

Drugs, vaccines and natural products for coccidiosis control - will they help the poultry industry grow better chickens?

H. D. Chapman

Department of Poultry Science, University of Arkansas

Abstract

In the USA, chemotherapy is widely used to control coccidiosis. In this article, problems that accompany this approach are described and potential problems for the future are considered. Drug programs that are believed to ameliorate resistance are discussed. Live vaccines and natural products are considered alternatives to medication but in most cases a lack of research coupled with inadequate experimental design prevents an accurate evaluation of their efficacy. Progress in our understanding of this disease will depend upon continuing collaboration between researchers in academia, government, and industry that has served so well in the past. Funding for basic and applied coccidiosis research is presently almost impossible to obtain and if this situation is not remedied then optimal productivity in poultry production will be difficult to achieve in the future.

Costs of coccidiosis

There is a perception among some in the poultry industry that coccidiosis is not the problem it once was. Many improvements have been made in the way we raise poultry that may mask the costs of this disease. The parasites responsible (protozoa of the genus *Eimeria*) are still widespread in poultry flocks and it is possible to isolate these organisms from any poultry house with little difficulty. Whereas in the past clinical coccidiosis was frequently diagnosed this is less so today. The principal affect of coccidiosis is reduced growth rate and poor feed conversion but this is not easy to measure in the field since data from uninfected flocks (that may serve as a control) is unavailable. One recent estimate is that coccidiosis may cost the US chicken industry about \$127 million annually (Chapman, 2009) and proportionally similar losses may occur in turkeys. Thus coccidiosis is probably the most expensive disease that afflicts intensively raised poultry. Almost all chickens are reared with an anticoccidial drug in the feed, at considerable expense, testimony that coccidiosis remains an important problem.

Drugs for coccidiosis control

The use of drugs for coccidiosis control commenced in the early 1940s and many scientists from government, university, and private institutions were involved in this work. A pioneering publication from the Rhode Island Agricultural Experiment Station was the first to show that coccidiosis could be prevented by incorporating a drug in the feed and this was to revolutionize control of the disease (Chapman, 2009). Subsequently many novel compounds were introduced, with varying success, and some of these are

still in use today. In the last 20 years, however, only two new drugs have been introduced in the USA (Table 1). How has this parlous situation come about?

Drug discovery and introduction

Unlike other parasitic diseases of livestock, coccidiosis is unusual in that a dozen or so compounds have been shown to be effective against the disease. However, tens of thousands of molecules were screened to discover these compounds. Developing a drug and bringing it to market is a very expensive process and in the USA it has been estimated that \$25 million and at least 10 years work is necessary to obtain approval for an anticoccidial drug (Duquette, 2005). In addition to problems of drug resistance and public perception discussed below, competition between similar products and brands of the same product has lowered the price of drugs to the point where profit margins are very low. As a result many companies are no longer involved in the discovery process. Furthermore, existing drugs are often sold by organizations with little or no research facilities or expertise.

Drug resistance

Resistance has been documented to all compounds introduced to control coccidiosis and many surveys conducted in the USA and elsewhere have shown that resistance is widespread (Table 2). In some cases, resistance has appeared within a year of introduction (Chapman, 1997). This is not surprising because extensive use (in the USA more than 90% of broilers are raised with a drug in one or more feeds) has resulted in relentless selection pressure in favor of resistance.

This raises the question why, if resistance is widespread, are anticoccidial drugs so widely used? One suggestion is that the tests used to determine whether field strains are resistant to drugs involve experiments in which chickens are infected with large numbers of parasites, and that these do not reflect infection levels in the field. However, we have shown that resistance can be demonstrated in such tests regardless of the magnitude of infection (Chapman, 2005). Our work indicates that although drugs often show only partial activity, they do allow the natural acquisition of immunity (Fig.1). Sufficient protection may be acquired to prevent clinical coccidiosis (Chapman, 1999). Improved genetics and better nutrition may have reduced susceptibility to disease, and improved housing, husbandry, sanitation, and control of other diseases may have contributed to fewer parasites being present in the environment.

Public perception

Scientific publications concerned with vaccination and the use of “natural” products, often refer to negative public attitudes to the use of drugs in animal feeds. The public perception concerning the use of growth promoters and antibiotics may color opinions regarding anticoccidial agents even though these are approved for disease control rather than growth enhancement. This view is not new and it is worth quoting the veterinarian P. P. Levine (1945) who was the first to describe anticoccidial activity in a drug:

“medication can never take the place of proper husbandry ---- if domestic animals, including poultry, have to be medicated continually to keep them healthy or alive, there is something fundamentally wrong”.

Unfortunately, these sentiments did not help the poultry farmer faced with catastrophic losses caused by coccidiosis. Today, newsletters circulated by the pharmaceutical industry, suggest that the issue of public perception is a matter of concern (Anon, 2009). According to Duquette (2005) however:

“the good news is that currently marketed anticoccidial drugs will remain on the market, as there is no indication that CVM has any concerns with these compounds -- - The anticoccidial drugs are amongst the most important tools that allow the broiler producer to produce healthy birds, because they are the safest and most effective method to control coccidiosis. In turn, the consumer benefits through low-priced, high quality animal protein, produced using drugs that have been proven safe and effective in rigorous scientific studies”.

Extending the use of drugs

Shuttle and rotation programs involving anticoccidial drugs have long been practiced by the poultry industry and this may have ameliorated the development of resistance. Alternation between drugs with a different mode of action may slow the emergence of resistance although will not prevent its appearance. Another approach involves alternating the use of drugs with a coccidiosis vaccine (Fig.2). Some vaccines comprise live oocysts of strains that were isolated before most drugs were introduced and are inherently drug-sensitive. Thus use of such vaccines should in theory replace “resistant” strains with those that are “drug sensitive” resulting in improved efficacy when drugs are subsequently employed. Support for this contention has been obtained (Chapman, 1994), but there is little evidence that this approach has been widely adopted by the poultry industry.

Vaccines

An alternative approach to the control of coccidiosis involves vaccination with live, potentially virulent parasites (Chapman, 2000). Litter management is important (to reduce infection levels) because these vaccines can cause the disease they are designed to prevent. Attenuated vaccines (with reduced pathogenicity) have been developed but these are expensive to produce. The first coccidiosis vaccine was introduced in the 1950s but although often employed during the rearing phase of broiler breeder production its use in broiler flocks has been limited. In the last few years there has been increased interest in the use of vaccines and several new products have appeared, with more anticipated in the near future. The introduction of spray techniques allowing vaccination in the hatchery has improved the utility of coccidiosis vaccines. In some countries vaccines have been widely adopted but in others (USA) presently this is not the case. Some characteristics of the ideal vaccine are listed in Table 3 (Chapman et al., 2005). Most vaccines currently available fail in one or more of these criteria.

It has been standard practice to evaluate the efficacy and safety of anticoccidial drugs in three types of experiment. The first involves short term battery studies to determine efficacy during the acute phase following infection, the second involves floor-pen experiments to examine effects upon performance during the life of the bird, and the third involves field trials at commercial locations. For vaccines, an additional requirement is challenge tests demonstrating that immunity has developed. Properly designed battery experiments and floor-pen trials permit adequate replication, but this is difficult to achieve in field trials, hence their main value is to demonstrate product safety.

Unfortunately, vaccine producers often omit, or limit the second step moving directly to field trials. As a consequence, data generated with appropriate controls and adequate replication published in peer reviewed Journals is either lacking or very limited in extent. An extensive literature has been established in recent years regarding the cellular immune responses to *Eimeria* infections in chickens but apparently no studies have been published documenting these responses in birds given commercial vaccines.

Research has been underway for many years to develop a coccidiosis vaccine using recombinant DNA technology. This has involved attempts to identify important antigens capable of stimulating a protective immune response in the bird. So far, however, probably because of the complexity of host immunity and the parasite life cycle, this approach has not proved successful.

Natural products

An alternative approach involves utilizing so-called natural products. This is a heterogeneous assemblage of plant, bacterial, and other substances claimed to alleviate coccidiosis either directly or indirectly by improving “gut health” or the chicken immune system. This approach would be particularly useful in organic poultry production where use of chemical agents and antibiotic growth promoters is circumscribed.

Finding ways to boost the innate resistance of poultry to *Eimeria* infection by identifying natural substances capable of modifying the intestinal micro environment has been investigated (Allen et al., 1998). *Pediococcus*, *Saccharomyces*, and *Lactobacillus* based probiotics have been used to enhance the local cell mediated immune response in poultry. Various substances, including many plant based extracts, such as menhaden oil, flaxseed oil, artemisinin, betaine, and proanthocyanidin, have been claimed to have such an effect because of their antioxidant properties.

Many studies intended to demonstrate the efficacy of natural products are poorly designed, lack appropriate controls, and have insufficient replication. Guidelines to aid investigators in the design, implementation, and interpretation of studies for the assessment of product efficacy have been published (Holdsworth et al., 2004). As in the case of vaccines there is a need for floor-pen experiments as well as field trials. Often inclusion levels are unrealistically high and therefore would be difficult to accommodate in commercial feed formulations. Claims for efficacy are often based upon marginal reductions in oocyst production and lesion scores. Such claims would not be acceptable if an anticoccidial drug were under investigation.

Conclusions

The parasites that cause coccidiosis have an oro-fecal method of transmission and produce a stage of the life cycle (oocyst) that is resistant to most chemicals likely to be encountered in the poultry house. Raising poultry under intensive conditions in direct contact with their feces in a moist environment therefore ensures survival of the oocysts in the litter and their transmission from flock to flock. Drugs have been used extensively for more than forty years with varying degrees of success and yet eradication has proved impossible. Nevertheless the adoption of appropriate drug programs, in which compounds of different mode of action are alternated in successive feeds and in consecutive flocks, can help reduce the impact of the disease. The lack of new drug discovery, coupled with the development of drug resistance is of concern. Whether public perception regarding the use of drugs limits the application of chemotherapy in the future remains to be seen. Vaccines and natural products have been promoted as alternatives to chemotherapy. If these approaches are to be successful, however, and enable us to grow better chickens, we need much more data than has so far been provided.

References

- Allen, P. C., Danforth, H. D. & Augustine, P. C. (1998). Dietary modulation of avian coccidiosis. *Int. J. Parasitol.* 28:1131-1140.
- Anon (2009). *For The Record*. 8, Issue 2. ALPharma Inc.
- Chapman, H. D. (1997). Biochemical, genetic and applied aspects of drug resistance in *Eimeria* parasites of the fowl. *Avian Pathol.* 26:221-244.
- Chapman, H. D. (1999). Anticoccidial drugs and their effects upon the development of immunity to *Eimeria* infections in poultry. *Avian Pathol.* 28:521-535.
- Chapman, H. D. (2000). Practical use of vaccines for the control of coccidiosis in the chicken. *Wld's Poult. Sci. J.* 56:7-20.
- Chapman, H. D. (2005). Perspectives for the control of coccidiosis in poultry by chemotherapy and vaccination (pp. 99-104). In: *Proceedings of the Ninth International Coccidiosis Conference, FACTA, Foz do Iguazu, Brazil.*
- Chapman, H. D. (2009). A landmark contribution to poultry science – prophylactic control of coccidiosis in poultry. *Poultry Sci.* 88:813-815.
- Chapman, H. D. (1994). Sensitivity of field isolates of *Eimeria* to monensin following the use of a coccidiosis vaccine in broiler chickens. *Poultry Sci.* 73:476-478.
- Chapman, H. D., B. Roberts, M. W. Shirley, & R. B. Williams. (2005). Guidelines for evaluating the efficacy and safety of live anticoccidial vaccines and obtaining approval for their use in chickens and turkeys. *Avian Pathol.* 34:279-290.

Duquette, P. (2005). A US perspective on the current and future regulation of anticoccidial drugs and vaccines (pp. 117-125). In: Proceedings of the Ninth International Coccidiosis Conference, FACTA, Foz do Iguazu, Brazil.

Holdsworth, P. A., Conway, D. P., Mckenzie, M. E., Dayton, A. D., Chapman, H. D., Mathis, G. F., Skinner, J. T., Mundt, H. C. & Williams, R. B. (2004). World Association for the Advancement of Veterinary Parasitology (WAAVP) guidelines for evaluating the efficacy of anticoccidial drugs in chickens and turkeys. *Vet. Parasitol.* 121:189-212.

Levine, P. P. (1945). Specific diagnosis and chemotherapy of avian coccidiosis. *J. Am. Vet. Med. Assoc.* 106:88-103.

McDougald, L. R. (2003). In: *Diseases of Poultry* 11th edition, Y. M. Saif (ed) Iowa State press, Ames, IA.

Table 1. Number of drugs introduced to control coccidiosis in the USA¹.

1940s	1950s	1960s	1970s	1980s	1990s	2000+
7	7	7	5	5	2	0

¹Data based upon McDougald (2003).

Table 2. Resistance in field strains of *Eimeria* to anticoccidial drugs.

Drug	Resistance described	Rate	Drug	Resistance described	Rate ¹
Sulfaquinoxaline	1954	Slow	Monensin	1974	Slow
Nitrofurazone	1955	Slow	Robenidine	1974	Slow
Nicarbazin	1964	Slow	Lasalocid	1977	?
Dinitolmide	1964	Slow	Narasin	1977	?
Amprolium	1964	Slow	Arprinocid	1982	Rapid
Buquinolate	1968	Rapid	Salinomycin	1984	?
Clopidol	1969	Moderate	Maduramicin	1987	?
Met. benzoquate	1970	Rapid	Toltrazuril	1993	Moderate
Decoquinate	1970	Rapid	Diclazuril	1994	Moderate

¹In the case of drugs with a common mode of action (e.g. ionophores), it is not possible to determine rate because resistant strains were already present in the field.

Table 3. Characteristics of the ideal vaccine.

<p>Induce specific immunity against economically important species of <i>Eimeria</i></p> <p>Be safe for the target host species, non-target animals and humans</p> <p>Not represent an environmental hazard</p> <p>Comprise parasites of normal or low virulence, the latter trait being stable during propagations through the host</p> <p>Comprise parasites that remain viable during storage under optimal conditions for a reasonable period of time</p> <p>Protect against field strains from different geographical areas, including those where the vaccine is intended to be used</p> <p>Be administered by a commercially practical method to ensure that as many birds as possible receive a similar dose</p> <p>Have no adverse effects upon final performance or other production criteria</p> <p>Be compatible with other poultry vaccines</p> <p>Be free from viral, bacterial, mycoplasmal, fungal, and chemical contaminants</p> <p>Be cost effective when compared with other methods of coccidiosis control</p> <p>Include drug-sensitive lines so they may interbreed with drug resistant field populations and thus reduce overall local resistance</p>
--

Fig.1. Development of immunity to three species of *Eimeria* in birds reared on anticoccidial drugs.

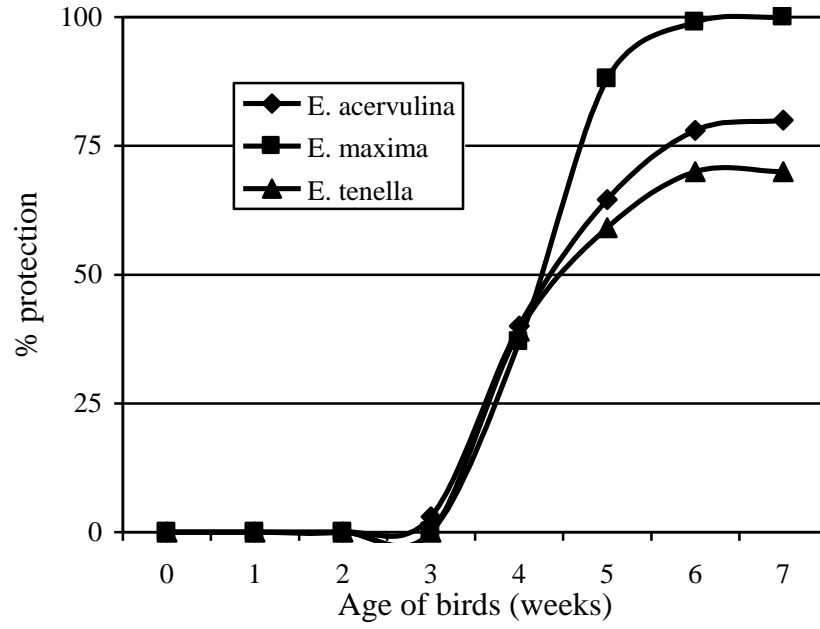


Fig.2. Rotation program with drugs and vaccines.

