An overview of intestinal coccidiosis in sheep and goats

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SUMMARY

Intestinal coccidiosis is one of the most important parasitic diseases of small ruminants worldwide. Several Eimeria species including E. arloingi, E. ninakohlyakimovae and E. christenseni in goats and E. ovinoidalis, E. ahsata and E. bakuensis in sheep are the most pathogenic. The disease is more serious in 4-6-month old kids and lambs and also when animals of any age are kept under conditions of intensive husbandry. Stress factors such as weaning, inclement weather, dietary changes, traveling and regrouping have important roles in small ruminant coccidiosis. The pathogenesis comprises three phases including one or more generations of asexual multiplication by merogony, sexual reproduction by gamogony, and asexual reproduction by sporogony. The most common gross lesions are multiple small pale nodules 1-2 mm in diameter on mucosa of small intestines especially jejunum and ileum. In advanced cases, multifocal to coalescent thickening, folding or corrugating to pseudoadenomatosis of the intestinal mucosa associated with numerous well-raised whitish nodules are seen that may be the result of mitogenic stimuli of progamonts. The main histopathologic lesions are papillary hyperplasia of villi epithelium associated with the presence of intracytoplasmic developmental stages of the parasite and infiltration of inflammatory cells. Accurate diagnosis of clinical and subclinical infections and prompt treatment, control and prevention is quite necessary for preventing of great economic losses of this disease in the herds.

Keywords: intestinal coccidiosis, Eimeria species, pathology, small ruminants

Introduction

Coccidial infection is universal in sheep and goats, and coccidiosis can be a significant problem in the young of both species. The coccidians are members of the protistan phylum Apicomplexa, subclass Coccidiasina, intracellular parasites, characterized at some stage of the life cycle by a typical apical complex of organelles at one end of the organism. Members of the genus Eimeria and Isospora are homoxenous with sexual and asexual development taking place in a single host. The etiology of coccidiosis in sheep and goats is complicated by the morphologic similarity of the coccidia infecting these species [18, 67].

Recent studies and reports in some countries such as Sri Lanka [16], Iraq [2], Jordan [1], Austria [56], Turkey [22], Saudi Arabia [66], China [69], brazil [61] and Iran [26, 38, 40, 57, 75] have indicated that small ruminant coccidiosis is an important clinical and subclinical disease which may be associated with significant economic losses, particularly in intensive breeding conditions accompanied by a high animal density and high productivity [17].

The economic impact of coccidiosis in small ruminants is not well documented and there is no published data about estimate for economic losses due to subclinical or clinical disease in tropical regions. The economic cost is considerable, in terms such as low growth performance, decrease in productivity, mortality, morbidity, and the cost of prevention and treatment. These losses can be linked to reduced production, in the case of moderate infection without clinical signs or direct consequences of diarrhea on the growth of the animals and on mortality, in the case of clinical coccidiosis [8, 17]. Some assumed parameters for estimation of economic losses are summarized in Table I.

Coccidia can invade and destroy intestinal cells of the hosts, causing anemia, electrolyte loss and poor absorption of nutrients. The most common clinical sign of infection is diarrhea, and affected sheep and goats can show a rough hair coat, poor weight gain and weakness [69].

RéSUMÉ

La coccidiose intestinale chez les moutons et les chèvres : revue bibliographique

La coccidiose intestinale est l’une des maladies parasitaires les plus importantes des petits ruminants dans le monde entier. Différentes espèces d’Eimeria, dont E. arloingi, E. ninakohlyakimovae et E. christenseni chez les chèvres et E. ovinoidalis, E. ahsata et E. bakuensis chez les moutons sont les plus pathognomes. La maladie est plus grave chez les jeunes et lorsque les animaux de tout âge sont maintenus dans des conditions d’élevage intensif. Les facteurs de stress tels que le sevrage, les intempéries, les changements alimentaires, les déplacements et le regroupement ont un rôle aggravant importants. La multiplication du parasite comprend trois phases incluant un ou plusieurs cycle de multiplication asexuée par merogonie, la reproduction sexuée par gamogonie et la reproduction asexuée par sporogonie. Les lésions macroscopiques les plus courantes sont des petits nodules multiples pâles de 1-2 mm de diamètre sur la muqueuse de l’intestin grêle notamment le jéjunum et l’iléon. Dans les cas avancés, on constate un épaisseissement multifocal à coalescent, un pliage ou des ondulations pseudoadénomatoses de la muqueuse intestinale associées à la présence de nombreux nodules blanchâtres élevés qui peuvent être le résultat de stimuli mitogènes de progamonts. Les principales lésions histopathologiques sont une hyperplasie papillaire de l’épithélium des villi associées à l’infiltration par des cellules inflammatoires. Un diagnostic précis des infections cliniques et subcliniques et un traitement, un contrôle et une prévention sont nécessaires pour limiter l’importance de cette maladie.

Mots-clés : coccidiose, Eimeria, mouton, chèvre, petits ruminants
Pathologic lesions vary from proliferative in sheep and goats to necrotic-hemorrhagic in cattle, avian species, dogs and cat [18, 67]. This paper reviews the prevalence, pathology, pathogenesis, immunity, diagnosis and control of intestinal coccidiosis in sheep and goats.

Coccidian of sheep and goats

The number of *Eimeria* species considered to be parasites of sheep and goats is variable and controversial, and depends upon the acceptance of the validity of some species [59]. Several species considered as parasites of both goat and sheep were not able to infect one or other of those hosts in cross transmission studies [48, 50]. *Eimeria* species of goat and sheep are listed in Table II. In sheep, fifteen species of coccidia have been described, of which *E. ahsata*, *E. ovinoidalis*, and *E. bakuensis* are considered serious pathogens [58]. Of 16 species of *Eimeria* have been described from goats in different parts of the world, *E. christenseni*, *E. arloingi*, *E. caprina*, and *E. ninakohlyakimovae* are reported as the most pathogenic species [38, 57].

Most species of coccidian look and behave similarly in sheep and goats, but do not cross-infect. Only three species including *E. pallida*, *E. caprovina* and *E. punctata* may occur in both sheep and goats, although the validity of *E. punctata* as a species is questioned [67].

Prevalence and geographical distribution

Coccidia of small ruminants are present worldwide and it seems difficult to say that there is any particular geographical distribution for one or the other species of coccidia. Although, a dozen species of coccidia are found in each of sheep and goats; of these a few are potentially highly pathogenic, whereas several others have little pathogenic effect under normal circumstances.

In the literature review of mostly recent decade, there are various reports on prevalence rate of *Eimeria spp.* in sheep and goats as summarized in Table III.

According to these studies, the variation in prevalence and distribution of coccidiosis may be attributed to the differences in management and hygienic conditions, temperature, agroecology, climate, weather conditions, the immune state of the host, sample size, sampling period and breed susceptibility to coccidia in different areas.

The evaluation of the influence of management conditions on the prevalence of *Eimeria* infections showed that the lower incidence of disease observed in large farms, which did not necessarily correspond to farms with intensive systems, were probably related to the stricter hygienic measures and deparasitation strategies employed in these farms, although other aspects such as the degree of immunological

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Subclinical coccidiosis</th>
<th>Clinical coccidiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor feed conversion rate</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Poor body weight gain</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Weight loss</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Intercurrent or concurrent diseases</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Reduce productions (milk, wool, hair)</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Losses due to mortality</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Chemoprophylaxis</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Treatments</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Carcass deletion in slaughterhouse</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Intestine deletion in slaughterhouse</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Reduced fertility</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Table I: Assumed parameters for estimation of economic losses due to coccidiosis in sheep and goats.

<table>
<thead>
<tr>
<th>Animals</th>
<th>Eimeria species</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep</td>
<td><em>E. ahsata</em>, <em>E. bakuensis</em>, <em>E. crandallis</em>, <em>E. faurei</em>, <em>E. granulosa</em>, <em>E. gonzalezii</em>, <em>E. gilruthi</em>, <em>E. intricata</em>, <em>E. marsica</em>, <em>E. ovinoidalis</em>, <em>E. pallida</em>, <em>E. parva</em>, <em>E. weybridgetensis</em>, <em>E. punctate</em>, <em>E. dalli</em></td>
<td>[9, 15, 46, 51]</td>
</tr>
</tbody>
</table>

Table II: Eimeria species of goats and sheep.
competence due to differences in nutritional status should also be taken into account [37].

Poor hygienic sanitation could be considered as a risk factor for coccidiosis, as it can increase levels of infection/exposure and incidence of the disease due to feed and water contamination and stress-induced immunosuppression. Also, it has been reported that overcrowded conditions may result in the development of higher levels of infection in the presence of noncemented floors, a closed housing system, and large herd size, due to greater contamination of overcrowded animals and feeding and watering troughs [3].

Some researchers reported that female are more susceptible to Eimeria infection than male. This might be ascribed to sex-related factors, such as the physiological stress experienced by female animals in relation to pregnancy; giving birth and lactation could also cause female animals to be more susceptible to Eimeria infections [74].

A significant association has also been recorded between body condition score and Eimeria infection. Khan et al. (2011) reported a higher infection rate in sheep with poor body scores than in sheep with good body scores. This might be due to the weak immune status of poorly scored animals as a result of malnutrition and other parasitic infections, which results in immunocompromised [36].

Moreover, the positive correlations between the temperature and the intensity of the infection has been reported previously for semi-arid or even subhumid areas [5; 23, 68]. This correlation might be explained by the temperature-dependent sporulation rates of the Eimeria oocysts and the influence of temperature on the onset of the sporulation [19].

Differences in breed susceptibility to coccidia may also exist. In Zimbabwe, indigenous goats were found to be more resistant to coccidiosis than introduced Boer, while Angora and feral goats were reported to be more susceptible to clinical coccidiosis than dairy breeds goats [7].

### Table III

<table>
<thead>
<tr>
<th>Country</th>
<th>Goat (Species/Prevalence)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Southern Portugal</td>
<td>E. ninakohlyakimovae(88%), E. arloingi(85%), E. alijevi(63%), E. caprovina(63%)</td>
<td>[62]</td>
</tr>
<tr>
<td>Czech Republic</td>
<td>E. arloingi (84%), E. hirci (63%), E. ninakohlyakimovae(56%), E. christenseni (55%)</td>
<td>[42]</td>
</tr>
<tr>
<td>Poland</td>
<td>E. arloingi (80%), E. christenseni (70%), E. ninakohlyakimovae (40%), E. caprina (20%)</td>
<td>[5]</td>
</tr>
<tr>
<td>Gran Canaria (Spain)</td>
<td>E. ninakohlyakimovae (30.0%), E. arloingi (28.6%), E. alijevi (20.5%), E. caprina (9.1%)</td>
<td>[60]</td>
</tr>
<tr>
<td>Nigeria</td>
<td>E. jolchiev (24%), E. pallida (22%), E. arloingi (18%), E. apsheronica (16%)</td>
<td>[71]</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>E. alijevi (99%), ninakohlyakimovae, (99%), E. hirci, (83.5%), E. arloingi, (80.6%)</td>
<td>[7]</td>
</tr>
<tr>
<td>Tanzania</td>
<td>E. alijevi (63%), E. arloingi (55%), E. caprina (26%), E. ninakohlyakimovae (26%)</td>
<td>[44]</td>
</tr>
<tr>
<td>South Africa</td>
<td>E. arloingi (97.47%), E. hirci (84.34%), E. caprovina (61.11%), E. ninakohlyakimovae (45.95%)</td>
<td>[23]</td>
</tr>
<tr>
<td>Southeastern Iran</td>
<td>E. arloingi (68.26 %), E. christenseni (50.9 %), E. ninakohlyakimovae (41.8 %), E. caprina (31.7 %)</td>
<td>[37]</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>E. ninakohlyakimovae (31%), E. alijevi (29%), E. arloingi (21%), E. christenseni (7%)</td>
<td>[16]</td>
</tr>
<tr>
<td>Malaysia</td>
<td>E. arloingi (71%), E. ninakohlyakimovae (67 %), E. christenseni (63%) and E. alijevi (61%)</td>
<td>[31]</td>
</tr>
<tr>
<td>North of Jordan</td>
<td>E. caprina (13.5%), E. ninakohlyakimovae(12.5%), E. arloingi (11%), E. apsheronica (10%)</td>
<td>[1]</td>
</tr>
<tr>
<td>Northeast China</td>
<td>E. christenseni (78.3%), E. alijevi (73.7%), E. caprina (62.3%), E. arloingi (44.6%)</td>
<td>[69]</td>
</tr>
<tr>
<td>Turkey (Van province)</td>
<td>E. arloingi (40.9%), E. christensini (34.3%), E. alijevi (32.6%), E. pallida (31.0%)</td>
<td>[13]</td>
</tr>
<tr>
<td>Turkey (Igdir province)</td>
<td>E. arloingi (47.43%), E. christenseni (45.14%), E. ninakohlyakimovae (36%), E. alijevi (26.85%)</td>
<td>[22]</td>
</tr>
</tbody>
</table>

### Table III: Prevalence and geographical distribution of reported Eimeria species in sheep and goats.

<table>
<thead>
<tr>
<th>Sheep (Species/Prevalence)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>E. ovinoidealis (28.3%), E. crandallis (27.3%), E. weybridgeensis (27.3%), E. ahsata (19.1%)</td>
</tr>
<tr>
<td>Kenya</td>
<td>E. bakuensis (43.6%), E. ovinoidealis (23.6%), E. ahsata (15.2%), E. intricata (8.27%)</td>
</tr>
<tr>
<td>Tanzania</td>
<td>E. crandallis (96%), E. parva (92%), E. ovinoidealis (29%), E. weybridgeensis (29%)</td>
</tr>
<tr>
<td>Northwestern Iran</td>
<td>E. intricata (35%), E. ovina (18%), E. faurei (18%), E. parva (13%)</td>
</tr>
<tr>
<td>Western Iran</td>
<td>E. ahsata(81.46%), E. parva(67.46%), E. pallida(58.4%), E. weybridgeensis (56.26),</td>
</tr>
<tr>
<td>Northeast China</td>
<td>E. ahsata (67.2%), E. parva (59.9%) and E. weybridgeensis (44.3%), E. faurei (17.1%)</td>
</tr>
<tr>
<td>Turkey (Kars province)</td>
<td>E. ovinoidealis (47.7%), E. weybridgeensis (46.6%), E. parva (37.1%), E. granulosa (27.7%)</td>
</tr>
<tr>
<td>Turkey (Antakya province)</td>
<td>E. crandallis (64.91%), E. ovinoidealis (55.24%), E. weybridgeensis (38.70%), E. weybridgeensis (30.24%)</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>E. parva (31.7%), E. intricata (26.8%), E. arloingi (22%), E. ovina (17.1%)</td>
</tr>
</tbody>
</table>
Pathogenesis

The pathogenesis and life cycles of coccidia must be understood in order to visualize their effects upon the host. Coccidia are obligate intracellular parasites whose development within the cytoplasm of epithelial cells result in the hyperplasia or death of each cell that is parasitized. Mechanisms and degree of tissue damage depend on the species of *Eimeria* involved, the size of the infective dose of oocysts, stress, and various host-related factors including age, physical condition, genetic susceptibility, and degree of immunity that has developed from a previous low levels of infection. Because of diminished epithelial turnover in young animals, they are most susceptible to disease [32]. The life cycle of *Eimeria* species includes an exogenous phase of maturation of the oocyst (sporogony), and a parasitic endogenous phase within the host with an asexual followed by a sexual multiplication.

The unsporulated oocysts are passed in the faeces and develop into the infective stage after 2–7 days according to the species of *Eimeria* and the environmental conditions, moisture, oxygen and temperature. The original single cell divides, forming four sporoblasts, each of which develops into one sporocyst, and within each sporocyst two sporozoites develop. The pathogenesis begins with infection of a cell in the intestinal mucosa, by a sporozoite released from a sporocyst in the lumen of the gut. The life cycle of coccidia are similar and comprises three phases including one or more generations of asexual multiplication by merogony, sexual reproduction by gamogony, and asexual reproduction by sporogony. Gamogony is characterized by the independent development of macrogametocytes (female) and microgametocytes (male), with the latter being motile and often produced in large numbers. In addition, the sporozoites are typically enclosed in sporocysts that form within oocysts which are passed into the environment as a resistant stage [30, 45].

The sporulated oocysts show a great resistance in the external environment. They can survive several months or even more than one year. However, extreme desiccation, direct exposure to the sun limit the survival of the oocysts and temperatures below −30°C or above 63°C are lethal. The oocysts are thick-wall, usually ovoid forms of the organism and resist drying and provide the means of transfer of oocysts are thick-wall, usually ovoid forms of the organism. The pathogenesis and life cycles of coccidia must be understood in order to visualize their effects upon the host. Coccidia are obligate intracellular parasites whose development within the cytoplasm of epithelial cells result in the hyperplasia or death of each cell that is parasitized. Mechanisms and degree of tissue damage depend on the species of *Eimeria* involved, the size of the infective dose of oocysts, stress, and various host-related factors including age, physical condition, genetic susceptibility, and degree of immunity that has developed from a previous low levels of infection. Because of diminished epithelial turnover in young animals, they are most susceptible to disease [32]. The life cycle of *Eimeria* species includes an exogenous phase of maturation of the oocyst (sporogony), and a parasitic endogenous phase within the host with an asexual followed by a sexual multiplication.

Once ingested by the host, the oocysts undergo a process of excystation. The sporozoites penetrate into an epithelial cell of the small intestine to transform into a schizont. Two asexual multiplication cycles (schizogonies) occur in the small intestine only, or in the small then large intestines, according to the *Eimeria* species. Eventually, the schizonts penetrate the epithelial cells (sexual phase or gamogony) that lead to the production of gamonts, gametes and then non sporulated oocysts that are released with the faecal matter (Fig. 1).

When ingested by the host, the wall of the oocyst breaks down and the sporozoites are released. The sporozoites penetrate into an epithelial cell of the small intestine to transform into a first generation schizont. The schizont produce motile merozoites, which may initiate another generation of schizonts in other intestinal cells or become gamont, gametes and then non sporulated oocysts that are released with the faecal matter. The second generation schizogony occurs usually in the large intestines followed by the release of another generation of merozoites, which invade epithelial cells and produce the sexual stages, the macrogametocyte and the microgametocyte. The second generation schizogony and fertilization of the macrogametocyte by the microgametocyte (gametogony) are the stages of the life cycle that cause functional and structural lesions of the large intestine [17].

Host specificity and immunity

*Coccidia* of domestic animals are relatively host, organ and tissue specific. Interestingly, sporozoites have tropisms for specific populations of villus enterocytes in specific segments of the small and large intestine. Rarely does one species of *Eimeria* complete an infectious cycle in more than one host species. Exceptions have been noted under experimental conditions. The underlying mechanisms of host specificity are not well understood, but most likely include genetic, nutritional/biochemical, and immune factors. Recently, the role of surface microneme proteins (MICs) that appear to be unique to each species of the protozoan has been established. Sialic acid, galactose, and many forms of these molecules act as receptors and are arrayed on enterocyte membranes. Patterns of these receptors likely determine the specificity for microneme proteins unique to individual species of coccidia [77].

Virulence reflects a number of factors such as the location and type of cell infected by various stages of the organism,
the function of infected cells, and the degree of host reaction stimulated by infection [67].

Immune responses to coccidia are extremely complex and different effector mechanisms may be involved depending on the stage of parasite development, prior host exposure to parasites, the nutritional status of infected animals, and the genetic makeup of the host.

Life cycle of *Eimeria* comprises several stages including intracellular, extracellular, asexual, and sexual, hence the host immunity is complex and involves many facets of non-specific and specific immunity, the latter encompassing both cellular and humoral immune mechanisms [49]. Non-specific factors include physical barriers, phagocytes and leukocytes, and the complement system. Specific host immunity is mediated by lymphocytes and their secretions such as antibodies and cytokines [76].

Specific immunity to each coccidial species develops after infection, so that young animals exposed for the first time are often more susceptible to a severe infection and clinical disease than other animals. The immunity induced by the first infection seems to protect most lambs from reinfections later in the grazing season [6].

It seems that, the age of animals plays an important role in the immune responses. Very young lambs are relatively resistant to infection with a mixture of pathogenic species of coccidia, but susceptibility increases progressively up to at least 4 weeks of age. The lambs inoculated at 4-6 weeks of age, develop severe diarrhea, whereas the same inoculum given at 1 day of age causes no clinical disease [20].

Some researchers have confirmed a protective role of maternal antibodies against *Eimeria* infection in lambs and kids. IgG1 is a predominant isotype transmitted in sheep with colostrum and its half-life time comes up to 11–13 days after birth. However, maternal antibodies will be present until 40 days after birth and can protect the animals against *Eimeria* infection. Afterwards, the level of maternal antibodies is reduced and the animal becomes susceptible to disease [14, 58].

Although, Gregory and Catchpole (1989) stated that animals with low initial antibody levels to *Eimeria* antigens tend to reach finally high titres [20], but this hypothesis is not acceptable. Otherwise, the antibody response of ageing lambs is the result of a complicated interplay between passive maternal immunity and active immunization, the type of antigen and other factors and thus not always predictable [53, 70].

In addition to the age of infected animals, differences in breed susceptibility to coccidia is also proposed. It is noted that indigenous goats are more resistant than introduced Boer goats, while Angora and feral goats were reported to be more susceptible to clinical coccidiosis than dairy breeds. Among sheep breed, Merino was found to be more resistant to coccidiosis. A similar situation was reported for *Eimeria* infections in some chicken lines [55, 76].

Although many studies have been conducted with regards to differences in a variety of immune parameters, particularly intestinal lymphocyte subpopulations and cytokine production, to ascertain the important components of acquired immunity to poultry coccidiosis, there is not enough information about small ruminant coccidiosis in this field and more studies are needed.

In the natural host, immunity is species specific such that lambs immune to one species of *Eimeria* are nevertheless susceptible to others. Additionally, different species of *Eimeria* demonstrate different tissue and organ specificity in the infected host [76].

Immunoinflammatory reactions may be incited by coccidial infection. In experimental systems, resistance to coccidial infection is thymus dependent, and is largely mediated by T-cell-promoted intracellular killing directed mainly against asexual stages in the life cycle. In mammals, acute inflammatory reactions in intestinal coccidiosis are most commonly associated with heavy infection and destruction of cells by the sexual stages and oocysts, rather than in response to asexual stages. Generally, cellular immunity is more important in resistance against reinfection than humoral immunity [67].

**Clinical signs**

Clinical coccidiosis occurs mainly in 4-6-month old kids and lambs and age, genetic susceptibility, physical condition, the degree of immunity and stress factors, such as inclement weather, weaning, dietary changes, traveling, and regrouping have important roles in clinical coccidiosis [11, 22]. The stress factors results in immunocompromised, so these animals could be more susceptible to *Eimeria* infections.

Review of experimental studies shows that the advanced clinical signs of the infected lambs or kids have no prominent difference with the used inoculated doses, but the beginning and the severity of symptoms are dose dependent [12, 25]. The main symptom is diarrhea, which can be haemorrhagic in sheep but less frequently than in cattle, while in goats is usually watery, but not bloody. The change in the feces appearance is coincided with the first appearance of oocysts which varies according to the prepatent period of each species. In many cases, the faeces are watery with clumps of mucus and color changes from brown to yellow or dark tarry [17, 42, 67].

During the period of diarrhea, the affected animals rapidly show marked dehydration, paleness of conjunctiva, listlessness, abdominal pain, tenesmus, and weight loss. The general condition of the animal is worsened because of decreased appetite. In certain conditions, coccidiosis can be characterized by sudden mortality without preceding
digestive signs, in particular amongst young animals between 2 and 4 months old. Impairment of growth is the main sign of subclinical coccidiosis [8].

**Gross pathology**

Gross lesions of coccidiosis are variable by host species, parasite species, and intestinal location. Lesions vary from proliferative in sheep and goats to necrotic-hemorrhagic in cattle, avian species, dogs and cat [18, 67]. In small ruminants, coccidial-induced enterocyte hyperplasia results in nodule formation and thickening of the intestinal wall can cause reduction in food absorption, emaciation, serous atrophy of fat, diarrhea, and dehydration. Gross lesions, even in heavily infested animals, may be minimal to absent. The minimal to moderate changes are observed as thickening of the intestinal mucosa associated with a few scattered whitish 1-2 mm in diameter non-pedunculated plaques or nodules (Fig. 2). The large schizonts of some species are sometimes grossly visible as well.

The most common lesions of clinical coccidiosis in young sheep and goats are scattered whitish non-pedunculated plaques to nodules on mucosa of small intestines. In advanced cases, multifocal to coalescent progressive thickening, folding or corrugating (Fig. 3) to pseudoadenomatosis of the intestinal mucosa associated with numerous well-raised whitish nodules (Fig. 4) are seen. These nodules, sometimes pedunculate, and about 0.3-1.5 cm in diameter are comprised of hypertrophic crypt-villus units, in which virtually every epithelial cell is infected by mainly gametocytic stages of coccidia, which, in sheep, are probably *E. bakuensis* and *E. ahsahta* and in goats, is *E. arloingi* [18, 21, 25, 28, 40, 67].

The term pseudoadenomatous has been used to describe the polypoid lesions and the oocyst patches or plaques in coccidiosis of small ruminants and may be the result of mitogenic stimuli from progamonts of the parasite. In some cases, a particular pattern of projections are visible from the serosa of affected intestines. Recently, the term of cerebriform or gyrate pattern (Fig. 5) was used as a diagnostic gross lesion of advanced naturally occurring coccidiosis in kids and lambs [40].

**Figure 2**: Clinical coccidiosis. Kid. Thickening of the jejunal mucosa and presence of scattered whitish nodules (arrows) (Scale Bar=5 mm).

**Figure 3**: Advanced clinical coccidiosis. Lamb. Thickening, folding and corrugating of the mucosa of small intestine (Scale Bar=10 mm).

**Figure 4**: Clinical coccidiosis. Lamb. Pseudoadenomatous pattern of affected mucosa of jejunum is seen due to papillary hyperplasia of epithelium (Formalin-fixed tissue; Scale Bar=5 mm).

**Figure 5**: Advanced clinical coccidiosis. Kid. Cerebriform or gyrate pattern is seen on the serosal surface of small intestine especially jejunum (Scale Bar=12 mm).
Histopathology

Although the main histopathological lesion of coccidiosis is hyperplastic or proliferative enteritis in sheep and goats, but the pathological changes vary in detail according to the species concerned. *E. ninakohlyakimovae, E. arloingi, E. christenseni* and *E. caprina* in goats and *E. ovinoidalis, E. ahsata* and *E. Bakuensis* in sheep are considered to be the most pathogenic species [12, 21, 25, 31, 42].

In most cases, loss of surface epithelial cells and villous atrophy are associated with first generation schizonts, while crypt destruction or hyperplasia are associated with gamonts [65].

*E. ninakohlyakimovae* occurs in the lower small intestine and large intestine. Hyperplasia of intestinal epithelium and subacute to chronic enteritis characterized by multifocal infiltration of lymphocytes in the small and large intestine are the main pathological changes associated with this species. Lymphoid hyperplasia in the mesenteric lymph nodes, chronic cholecystitis and focal degeneration and necrosis in the liver are also reported [12]. Ileoileal intussusception associated with coccidiosis is reported in a sheep [39].

*E. ovinoidalis* has giant schizonts up to 300 μm in diameter develop in cells deep in the lamina propria, in the terminal ileum. They release merozoites that enter epithelium in the glands of the cecum and colon, and perhaps distal ileum. Here small second-generation schizonts evolve, and other cells in glands in the same area subsequently become infected by the gametocytes. It seems that second-generation schizogony and gametogony are responsible for lesions related to diarrhea, dehydration, and hypoproteinemia which are limited to the terminal ileum, and especially the cecum and proximal colon.

*E. arloingi* and *E. christenseni* in goats and their analogues, *E. ahsata* and *E. bakuensis* in sheep, seem to have somewhat similar developmental cycles and histopathological lesions.

*E. arloingi* has a developmental cycle that involves large schizonts up to nearly 200 μm across in the endothelium of the lacteals in villi in the upper small intestine. Early histopathologic lesions due to schizogony phase are including the presence of intracytoplasmic developmental stages of the parasite such as trophozoites, immature to mature schizonts and mild infiltration of inflammatory cells (Fig. 6). The mature first generation schizonts are observed in the lacteals of villi in the proximal part of the jejunum. In this stage, there is no remarkable hyperplasia of epithelial cells of affected villi and crypts. In late lesions due to various stages of gametogony, the histological pattern is mainly remarkable hyperplasia of the epithelial cells with the presence of intracellular developmental stages of the coccidia and infiltration of inflammatory cells. Second generation schizonts and merozoites, and also gamonts, macrogametocytes, microgametocytes and oocysts are seen in the epithelial cells of affected villi and crypts (Fig. 7). The most histologic lesions are seen in the jejunum and ileum. Schizogony in intestinal epithelium induced necrosis and subsequent hyperplasia due to second generation schizonts and gamonts, eventually developed into papillary projections of reactive epithelium (Fig. 8). Infiltration of inflammatory cells especially lymphocytes and eosinophils is prominent in advanced lesions [25].

**Figure 6**: A) The presence of mature schizont in the endothelium of the lacteal in villi (H&E staining; Scale Bar=35 μm) and B) Trophozoites in the cytoplasm of enterocytes (arrow) (H&E staining; Scale Bar=5 μm).

**Figure 7**: Hyperplasia of epithelial cells of intestinal mucosa and presence of intracellular developmental stages of the parasite (H&E staining; Scale Bar=80 μm).
E. christenseni undergoes a development similar to that of E. arloingi and causes similar gross and microscopic lesions in goats, with minor differences. First-generation schizonts are most numerous in the lacteals of villi in the middle small intestine, and the associated grossly visible plaques are more common in the small intestine, while these plaques in E. arloingi may tend to be more distal in the small intestine, and occasionally involve the large intestine.

E. crandallis in sheep is characterized by villus atrophy and marked loss of crypts in infected areas of intestine. Giant first-generation schizonts develop in crypt cells that after infection migrate into the lamina propria. As the infection progresses, villi become stumpy or disappear, and in the small intestine and cecum, crypts are hyperplastic, with large, basophilic enterocytes, and reduced goblet cell numbers. Asexual or, more commonly, sexual stages of coccidia are present in the epithelium on the surface of the mucosa. In hyperplastic crypts, epithelial cells are infected by progamonts, which seem to be divided in synchrony with host cells. During the development of progamonts, infected crypts undergoing degeneration associated with infiltrations of macrophage-like cells in close proximity to crypt epithelial cells. Apoptosis of infected and uninfected cells may occur, resulting in attenuation of surviving crypt epithelium. It is unclear whether atrophy of villi is the result of excess loss of epithelium directly due to the effects of coccidial infection, or whether it is mediated by an immune response [67].

E. bakuensis like E. crandallis, forms progamonts that divide in synchrony with the cells they infect, but the lesions produced differ markedly. E. bakuensis produces well circumscribed oocyst patches and polyps, whereas E. crandallis caused diffuse hyperplasia. The difference can be explained by the mode of release of merozoites. E. bakuensis appears to release them into the lamina propria, producing a local lesion, whereas E. crandallis releases them into the gut lumen, to be scattered widely [21].

E. apsheronica occurs throughout the small intestine and in the cecum. This species has minor pathogenic potential in the goat. First and second-generation schizonts develop in the lamina propria of villi and in the epithelium on villi, respectively. Gametocytes have the same distribution. Pale foci in the mucosa, where gametocytes are concentrated, and focal areas of erosion and hemorrhage may occur in heavily infected animals.

Large schizonts are often encountered incidentally in submucosal lymphatics, or in the subcortical or medullary sinuosids of mesenteric lymph nodes in sheep and goats infected with E. bakuensis, E. ninakohlyakimovae and E. arloingi. Sometimes they may be visible grossly in these locations as pinpoint white foci. The presence of schizonts or other stages in lymph nodes are the result from establishment of sporozoites or merozoites migrating from the lacteals into the lymphatic drainage in early infection [12, 67].

**Diagnosis**

The diagnosis of coccidiosis depends on the clinical findings (diarrhea, dehydration, and progressive emaciation), the presence of large numbers of oocysts in the feces, appropriate signalment and intestinal lesions at necropsy and history [43]. Diagnosis is not easy because clinically normal sheep and goats often shed coccidial oocyst. Furthermore, there may be considerable intestinal damage and scouring even before oocysts appear in the faeces.

The developmental stages of Eimeria spp. in the intestinal cells can be demonstrated in Giemsa-stained intestinal smears or scrapings and, in haematoxylin eosin stained histological sections. The demonstration of various developmental stages of Eimeria spp. and the denudation of the intestinal epithelium in dead or sacrificed animals is considered to be a positive diagnosis for coccidiosis. Postmortem examination is the best means of confirming the diagnosis, providing is performed immediately after death. The intestines may be slightly reddened and full of fluid, but the most characteristic feature of coccidial infection is the presence of multiple small pale nodule 1-2 mm in diameter in the intestinal wall [8, 18, 40, 43, 67].

Microscopic analysis of faecal samples makes it possible to quantify the rate of infestation by counting the number of oocysts excreted per gram of faeces (OPG). Although this method can support the diagnosis, but it is usually not very
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Faecal oocyst counts on about 10 kids are needed in order to obtain a correct estimation of the average excretion of a group of animals. Despite the general relationship between clinical coccidiosis and high excretion of oocysts, a clear-cut threshold for coproscopical values is difficult to assess.

Accurate diagnosis of the causative agent of coccidiosis is very important and helps us to have a better understanding of the biology and life cycle of this parasite. The traditional methods are not only very subjective and time consuming but are also unreliable since the different species have overlapping properties [29]. Furthermore, morphological examinations combined with faecal examination are very labor-intensive and require skillful technique. It is essential to develop a more rapid, convenient, and accurate diagnostic method. Thus, molecular tools have recently been proven useful for the species identification or classification of this genus to overcome the limitations of traditional methods [72] and have furthermore demonstrated the phylogenetic position of each *Eimeria* spp. and host–parasite relationship by forming some phylogenetic clades [54, 78].

Although many studies were conducted to find molecular characterization and phylogenetic position of avian *Eimeria*, but there are a little information about *Eimeria* species in ruminants and it is only limited to studies of Kawahara et al. (2010) and Khodakaram-Tafti et al. (2013) in cattle and goats, respectively. These researchers showed that 18S rDNA gene sequences and the internal transcribed spacer1 (ITS1) region derived from the ribosomal RNA (rRNA) genes can be used effectively to define the genetic characterization and phylogenetic analysis of some *Eimeria* species [34, 41].

In details, the phylogram based on the ITS1 sequences shows that the *E. arloingi* in goats and *E. bovis* and *E. zuernii* in cattle form a distinct group separate from the other *Eimeria* species in spite of many different biological characteristics and the pathological lesions. Moreover, the 18S rDNA sequence derived from *E. arloingi* shows 99% similarity to *E. ahsata* and differences are found in only three nucleotides. It is quite interesting that these two species have similar pathologic lesions in spite of many different morphological features of the oocysts and different host [67].

The use of acute phase proteins (APPs) and inflammatory mediators such as haptoglobin (Hp), serum amyloid A (SAA), TNF-α and IFN-γ have been suggested as a non-specific marker for disease as well as for monitoring the response to treatment in coccidiosis. Measuring APPs along with clinical signs and oocysts per gram (OPG) can be useful for providing information about the stages of clinical and subclinical coccidiosis [24]. Mucosal scrapings or tissue sections of mucosa containing large numbers of asexual and gametogenous coccidial forms in association with diarrhea and perhaps some hemorrhage into the intestine, support the diagnosis, in the absence of other syndromes such as gastrointestinal helminthosis [67]. Accurate diagnosis of clinical and subclinical infections and prompt treatment, and prevention is quite necessary for preventing of great economical losses of this disease in the herds.

**Treatment**

Treatment must be done as early as possible and concern the whole group of animals (age, paddock) as animals showing no obvious signs may contaminate the environment. Treatment has to be associated with a move of the animals to a cleaner environment [8].

Coccidiosis can be treated using decoquinate (0.5 mg/kg BW) and lasalocid at a dose of 25-100 mg/kg feed from weaning until market [10]. Sulfonamides at dosage rates of 25 to 35 mg/kg BW for at least 15 days are effective against coccidiosis in small ruminants. A combination of chlorotetracycline and sulfonamide has provided protection in lambs. Amprolium in feed is also used to treat the disease in goats (100 mg/kg BW for 21 days) and sheep (50 mg/kg BW for 21 days) [10]. Other drugs include monensin (20 and 16 g/ton of feed for sheep and goats, respectively), toltrazuril (20 mg/kg BW as a single oral dose) and diclazuril (2 mg/kg BW as a double oral dose) [10, 43, 59]. Decoquinate, toltrazuril and diclazuril are molecules which act on the whole cycle of the coccidia and this allows both a curative and a preventative effect [10, 65].

**Prevention**

The control of coccidiosis assumes greatest importance in kids and lambs, and has been difficult to achieve with reliability. Prevention relies on the control of hygienic conditions, the reduction of stressors, an adequate nutrition and the use of anticoccidial drugs [17].

Proper hygiene in the house and minimization of predisposing factors are important factors to be considered in the control strategies of coccidiosis [10]. Lambing and
kidding grounds should be well drained and kept as dry as possible. Lambing pens should be kept dry, cleaned out frequently, and bedding disposed of so that oocysts do not have time to sporulate and become infective. One animal, or only a few animals at a time, should use maternity areas. The cleaning and disinfecting of the buildings must be done with boiling water under pressure and gaseous ammonia when possible [64].

Long kidding/lambing seasons predispose to a progressive heavy contaminated environment and to mixing of different age groups that is very favorable to clinical coccidiosis. In this situation, the main objective is to raise later-born lambs or kids on different paddocks/pastures from early animals in order to avoid highly contaminated areas [6].

All measures that minimize the amount of fecal contamination of hair coats and fleece should be practiced regularly. Feed and water troughs should be high enough to avoid heavy fecal contamination. Feeding animals on the ground should be avoided if possible, particularly when overcrowding is a problem. In groups of lambs at pasture, the frequent rotation of pastures for parasite control will also assist in the controls of coccidial infection. However, when lambs are exposed to infection early in life, a solid immunity usually develops and only when the stocking density is extremely high will a problem develop [10].

To reduce the risk of introducing infected animals, several points need to be considered. The herd or flock should be tested to identify infected animals that are, or probably will be, shedding the oocysts. Based on the test results, chronically infected animals with persistent infection that are not responding to treatment should be removed to prevent infection in lambs and to allow the flock a chance to become reinfected. Chronically infected animals that are not responding to treatment should be removed to prevent infection in lambs and to allow the flock a chance to become reinfected. The medication of feed for ewes may reduce the output of oocysts but may not prevent infection in lambs and thus a regular monitoring of the treated animals is needed. The medication of feed unpalatable and toxic [17, 73].

Coccidiosis prophylaxis by coccidiostats in drinking water or feed are commonly employed to control the disease in intensive production systems. Decoquinate (0.5 mg/kg) in feed mixtures is a safe and very effective coccidiostat in goats and sheep. Monensin fed prophylactically at 20 mg per ton of feed controls shedding of oocysts and increases feed conversion. However, high levels of monensin render the feed unpalatable and toxic [10]. The continued use of coccidiostats lessen the number of oocysts passed in the faeces over time, but may also lead to selection for resistance and thus a regular monitoring of the treated animals is needed. The medication of feed for ewes may reduce the output of oocysts but may not prevent infection in lambs and thus seems not advisable [17, 73].

Competing interests

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.

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