Host resistance to ectoparasites

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Summary: Examples of immunological reactions to arthropod parasites include responses by hosts to the following stimuli:

- excretory and secretory antigens produced by myiasis-producing larvae or skin-dwelling (mange) mites
- salivary antigens of blood-sucking arthropods.

In many cases, these are hypersensitivity reactions, which often appear not to produce very deleterious effects on the parasites. However, some reactions - such as those induced by natural infestations with ixodid ticks and certain mange mites - damage the parasites and protect the hosts.

Recently, successful vaccines have been devised to protect cattle from Boophilus microplus ticks. The antigens used, which are believed not to be introduced into the host during natural infestations, came from the midgut of the ticks. Such antigens, which are normally 'concealed' from the host, appear to induce 'novel' immunological responses which are difficult for the parasite to combat. Similar 'concealed' antigens have also been investigated in potential vaccines for use against other ectoparasitic arthropods.


MYIASIS

During infestations with myiasis-producing larvae, one would expect the parasites to present a number of potentially antigenic materials to the immune system of the host, and that the host would respond to these antigens. Both of these things happen but in natural infestations, which are the result of long-term evolutionary host/parasite associations, the responses of the hosts provide only a moderate degree of protection and rarely destroy all the parasites. A balance has been reached between the protective immunological responses of the hosts and the protective counter-measures of the parasites.

In blowflies, such as Lucilia spp., the larvae develop in subcutaneous sites in the hosts. The parasites develop through three larval stages before leaving the host to pupate on the ground.

Blowfly infections in sheep are of particular importance in Australia, and many investigations into immunological reactions to these parasites have been conducted in this country (59). The parasitic larvae in the skin of the sheep present a number of antigenic components (including excretory and secretory materials) to the immune system of the host, and there is some evidence to suggest that multiple infections with

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blowfly larvae do indeed induce a measure of resistance in sheep (25). However, up to seven or eight repeated infections may be required to induce demonstrable acquired immunity. Some of the secretions or excretions produced by the parasitic larvae are powerfully immunosuppressive (41) and this may partly explain why resistance to the larval infections is not readily induced in natural infestations.

Investigations of immunological responses in sheep infected with blowfly larvae have shown that antibodies to larval antigens do occur. Some of these antibodies reacted with antigens from the larval gut and salivary glands of the blowfly larvae (63). This is reminiscent of a report, published in 1930, on resistance in guinea-pigs to larvae of another myiasis-producing species, *Cordylobia anthropophaga*, in which death of larvae in the immune animals was associated with a reaction between the larval gut contents and sera from immune animals (11). At present it is uncertain to what extent antibodies protect infected sheep, but serum samples from repeatedly-infected sheep significantly inhibit larval growth *in vitro* (62).

Two intriguing reports published recently have shown that a protein component of the peritrophic membrane from the gut of *Lucilia cuprina* larvae can be used to immunise sheep and induce significant protection (24, 26). The gene responsible for this protein has been sequenced, and trials with recombinant antigens have commenced (71). It has been suggested that this antigen may be a ‘concealed’ antigen, which is unavailable to the host during a normal infestation; therefore, when the antigen is used in a vaccine, the host responds with a ‘novel’ immunological attack to which the parasite has evolved no counter-measures (71) (see description of the ‘concealed’ *Boophilus microplus* antigen in the section on artificially-induced tick resistance).

Another indirect approach to immunological control of blowfly infections has been to use bacterial antigens to vaccinate sheep against the bacterial infections of the skin which cause lesions (fleece rot) that are attractive to egg-laying female blowflies (59). However, as many different bacterial species may be involved in fleece rot, multivalent vaccines of this type would presumably be required.

In other studies, strains of sheep have been selected as innately resistant or susceptible to fleece rot and blowfly myiasis. The exact reasons for the resistance or susceptibility of the two strains are not known, but innately resistant sheep were found to react more strongly to intradermal injections of excretory/secretory products of *L. cuprina* larvae. This might be due to innate reactivity to pro-inflammatory components of the larval materials, or to an enhanced ability to acquire (protective) hypersensitivity responses to larval allergens (51).

The larvae of *Hypoderma* spp. infect cattle and parasitize their hosts for much longer periods of time than the blowfly larvae. *Hypoderma* spp. larvae also induce immunological responses and a degree of protection against reinfection in their hosts (49).

A recent review on the biology of cattle grubs includes a section on immunological responses and potential vaccines (61). Infected cattle have long been known to produce anaphylactic responses when injected with extracts of *Hypoderma* larvae, and it appears that the massive inflammatory reactions which occur at spinal or oesophageal sites when larvae are destroyed there by insecticidal treatments of infected animals, are also anaphylactic responses due to the release of larval antigens in sensitized animals.

Cattle may acquire variable degrees of resistance following infections (28). Antibody responses, including immediate hypersensitivity reactions and cell-mediated immunological responses to larval antigens, are demonstrable in infected animals, but
the exact ways in which such responses might damage the parasite or protect the host are still unknown.

Early investigations of potential vaccines made use of crude extracts of *Hypoderma* larvae (28). Extracts of first-stage larvae, but not third-stage larvae, were found to produce measurable protection in vaccinated animals.

More recently, studies have focused on a number of isolated and purified protease enzymes derived from first-stage larvae. Of these, the so-called hypodermins A, B and C have been evaluated in vaccination trials. Significant levels of protection have been obtained in animals vaccinated with various combinations of the hypodermins (8). However, in a trial in which animals vaccinated with hypodermin A were subjected to natural infestations, no significant protection was demonstrable (15).

Apart from investigations of their potential use in anti-*Hypoderma* vaccines, hypodermins A and B have also been shown to degrade bovine complement (6,12). This ability may well represent an important mechanism whereby the parasites interfere with the protective inflammatory and immunological responses of the host.

**BLOOD-SUCKING ARTHROPODS**

Hosts of blood-sucking arthropods respond with hypersensitivity reactions to antigens in the saliva of the arthropods. These reactions usually irritate the host and, in some cases, appear to produce deleterious effects on the parasite. Several of the parasites which take prolonged blood meals, or are permanent inhabitants of the skin of the host, cause significant immunosuppression.

In some cases, antibodies from hosts which have been artificially immunized with antigens other than the salivary antigens of the parasites, may deleteriously affect the arthropod when a blood meal is taken.

**MOSQUITOES**

From a review published in 1987 (49), it appears certain that skin reactions to the bites of mosquitoes represent hypersensitivity responses to allergens in the saliva of the female mosquitoes. These reactions are of two types. The 'immediate' reaction is a wheal and flare reaction which begins 1-2 min after the bite and lasts for approximately 1 h. The 'delayed' reaction commences approximately 24 h after the bite and may last for a further 24 h.

If human volunteers or experimental animals are subjected to repeated bites by the same mosquito species over prolonged periods, the sequence of skin reactions occurs in five stages (Table I). No reactions occur to the first few bites (stage 1), and only delayed reactions occur in stage 2. Later in the series, a single bite induces both an immediate and a delayed response (stage 3). Later again, only an immediate response occurs (stage 4), and eventually (if the bite series continues long enough) most individuals may become unresponsive again (stage 5).

The same series of skin reactions can be produced by repeated intradermal injections of small doses of other foreign proteins (48), and the reactions in stages 2 and 3 are now known as cutaneous basophil hypersensitivity (CBH) reactions, as they involve large numbers of basophil leukocytes in the reacting skin (57).
Evidence exists to show that some salivary antigens are shared among several species and at least two genera of mosquitoes, while other antigens appear to be specific for a given mosquito species (49).

Both immediate and delayed skin reactions are itchy and irritating to the host, and it is possible that the immediate skin reaction may occur rapidly enough for the host to dislodge or swat the feeding mosquito, but neither reaction causes direct harm to the mosquito, which has usually fed and departed within a couple of minutes of first probing the skin.

A few human subjects show very serious systemic reactions to mosquito bites. Attempts to desensitize such patients using increasing doses of mosquito allergens have not generally been successful (42), possibly due to the impure nature of the antigenic extracts used in such trials.

In several studies, mosquitoes have been allowed to feed on hosts which have been experimentally immunized with extracts of mosquito tissues. These hosts produced antibodies specific for antigens in the mosquito tissues. The antibodies were taken in by the blood-feeding mosquitoes and entered the haemocoel. In some cases, it was possible to demonstrate significant reductions in fecundity or increased mortality in such mosquitoes, and these effects were apparently associated with the antibodies picked up by the feeding mosquitoes (1, 34, 35, 54). There has been speculation that suitable vaccination of mosquito hosts with various mosquito antigens might result in sufficient disruption of the normal physiology of the parasite, and thus effect some reduction in the transmission of mosquito-borne pathogens (54). It has also been shown that immunizing mosquito hosts with antigens from sexual stages of mosquito-borne malaria parasites can exert control on the transmission of the protozoan parasite (10).

**CERATOPOGONIDAE**

Repeated bites from *Culicoides* species and other ceratopogonids cause severe skin reactions in horses and other hosts. Again, there is firm evidence to suggest that these are hypersensitivity reactions to *Culicoides* antigens (49). As with many other diseases involving allergies, very severe skin hypersensitivity reactions are found to occur in a relatively small proportion of the host population at risk, and there is a hereditary predisposition for such responses. There is some evidence for the existence of a significant association between the possession of one particular equine leukocyte antigen and the occurrence of severe skin reactions in horses (32).
SANDFLIES

In human volunteers subjected to repeated bites from sandflies (*Phlebotomus* sp.), a series of reactions was observed which was quite similar to the five-stage series found to result from repeated mosquito bites (49). Also, in guinea-pigs which were given repeated bites from *Lutzomyia longipalpis*, the changes in numbers of basophil leukocytes in the peripheral blood were interpreted as indicating that CBH reactions were occurring in the skin of the bitten hosts (14).

Salivary gland components of female *L. longipalpis* have been shown to enhance the infectivity of *Leishmania major* organisms which are transmitted by this species of sandfly. The salivary gland components appeared to cause some inhibition of the antigen-presentation function of macrophages (64).

BLACKFLIES

Although blackflies cause serious problems to humans and livestock, reactions to blackfly bites have received relatively little immunological study (49). Cattle are known to have succumbed following massive numbers of bites from *Simulium* spp., showing signs similar to anaphylactic (systemic allergic) reactions. However, it remains uncertain whether these responses are mediated immunologically or by toxins. In more recent studies, mice subjected to bites from *Simulium vittatum* were found to produce antibodies (of IgM, IgG and IgE isotypes) specific for antigens in salivary gland extracts (16).

STOMOXYS, HAEMATOBIA AND GLOSSINA SPECIES

*Stomoxys calcitrans* (stable fly) is known to induce quite severe skin reactions and cause serious productivity losses in domestic animals.

Schlein and Lewis (60) investigated the effects of allowing these flies to feed repeatedly on rabbits which had previously been immunized with various fly tissues. Mortality of stable flies feeding on rabbits immunized with fly muscle tissues was twice that of flies feeding on control rabbits; similar effects were observed in *Glossina* which had fed on rabbits immunized with *Stomoxys* tissues. These experiments, together with those of Alger and Cabrera (1) on mosquitoes, represent the first successful uses of 'concealed' antigens to produce deleterious effects on blood-sucking arthropods which had fed on animals vaccinated with such antigens. Schlein and Lewis (60) suggested that antibodies in the blood meal would be able to pass intact from gut to haemocoel. More recent experiments (67) showed similar mortalities in stable flies feeding on immunized rabbits, and it was suggested that (despite the fairly wide range of potential host species for stable flies) vaccination of individual cattle herds might provide a measure of local control of these flies (67).

The salivary antigens of *Haematobia irritans exigua* (buffalo fly) have been shown to induce immunological responses, and cattle exposed to these flies show immediate hypersensitivity reactions to such antigens (40). However, no significant deleterious effects were observed in flies feeding on previously-exposed cattle with high titres of anti-salivary antigen antibodies. It has been shown that host immunoglobulins can pass into the haemolymph of blood-feeding flies (3). Potential vaccines using other antigens (such as midgut antigens) are being investigated.
Human skin reactions to bites from tsetse flies, as with bites from other blood-feeding insects, are caused by allergenic components in the saliva of the insects (29). Guinea-pigs subjected to repeated bites from Glossina morsitans produced increased numbers of basophil and eosinophil leukocytes both in the circulating blood and in the bitten skin (14).

Rabbits bitten repeatedly by tsetse flies have been shown to produce antibodies to components of the salivary glands of the flies, but the presence of such antibodies was not associated with demonstrable changes in longevity, mortality or pupal production in the flies feeding on these rabbits as opposed to naive rabbits. However, flies feeding on multiply-exposed ears were thought to find difficulty in obtaining the normal volume of blood (49). More recently, claims have been made that resistance to tsetse flies (a killing effect) could be transferred passively from one rabbit to another with intravenous inoculations of serum (45).

In experiments designed to monitor the effects on Glossina fuscipes fuscipes of feeding on rabbits which had previously been immunized with extracts of intestinal tissues of the tsetse flies, the use of these ‘concealed’ antigens produced statistically-significant but minor increases in mortality among the flies (18).

A different means of controlling tsetse flies has been suggested, using the immunological responses of the host, following the demonstration that it is possible to rid tsetse flies of the symbiotic organisms which normally supplement the nutrient requirements of the flies (50). This can be achieved by feeding the flies on hosts which have been immunized with the symbionts of the flies. The blood of these hosts contains anti-symbiont antibodies. Flies lacking symbionts have severely reduced fecundity, and it is suggested that a measure of tsetse fly control might be obtained if it were possible to vaccinate virtually all potential hosts in a given area (43).

**BLOOD-SUCKING HEMIPTERA**

Of the blood-sucking Hemiptera, bedbugs have long been known to cause skin reactions, apparently due to salivary antigens (49). The larger reduvid bugs, such as the many Triatoma species, induce the production of antibodies specific for salivary antigens in bitten hosts (66) and are infamous for causing serious and sometimes fatal systemic anaphylactic reactions to salivary antigens in sensitized human hosts. Offending allergens in the saliva of different species of Triatoma are multiple, but appear not to cross-react with those of different Triatoma species (44).

**FLEAS**

Early studies with guinea-pigs subjected to repeated flea bites revealed exactly the same five-stage series of skin reactions as shown for repeated mosquito bites, and the components responsible for the reactions were demonstrable in the oral secretion (saliva) of fleas (49). It was suggested that a haptenic component in the saliva reacted with collagen components of the skin to produce a complete allergen (49). Saliva from Ctenocephalides felis fleas has more recently been shown to contain many different allergens and to provoke a great diversity of serological responses in individual host animals (30).
Cutaneous basophil hypersensitivity reactions have been demonstrated in guinea-pigs receiving multiple flea bites (38), and skin reactions in flea-sensitized dogs appear to involve both CBH reactions and (later) IgE-related skin responses (22, 33).

Flea allergy dermatitis can be a very serious problem in cats and dogs (22). Diagnosis of the condition using intradermal tests with relatively crude extracts of fleas has been somewhat unreliable, and attempts to ‘desensitize’ dogs with increasing doses of such flea allergens have been far from universally successful (22). Impressively recent investigations using one flea species (C. felis) obtained flea allergens of increased purity and revealed a means of obtaining large quantities of recombinant antigens (30, 31). Such allergens may well improve the efficacy of diagnostic or desensitization procedures.

A recent attempt to protect cats against infestations with C. felis, using a vaccine which included antigens extracted from the midgut of unfed fleas, proved unsuccessful (52). However, another publication has claimed marginal success in protecting dogs from infestation with the same flea species using antigens extracted from the gut of blood-fed fleas (36). It is perhaps rather unlikely that vaccines against the fleas which affect cats and dogs will provide much control of the flea populations. The flea species which infest these hosts also make use of a large number of non-canine and non-feline hosts, and thus vaccination of cats and dogs would not necessarily reduce their numbers significantly. In addition, the skin hypersensitivity reactions which cause so much trouble to sensitized dogs and cats would probably not be reduced greatly by the use of such vaccines.

**SHEEP KEDS**

Adult keds (Melophagus ovinus) are the only blood-feeding stage in the life cycle of these parasites. The adults remain on the host continually and feed frequently. The number of keds on sheep fluctuates annually, with peak numbers in winter. The subsequent decline in ked numbers may be due to an immunologically-mediated acquired resistance (7, 49). Antibodies specific for ked antigens and lymphocyte blastogenic responses to these antigens have been demonstrated in infested sheep, but it is not known how such immunological responses relate to resistance.

In resistant sheep, histological evidence has suggested the occurrence of significant arteriolar vasoconstriction in the outer layers of the dermis, together with hypersensitivity reactions in the skin. However, the exact mechanisms responsible for the arteriolar vasoconstriction remain unknown (49).

Immune responsiveness (estimated by responses of the sheep lymphocytes to the polyclonal T-cell activator PHA) was reduced in heavily-infested sheep, leading to the suggestion that the ectoparasites may cause a degree of immunosuppression (7).

**LICE**

Lice, like the sheep ked, are long-term skin-inhabitants, spending their entire life cycle on the host. Blood-sucking lice (Syphunculata or Anoplura) take repeated blood meals as both nymphs and adults. Most experimental studies of immunological responses to Anoplura have made use of mice with restricted grooming abilities and the
louse species *Polyplax serrata* (49). In strains of mice which acquire resistance, large louse populations build up over a period of about four weeks and the louse burdens then fall markedly as resistance develops. Histological studies showed responses similar to those found in ked-resistant sheep (49). The acquisition of resistance has been prevented by treating infested mice with various immunosuppressant drugs (7), which lends support to the suggestion that immunological responses are at play in the resistance. However, the resistant state appeared to be confined to areas of skin that had previously been heavily infested, which was taken to imply that circulating antibody played no role in the resistance (7).

More recent experimental studies with the louse/mouse system have shown that cell-mediated immune responses to louse antigens occurred at the same time as development of resistance (55), and that resistance was expressed at skin sites other than those originally infested. In addition, skin reactions in mice to louse antigens followed the same sequence as those shown by guinea-pigs in response to repeated mosquito or flea bites. Furthermore, resistance was artificially induced using soluble antigens from disrupted lice (55).

It has been suggested (but not proved) that hosts of mallophagan lice also become sensitized by salivary or excretory antigens, and that this may account for the irritation associated with such infestations. Some recent studies of a mallophagan louse species, *Bovicola ovis*, have shown that these non blood-sucking lice may ingest antibody molecules from hosts, but the amounts ingested were so low that it was thought unlikely that louse ‘concealed’ midgut antigens would provide a successful vaccine similar to that for *Boophilus microplus* ticks (see below) (27).

**TICKS**

For over 75 years it has been recognized that a condition known as tick resistance occurs in certain cattle, and many studies of this phenomenon have been performed using the single-host tropical cattle tick, *Boophilus microplus*, in Australia (2). The tick-resistant state is not innate but is acquired following tick infestations; this state is not absolute and may be reduced under conditions which are stressful to the resistant animals. However, highly-resistant animals allow less than 1% of infesting larvae to develop through to become engorged adult ticks. The ability to acquire such resistance is hereditary, and occurs more often in *Bos indicus* animals (and cross-breeds involving *B. indicus*) than in *B. taurus* animals. The selection of cattle known to acquire high levels of resistance has therefore formed an important part of cattle-tick control schemes in Australia and elsewhere (2).

Cattle have also been shown to acquire resistance to other species of ixodid ticks, including *Amblyomma*, *Ixodes*, *Rhipicephalus*, *Haemaphysalis* and *Hyalomma* spp. (2), and other large domestic mammals such as sheep and horses have also been reported to acquire resistance to various species of ixodid ticks (2).

The acquired resistance tends to be more effective against larval ixodid tick infestations than against infestations of nymphs or adults. Most of the larvae feeding on a resistant animal tend to detach after a short time. They may re-attach briefly at other sites before leaving the host or dying (2).

The mechanisms of acquired tick resistance are not completely known, but there is strong evidence to suggest that the resistance is immunologically mediated and that it is
associated with a complex set of hypersensitivity reactions to tick salivary antigens in the skin of resistant animals. Much of the evidence to support this statement has been obtained from guinea-pigs, rabbits, mice and other rodents, as well as domestic animals subjected to infestations with ixodid ticks (2).

The current dogma claims that tick salivary antigens sensitize the host, with Langerhans cells in the epidermis participating in this process by trapping antigens and carrying them to local lymph nodes where the antigens are presented to appropriate lymphocytes. When ticks feed on sensitized hosts, it is thought that Langerhans cells in the epidermis again trap the antigens, and reactions between antigens and antibodies then occur in the epidermis, leading to the development of epidermal vesicles just below the sites of tick attachments.

CBH reactions to tick salivary antigens occur, and large numbers of basophil leukocytes are attracted—apparently by complement-mediated chemotactic factors—to accumulate in the epidermal vesicles at tick attachment sites. The basophils, with specific antibodies attached to their membranes, degranulate when the salivary antigens meet the membrane-bound antibodies. Pro-inflammatory mediators (such as histamine) are released locally, affecting the attached ticks in two ways:

- directly, by causing the ticks to cease feeding and detach from the host
- indirectly, by inducing local grooming activity (itch/scratch reflex) leading to the mechanical removal of ticks (2).

Most argasid ticks also seem to induce similar hypersensitivity reactions in the skin of their hosts, but no tick resistance is demonstrable. This may be due to the relatively rapid feeding of these species, which normally leave the host within a few hours of the commencement of feeding; the skin reaction may thus occur too late to have a deleterious effect on the feeding ticks (2). However, some argasid larvae, such as those of *Argas polonicus*, normally require several days to engorge. Repeated infestations of pigeons with these larvae have been shown to induce CBH reactions and marked resistance, reaching larval rejection rates of 90-95% (23).

Resistance to ixodid ticks has not been demonstrable in all tick/host associations. Particularly where there have been long evolutionary associations between certain tick species and their ‘natural’ hosts, it seems that the ticks have developed mechanisms to evade or restrict the immune-mediated resistance mechanisms of the host species, allowing the ticks to survive and prosper. Several components of the saliva of the ticks have been shown to produce specific effects of this sort (56).

Immunosuppression of hosts during ixodid tick infestations has been shown to occur both in laboratory animals and in cattle (2, 37, 69). It seems likely that such immunosuppressive effects produced by ticks would reduce both the immune responses responsible for tick resistance and those responsible for protection against tick-borne organisms. The precise mechanisms responsible for such immunosuppression are unknown, but salivary gland extracts of *Dermacentor andersoni* have been found to cause changes in the production by murine leukocytes of cytokines known to exert control over the immune response (69).

**Artificially-induced tick resistance**

Some success has been achieved in attempts to immunize animals artificially with tick salivary antigens. Using relatively crude extracts of salivary glands, some resistance has been induced in guinea-pigs, but the levels of resistance did not reach those
achieved by repeated natural tick infestations (2). More recent reports describe significant but very modest levels of resistance achieved in cattle vaccinated with tick salivary antigens (5, 52). If the resistance mechanisms induced artificially with salivary antigens are similar to those induced naturally by repeated tick infestations, one would expect a high level of resistance to be induced only in cattle with the genes which allow such a response (usually Bos indicus and related cross-breeds).

A very different type of vaccine has been devised by two Australian groups to induce resistance against B. microplus in cattle (39, 53). Such vaccines make use of glycoprotein antigens which are associated with tick midgut cell membranes. The resistance mechanism induced in vaccinated cattle appears to be completely different from that of naturally-acquired resistance and depends on antibodies specific for these midgut antigens. When a tick of this species feeds on a vaccinated animal, the ingested antibodies apparently react with antigens in the midgut cell membranes and, with or without the help of ingested complement components, cause damage to the gut membranes of the ticks, often leading to cell lysis and leakage of the ingested blood into the haemocoel of the ticks and cell-mediated damage to other tick organs (52, 70). Such vaccines have been found to be effective in trials with Bos taurus, providing up to 90% protection in many animals.

It has been suggested that these midgut antigens do not enter the host during the normal feeding activities of the tick, and they have been described as 'concealed' or 'novel' antigens which the host would not encounter under normal circumstances during tick infestations. It is proposed that success in using such 'concealed' antigens can be expected because the parasites would have had no chance to evolve specific counter-measures to cope with the immunological responses of the vaccinated cattle (52, 70, 71).

The ‘midgut’ vaccines appear to be effective using relatively very small doses of antigens together with appropriate adjuvants (52). In attempts to produce sufficiently large quantities of antigens for commercial purposes, it has been possible to use recombinant deoxyribonucleic acid techniques to produce antigenic material in various expression vectors (71). However, the ‘midgut’ vaccines appear to provide no cross-protection against other tick species.

Although the ‘midgut’ vaccines have produced remarkable results, there is some variation in the abilities of individual vaccinated cattle to achieve high-level resistance (52). To date, attempts to correlate the ability to respond well to the vaccines with major histocompatibility complex I (MHC I) antigens of the individual cattle have met with little success, but further work in this domain could be valuable, when it is easier to reveal the MHC II antigens of individual animals (52). Other factors which may improve the performance of the vaccines include means of circumventing the immunosuppressive effects of tick infestations, and the provision of improved methods for (long-term) delivery of antigens when vaccinating cattle (52).

It would probably be unwise to expect similar ‘midgut’ vaccines to be equally effective against all tick species. The effectiveness of the B. microplus ‘midgut’ vaccines depends, to a large extent, on the fact that this species is highly host-specific, almost exclusively parasitizing cattle. Thus, if most of the cattle in a given area were immunized, one could expect to cause a large reduction in the tick population of that area. Similar success could not be expected in controlling other tick species which parasitize many different host species, unless it were possible to vaccinate a large proportion of all the potential host species, both domestic and wild.
The effectiveness of the *B. microplus* 'midgut' vaccines may also depend, to some extent, on the fact that this is a single-host tick. Although the major effects of the system appear to act on the adult tick (70), vaccinated cattle potentially have three 'shots' at each tick: as a larva, as a nymph and as an adult.

**SKIN-INFESTING MITES**

The antigens of skin-infesting mites (mange mites) induce immunological responses in the host, including the same types of hypersensitivity reactions known to occur in response to blood-feeding arthropods. These reactions exert some control over the mite populations, particularly in mites which are long-term skin-inhabitants. In return, some species of mites appear to induce immunosuppression in the hosts.

*Sarcoptes scabiei*

*Sarcoptes scabiei* infests the skin of many different species of mammals. Female mites, and some of the other stages in the life cycle, burrow in the epidermis depositing eggs, excretions and secretions in the skin. Immunological responses to the mite antigens occur, and delayed and immediate hypersensitivity reactions appear in hosts following sensitization (2).

It appears that *Sarcoptes* mites are normally under considerable immunological control in humans, as immunodeficient or immunosuppressed patients (including patients suffering from acquired immune deficiency syndrome [AIDS]) have been found to harbour extremely large mite populations (2, 21). This condition in humans is termed 'Norwegian scabies' and consists of crusted skin lesions, containing massive numbers of mites, over large areas of the skin. Similar lesions occur in other stressed or immunosuppressed domestic and wild mammals (2). The exact mechanisms of immunological control have not been elucidated, but it appears that immune-mediated reactions in the skin, including immediate hypersensitivity reactions and the deposition of complement components and immune complexes, combine to produce adverse conditions for the mites in the epidermis (2).

In recent investigations of swine infested with *Sarcoptes* mites, the hosts have been observed to progress through the first four stages of skin hypersensitivity reactions previously shown to occur in hosts subjected to repeated bites from fleas or mosquitoes (17).

*Psoroptes* spp.

Serious dermatitis can be caused by *Psoroptes* mites in rabbits and large domestic and wild animals. It has been established that *Psoroptes* infestations induce both antibody- and cell-mediated immunological responses in such hosts (2, 13, 65, 68).

There is some indirect evidence to suggest that delayed cutaneous hypersensitivity reactions may result in a measure of control of the mite populations on the skin of infested cattle (2).

*Demodex* spp.

Mites of the genus *Demodex* inhabit the hair follicles and associated sebaceous glands of mammalian hosts. In most host species, these mites occur only in small numbers and appear to cause no disease, but in immune-compromised hosts
(particularly dogs) the mites may proliferate dramatically and produce very severe generalized dermatitis (2).

Clinical demodectic mange has been experimentally induced in normal dogs (which harbour the usual small number of mites) by treating the animals with anti-lymphocyte serum. This has provided support for the suggestion that cell-mediated immune responses, in particular, are usually responsible for controlling the mite populations. There is also evidence to suggest that the familial predisposition to generalized demodectic mange in certain strains of dogs is associated with defects in the cell-mediated immune capabilities of these hosts (2). There have been suggestions that large populations of *Demodex* mites are themselves capable of causing immunosuppression in canine hosts (2, 9), but it is unclear whether the immunosuppressive effects are associated with the mites or with the accompanying bacterial infections.

In a human patient, chemotherapeutic treatment of acute lymphoblastic leukemia was followed by an episode of demodicosis (58), and patients with AIDS have shown similar outbreaks of disease associated with these mites (4, 20).

The immune mechanisms responsible for control of *Demodex* mite populations in hair follicles are unknown, but it is possible that Langerhans cells and other components of the naturally-acquired tick resistance mechanisms may also be involved here.

*Ornithonyssus sylviarum*

Immunological responses of chickens infested with *Ornithonyssus sylviarum* have been studied by several investigators. The sera of infested birds contain mite-specific antibodies, and infested birds have been reported to acquire a degree of resistance (2, 19). Attempts to induce resistance artificially, using mite antigens, have been essentially unsuccessful (47).

*Trombiculid mites*

The larval stages of trombiculid mites feed on fluids and lysed tissues while attached to the skin of many different host species. They feed through a 'feeding tube' or stylostome which forms from salivary secretions. Trombiculid mites induce immunological responses in hosts, and both immediate and delayed cutaneous hypersensitivity reactions occur in sensitized hosts (2, 72).

It appears that skin-dwelling mites (like many other arthropod parasites) may induce hypersensitivity reactions, many of which appear to be protective to their hosts. Presumably – as discussed by Miller (46) in relation to other metazoan parasites – many arthropod antigens also tend to cause the immune responses of the host to be switched into the immediate or cutaneous basophil hypersensitivity mode due to the activities of the appropriate T-helper cells (Th2 cells).

To date, no successful vaccine against skin-dwelling mites has been produced. Perhaps the best advice concerning immunological control of these mites at present would be to avoid causing stress to the hosts, or provoking immunosuppression in any other way, thus enabling the development of maximum protective immune responses.

Résumé : Les réactions immunologiques aux arthropodes parasites consistent notamment en la réponse de l'hôte aux stimuli suivants :

– antigènes d'excrétion et de sécrétion, produits par des larves responsables de myiases ou par des acariens de la gale ;
– antigènes salivaires d'arthropodes hématophages.

Dans de nombreux cas, ce sont des réactions d'hypersensibilité. En général, ces réactions ne semblent pas avoir d'effets très nuisibles sur les parasites. Cependant, certaines d'entre elles, telles que celles induites par des infestations naturelles de tiques et d'acariens de la gale, attaquent les parasites et assurent la protection de l'hôte.

Des vaccins efficaces ont récemment été mis au point pour immuniser les bovins contre la tique Boophilus microplus. Les antigènes utilisés, qui ne pénètreraient pas dans l'hôte pendant les infestations naturelles, proviennent de l'intestin moyen des tiques. Ces antigènes, qui sont normalement « dissimulés » à l'hôte, semblent induire de « nouvelles » réponses immunitaires que le parasite a du mal à combattre. Des vaccins contre d'autres arthropodes ectoparasites sont également à l'étude à partir d'antigènes similaires.


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Resumen: Los ejemplos de reacciones inmunológicas a los artrópodos parásitos incluyen las respuestas del huésped a los estímulos siguientes:

– antígenos de excreción y de secreción, producidos por larvas responsables de miasis o por acáridos responsables de la sarna;
– antígenos salivales de artrópodos hematofagos.

En muchos casos, se trata de reacciones de hipersensibilidad que, en general, no parecen producir efectos muy destructores en los parásitos. Sin embargo, algunas de estas reacciones, como las que son inducidas por infestaciones naturales de garrapatas y acáridos de la sarna, atacan los parásitos y protegen al huésped.

Recientemente se han desarrollado vacunas eficaces que inmunizan a los bovinos contra la garrapata Boophilus microplus. Los antígenos usados, que al parecer no penetran en el huésped en las infestaciones naturales, proceden del intestino medio de las garrapatas. Normalmente «dissimulados» en el huésped, estos antígenos parecen inducir respuestas inmunitarias difíciles de combatir por parte del parásito. Se está estudiando la posibilidad de desarrollar vacunas contra otros artrópodos ectoparásitos a partir de antígenos similares.


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REFERENCES


