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Immunization against nematodes (Helminth): A review

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Abstract
Helminth word is originated from the Greek which means "worms". Clinical features of helminth infections are known from the ancient writings of Hippocrates, Egyptian medical papyri, and the bible. Helminths are multicellular parasitic organism having medical and economic value. Many human beings and domesticated animals were found infected worldwide by parasite of helminth. Helminths were key factor of morbidity and mortality, especially in developing countries. The World Health Organisation report indicates that more than 2.5 billion human are found infected with parasitic. Intestinal helminths [23] infections are more in children. An estimate indicate that by year 2025, approximate 57% of human population (countries developing) may be by helminth infection. Helminth borne diseases are primary factor in lowering the productivity of useful animals. This was mainly due to mortality and reduced weight gains. This problem is severe in tropical countries where rains are good. Helminths infected rats and mice are responsible for transmitting the helminth disease to men and vertebrates. In helminths nematodes are also known as roundworms. This group is known to have second largest number of species in phylum among animal kingdom, encomprising up to 500,000 identified species. Nematode infections are common feature among vertebrate life. Infected hosts tried to respond to infections caused by nematode with 5 their immune response. While nematodes respond to host with three defence strategies i.e.: (1) Not persuading immune responses which are harmless (2) Compromise with selected parts of the host's immune response, and (3) Preventing the local effecter cell mechanisms of the host's response. In case of nematode infections, it was commonly observed that the, survival and fecundity of infectious agents are lowered in hosts due to an immune response Gastrointestinal nematodes are causing serious production losses. Parasites are highly successful organisms due to it's highly adaptability quality developed.

Keywords: helminth, parasites, nematodes and immune response

Introduction
Helminths are disease causing multicellular eukaryotic organisms. They are major productivity constraints among small sized ruminants belong to tropic and subtropics regions where humid climate provide favourable conditions for successful survival of parasite eggs as well larvae (Alam, 2003) [1]. Helminth also causes high morbidity and low production in stocks with a higher nematode pervasiveness. Helminths infection reduces the quality and quantity of meat, milk, and is also responsible for increased mortality, especially of young stock (Sorobetea *et al.*, 2018) [28]. Members of protozoa, helminths, fungi which act as parasitic pathogens considered to have strong forces of immune responses.

Long lived helminthic parasites have tremendous capabilities to provide host immunity, protect themselves against expulsion and minimize chronic infection. Helminth infections very rarely responsible for mortality, however pain in abdomen and lowering of haemoglobin is the immediate result, its long term impact can lead to the severe result in the form of lowered cognitive abilities and productivity (Gerbe *et al.*, 2016) [15].

WHO report states that 1/4th of the world's population is infected with helminths, presenting a major public health problem in developing countries, where the health and sanitation facilities issue were not dealt very well with the need of increasing population (WHO, 2005). The main effect of these infections in young children adversely effected both physical and mental development.

Chronic helminth infection leads to growth retardation, vitamin deficiency and poor cognitive function along with iron deficiency anemia in endemic area. Children of rural areas have high burden of helminth parasite in which major contribution is of hookworm, roundworm, whipworm and threadworm (Sorobetea *et al.*, 2018) [28].

Related Work
In the end quarter of 19th century chemical like carbon tetrachloride, nicotine sulphate, copper sulphate and arsenic were widely used chemical for parasite treatment, although these chemicals were highly toxic to host and parasite (McKellar and Jackson, 2004) [21].

According to McClure (2000) in young sheep, where GI infected with nematodes are unable to acquire early immunity against vaccination and natural boosting. Role of vaccination is also evident from the previous researches. The use of anthelmintics drugs created problems like, development of resistance (Waller and Prichard, 1985), toxicity problem via chemical residue (Kaemmerer and Butenkotter, 1973). The identification and recognition of complex nature of antigen lead to slow down the vaccine development. Research on helminth vaccines were carried out by various researchers.

Limited study was carried out to study the helminths induced immune response in human being. However, some studies are available which were carried out in natural and experimental model related auto 14 immune disorder (Khan, 2002).

Advance study in immunobiology and biotechnology defined the lab model of infection (Cox, 1993). Englund and

Sher (1988) [9] described the different immune based effector mechanisms. Stimulation of immunological killing of helminths by therapeutic agents is one such approach of utmost importance.

To prevent infection, host gradually developed resistant ability (Van Houtert and Sykes, 1996) [29]. Kahn (2002) observed natural resistant nematode of gastrointestinal tract. Such infection showed increased in proteins which develop endogenously in tract. Thus supplementary intake of protein may reduce losses and morality.

Parasites are highly successful organisms that have cleverly outwitted the developed adaptation against their hosts. Helminths parasites are seen affected by phagocytes (Nawa *et al.*, 1994). Therefore the host must destroy and kill helminths in alternate ways. T-cell and eosinophils are most likely to have direct effect on helminth. Immunity against helminth parasites is T-cell dependent. Initially, the work on immune-adaptation was focused on mechanism by which parasites evade or inactivate specific host effecter response (Sugawara *et al,* 2016).

In case of pinworm, mouse model, several studies have provided enough evidence regarding the involvement of cellular and humoral immunity, which play an important role in operating immune mechanism. Infection of *Aspicularis tetraptera* in mice through eggs produces a strong immune response induced by antigenic stimulation. Behnke (1974) [24] also observed the immune against Nematode (*Aspicularis tetraptera*) in mice by introducing primary challenge infection.

Scientists explained the role of somatic antigen (prepared from *Aspicularis tetraptera*) in family of oxyuridae which triggered immune system in lab mice. The expulsion of nematode parasite during 2nd and 3rd week of primary infection (*T. muris*) were observed in vaccinated mice (Gaherwal *et al.*, 2011, 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34].

Acquired immunity against *Trichuris muris* in albino lab mouse was studied by Wakelin *et al.* (1967). Immunity against *Trichinellu spiralis* III and longation of intestinal phase of infection in experimental mice was reported by Denham (1968). Ogilive (1973) reported the immunity & host-parasite relationship in infection of Nippostrogylus brasilensis. Acquired immunity against infection manifested by quiuck explosion of challenge infection was studied by Wakelin, (1973). Eosinophilic counts in blood of vaccinated and nonvaccinated mice with Hymenolips diminuta were studied by Gaherwal & Prakash (2009b and 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34]; Verma *et al.*, 2010a and b which indicate that eosinphilis has significant role in immune system of hosts (Sorobetea *et al.*, 2018) [28].

Observations on nematode infection in GI have revealed inhaled local cellular activity of mucosal mast cells, globular leucocytes, eosinophils and systematic humoral responses with specific antibody production of IgE (Sorobetea *et al.*, 2018) [28]. DTH reactions indicate cell-mediated immune responses which exert important immunopractive or immunopathologic effects (Sharma *et al.*, 2006) [26, 27].

Else (2003) [7] found that mice immunized with eggs showed a perfect resistance against challenged infection. Else *et al.* (1994) indicated that immunity is almost exclusively operative in the intestinal tissue of immunized mice. Protective action of immunity is undoubtedly directed against the eggs or larvae in the mucosa.

Koyama *et al.* (2000) [19] have suggested that primary infection with single eggs is sufficient to induce immunity. Immunity thus induced perfectly prevents the establishment of the larvae derived from the challenge egg infection and is also effective in killing to adult worms. Vaccine development against nematode is possible. Secondary infection of egg can be removed by immune mechanisms. Resistance to secondary infection may be developed either by primary infection or by immunization (using parasite extracts).

Several workers have attempted to immunize the host animals to nematode infections using antigenic materials from various stages of the worms (Vercruysse and Dormy, 1999). The eggs secretion may be used as potent source of immunogens.

Wakelin and Selby (1976) studied the immune explusion of *Trichuris muris* from resistant mice by transfer of lymphoid cells. Helminth parasites are multicellular organisms and thus they are not ingested by phagocytic cells such as macrophages or neutrophilis. Therefore, extracelluar digestion or/and granulomass are the available ways for the host to protect itself against helminth invaders. Eosinophils and mast cells are considered as appropriate cells because they contain large amount of various chemical mediators like hydrolytic enzyme and cytotoxic substances in their granules and also in their cytoplasm. They release these substances on degranulation or on stimulation. This may be the major reason why eosinophils and mast cells are affiliated with infections caused by helminths (Gaherwal *et al.*, 2014; Verma *et al.*,2018a and b).

RBC and haemoglobin lowered in the mice infected with *A. tetraptera* vaccinated with adult somatic antigen (Gaherwal and Prakash, 2012a, 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34]. Helminthic infection reduced albumin and elevated globulin contents along with significant changes in protein (Gaherwal *et al.*, 2012a and 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34]. Depletion in total serum protein was recorded, due to breakdown of protein. Albumin in important nutrient for developing worms. Increased albumin level in mice vaccinated indicates the killing or elimination of the worm by the immunogen. Globulin increased in vaccinated mice in comparison to infected non-vaccinated mice may be due to globulin containing antibodies (Gaherwal and Prakash, 2012a, 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34]. Increased globulin value indicates the production of antibodies which causes manifestation of host immunity against parasitic.

Specific antibodies against somatic components or excretory products of parasites are commonly detected in serum of the host infected with helminths. Detection of specific antibody or sensitized lymphocytes is useful tools for the diagnosis of the helminths (Nawa *et al.*, 1987). Usually nonspecific inflammatory responses were observed in helminthic infections which generated to protect and maintain homeostatic integrity of the host animals (Demri *et al.*, 2017). Eosinophils are considered as the effecter/regulator cells to fight against tissue migrating helminths and to encapsulate them, whereas mucosal mast cells are the effecter/regulator cells to expel lumen dwelling parasites from the intestinal tract.

Blackwell and Else (2001 presented a result which indicates that the protective antibody developed in four weeks after an oral egg infection and then potent immune serum of recipient mice killed almost all of the invaded larvae and adult worm. The antibody responsible for protective immunity to *T. muris* may be involved in IgG, or IgG 2a or

both classes of immunoglobulin (Koyama *et al.,* 2000) [19]. It is clear that increase in level of IgE occurs after egg infection although protective role of IgE is still uncertain.

Increase in the number of lymphocytes in the infected groups confirms the involvement of lymphocyte-medicated cellular immunity in *T.muris* mouse model (Else and Schoolmester, 2003) [7]. Lumphocytes were observed (Rothewell, 1989) associated with both immunized and challenged groups of mice.

The gastrointestinal helminths can present fascinating information about immune regulation, improved understanding of protective immune mechanism (Gaherwal *et al.,* 2012b, 2014) [10, 11, 12, 13, 14, 31, 32, 33, 34]. Hence gastrointestinal helminth are key organism for the development of vaccine. Above reviewed literature thus suggest that selected research problem is valid for further research investigation.

Conclusion

Helminths are multicellular parasitic organism having medical and economic value. Many human beings and domesticated animals were found infected worldwide by parasite of helminth. Helminths were key factor of morbidity and mortality, especially in developing countries. The World Health Organisation report indicates that more than 2.5 billion human are found infected with parasitic worm. Intestinal helminths infections are more in children. An estimate indicate that by year 2025, approximate 57% of human population (countries developing) may be infected by helminth infection.

The many of the available antiparasitic drugs are safe, cheap and effective against helminth parasites. However, the rapidly increase resistant in parasite species against drug is making the control of problem worst. One option available is to control the helminths infection or 3 prevent infection by parasite through vaccination. In other words we can say that by discontinuity in the life-cycle and we can keep away the infection source from animals or humans. Nematodes are occupying the gastrointestinal (GI) tract of animals where they released undefined chemicals (excretory-secretory antigens) into their environment. These chemicals elicit powerful and potentially damaging immune responses which are responsible for the expulsion of larval and adult.

In past few years the field of immunology has undergone a rapid expansion. The immunological techniques have allowed investigators to examine specific problems from new angle of approach. Immunological killing of helminths by therapeutic agents and immunological control through vaccination were studied by many past researchers.

Immunity or host resistance is the ability of a host to prevent from infection caused by parasites and expel settled parasites by two types of immune responses, innate and acquired. Innate immunity is inherent, whereas acquired immunity develops gradually in the animals after exposed to parasites. Most adult ruminants acquire naturally acquired protective immunity against GI nematodes. The protective characteristic generally exists by ability of host to reject larvae or to expel adult parasites. Immunity is supposed to be dependent on morphological and physiological status of host i.e. health, sex, age nutrition and stress etc. factors.

The parasitic infection generally stimulates many immunological defiance mechanism and responses that predominates and depends upon the identity of the parasite. Parasitic infections may become chronic. Consequences of chronic infections show the presence of circulatory antigens, persistent antigens stimulation and the formation of immune complexes. The subject of immunology rapidly develops in parasitology. Advanced immunological techniques have allowed researchers to evaluate problems from a new angle. Immunological killing of helminths by therapeutic agents is one of such new approach which needs much attention.

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