosis should be focused on the general situation of the herd and not on an individual basis (Hidalgo Argüello and Cordero del Campillo, 1999 [43929] [713]; Taylor et al., 2007; [44694] [1688]; de Waal, 2012 [43953] [351]).

Quantitive data on oocyst excretion are useful for diagnosis. One of the classic procedures include various modifications of the McMaster method. Nevertheless, the observation of large oocysts numbers in fecal samples is not always indicative of coccidiosis, especially when the species involved have a low pathogenicity, so a large number of oocysts can be observed in apparently healthy animals (Taylor, 1995 [44189] [1683]). On the contrary, a moderate number of oocysts of pathogenic species could be a significant indicator of coccidiosis. It should also be considered that oocysts may not be observed in animals with clinical signs during the early stages of infection (Wright and Coop, 2007 [44693] [1822]).

As indicated above, in addition to the information provided by quantitative fecal analysis, it is of great interest to collect information on the *Eimeria* species involved, given the different degrees of pathogenicity that can be observed among species (Lima, 2004 [43934] [1020]). To achieve this objective, the most feasible and widely used procedure is stool culture in a thin layer of 2.5 % potassium dichromate for 7–10 days at 20-27 °C. *Eimeria* species of each oocyst was determined by light microscopy according to the characteristics of the oocysts after sporulation (size, shape, color, presence or absence of micropyle and its cap, presence or absence of residual, polar and Stieda bodies) described by Eckert et al. (1995) [41864] [459] (Figures 9.1 and 9.2), Hidalgo Arguello and Cordero del Campillo (1999) [43929] [713] and Taylor et al. (2007) [44694] [1688] (Table 9.1). After sporulation, it is possible to differentiate between species whose nonsporulated oocysts are very similar (*E. crandallis* and *E. weybridgensis*), taking into account the size and shape of the sporozoites (Eckert et al., 1995 [41864] [459]). The same has been described by Engidaw et al., (2015)[43922] [494] for *E. parva* and *E. pallida.*

Based on the data obtained by quantitative coprological analysis and the identification of *Eimeria* spp., the participation of this protozoan in the development of intestinal diseases should be considered with counts from 50,000 OPG or higher, if a predominance of pathogenic species is found. However, a differential diagnosis has to be performed with other diseases that cause ovine diarrhea (Hidalgo Argüello and Cordero del Campillo, 1999 [43929] [713]; Chartier and Paraud, 2012 [42418] [247]; Andrews, 2013 [43915] [41]).

9.5.2 Molecular methods

Limited molecular data are available concerning molecular characterics of ovine *Eimeria* and the usefulness of PCR for differential diagnosis of ovine *Eimeria* species. It could be highlighted a quantitative PCR (qPCR) based on the amplification of a fragment of the 18 S rRNA locus and subsequent sequencing, which allows speciation and quantification of *Eimeria* spp. oocysts from fecal samples. This method is able to detect the two most pathogenic species *E. ovinoidalis* and *E. crandallis* in addition to differentiating between species with oocysts of similar size and shape (*E. crandallis/E. weybeidgensisis*) (Yang et al., 2014; [42125] [1850] Nahavandi et al., 2016 [43936] [1229]).

9.6 TREATMENT

Many anticoccidials **(see Chapter 6)** used for poultry coccidiosis have also been used to treat ovine coccidiosis (Tables 9.5, 9.6).

During an outbreak of coccidiosis, all sheep (ill and healthy) should be treated. The aim of this measure is to reduce the damage caused by the parasite to the intestinal mucosa and to ensure that subsequent recovery takes place more quickly. In these cases, if a large number of animals need to be treated, lambs may be group treated through feed or drinking water. However, in some cases, treatment must inevitably be applied on an individual basis, for example when the animals are very young, unweaned or extremely ill, and do not have regular consumption of feed or water (Taylor et al., 2007 [44694] [1688]; Andrews, 2013 [43915] [41]). Sulphonamides, amprolium, ionophores, and various triazines have been used to control coccidiosis in sheep (Engidaw et al., 2015 [43922] [494] Paula et al., 2018 [43942] [1331], Witcombe and Smith 2014 [43954] [1811]).

Triazines commonly used in veterinary species include toltrazuril, diclazuril, ponazuril (toltrazuril sulfone), clazuril, and nitromezuril, the first 2 being the most commonly used in control and treatment of ovine coccidiosis. With regard to diclazuril, although its mechanism of action is not fully known, in lambs infected with *Eimeria* spp. its activity appeared to have a direct effect on several stages of the parasite life cycle, in particular, the large first generation schizont, but also against other specific endogenous stages such as second generation schizonts and gamonts (Taylor et al., 2003 [42099] [1687]; Mundt et al., 2009 [40310] [1217]; Diaferia et al., 2013 [41854] [368]).

Several studies have been performed in sheep testing the effect of either toltrazuril and diclazuril in reducing oocyst excretion and clinical signs. In general, these studies show that clinical efficacy of toltrazuril against *Eimeria* spp. under field conditions appears to be superior to diclazuril in naturally infected lambs, as evidenced by a greater decrease in oocyst shedding, decreased diarrhea duration, and increased weight gains. However, it should be noted that the toltrazuril dose was 20 times of diclazuril (20 mg/kg toltrazuril vs. 1 mg/kg diclazuril) (Le Sueur et al., 2009 [39710] [950]; Taylor et al., 2011 [42100] [1689]; Diaferia et al., 2013 [41854] [368]; Saratsis et al., 2013 [42063] [1495]). According to the reviews carried out by Grilo and de Carvalho (2014) [43926] [628] and Engidaw et al., (2015) [43922] [494], Table 9.4 contains information on the dosage and certain properties of all these active principles for treatment of coccidiosis in lambs, which as indicated above should be subject to the corresponding sanitary legislation in each country.

When the treatment of infected animals is inevitable in coccidiosis outbreaks and the proper treatment protocols have been selected, the first control measure to be implemented should be isolation of diarrheic animals from the group to stop environmental contamination. Lambs should be treated and moved as soon as possible to uncontaminated pasture or clean and dry pens to prevent reinfection (Taylor et al., 2007; [44694] [1688]Andrews, 2013 [43915] [41]).

In very ill animals, in addition to individual coccidiosis therapy, supportive care should be taken into account in order to correct dehydration, electrolyte imbalances and re-establish homeostasis. Additionally, broad-spectrum antibiotics have been shown to prevent

secondary bacterial infections in the digestive system or respiratory complications that are frequently associated with coccidiosis in lambs. The treatment of septicemia due to alteration of the intestinal mucosal barrier induced by parasites is another complication that should be considered in more severe cases (Sudhakara Reddy et al., 2015 [41236] [1640]).

9.7 CONTROL

9.7.1 Management

A hygienic measure that seems to provide good results in housed lambs is the deep cleaning of facilities before lambing. For this purpose, a blowtorch designed to avoid fecal contamination can be used on flooring, feeders, and drinkers. If the pens do not have slatted floors, the animals should be provided with clean and dry bedding regularly replaced, and disinfected (Foreyt, 1990 [38906] [546]; Lopes et al., 2014 [43935] [1088]; Taylor et al., 2007 [44694] [1688]; Saratsis et al., 2013 [42063] [1495]; Engidaw et al., 2015 [43922] [494]).

Another measure used to prevent coccidiosis outbreaks in lambs is nutritional management. It is recommended that ewes receive good nutrition before lambing, and newborns get enough colostrum as well as vitamin and mineral supplements. Other management practices that can contribute to an environment with little oocyst contamination have already been considered in previous sections (See 3. Epidemiology), among them the rearing of animals of similar age and avoiding overcrowding are considered the most important (Taylor, 1995 [44189] [1683]; Alzieu et al., 1999 [42368] [36]).

Some of these approaches can be applied to lambs outdoor in pastures. In this case adequate turnout, grazing period, composition by age of flocks, as well as the duration of pasture rotations have to be established. Given the specificity of *Eimeria* spp., other animal species could be included in rotation programs to optimize grazing resources (Kumar et al., 2013 [43933] [921]).

9.7.2 Chemoprophylaxis/Metaphylaxis

In sheep production, management measures are generally not sufficient either to prevent the development of coccidiosis outbreaks or production losses caused by subclinical disease, so anticoccidial drugs are commonly used for preventive purposes (Platzer et al., 2005 [42038] [1359]; Le Seur et al., 2009 [39710] [950]; Taylor et al., 2011 [42100] [1689]; Saratsis et al., 2013 [42063] [1495]; Odden et al., 2017 [37570] [1263]).

The chemoprophylactic treatments with this class of drugs are usully applied in feed or drinking water for a sufficiently long time to cover the period in which there is a risk of clinical outbreaks or economic losses (Taylor and Bartram, 2012 [43949] [1685]).

a) Decoquinate: Although it can be used for curative purposes, there are several studies reporting the benefits of feeding lambs with decoquinate to control coccidiosis. The treatments may include dosing of ewes 28 days before lambing (0.5 mg/Kg body weight/day), as well as lambs for at least one month from 2 weeks of age at a daily dosage of 1 mg/kg body weight. Decoquinate should not be

administered to sheep used to produce milk for human consumption (Taylor and Bartam, 2012 [43949] [1685]; Andrews, 2013) [43915] [41].

b) Other chemoprophylactic drugs: Clopidol, robenidine, and sulphonamides included in sustained-release intra-ruminal boluses be used to control ovine coccidiosis (Gutiérrez-Blanco et al., 2006 [43927] [649]; Grilo and De Carvalho, 2014 [43926] [628]).

Some preventive protocols in which all these products are used as have been reviewed by Grilo and de Carvalho (2014) [43926] [628] and Engidaw et al., (2015) [43922] [494] (Table 9.5).

When anticoccidial agents develop an activity against all parasitic stages, they are usually applied as therapeutic agents or in a metaphylactic basis before the clinical signs of the disease develop, to futher allow the generation of protective immune responses against later reinfections. In these cases, the application of the drug at a more specific time (1 or 2 treatments, 2 or 3 weeks apart), which usually coincides with the pre-patent period, but established on the basis of the history of the farm as well as the management and rearing systems carried out, aiming for the desired effect in terms of reducing the negative impact of the disease, and also enabling the development of protective immune responses. Therefore, the same pharmacological groups considered in the treatment of ovine coccidiosis, for example the triazines, could also be used for metaphylactic purposes, even at the same dose (Mundt et al., 2009 [40310] [1217]; Taylor et al., 2011 [42100] [1689]; Ruiz et al., 2012 [40864] [1460]; Andrews, 2013 [43915] [41]; de Souza Rodrigues et al., 2017 [41842] [347]).

9.7.3 Anticoccidial Drug Resistance

Testing for anticoccidial efficacy are not standardized for sheep as in other species, so the most advisable method would be controlled efficacy test based on experimental infections with both suspected resistant and known sensitive strains. These procedures have also been able to demonstrate that also in sheep the intensive long-term use of anticoccidial drugs has to the emergence of resistant *Eimeria* spp. strains although the number of reported cases is still low for the moment (Joachim et al., 2018a [42235]; Odden et al., 2018b [43938]).

9.7.4 Alternative Control Methods

There is a current interest in the use of so-called natural products, which include fungal extracts, plant extracts, and probiotics to reduce problems caused by coccidiosis. Accordingly, there are many studies that have been conducted, especially in the control of avian coccidiosis, which have resulted in the use of dietary supplements with anti-inflammatory, antioxidant activities, or immune system stimulating effects. Among these supplements are some fats, natural antioxidants, essential fats, and herbal extracts or medicinal plants (Quiroz-Castañeda and Dantán-González, 2015 [40652]).

In relation to the control of coccidiosis in sheep, most of the information available on the use of natural supplements focuses on the use of medicinal plants. That is the case with tanniferous plants such as sainfoin (*Onobrychis viciifolia*) or sericea lespdeza (*Lespedeza cuneata*). These plants, which have also shown anthelmintic activity, have demostrated their effect to control coccidiosis when used as a supplement in ewes (from before lambing to weaning) or in lambs (Saratsis et al., 2012 [42062] [1496]; Burke et al., 2013 [41798] [164]; Saratsis et al.,

2016 [42064] [1497]).

Some other extracts from curcuma or from some citric fruits have also been preliminarily evaluated in the control of ovine coccidiosis, which have shown interesting results, but require further research to confirm a possible use as natural supplements in the control of coccidiosis in this ruminant species. Similarly, given the role that some minerals play in generating immune responses, and that some of them are affected in the course of infection, mineral supplementation could also be a future alternative (Davoodi and Kojouri, 2014 [44182] [342]; Cervantes-Valencia et al., 2016 [42483] [199]; Pérez-Fonseca et al., 2016 [42037] [1352]).

In contrast to avian coccidiosis, where vaccination is a control alternative to the use of anticoccidial drugs, only a few preliminary trials have been carried out for the development of vaccines against *Eimeria* spp. in small ruminants, so the use of vaccines in sheep does not seem feasible in the short term (Catchpole et al., 1993 [38333] [186]; Ruiz et al., 2014 [40865] [1462]).

Figure 9.1. Morphological characteristics of oocysts of *E. ovinoidalis* (A=unsporulated, B=sporulated), *E. crandallis* (C= unsporulated, D= sporulated), *E. ashata* (E), *E. bakuensis* (F), *E. marsica* (G), and *E. parva* (H).

Figure 9.2. Sporulated oocysts of ovine *Eimeria* spp. (From Eckert et al., 1995) [41864]

Figure 9.3 Lesions in lambs infected with *Eimeria* spp. (**A**) Thickened ileum. (**B**) Thickening of the mucosa with scattered whitish nodules (arrows). (**C**) Blunt ileal villi: hyperemia and hemorrhage were observed below the epithelium. H&E. Bar= 240 µm. (**D**) Ileal villi with many *Eimeria* spp. (arrows) in both the epithelium and the lamina propria. H&E. Bar= 60 µm. (**E**) Crypt abscesses (arrows) in the ileum; note the infiltration of inflammatory cells in the lamina propria. The surface epithelium is flat and villi are absent. H&E. Bar= 240 µm. (**F**) *Eimeria* spp. stages in the crypt epithelium and lamina propria of the cecum (arrows). There is hypertrophy of the crypt epithelium and infiltration of inflammatory cells in the lamina propria. H&E. Bar= 60 µm. (Photos: Courtesy of A. Odden).

Table 9.1 Morphological characteristics of *Eimeria* Species of Sheep (Hidalgo Argüello and Cordero del Campillo, 1999; [43929] [713] Taylor et al., 2007) [44694] [1688].

***Eimeria* spp.**	**Size (µm)**		**Oocyst shape/color**	**Micropile**	**Polar cap**	**Residual body**		**Polar granules**
	Oocyst	Sporocyst				Oocyst	Sporocyst	
E. ahsata HONESS, 1942	29-37 x 17-28 (33.4-22.6)	18-20 x 6-10	Ellipsoidal/ yellowish-green to yellowish-brown	+	+	-	+	+
E. bakuensis MUSAEV, 1970	23-33 x 18-24 (31 x 20)	11-17 x 6-9	Ellipsoidal/Light green to brown	+	+	-	+	+
E. crandallis HONESS, 1924	18-25 x15-23 (21.9 x 19.4)	8-11 x 5-8	Ellipsoidal/Colorless-yellowish brown	+	+	-	+	+
E. faurei MOUSSOU and MAROTEL, 1902	28-37 x 21-27 (32 x 23)	14-16 x 8-9	Ovoid/ Colorless or yellowish brown	+	-	-	-	+
E. granulosa		13-16 x 8-9	Urn-shape/ Yellow-greenish	+	+	-	+	-

CHRISTENSEN, 1938								
E. intrincata SPIEGEL, 1925	22-35 x 17-25 (29.4 x 20.9)	16-18 x 8-10	Ellipsoidal/ Dark brown	+	+	-	+	-
E. marsica RESTANI, 1971	40-56 x 30-41 (48 x 34)	8-11 x 4-6	Ellipsoidal/ Colorless to light yellow	+	+	-	+	+
E. ovinoidalis McDOUGAL, 1979	15-22 x 11-14 (19 x 13)	5-6 x 3-4	Ovoid-Spherical/ Colorless to light greenish-grey	-	-	-	+	-
E. pallida CHRISTENSEN, 1938	17-25 x 13-20 (23-18)	6-9 x 4-6	Ellipsoidal/ Colorless to light yellow	-	-	-	+	±
E. parva KOTLAN, MOSCSY and VAJDA, 1929	12-20 x 8-15 (14 x 10)	6-13 x 5-8	Subspherical-Spherical/Colorless or slightly brownish yellow	-	-	-	+	-
E. weybridgensis NORTON,		13-15 x 6-8	Ellipsoidal-Subspherical/ Colorless and dark inner membrane	+	+	-	-	+

JOYNER and CATCHPOLE, 1974	13-22 x 11-13 (16.5 x 14)	**Table 9.2 Sporulation Time at 20 ºC and 27 ºC of Ovine *Eimeria* spp. Oocysts** (Hidalgo Argüello & Cordero del Campillo, 1999; [43929] [713] Engidaw et al., 2015) [43922] [494].
	17-30 x 14-19 (24 x 17)	

***Eimeria* spp.**	**Sporulation time at 20 ^{0}C (hours)**	**Sporulation time at 27 ^{0}C (hours)**

Table 9.3 Endogenous Stages, Site of Infection and Prepatent Period of Most Prevalent *Eimeria* spp. in Sheep (Data compiled and adapted from Levine and Ivens, 1986, [10121] [10122] Hidalgo Argüello and Cordero del Campillo, 1999; [43921] [43] Taylor 1995 [44189] **1683** and Taylor et al., 2007) [44694] **1688**.

E. ahsata	48-72	16-32
E. bakuensis	48-96	24-42
E. crandallis	24-72	41-65
E. faurei	24-72	24-41
E. granulosa	72-96	36-41
E. intrincata	72-168	68
E. marsica	72	72
E. ovinoidalis	24-72	24-44
E. pallida	24-72	24-44
E. parva	72-120	48-68
E. weybridgensis	24-72	45

Site of Infection	Prepatent Period (Days)	Meronts/Schizonts, merozoites	Gamonts
Small Intestine	18-30	1G: 256 x 162 µm. Thousands merozoites 2G: 52 x 30 µm. 48 merozoites aprox. (1.6-5 µm)	Macro: 35-45 µm Micro: 26-36 µm
Small Intestine	18-29	1G: 122-146 µm. Thousands merozoites (2 x 9 µm) 2G: 10 X 15 µm	NS
Ileum and cecum, colon	15-20	1G: 250 µm. 250,000 merozoites aprox. (1.7 x 10 µm)	NS
Small and large Intestine	13-15	2G: 5-9 merozoites 1G: 45-100 µm. Large merozoites (4 x 19.5 µm)	Macro: 25-54 µm Micro: 36-71 µm
NS	NS	NS	NS
Small intestine	23-27	G1: 37,5-75 400 merozoites (1.7 x 12 µm)	Macro: 29-32 µm Micro: 34-52 µm
NS	14-16	NS	NS
Ileum and cecum, colon	12-15	1G: 290 µm. Many thousands of merozoites (2 x	Macro: 12 x 16 µm Micro: 12 x 15 µm

		12 µm). 2G: 12 µm 24 merozoites (1.4 x 5.5 µm)	
	NS		NS
NS		NS	
	12-14		Macro: 10-19 µm
Small intestine		G1: 128-256 µm. Thousand of merozoitos (12	Micro: 10-19 µm
	23-33	µm)	NS
Small intestine,		G2: 60 µm	
Mesenteric lymph node		NS	

1G: First generation schizonts. 2G: Second generation schizonts. Macro: Macrogamonts. Micro: Microgamonts. NS: Not stated.

Table 9.4 Drugs Used in the Treatment of Coccidiosis in Lambs (Grilo and de Carvalho, 2014 [43926] [628]; Engidaw et al.,2015 [43922] [494]).

Chemical group	Active principle	Dosage/remarks
Nitrofurans	Amprolium	40-50 mg/Kg BW. Orally for 5-7 days.
Sulphonamides	Sulfaguanidine	100-280 mg/Kg BW. Orally for 4-7 days.
	Sulfadimethoxine	20-75 mg/Kg BW. Orally for 3-5 days.
	Sulfadimidine	135-200 mg/Kg BW. Orally for 3-5 days
	Sulfadoxine	16-24 mg/Kg BW. Intramuscular. 3 days.
Triazines	Diclazuril	1 mg/Kg BW. Orally.
	Toltrazuril	

20 mg/Kg BW. Orally.

BIBLIOGRAPHY