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Comparison of the Use of Vaccines or Drugs against Parasitic Diseases

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***Abstract*—**The viewpoint towards the use of drugs or vaccines against avian parasitic diseases is one of the most striking challenges in avian medical parasitology. This includes many difficulties associated with drug resistance and in developing prophylactic vaccines. In many instances, the potential success of a vaccination in controlling parasitic diseases in poultry is well-documented. However, some medical, technical and financial limitations are still paramount. On the other hand, chemotherapy is not very well-recommended due to a number of medical limitations. But in the absence of an effective vaccine, drugs are used against parasitic diseases. This paper sheds light on some the advantages and disadvantages of using vaccination and drugs in controlling parasitic diseases in poultry species. The usage of chemotherapeutic drugs is discussed with some examples. Then, more light will be shed on using vaccines as a potentially effective and promising control tool.

***Keywords*—**Drugs, parasitology, poultry, vaccines.

I. Introduction

THE use of vaccines as a means to control a large number of parasitic diseases in humans as well as animals, has been considered and implemented to a certain extent for a long period of time. However, this holds a limitation as the number of parasitic vaccines available much less, and out of these, most are used for veterinary species [1].

Drugs have been used to treat all the common parasitic diseases of human and domestic animals. Chemoprophylactic drugs are also available against some diseases. In the absence, in most instances, of vaccines, they together with other measures are used. Most of the antiparasitic drugs are efficient in clearing the parasite. On the other hand, there are many medical disadvantages associated with drugs. These include toxicity, drug resistance, incubation period, adverse reactions, short-lasting effect, possible carcinogenicity, interaction with other compounds, inability to be used in some cases, diagnosis difficulties, contamination and expensive cost. These disadvantages will be discussed separately [1]. The disease haemonchosis caused by Haemonchus contortus affects millions of livestock worldwide causing gastritis, anaemia and ultimately death, a vaccine Barbervax was released to combat this, but ultimately leading to resistance due to excessive drug use. So a study using plant extracts from Picria fel-terrae Lour, a rich source of anthelmintics showed significant inhibitory effect on motility and development of H. contortus [2].

Most antiparasitic drugs are registered as toxic chemical substances in the National Institute for Occupational Safety and Health in the USA. For example, quinine is the first drug used to treat malaria; it is potentially toxic and cannot be used as a prophylactic drug. Melarsaprol (an arsenical) is another example of toxic antiparasitic drugs; it is used against kinetoplastid protozoa in the brain. Chagas disease is treated with toxic drugs including antimonials, pentamidine and amphotericin B [3].

Chagas disease (American trypanosomiasis) results from infection by Trypanosoma cruzi and is a cause for serious concern, particularly in the Americas. It is currently being treated with two chemotherapeutics: benznidazole and nifurtimox, which have proven to be effective. Benznidazole, should, however, be avoided during pregnancy and during kidney or liver failure, while nifurtimox should be avoided in people with neurological and psychological disorders [4].

Nitazoxanide has been the only clinically approved drug to treat diarrhoea caused by C. parvum; it is also used to treat diseases caused by other parasites, and has been shown to promote Hepatitis C elimination and been effective against certain types of cancer cells [4].

Acquired resistance has been a problem in using antiparasitic drugs. Several genetic and biochemical mechanisms are involved in drug resistance. These include: point mutations, alternation in the biochemical targets, bypass of the target lesion due to the development of an alternative pathway, metabolic inactivation of the drug and change in the permeability, so that the drug is no longer taken up. For example, anti-trypanosomal resistance to pentamidine is due to the alternation in the drug uptake system. Resistance to antimalarial, and chloroquine, is due to the loss of a high affinity chloroquine-binding site as well as to mutations in oxygenase enzymes [5].

The subclinical incubation period is the period of time after infection and the appearance of the clinical signs of the disease. Chemotherapeutic treatment begins after that period. By this stage, the parasites may have reached an advanced number, so that the antiparasitic drug is not effective. Misuse of antimalarial drugs and availability of low quality medicines brought about the problem of drug resistance. In recent studies, artemisinin, a traditional Chinese medicine, is now considered as the key to fighting malaria. In order to delay parasite resistance, it was suggested that the artemisinin be used in combination with other antimalarials. However, a number of other problems arose such as wrong dosing, inadequate knowledge and training of service providers, and self-medication with inadequate doses [6].

Onchocerciasis has been treated with diethylcarbamazine and suramin but these drugs may cause severe adverse

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reactions, including death. Other drugs like metronidazole, pentamidine, amphotericin B, diloxanide, melarsoprol and nifurtimox are known to cause headache, gastrointestinal irritation, stomatitis, candidiasis, nephrotoxicity, hypotension, pancreatic damage, hypocalcaemia, hallucination, cardiac dysrhythmias, muscle pain, anorexia, bone-marrow depression micturition and other severe side effects [7].

Antiparasitic drug treatment is considered to be short-lasting. It may protect the individual but does not produce a herd-immunity for community protection. The short half-life factor means that repeated doses are required. The antimalarial drug, Mefloquine, has an advantage of having a long half-life (up to 30 days) and lower side effects [8].

According to Cheah and White [9], Malaria is known to be a leading cause of death in third world countries and one of the promising ways to eliminate malaria was through Mass Drug Administration (MDA), i.e. to give the entire population malaria treatment. The key limitation to this method is that the entire population might not participate.

Some chemical drugs have cross reactions with other compounds. For example, metronidazole has reported to have interaction with alcohol. Drug interactions of sulfamethoxazole and trimethoprim with some plasma proteins may cause megaloblastic anaemia. In addition, methotrexate interferes with folic acid metabolism in cells [7].

Most of the known chemical drugs are dangerous to be used during pregnancy. Diloxanide (amoebicide) is toxic to the fetus. Some drugs like pentamidine cause abortion. Chemical drugs are reported to cause hypersensitivity reactions to the mother. However, if the parasitic disease is life-threatening, treatment should not be delayed [7].

Another limitation is that treatment occurs after a specific medical diagnosis. Sometimes, unavailability of specific diagnostic tests is a big problem, especially in developing countries.

Egypt holds the record for the highest prevalence of Hepatitis C viral infections, the major cause being the wrongful use of tartar emetic injections. Present day treatment involves the use of direct acting antiviral drugs (DAA) in combination with sofosbuvir and ribavirin, which have proved to be revolutionary in treating HCV. The major limiting factor here is the high cost of treatment; however, the Egyptian government is coming up with schemes to tackle the issue [7].

Contamination with chemical drugs is considered to be a problem in the case of the coccidial ionophores that is used to treat chicken broilers. Accumulation of that chemical in the broiler meat may cause adverse effects in humans. Vaccination, on the other hand, remains the method of choice against parasitic diseases; although, no vaccines are commercially approved to be used against human parasites. It has a lot of advantages over chemical drugs because prevention is always better than cure. It also has some medical limitations, as will be shown later. Unlike drug treatments, vaccination induces immune response that provides herd immunity on a long-lasting basis. It also has a history of success in other viral and bacterial diseases.

There are some successful vaccines against parasitic protozoa of veterinary importance. Vaccines are well known to be safe without severe side effects or cross reactions. Sometimes, an important advantage of vaccines is their wide application against more than one parasite if the parasitic antigen carries epitopes which are present in other species. For example, gp 28 is an antigen present in *Schistosoma mansoni*; it carries epitopes that are present in other species including the human parasites *S. japonicum* and *S. haematobium* and the bovine parasite *S. bovis* [10].

There are several sources of antiparasitic vaccines. These include: whole killed parasites, attenuated live or low virulence parasites, peptide vaccines and nucleic acids vaccines.

Irradiated larval vaccines like Dictol are used against some animal parasites contortus in sheep. Although they give good results against the pathological signs of infection, they did not give complete resistance. Leishmaniasis is the second most severe parasitic disease that affects humans and dogs worldwide, caused by the protozoan of the genus Leishmania. A vaccine formulation containing naturally excreted secreted (ES) antigens was prepared from *L. infantum* promastigote culture. When administered to infected dogs, it was seen that parasite burden was reduced. Also, there were clear differences between the humoral and cellular immune response between vaccinated and control dogs. This kind of vaccine is used mainly in animals and cannot be used as a human vaccine due to the fact that it may cause serious side effects, vaccine failure and incomplete attenuation. If the inoculum contains larger proportions of living parasites than the dead ones, the host's immune system may not be able to manage at the site of the vaccination, resulting in a systematic spread of the parasite that is supposed to be localized. Living parasites are also not safe to handle. There are some people that should avoid taking a toxoplasmosis vaccine such as pregnant women, young fertile women, and those with poor immune systems [10].

Peptide vaccines have some advantages including the ability to stimulate specific B and T cell-mediated responses, stability, and being chemically defined products which are cheap. Usually only one peptide is used, which is considered to be a disadvantage when dealing with a parasite that exhibits variation in the antigenic proteins [10].

Most of the currently available vaccines are prophylactic, they prevent the effect of a future infection; however, there are no licensed therapeutic vaccines for any chronic infectious disease. Some of the diseases for which prophylactic vaccines have been developed are the human papillomavirus (HPV) and hepatitis B virus (HBV) [10].

Molecular approaches including recombinant vaccines, screening cDNA libraries and protein and cloning gene encoding antigen have a lot of advantages including the ease of manipulation, speed of growth and the cheap production in bacteria, yeast or cell lines. Vaccination with plasmid containing a gene encoding antigen or using a mixture of synthetic peptides is an advantage because they are well defined in terms of the desirable epitopes. Also, they are stable at ambient temperatures and they stimulate the correct

immune response [8]. Using adjuvants with vaccines help stimulate antigen-presenting cells and lymphocytes proliferation. They perform a 'depot effect' like in the case of aluminium hydroxide and oil emulsions that act as a long-lasting reservoir of antigen in the lymph nodes. On the other hand, adjuvants are active only if used in high doses which may cause other pathological side effects. Muramyl Dipeptide (MDP) is being used in animal vaccine adjuvants, however, it is toxic for clinical use [8]. The fact that parasite populations might be polymorphic is a limiting factor in recombinant DNA technology. Also, a simple recombinant might not stimulate all required immune components.

If the vaccine is targeted at a self-like molecule, it causes serious autoimmune reactions that damage the cells of the host [7]. Vaccines sometimes do not stimulate sufficient amount of cell-mediated immunity. More understanding of T-cell epitopes would certainly solve this problem. A considerable disadvantage of vaccination occurs in the case of genetic mutation that alters the epitope pattern and cause the T-cell recognition to be lost [8]. In addition, vaccines have to stimulate the right type of immune responses to avoid enhancement of immunopathological responses. One of the technical limitations of effective vaccination is the failure to vaccinate under field conditions, especially if multiple visits are required. Another problem that is associated with field conditions is the genetic heterogeneity of both hosts and parasite. This problem can be solved by using a cocktail of parasites. Heat stability and transport of the vaccine is another limiting factor under field conditions. Many developing countries suffer from inadequate sterilized syringes and needles, and the reuse of disposable equipment. Also, financial problems are usually faced in developing countries [7]. In endemic areas, the efficiency of vaccination can be affected by the fact that young children may have the infection even before birth. Also, under-nutrition that is usually associated with immune depression affects the efficiency of vaccination [7].

Although there have been some promising advances in malaria vaccine development, the best protection achieved so far is partial and short-lived. One vaccine of interest is SPf66 that contains sequences from both sporozoite and merozoite proteins. It protects monkeys and humans against challenge infection [7]. Using small peptide sequences as the basis of the vaccine is a disadvantage, because these sequences are different between strains of *Plasmodium falciparum* in endemic areas. However, successful approaches have been done to develop vaccines against the erythrocytic stages depending on antigens on the surface of the parasitized red blood cell (PRBC) [11]. Scientists have found that when irradiated sporozoites were delivered via mosquito bites to volunteers, they were protected against subsequent infection. The transient nature of the immunity reveals that this vaccine can be used for short-term instances [7].

The use of a transmission-blocking vaccine in malaria control includes passive transfer of antibodies that attack the parasite in the gut of the mosquito, this vaccine is important to control the spread of the parasite within a population, but does not treat infected individuals. A trial was done to compare between using vaccination or impregnation of mosquito nets with permethrin chemical to reduce mortality due to Plasmodium falciparum malaria. Results have shown that a malaria vaccine would be extremely effective in terms of cost and prevention of death when compared with the permethrin impregnated nets (Table I) [12].

TABLE I
ESTIMATES OF EFFICIENCY FOR MALARIA VACCINE AND NET IMPREGNATION

Outcome	Intervention	Base-case estimate %	Range %
Malaria attack	Net impregnation	50	41-58
Death	Vaccine	39	30-48
Malaria attack	Net impregnation	35	17-63
Death	Vaccine	20	10-30

The BCG (Bacille Calmette-Guerin) vaccine is the only available vaccine for tuberculosis licensed under the WHO Expanded Programme on Immunisation (EPI) and is normally administered after birth in countries with high incidence of TB, but is not recommended to immunocompromised individuals as it can pose a risk for the development of disseminated BCG disease. It has had little impact on overall improvement. Currently, a number of studies are being done to improve the BCG vaccine or to altogether replace it with a new one [13].

Vaccines against schistosomiasis are still under development, but none are currently available. Vaccines against African trypanosomiasis are really difficult to be developed because the parasite has the potential to change its variant surface glycoprotein (VSG). The American trypanosomes do not exhibit antigenic variation but their antigens have great cross-reaction with the host antigens causing chronic autoimmunity. In the case of leishmaniasis, subunit vaccines are mostly recommended for the more serious forms of the disease than other kinds of vaccines. Gp 63 is an antigen found on the surface of the promastigote. It is being evaluated [8].

Plant-based oral vaccines are a promising aspect to the vaccine industry as they offer several advantages such as low cost of production, heat stable, ease of storage and transportation and lack animal-pathogen contamination. For example, Toxoplasmosis caused by the parasitic protozoan *Toxoplasma gondii* is known to cause complications in pregnant women and in individuals suffering from AIDS and organ transplant recipients. Oral immunization with chloroplast-transformed GRA4 antigen showed mucosal and systemic immunity, with a 59% decrease in brain cyst load when studied in mice, it also induced a protective immune response against *Toxoplasma* infection [14].

DNA vaccines along with DNA-based dMAB (monoclonal antibody) used in combination was studied showing promising results to provide both, short-term and long-term protection against the Chikungunya virus [15].

II. CONCLUSION

In conclusion, vaccines have many advantages over

chemical drugs. They are urgently and honestly required to be used as an effective epidemiological tool to maintain a low level of parasitic infection, and in some cases, as a weapon to eradicate infection completely. Efforts by immunologists and molecular biologists to achieve that dream have been made. Many biologists are currently working hard on vaccine development products for the sake of this dream. When these vaccines are introduced, there will undoubtedly be a big breakthrough in this field. Will these new vaccines be produced in the near future? Or, will they meet the requirements effectively and with minimum side effects? The future will tell.

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