HOST IMMUNE MECHANISMS OF PARASITE DESTRUCTION.

Immune Response

The immune response to parasitic invaders is in principle based on the same components as the response to other infectious agents. The relative importance of the single components, the interaction between them, and the resulting effector mechanisms are highly variable, depending both on the species of parasite and host.

Mechanism of Immunity

The immune system exhibits a range of responses involving humoral factors, immunoglobulin, and sensitized calls of the lymphoid system. The immunoglobulin which posses antibody activity comprise distinct classes of which IgG, IgM, IgA and IgE are the most important, IgG is the predominant class circulating in the blood stream. IgA may be involved in local immune response through its capacity to cross-epithelial surfaces of e.g. the gut, the bronchi or the mammary gland. IgE may be associated with cells in immediate hypersensitivity reactions. Also additional humoral factors like complement are involved in many immune responses. The cells may be lymphocytes derived from stem cells in the bone marrow. There are two major categories of these cells, namely; the B-cell lymphocytes which give rise to plasma cells whose main function is the production of immunoglobulin and the T-cell which develop under the influence of thymus, and transform into cell populations such as the so-called helper and suppressor cells. There is a close and complex cooperation between the B- and T-cell systems and other cells like macrophages, mast cells, and polymorphonuclear leucocytes. One cell type within great number in helminth infection especially where the association of parasite with host tissue is close. Several arms of the immune response must interact before the animal can effectively control its parasites. Thus, simple neutralization by antibody, which may operate against bacteria and viruses, is usually incapable of affecting parasite. Composite effector mechanism like antibody mediated cell lysis by lymphocytes may be effective although much more complex reactions are usually required. Immediate hypersensitivity reactions are often encountered in the local environment of the parasite in that mast cells become sensitized with antibodies of the IgE class.

On contact with a parasite antigen, the mast cell releases so called vasoactive amines, which cause smooth muscle concentrations and increased permeability of blood vessels. Evidence suggests that this may demolish parasites either because of physiological changes of their environment or because they come in closer contact with antibody and other defense factors of the host. Other parasites induced tissue lesions, with or without an immune background may also create unfavourbale conditions. This it is believed that parasites may be trapped and immobilized by granulomas and connective tissue formations.

Manifestation of Immunity on the Parasite Population

Whereas immunity to bacteria or viruses is often able to protect the animal from initial attack or to destroy the invaders – this is not characteristic for immunity to parasites. There immunity develops slowly, and seldom cause total elimination of the parasite population.

In helminth infections immunity may affect parasites in at least three characteristic situations:

i. The parasite population or sub-population may be markedly reduced
either because it is trapped and killed in the tissues or because it is expelled from the host, e.g. via the gastro-intestinal tract. In domesticated animals, probably the best known of all expulsion phenomena is the so-called self-sure reaction described in haemonchosis in sheep. The major responsible factor for this phenomenon may be local hypersensitivity reaction of the immediate type triggered off by the antigenic stimulus provided by the introduction of infective larvae, although it has been indicated that under certain conditions it may be induced by dietary factors.
This pattern of expulsion may also operate in other helminth infections like dictyocaulosis and ostertagiasis of ruminant. In these infections, immunity is associated with a terminal exponential expulsion of adult worms.

ii. A number of parasite species may become arrested in their larval
development as a result of acquire immunity. Larvae may also become temporarily arrested due to prior experience of certain climatic and environmental factors. This process referred to as hypobiosis is comparable with the diapause phenomenon encountered in insect physiology.

iii. Reduction of size and egg-laying capacity of adult worms observed
in chronic infections may be a result of acquire immunity.

In protozoan infections, acquire immunity may exert the influence in a number of ways including agglutination, immobilization, lysis or phagocytosis, and reproduction/multiplication may be inhibited.
In both helminth and protozoan infections, a complete elimination of the parasite population may not always be entirely beneficial. Long-term protection by the continuing stimulation of the immune apparatus may acquire persistence of at least a few parasites, a state that is usually designate premunity or concomitant immunity.
It is evident that the capability of the host to acquire immunity to a given parasite plays an important direct role in limiting the incidence and severity of clinical disease.

Evasion of the Immune Response

Many parasites appear not to elicit or not to be affected by their hosts' immune response. Any parasite which can survive in its mammalian host for appreciably more than nine days must be assumed to have some mechanism for avoiding or mitigating their hosts' immune response. The evasion strategies can include: surface absorption of host antigen, molecular mimicry, loss or masking of surface antigens, antigenic variation, the occupation of immunologically incompetent sites and immunosuppression. There is no evidence for specific immunological tolerance.

Invertebrates have innate, but not aquired immune responses, invertebrates have no 'immunological memory'. However, the evasion strategies used by parasites of invertebrates show many parallels with those used by the parasites of mammals.

There is a complex interaction between parasites and their hosts' immune system and parasites may provide unique systems in which to study immune responses.

Many parasites may survive for long periods in immuno-competent hosts. A number of mechanisms have been recognized which may explain how the parasite avoid the potential lethal consequences of the host response. Three relative well-described mechanisms are;

i.   Parasites may be shield from interaction with immune factors in
        special anatomical sites or by intracapsular or intracellular locations, e.g. it is believed that the blood protozoa *Trypanosoma brucei* may be secluded from the host reaction, when it is localized in the central nervous system, and *Toxoplasma gondi*, another protozoa protected with host cells.

ii.   The parasite may avoid the host's immune response by shifting
        antigenic structure. This is a prominent feature of trypanosomiasis and it helps to explain why the immune response is more or less in capable of controlling the disease. Trypanosomes are apparently able to synthesize an unlimited number of variant antigens – at intervals of a few days. The immune response (although effective) occurs invariably too late to affect the parasite because it has altered its antigenicity.

iii.   The parasite may present surface which the host cannot detect or
        attack. In chronic schistomiasis, concomitant immunity is a characteristic feature.

Adult worms persist unaffected in hosts which may be highly resistant to re-infection. The parasite apparently acquires a coating of host antigens on its surface preventing the host from identifying it as non-self. Alternatively, the parasite itself may produce antigens indistinguishable from those of the host, it is also possible that the surface layer (tegument) turns over so rapidly that adhering antibodies or cells are discarded. Immuno suppressive effect exerted by certain protozoan e.g. trypanosomes may be another important factor for the parasite to avoid host reactions.

NEONATAL UNRESPONSIVENESS

The capacity of neonates to respond immunologically to infection varies with the species of animal and with the kind of antigen to which it is exposed. Among domestic animals, sheep fail to develop significant resistance to helminth infection until they are several months old. This has important implications in the field because the animals may be exposed to high levels of infection during the vulnerable period. The phenomenone has been described for *Haemonchus contortus* and *Trichostrongylus colubriformis* and it has been demonstrated in neonatal cattle affect with eggs of the Cestode *Taenia saginata*.

🟢 **Pathology of Helminth Infections:**

In terms of pathology both adult and larval helminths may cause pathology and disease. An important difference between infection with parasitic helminths, and infection with bacterial, viral or protozoan parasites is that, in most cases, the parasites do not increase in numbers within their hosts, (exceptions to this general rule may however be found with larval helminths, or some nematodes such as *Strongyloides* sp.). That is, each larval helminth that infects the definitive host will give rise to only one adult parasite. Therefore, as pathology due to helminth infection is usually density dependent, (i.e. only with high worm burdens is severe pathology present) this parasite density, and therefore degree of pathology, is governed by the rate at which larval parasites enter the definitive host. This aspect of these diseases has important implications for the control of helminth parasites in that the diseases that they cause may be reduced or even eliminated by control measures that do not completely eliminate the parasite. This is the basis for control of many trichostrongylid nematodes of veterinary importance, where it is impractical to completely eradicate the parasite, but the disease caused by the parasite may be eliminated by controlled use of drugs at strategic times of the year. This is not the case with parasites that can divide asexually in their hosts such as bacterial, viral or protozoan parasites, where, for example, a single malaria parasite is capable, (at least in theory), of causing a fatal illness.

In terms of veterinary importance the strongylid nematodes are of greatest economic importance. As has been said above, larval helminth infections in their intermediate hosts may also be important disease organisms, for example hydatid disease in man and domesticated animals (caused by *Echinococcus granulosus* infection), or hyper infections of *Trichinella spiralis* L_3 larvae in their host's muscle tissues. With viviparous helminths larvae may also cause problems in the definitive host. The most important example of this is with river blindness, due to *Onchocerca volvulus* infection, with microfilaria (a pre larval L_1 stage) migrating through cutaneous tissues (causing skin pathology) and the eye (eventually causing blindness).

Pathology with infection of adult helminths may be due to a number of reasons, including:

⭐ Immune responses to adult, larval or eggs stages of the lifecycle (for example with the schistosomes).

⭐ High densities of adult parasites feeding on host tissues, causing tissue damage (for example many of the digenean flukes), or obstruction of the gut, (as may be the case with *Ascaris* infections) or lymphatic drainage (as seen with lymphatic filariasis, although in this case this is a gross simplification of what happens).

⭐ Depletion of nutrients or other metabolites required by the host (for example vitamin B12 depletion, leading to pernicious anaemia with infection by *Diphylobobrium latum*)

⭐ Parasites feeding on blood, causing anaemia (for example infection with hookworms)

⭐ Other reasons

Other parasitic infections however, where the association is much closer, are generally less pathogenic, extreme pathology generally only being associated with high parasite loads. That both parasite and host undergo this evolution may be seen with the association between the protozoan parasite *Trypanosoma brucei brucei*, which in its natural hosts (wild animals such as Zebra and Antelope) do not cause disease. Domesticated animals such as cattle or horses (which have not undergone this co-evolution) when introduced into trypanosome endemic areas are rapidly killed by the same parasites however. The reason for this co-evolution is probably because it is not in the interest of the parasite to kill its host, and the parasite may have evolved ways of reducing any pathogenic effects it may have. This growing association may even go to the extent of the parasites limiting their own densities of infection, (for example the concomitant immunity reported with schistosome infections).

There are however important exceptions to this, particularly for example with infection of intermediate hosts with larval helminth parasites. Here it is often the case that the intermediate host must be eaten by its definitive host to complete its lifecycle. If this is the case, the larval parasites have often evolved to facilitate this, either actively or passively. Examples of parasites actively aiding the predation of their intermediate hosts have been reported from a number of species of helminths that modify the behaviour of these intermediate hosts. For example metacercarial infections of ants by *Dicrocoelium dendriticum* causes the ants to change their behaviour, by running up, and attaching themselves, by their jaws, to the tops of blades of grass, where they can be accidentally ingested as their herbivorous definitive hosts graze. Other behavioural modifications include the intermediate host not hiding itself from predators, as has been reported in fish infected with larval pseudophyllidean cestodes (e.g. *Schistocephalus solidus*), or arthropod intermediate hosts infected with larval acanthocephalans. Other more passive means include infection with many larval cyclophyllidean cestodes, where the larval cestode may, as it develops to maturity, cause extreme pathology (for example infection with species of *Echinococcus*), which will eventually kill the intermediate host. The dead intermediate host is then available for scavenging by the carnivorous definitive hosts, who then become infected, completing the parasites lifecycle. Larval helminths in accidental or paratenic hosts may cause pathology, two types of condition being important. Firstly **Visceral Larval Migrans**, as seen with *Anisakis* and *Angiostrongylus* infections, and importantly with the larvae of the nematode *Toxocara canis*, where migrating larvae may causes blindness in infected humans (usually children). Here larvae migrate deep within the paratenic hosts tissues. Secondly **Cutaneous Larval Migrans**, where the larvae migrate through the skin and subcutaneous tissues. Examples here include dog hookworms of the genus *Ancylostoma*. Some larval helminths may cause both conditions in paratenic hosts, such as is the case with plerocercoids of Pseudophyllidean Cestodes such as *Spirometra*, where the condition is known as sparganosis.

THE PRINCIPLE OF DIAGNOSIS, TREATMENT AND PREVENTION

Immunodiagnosis of Parasitic Infection

The available immunodiagnostic procedures in parasitism comprises serodiagnostic test base on detection of specific antibody in the serum.

Serodiagnosis

The humoral immune response to parasitic infection involves the occurrence of varying levels of specific antibodies in the blood stream. Description of fluctuation in antibody titre (and immunoglobin levels) has for many years been included in studies on immunology of parasite/host relationship. The importance of serology lies in its diagnostic capacity. Routine diagnosis usually depends on direct identification of the parasite, but there is a number of infections where parasite stages are not excreted with faeces or urine or released to the blood stream, and therefore not directly identifiable by isolation and microscopy. This applies to infections like trichinelosis, hydatid disease, toxoplasmosis etc., where indirect method such as serology are needed. Serology may be relevant in other infections because direct demonstration of the parasite may be tedious and time-consuming. In addition, direct and indirect approached may be complementary. Serology may, for instance, be applied during prepatent, hypobiotic - or other non-reproductive phase of helminth infections. Serodiagnosis may also be helpful in many haemoprotozoan diseases where parasitaemia is restricted to certain phases of the infection.

The qualification of a serological method in animal parasitology is determined by its degree of sensitivity, specificity and reproducibility, weighed against cost and capacity for routine applications. Methods in use include the Complement Fixation Test (CFT), the Indirect Haemagglutination Test (IHT), Indirect Flourescent antibody Test (IFT) and the Enzyme Linked Immunosorbent Assay (ELISA). Whatever the test may be, it's major limitation seems to be specificity and to a lesser extent sensitivity. Parasite antigens are very complex mixtures and no serological test can be more specific than the antigen used.

Examination of the Body

The body is searched for external parasites or their eggs (bots, oxyurids), not only the surface but also in the ears and in the conjunctival sac (eye worm), and the skin should be palpated to determine the presence of subcutaneous larvae. If mange like lesions are present, the hair round the affected area should be clipped and scrapings made with a scalpel, the blade being held at such angle that the material scraped away falls into a piece of card or paper or a microscope slide held underneath. A little oil on the blade used will cause the material to adhere tot he blade, so that it is not lost. Scraping should continue until suspected. The lesion should then be dressed and the material examine for the presence of mites or of fragments of them. Some material may be examine directly, either in water or saline or in light oil, e.g. clove oil. It is too dense for direct examination, it should be brought just to the boil in 10% caustic soda or caustic potash to break it up. It may then be examined in the hydroxide used, but it is better to centrifuge it lightly and examine the sediment. It may be possible to find mites in the external auditory canal by rotating a cotton-wood swab in this canal. A little oil on the swab will help to capture the mites. Examination with an illuminated auriscope may be useful.

Examination of Excretions

Excretions of the body may contain parasite eggs or larvae. The nasal discharge and the sputum may, therefore, aid in the diagnosis of parasites in the air-passages, the vomit may bear evidence of parasites in the stomach, and the urine may contain eggs which can be concentrated by centrifuging. The faeces are by far the most important, as eggs or larvae of gastro-intestinal parasites and may others leave the body in the faeces. It should be remembered, however, that no eggs may be found if the worms are still immature of it only male are present.

Faeces

Faeces are examined in the first place for adult parasites, larval stages insect (e.g. bots) or segments of tapeworm. If a tapeworm infection is suspected, a purgative may be given to cause the expulsion of segments in case they are not readily found.

Birds that have caeca, as the domestic fowl for example pass two kinds of faeces, those from the small intestine being relatively coarse and loose with particles of varying colour, while those from the caeca are of a fine, pasty nature with a homogenous brown or brownish-green colour. The eggs of small intestine worms will be found in both types of faeces, while those of caecal worms are found only in the caecal faeces.

Blood Examination of Larvae

The microfilariae of most filarial worms are found in the blood and the diagnosis of filariasis is made by finding them in blood examination.

i. A drop of fresh blood is placed on a slide, covered with a cover-slip and examined immediately. The microfilariae will be seen moving about. This method can be carried out as a preliminary, but is not suitable for a specific identification.

ii. If the larvae are abundant, a thin smear can be made; if they are rare; a thick film is made and this gives better results in the majority of cases. The films are completely air-dried as quickly as possible and the thick film is them placed into vessels of distilled water in a slanting position and facing downwards, until it has been completely dehaemoglobinished. It is then air-dried again, fixed in methyl alcohol for ten minutes and then stained.

iii. When the microfilariae are rare concentration techniques such as the knot technique are applicable.