COCCIDIOSIS

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Introduction

Coccidiosis, a protozoal disease of many mammalian, and all domestic livestock species, is caused by infection with species of the genera *Eimeria* or *Isospora*. Clinically it is characterized by enteritis although subclinical infections are frequent. The disease is relatively common in sheep, goats and cattle, rare in horses and an important disease of pigs in North America and Europe. It is of major economic importance to the poultry industry worldwide and has also been reported to be of economic significance in turkeys and pigeons. It has been described in a large number of different wildlife species.

Clinical disease is most prevalent where animals are subjected to overcrowding, unhygienic environments, or when animals are stressed. Coccidia are generally host-specific parasites, and very specific to a particular region in the intestines. *Eimeria* infections are more specific compared to *Isospora* infections. Economic loss in clinical disease is mostly attributed to mortality, poor performance, and the costs of treatment and prevention and although subclinically infected animals may appear normal they may have reduced feed consumption, feed conversion and growth performance. This article will mainly deal with disease in domestic ruminants.

Aetiology and life cycle

The most important species in sheep are *Eimeria ahsata*, *E. ovinoidalis* and *E. bakuensis*. The more important species in goats are *E. arloingi*, *E. chistenseni*, *E. hirici*, *E. jolchijevi*, *E. alijevi*, *E. kocharli*, *E. apsheronica*, *E. ninakohlyakimovae*, *E. caprina* and *E. caprovina*. A large number (approximately 20) of *Eimeria* species have been identified in cattle and most are relatively non-pathogenic. Field outbreaks of coccidiosis are generally caused by mixed infections of *E. zuernii* while infections with *E. bovis* is playing a lesser role. *E. debliecki*, *E. neodebliecki*, *E. porci*, *E. suis*, *E. scrabra*, *E. polita*, *E. perminuta* and *E. spinosa* are common in pigs and are considered to be either non- or mildly pathogenic and are not significant causes of disease in pigs. *Isospora suis* occurs in the small intestine and sometimes the colon of pigs giving rise to porcine neonatal coccidiosis. *Eimeria leuckarti* is occasionally diagnosed in horses and although it may be pathogenic it is usually an incidental finding.
In a recent CPD article published by Penzhorn (2009) a good overview is given on the current knowledge of coccidiosis in wildlife in South Africa. It has been described to be of clinical importance in buffalo, impala and springbok under certain and favourable conditions and game farming/management systems (breeding programs, captivity etc). Other African wildlife species in which infection has been described include Eland, Generuk, Hartebeest, Impala, Waterbuck, Defassa and Blue wildebeest.

Coccidia are primarily intracellular parasites targeting the gastrointestinal tract and has three stages of the life cycle namely merogony (asexual cycle), gametogony (the sexual cycle) and sporogony. The first two stages occur within the host cells and sporogony outside the host. After ingesting sporulated oocysts, sporozoites are released. Sporozoites enter epithelial or other cells of the mucosa where they become meronts and multiply by merogony (schizogony) to produce merozoites, the segment of intestine affected and the number being produced depending on the species of coccidian. These merozoites enter neighbouring epithelial cells in the gut and multiply again by merogony. The number of asexual generations remains constant for each species and the last generation merozoites infect new host cells and become gamonts. This initiates the sexual stage of the life cycle. Some of these gamonts will develop into macrogametes without further multiplication, and others will form a large number of flagellated microgametes by multiple fission. Microgametes are released and penetrate the macrogametes to form a zygote and a thick encompassing wall is formed around each zygote - forming the oocyst. When cells rupture oocysts are released into the intestinal lumen of the gut, and are excreted in the faeces as unsporulated oocysts. These oocysts sporulate and sporocysts containing infective sporozoites are formed taking between two and five days under optimal environmental conditions, which include temperature of 24°C to 30°C, sufficient humidity and oxygen. It takes approximately 14 to 21 days to complete the cycle from the beginning of merogony to the release of newly produced sporozoites depending on the species of *Eimeria* and the host. Clinical coccidiosis is usually seen during the late stages of gamogony.

**Epidemiology**

Coccidiosis is mostly a disease of young animals raised and kept under intensive management systems although older animals may occasionally be clinically affected. Disease usually occurs when the resistance of the host is lowered following stress, overcrowding, weaning, transportation, housing under conditions of poor hygiene, food changes, nutritional deficiencies, concomitant infections with other parasitic/infectious agents and adverse weather conditions.

High temperatures and humidity encountered in overstocked feedlots, pens containing straw bedding, or in kraals and irrigated pastures, are favourable for the survival of oocysts and therefore higher infection rates compared to extensive farming systems. Animals housed in separate pens may also be infected by airborne transfer of oocysts. Most infected animals become subclinically infected and continual reinfecion may occur. These animals then shed small numbers of oocysts in their faeces for long periods of time. Sporulated oocysts are very resistant to adverse environmental conditions and may survive on the pastures until the next season which then act as a source of infection when climatic conditions become favourable.
In a study commonly increased with age. Anti significantly decreased with increasing age of the calves, while the percentage of positive samples was significantly correlated with the OPG values. Clinical coccidiosis OPG values were significantly positively correlated with the cattle density in the different districts. Of 1000 or less identified per farm. Infections in calves, which were sampled early after housing being reared on slatted floors. Younger calves and calves which were sampled early after housing shed higher amounts of oocysts compared to older calves and calves stabled for a longer period. In a study by Koutny (2011) the occurrence of different Eimeria spp in 868 individual calves from 296 Austrian farms was reported. It was found that in 97.97% of the investigated farms, calves excreted Eimeria oocysts, and 83.67% of the individual samples were positive. In total eleven Eimeria species were found, with E. bovis, E. zuernii, E. auburnensis and E. ellipsoidalis being the most prevalent, followed by E. alabamensis, E. subsphérica, E. cylindrica, and E. canadensis. Some species such as E. wyomingensis, E. pellita and E. bukidnonensis were only found sporadically. Mixed infections were present on all the farms investigated and between 2-9 Eimeria species were identified per farm. Individual OPG values were generally low and 75% of the samples had an OPG of 1000 or less with the highest detected OPG being 72400. The mean OPG was 2525 and mean OPG values were significantly positively correlated with the cattle density in the different districts. Clinical coccidiosis characterized by diarrhoea was observed in 74 cases, and (semi-)liquid diarrhoea was significantly correlated with OPG. Linear regression on the OPG data showed that OPG values significantly decreased with increasing age of the calves, while the percentage of positive samples increased with age. Anti coccidial treatment was given to 13.51% of animals with toltrazuril most commonly used.

In a study by Almeida et al (2011) to determine the presence of species of the genus Eimeria in...
naturally infected bovines in Southern Bahia, Northeast Brazil it was found that 33.33% were positive, and ten different species were identified in the infected animals. Species identified were *E. bovis* (24.79%); *E. canadensis* (8.55%); *E. zuernii* (6.83%); *E. ellipsoidalis* (5.99%); *E. cylindrica* (3.42%); *E. auburnensis* (3.42%); *E. brasilensis* (2.56%); *E. bukidnonensis* (1.71%); *E. alabamensis* (0.85%), and *E. subspherica* (0.85%). Higher levels of parasitaemia was observed in animals up to one year of age but no animal presented with clinical signs of the disease.

In sheep the most important species are *E. ovinoidalis*, *E. crandallis* and *E. ahsata*. Coccidiosis is often a serious problem in feedlots and clinical signs may develop 10 to 20 days after new lambs are introduced. Mortalities in feedlots may be high and often associated with sudden outbreaks of clinical disease.

The findings of a study by Silva *et al* (2011) into *Eimeria* infection in lambs of mixed breed raised extensively on a farm in northeastern Brazil revealed that oocysts were detected in 17% of the lambs by week 3 and in 100% of animals by week 6. Eight species of *Eimeria* were identified and in decreasing order of prevalence they were *E. crandallis*, *E. parva*, *E. granulosa*, *E. ovinoidalis*, *E. ahsata*, *E. ovina*, *E. faurei* and *E. intricata*. Of the 191 faecal samples that contained *Eimeria* oocysts, only 32 (16.8%) were infected with a single species whereas 23 (12.0%) were infected with at least two species and 136 (71.2%) harboured three or more species.

In a study conducted by Saratsis *et al* (2011) to investigate ovine coccidiosis in dairy sheep production systems in the Mediterranean area the faecal consistency and oocyst excretion were recorded in lambs. Faecal samples were collected from 220 lambs in total and from six (intensive and semi-intensive) dairy sheep flocks and from groups of lambs born during two consecutive lambing periods (autumn, spring) from each flock. Sampling started at days 7-9 after lambing and the subsequently every 6 days for 5 times. Eleven *Eimeria* species including the highly abundant pathogenic *E. ovinoidalis* and *E. crandallis* were detected. Excretion was observed to start from day 13 to 33 after birth with a peak at 19-21 days. The cumulative incidence of infection per flock until the end of the study ranged from 64.29% to 100% during both lambing periods. The authors reported a significant tendency for animals to get infected earlier during spring lambing. They also observed subclinical cases of coccidiosis during the course of the study, and a relatively low proportion of diarrhoeic animals which did not significantly differ between the two rounds of sampling.

### Pathogenesis

The coccidian species involved, prevailing environmental conditions, the size of the infective dose, the age of the host, the number of host cells destroyed, the location of the parasite in the tissues and the presence or absence of acquired immunity all will play a role in the pathogenesis, or pathogenicity, once a host animal is infected. Pathology and clinical signs of coccidiosis are nearly always caused by the development of the gamont and oocyst in the lower ileum, cecum, and colon. Most coccidia develop in epithelial cells of the lamina propria but exceptions include the first meront of *E. bovis* in the endothelial cells in the lacteals of the villi in the lower ileum of calves. Another exception is the meronts found in the intestinal lymph nodes of some sheep.

Cytokines and other factors derived from epithelial cells play important roles in inflammatory and immune responses in intestinal tissue. Once infected the intestinal epithelial cells are destroyed, or their function is impaired and, in more severe infections, an acute inflammatory reaction may be seen. The epithelium may become erosive or ulcerated resulting in haemorrhage from the capillaries in the denuded lamina propria with hypoproteinaemia and anaemia being the consequences. Secondary bacterial infections may aggravate the clinical expression of disease.
Furthermore increased rates of peristalsis and the loss of adsorptive surface or capacity may result in diarrhoea, loss of fluids, decreased absorption of electrolytes such as sodium and potassium and acidosis due to the loss of bicarbonate ions.

Depending on the severity of damage and whether the infected animal survives all the consequences of the epithelial damage, partial or complete tissue repair and recovery may occur. The combination of dehydration, acidosis, anaemia, hypoproteinaemia, and shock combined with secondary bacterial infection, are the main causes of death.

Immunity develops after infection and the cellular immunity is the most important as far as protection of the host is concerned. Drugs may also interfere with the development of immunity. The immunity that develops in response to an *Eimeria* sp infection is species-specific. Jonsson *et al* (2011) quotes that the immune response in bovines seems to follow a sequential Th1 then Th2 pattern and elevations of CD4+ lymphocytes in the circulation and lymph nodes of primarily infected calves were reported. Early primary infection is characterised by IFN-gamma and IL-2 production by lymphocytes, whilst in later phases it is characterised by IL-4 production. After an initial expansion of CD4+ T cells and gammadelta (+) T cells in the intestines of animals following on primary infection, no increased infiltration of either cell type after challenge infection was observed. Phagocytosis of *Eimeria* by macrophages independent of the presence of immune serum has also been documented. The role of neutrophils in resistance to bovine *Eimeria* has been reported to include neutrophil extracellular trap (NET) activity on sporozoites of *E. bovis* with decreased parasite infectivity (*in vitro*) as consequence. However, the role played by neutrophils and macrophages have not been elucidated in infection and challenge studies using naive animals.

Worliczek *et al* (2009) studied the immunology in pigs which revealed a rapidly increasing age resistance prohibiting the development of clinical disease in piglets older than 3-4 weeks irrespective of the immune status. The authors hypothesised that the development of the innate immune system in the first weeks of life and its subsequent interactions with the adaptive immune system may explain this phenomenon. It is reported that following infection with *I. suis* migration of TcR-gamma delta(+) cells to the intestine is stimulated during the primary infection which leads to induction of IFN-gamma production by TcR-gamma delta(+) cells and CD4(+) T-helper cells in blood and various lymphoid tissues. It is thought that both innate as well as adaptive response mechanisms are activated during infection and both might not be completely developed in the first weeks of life which therefore leaves a window period for successful infection.

**Clinical signs**

In *bovines* clinical coccidiosis is primarily seen in calves between three weeks and six months of age, although older animals may show signs of infection. Clinical coccidiosis in cattle may be deceptive, with the primary clinical signs of diarrhoea often not apparent until 3–8 weeks after initial infection. The incubation period is usually about three weeks, although it may vary between a week to more than a month in some cases. Diarrhoea may start off as watery, becoming increasingly haemorrhagic. Fresh blood and blood clots may be present in the faeces and a mucoid to mucoid and fibrinous exudate may be seen as the clinical expression of the disease progresses. Faeces may become blackish-red to blackish, or greenish-black and it may become foul-smelling with the presence of shreds of mucosa. Tenesmus, pronounced borborygmi, constant grinding of teeth, abdominal pain, prolapse of the rectum, fever, an increased respiratory rate and loss of appetite may be seen. Severely affected animals may become extremely emaciated and anaemic.
A condition known as “nervous coccidiosis” may sometimes be seen in animals 6 months or more of age, after experiencing clinical coccidiosis caused by *E. zuernii*. Affected animals may spontaneously fall to the ground followed by spasmodic, bicyclic type of leg movement, contraction of the dorsal muscles of the neck and back, causing the head to be pulled backwards. This may last for a period of several minutes, after which they spontaneously recover, rise, and resume apparently normal function. The exact pathogenesis is unknown but believed to be related to plasma electrolyte imbalance. Animals with this condition may display these symptoms for months after apparently recovering from the primary infection.

In **sheep** disease is most severe in lambs two to eight weeks of age and in lambs two to three weeks after weaning. In sheep and goats the onset of diarrhoea is usually the first sign of illness and clinically affected animals may pass soft faeces, not forming pellets, which turns to a watery diarrhoea at later stages. Although blood may be present in the faeces this is less commonly seen in sheep and goats compared to cattle. The morbidity ranges from 10-50 % and the mortality may be as high as 100%. Angora goat flocks in the Eastern Cape Province of South Africa may suffer from morbidity rates as high as 100 % with mortality rates reaching 50 %. In the sandy, arid eastern parts of Namibia “boksieke” (goat disease) has been described due to a combined infection with coccidiosis and infestation with *Stongyloides papillosus*.

Clinical disease is usually encountered in 5 to 10 day old piglets characterized by the development of diarrhoea, dehydration and loss of condition. Vomiting may be seen in some animals. Faeces is yellow to grey and do not contain visible blood.

**Pathology**

Macroscopic lesions may be seen as small white spots in the mucosa of the ileum in **cattle** with *E. bovis* infection, but with *E. zuernii* similar lesions are not visible macroscopically. In severe cases, fibrino-haemorrhagic typhlocolitis may typically be seen and in many cases also an accompanying proctitis. The terminal ileum may sometimes also be affected. The caecal, colonic and rectal content may become semi-fluid and bloody in the early stages of infection and at later stages the sloughed mucosa, excessive amounts of blood and fibrin may form fibrinonecrotic pseudomembranes. The content may become malodourous, the mucosa erosive, the submucosa oedematous with petechiation and the lymph nodes oedematous and enlarged.

In **sheep** small, white, flat to dome shaped foci (1 to 2 mm in diameter) may be seen in the mucosa and also on the serosal surface of the small intestine which is typical of the schizont stages of *E. ovinoidalis* and *E. ahsata* (sheep) and *E. ninakohlyakinovae* and *E. christensenii* (goats). In *E. bakuensis* infection discrete opaque patches may also be seen and it may also develop into raised patches or even polyps. In severely affected animals the affected intestinal segments may become oedematous and thickened and focal or diffuse congestion and haemorrhages may be seen in the mucosa. In severe cases sloughing and ulceration of the intestinal mucosa may be a consequence. Haemorrhagic enteritis is commonly seen with *E. ovinoidalis* (sheep) and *E. ninakohlyakinovae* (goats) infections. The caudal part of the small intestine may become affected and blood may be detected in the faeces.
A fibrinous to fibrino-necrotic enteritis, in the caudal part of the small intestine, may be seen in some fatal infections in pigs.

**Diagnosis**

History, clinical signs, necropsy findings and demonstration of the parasite in fresh faecal samples forms the foundation of the diagnosis. Small quantities of faeces are required for analysis but accurate species identification of the coccidian may require the expertise of experienced laboratory personnel.

Estimates of the number of oocysts in faeces is possible but care should be taken as it may be difficult to interpret the results. High oocyst counts can be present in apparently healthy animals and in contrast low counts may be present in diseased animals. In the latter scenario the majority of the parasites may not have progressed to the oocyst stage at the time of clinical or post mortem examination. Scrapings from the intestinal lesions, or tissue sections of the intestine may be examined for the presence of meronts, gamonts or oocysts. It is not uncommon for mixed infections to be seen.

Serologic analytical methods by ELISA and Western Blot have been developed, but they are not as definitive as visual examination of faeces. The use of PCR assays has been more extensively pursued in the poultry industry compared to the situation in domestic ruminants.

**Control**

Control is mainly aimed at preventing the accumulation of large numbers of oocysts in the environment by creating an adverse environment for their development. Animals should be fed clean and dry food and feed spillage to the ground from feed troughs should not take place. Leakage from water troughs should be avoided and faecal contamination of feed and water troughs should be minimized. Proper drainage of paddocks, kraals and feedlot pens is essential. Special attention should be paid to all the young and susceptible groups of animals. Any potential form of stress such as may be experienced at weaning, sudden changes of diet and transportation should be minimized. In heavily infected environments, sterilization may be attempted and may be achieved but this is usually not a practical control measure. Exposure to sunlight for at least eight hours per day, and desiccation with a humidity of less than 25%, may be more cost-effective methods.

Clinical coccidiosis is difficult to treat and mostly supportive in nature which includes the administration of antimicrobials, antidiarrhoeal compounds and fluids, and when necessary, haematinics and blood transfusions. If animals are kept in pens, those showing clinical signs should be removed. They are not to be returned to the pens until at least two weeks after the clinical signs are no longer present, as oocysts shedding may persists for some time.

Anticoccidial compounds may be used either prophylactically or therapeutically although *Eimeria* has developed drug resistance against most anticoccidials currently used. Some of anticoccidials control of avian coccidiosis are too toxic for use in ruminants. Amprolium, decoquinate, lasalocid, lincomycin, monensin, and salinomycin have all been used to treat calves, lambs, and kids. Sulphonamides commonly used for treatment of coccidiosis in ruminants are only partially effective Gut-active sulphonamides (e.g. succinylsulphathiazole and phthalysulphathiazole) should not be used. Carboxylic ionophores (coccidioidal) have a broad-spectrum activity, a narrow margin of safety and are therefore best used prophylactically. Orally administered nitrofurazone at a dose of
10 mg/kg per day for five days is effective but is not tolerated for use in food producing animals in many countries due to persistent residues. Treatment with decoquinate controlled *E. bovis* in calves when administered as daily doses for three to four weeks, without relapse after withdrawal of medication.

Toltrazuril and diclazuril are symmetric triazinetriones advocated for the treatment of coccidiosis. Mundt *et al* (2005) investigated the efficacy of metaphylactic treatment with toltrazuril against natural infections with *E. bovis* and/or *E. zuernii* in 208 calves on five calf-rearing farms in Germany and the Czech Republic. All farms had a notable incidence of coccidiosis and animals were treated 14 days after stabling. It was found that the duration and rate of oocyst excretion, the number of scour days with *E. bovis* or *E. zuernii* oocyst shedding, and the severity of diarrhoea were significantly lower in the toltrazuril-treated groups. A single metaphylactic treatment with toltrazuril of housed calves under various field conditions seemed effective.

Toltrazuril has an effect on all intracellular forms of the parasite, primarily by interfering with cellular respiration and pyrimidine synthesis. The possible effect of toltrazuril on immune function has been investigated in poultry and mice. It was found not to interfere with the development of normal immunity, although it enhanced antibody production following treatment. Jonsson *et al* (2011) demonstrated an efficacy of toltrazuril for the treatment of *E. bovis* and *E. zuernii* infections in calves. It reached 99% efficacy within three days of treatment and remained at this level or above it for six days. Treatment did not have a significant effect on the pattern and extent of immune cellular infiltration in the mucosa of ileum and colon. However expression of the genes coding IL-2, IL-10 and TNF-a in the ileum and TNF-a in the colon were elevated in treated calves. Oocysts were shed at higher levels and treatment was associated with lower expression of genes coding for IL-2, IL-10 and higher for IP-10.

Toltrazuril has been shown to be effective in calves at 15-20 mg/kg live weight (Mundt *et al*. 2005). Similar studies were also conducted in lambs and piglets revealing this drug to be effective in these species as well (not discussed in detail in this article but listed in the references below for further reading).

Vaccination for control of bovine coccidiosis is currently not practical although research into the development and testing of vaccines is ongoing. In contrast far more attention seems to be given to the production of vaccines in the poultry industry and multiple articles have been published on this subject.

REFERENCES:


CPD Questionnaire

1. The most important species in bovines is:
   a. E. oviniodalis
   b. E. ashata
   c. E. bovis
   d. E. leuckarti
   e. E. zuernii

2. “Boksiekte” has been described as a co-infection of:
a. *E. oviniodalis* and *S. papillosus*
b. *E. ashata* and *S. papillosus*
c. *Emeris* spp and *S. papillosus*
d. *E. leuckarti* and *S. papillosus*
e. *E. zuernii* and *S. papillosus*

3. Which of the following would not be favourable to the development of clinical coccidiosis:
   a. immunosuppression
   b. overcrowding
   c. wet environment
   d. young age
   e. dessication

4. Worldwide coccidiosis is of the greatest economic impact in:
   a. poultry
   b. goats
   c. cattle
   d. sheep
   e. game

5. Mortality is usually due to:
   a. dehydration and acidosis
   b. anaemia, hypoproteinaemia
   c. shock
   d. secondary bacterial infection
   e. a combination of any, or all, of the above.

6. The effective dosage for Toltrazuril in calves is given as:
   a. 1,5 - 2 mg/kg live weight
   b. 15 - 20 mg/kg live weight
   c. 15 - 50 mg/kg live weight
   d. 1,5 - 10 mg/kg live weight
   e. 150 - 200 mg/kg liveweight

7. In cattle the immune response in early primary infection is characterised by:
   a. IFN-gamma and IL-2 production by lymphocytes
   b. IFN-gamma and IL-2 production by macrophages
   c. IFN- gamma and IL-2 production by eosinophils
   d. IFN- gamma and IL-1 production by lymphocytes
   e. IL-1 and IL-2 production by lymphocytes
8. An unreliable parameter to confirm a clinical diagnosis is:
   a. Typical history, clinical signs, necropsy findings and demonstration of the parasite in fresh faecal samples
   b. the presence of typical histological lesions and intralesional parasites
   c. the number of oocysts present in faeces
   d. all of the above
   e. none of the above

9. Control of coccidiosis may be achieved by:
   a. preventing suitable environmental conditions for oocysts development
   b. using anticoccidial compounds prophylactically
   c. treatment and isolation of clinical cases
   d. metaphalactic treatment with appropriate medicines
   e. all of the above.

10. Which chemical group is most effective against coccidiosis
    a. Macrolides
    b. Sulphonamides
    c. Triazinetrones
    d. Macrocyclic lactones
    e. Ionophores