

RABBIT COCCIDIOSIS AND ITS CONTROL : A REVIEW

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ABSTRACT : Coccidiosis caused by *Eimeria* species, is a major parasitic disease of rabbits and is responsible for a high incidence of morbidity and mortality. The incidence of this disease in European countries is 21-60% and in India 13-64%. In commercially reared rabbits; coccidiosis occurs in a subclinical form with growth retardation and altered feed conversion. The disease occurs in two forms, hepatic and intestinal, the latter being more common than the former.

Presently, the control of rabbit coccidiosis relies almost entirely on chemical coccidiostats. However, extensive use of such drugs in commercial rabbitries has already started creating problems of drug resistance. In view of the limitations of chemotherapy, it is imperative to develop immunoprophylactic measures against rabbit coccidiosis. These include development of live-attenuated and recombinant vaccines against the parasite.

RÉSUMÉ : La coccidiose du lapin et son contrôle : une revue.

La coccidiose provoquée par des espèces du genre *Eimeria* est la principale maladie parasitaire affectant le lapin. Elle est responsable de la morbidité et de la mortalité à fréquence élevée. Dans les pays européens, son incidence est de 21 à 60% dans les troupeaux, elle est de 13 à 64% en Inde. Dans les élevages commerciaux de lapins la coccidiose se manifeste sous forme subclinique provoquant des retards de croissance et une réduction de l'efficacité alimentaire. Cette maladie se manifeste sous deux formes, hépatique et

intestinale, la seconde étant plus fréquente que la première. Actuellement le contrôle de la coccidiose chez le lapin est presque exclusivement basé sur l'emploi de coccidiostats chimiques. Cependant l'usage intensif des ces médicaments commence à créer des problèmes de résistance aux anticoccidiens. Afin de limiter la chimiothérapie il devient impératif de développer des mesures immuno-prophylactiques pour lutter contre la coccidiose. Celles-ci incluent le développement de lignées atténuées et de vaccins recombinants utilisables contre le parasite.

INTRODUCTION

Rabbits, besides their use as laboratory animals, are raised for a variety of commercial purposes viz. wool, meat and fur. They are efficient converters of vegetable protein into high quality animal protein. In India, rabbit farming for wool and meat has developed into an important industry and it has brought handsome returns to the rabbit rearers (TRIPATHI *et al.*, 1995). These returns are often affected by the outbreak of various diseases, especially coccidiosis, in this animal. Coccidiosis caused by *Eimeria* species, not only results in tremendous economic losses to poultry industry world-wide (SHIRLEY, 1992 ; LILLEHOJ and TROUT, 1993), but is also responsible for major losses in rabbit industry (LEYSEN *et al.*, 1989). It is thus an emerging disease of increasing importance in commercial rabbits (LICOIS *et al.*, 1990).

THE PARASITE

The coccidia of the genus *Eimeria* are members of the subphylum Apicomplexa and the family *Eimeriidae*. The life cycle, in general, is the same for all *Eimeria* species. However, host specificity, developmental site, prepatent and patent periods, and pathogenicity varies from species to species. Generally, *Eimeria* species are very host specific and in natural infection, no species infects more than one host. The

Eimeria species parasitizing rabbits undergo a complex life cycle, having both intracellular and extracellular stages, and asexual and sexual reproduction, which is quite similar to that of *Eimeria* species parasitizing other hosts like chickens. The only peculiarity of the life cycle of rabbit *Eimeria* species is that two types of schizonts, which later on develop into microgamont and macrogamont for the formation of oocysts, can be distinguished even at the first schizogony (STREUN *et al.*, 1979 ; LICOIS *et al.*, 1992).

Rabbit coccidiosis, like other coccidiosis, is initiated by oral ingestion of the sporulated oocysts by the susceptible hosts and the infection develops into the disease in young rabbits primarily, whereas adults are mostly carriers. There are more than 25 species of *Eimeria* which are reported to cause coccidiosis in rabbits. However, till now, only 10 species have been isolated in pure culture and characterized without ambiguity (COUDERT, 1989). These species are : *E. magna*, *E. media*, *E. irresidua*, *E. flavescens*, *E. perforans*, *E. intestinalis*, *E. coecicola*, *E. piriformis*, *E. exigua* and *E. stiedai*. In addition, another species *E. vej dovsky* has been described by PAKANDL, 1988. This disease occurs in two forms, hepatic and intestinal, the latter being more common than the former. Liver coccidiosis is caused by *E. stiedai* and intestinal coccidiosis by the remaining species. The majority of the intestinal species develop in the small intestine. Only *E. flavescens* and

E. piriformis complete their development in the caecum and colon, respectively.

The symptoms of the disease include failure of young animals to gain weight, poor feed conversion, diarrhoea, anaemia and growth retardation. In intestinal coccidiosis, the disturbances in water and electrolyte balance occur in the parasitized part of the intestine before the appearance of the macroscopic lesions and are essentially characterized by a loss of water and sodium. The loss of sodium is compensated by the exchange of potassium from the blood, thereby leading to hypokalaemia and causing death of the animal (LEBAS *et al.*, 1986). The coccidia which parasitize the ileum, caecum or colon cause pathognomic lesions which are more characteristic of the organs involved than of the parasite species (PEETERS *et al.*, 1984 ; COUDERT, 1989). In hepatic coccidiosis, the parasite completes its development in the bile ducts of the liver which become enormously enlarged and thereby interfere with liver function. The liver eventually becomes markedly enlarged and white nodules or cords develop on it which later on tend to coalesce. The animals may have diarrhoea and their mucous membranes may be icteric (LEVINE, 1985).

The intestinal coccidial species can be classified into three types when clinical parameters like weight gain, diarrhoea and mortality are taken into consideration (LEBAS *et al.*, 1986). These are non-pathogenic to slightly pathogenic (*E. media*, *E. exigua*, *E. perforans*, *E. coecicola*), moderately pathogenic (*E. irresidua*, *E. magna*, *E. piriformis*) and very pathogenic (*E. intestinalis*, *E. flavescens*). *E. stiedai* can also be classified as moderately pathogenic. The prepatent period is quite precise for a particular species. It is 16-18 days for *E. stiedai*, 5-6 for *E. perforans* and *E. media*, 7 for *E. magna* and 9-11 days for all remaining intestinal coccidial species (ANONYMOUS, 1977). In all the intestinal types, the patent phase last for 5-35 days, whereas in *E. stiedai* it is 21-30 days and mortality generally occurs during this period. The average dimensions of the oocyst range from 14 x 13 µm in *E. exigua* to 38 x 23 µm in *E. irresidua* (LEVINE, 1985). The sporulation time of oocyst is one of the most important criterion in the identification of the species. It is mainly influenced by population density of oocysts, oxygen tension and ambient temperature. In controlled conditions, an incubation temperature of 28-30°C has been found to be optimum for sporulation for poultry coccidia (DAVIS, 1973) In rabbit coccidia, the temperature of sporulation must not exceed 28°C, the optimum being 27°C (COUDERT *et al.*, 1995).

PREVALENCE

A number of *Eimeria* species causing coccidiosis in rabbit have been reported from Britain, Belgium and France and of these *E. intestinalis* is one of the most pathogenic coccidial species (CATCHPOLE and NORTON, 1979 ; COUDERT, 1979 ; PEETERS *et al.*,

1981 ; COUDERT *et al.*, 1993). Although *E. intestinalis* is not the most common coccidium in European countries, PEETERS *et al.* (1981) have found it in more than 21% of their battery-reared animals. In these countries, three types of rabbit husbandry are practised: the farm rabbitry, the pre-industrial rabbitry and the industrial rabbitry. The farm rabbitry constitutes the deep litter system where typical lesions of coccidiosis can be seen and mortality is high as little or no treatment is given. Nearly all of the rabbit *Eimeria* spp. are found in animals raised in this system. The pre-industrial rabbitry is characterized by wire-netting cages, granulated food, bad hygiene and excessive medication. CATCHPOLE and NORTON (1979) found an infection level of 60% due to mixed infection in rabbits reared in this system. One mostly comes across from time to time, drug-resistant strains of various species of the parasite in this type of husbandry. The industrial rabbitry is distinct from the preceding types of husbandry as there is greater professionalism, good hygiene, less medication and consequently, a post-weaning mortality of less than 10% per year. These rabbitries are often unaffected by coccidiosis and the appearance of drug-resistant strains could have a devastating effect on this industry (COUDERT, 1989). More and more rabbitries in Europe are switching over to the industrial type of rabbit husbandry.

Rabbit coccidiosis is an emerging disease in India and is acquiring importance due to the rapid growth of rabbit husbandry. However, the Indian farmers are generally following the farm rabbitry and to some extent the pre-industrial rabbitry system. Earlier, there were only isolated reports on this disease (RAI *et al.*, 1985) but due to intensification of rabbit farming, prevalence and outbreaks of rabbit coccidiosis have been reported from various parts of the country. In the semi-arid parts of Rajasthan, SANYAL and SRIVASTAVA (1986) found a preponderance of *E. media*, *E. perforans* and *E. magna*. KRISHNA and VAID (1987) reported an outbreak of intestinal coccidiosis in Angora rabbits due to *E. perforans* in the Kangra valley of Himachal Pradesh (H.P.) and recently a number of reports from this area (BHAT and JITHENDRAN, 1996 ; JITHENDRAN and BHAT, 1996) have indicated that *E. magna* and *E. perforans* are largely prevalent in this region of which *E. magna* has been found to be moderately pathogenic (BHAT and JITHENDRAN, 1995). Earlier, JAIN (1988) showed that in cases of mostly mixed infections in Madhya Pradesh (M.P.), *E. media*, *E. perforans* and *E. magna* were generally present in the host, whereas MEITEI *et al.* (1988) reported that infection due to *E. magna*, *E. media* and *E. coecicola* were predominant in and around Ranchi region of Bihar. CHANDRA and GHOSH (1990) reported that *E. irresidua*, *E. media* and *E. perforans* were responsible for coccidial infections of rabbits in the North-East Hill (N.E.H) region of India. The incidence of the disease, as mentioned in these reports, varies from region to region with H.P. leading with 64%, followed by Bihar 54%, N.E.H. region 53%

Rajasthan 52.2%, and M.P. 12.8%. Thus it can be inferred that *E. magna*, *E. media* and *E. perforans* are the main cause of rabbit coccidiosis in India.

CONTROL

Presently, the control of rabbit coccidiosis is entirely dependant on prophylactic chemotherapy and a number of coccidiostats are used to control this disease (OKERMAN, 1988). The commonly used coccidiostats in India are Bifuran, Sulpha drugs and Amprosol (DASH and MAHAJAN, 1982 ; SHARMA and SRIVASTAVA, 1989). However, none of these drugs will cure a case of coccidiosis once signs of the disease have appeared. All of them are prophylactic and must be administered at the time of exposure to the parasite or soon thereafter to be effective (LEVINE, 1985). Since exposure in nature is continuous, these drugs must be used regularly in the non-immune hosts and this is usually done by mixing them with feed or water. Due to the continuous exposure of the host to these drugs, the appearance of the drug-resistant strains has been rapid and this has limited the useful life of many chemical coccidiostats (PEETERS *et al.*, 1987 ; JEFFERS, 1989). Recurring drug-resistance requires continuous development of new anticoccidial drugs, involving high costs. Together with increasing concern for the possible presence of drug residues in products for human consumption, this had led to an interest in alternative means of control. The appearance of coccidial drug resistance in rabbits has not been reported so far from India. However, due to the development of rabbit farming into an important animal husbandry practice, and extensive and intensive use of coccidiostats, the day is not far off when drug resistant strains will emerge on the scene. There is, hence, an urgent need for development of an immunoprophylactic control to replace the chemotherapy presently in use.

Generally, rabbit coccidia are very immunogenic and the phenomenon of natural resistance has been observed in animals infected with *E. intestinalis* (LICOIS and COUDERT, 1980 ; COUDERT *et al.*, 1993). Animals that survive the disease develop species-specific and, in some instances, strain-specific immunity. Both humoral and cell mediated immunity are involved, with the latter playing a predominant role. The immunological basis for resistance in rabbits is not yet fully understood but has been well worked out in poultry coccidiosis. The current research on development of an immunoprophylactic control for *Eimeria* species in rabbits is broadly representative of that being done on the other coccidial species, especially poultry coccidia. Vaccines using virulent strains are already in use against poultry coccidiosis e.g. **Coccivac** (Sterwin Laboratories of Pitman Moore Inc., Millsboro, USA) and **Immucox** (Vetex Laboratories, Rockwood, Ontario, Canada). Such types of live multivalent vaccines, although providing effective protection, run the risk of provoking

symptoms or outbreaks of the disease. JENKINS *et al.* (1991) have explored the possibility of vaccinating chickens with irradiated *E. acervulina* oocysts. However, no work is presently being done on the development of a vaccine against rabbit coccidiosis using virulent strains or irradiated oocysts of the parasite.

Recently, Pitman Moore Europe have come out with a vaccine **Paracox**, against chicken coccidiosis using precocious strains of the parasite (WILLIAMS, 1994). A similar approach for the development of live-attenuated vaccine using precocious strains is being followed in *Eimeria* species parasitizing commercial rabbits (LICOIS *et al.*, 1990 ; BRAUN *et al.*, 1992). Although, in the long run, subunit vaccines made by the recombinant DNA technology appear most attractive, precocious attenuated strains of *Eimeria* may be useful as vaccines for some years to come. These strains are strongly immunogenic and cause very little pathological changes because they go through one or two less cycles of replication at the schizont stage than do the wild type strains. Immunization using precocious strains does not lead to sterile immunity but considerably reduces pathological changes and morbidity (WILLIAMS, 1994).

In chicken coccidiosis, at least three cell types (sporozoites, first and second generation schizonts) have been shown to induce a protective response. An effective vaccine against a multi-stage protozoan parasite may require antigens from several stages. An approach which holds considerable promise is to search for exogenous and endogenous virulence factors which perhaps are not normally immunogenic but are critical for the well being and survival of this protozoan parasite. Such molecules have already been found in some parasites e.g. glutathione S-transferases of *Schistosoma* spp. and *Fasciola hepatica* (BROPHY and BARRET, 1990), protease of *Leishmania* spp. (ETGES *et al.*, 1986) and penetration enhancing factors in *Toxoplasma gondii*, identified as a 60 kD acidic protein (LERICHE and DUBREMETZ, 1991). The prospects of their use as candidate vaccines look bright (BUSHARA *et al.*, 1993) and similar possibilities can be explored in *Eimeria* spp. of chickens and rabbits. Experimental studies need to be conducted to identify the most pathogenic species of *Eimeria* and their strains in rabbits and the factors responsible for the selection of a suitable strain(s) for development of a vaccine.

Attempts to develop recombinant vaccines against poultry coccidia are continuing (BOGHAL, 1992). The vaccines are likely to consist of either purified coccidial antigens obtained from the large-scale fermentation culture of an appropriate recombinant micro-organism and intended for injection, or alternatively as live micro-organisms that, during the course of replication, will synthesize and release coccidial antigens within the host (ELLIS and TOMLEY, 1991). Development of a genetically engineered subunit vaccine using recombinant protein, for

immunoprophylaxis of rabbit coccidiosis, is at a preliminary stage (BRAUN *et al.*, 1992) and this work is yet to gather momentum.

Received : July 31, 1995

Accepted : March 1, 1996

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