Immunity to internal parasites *

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Summary: This review of internal parasitic diseases discusses methods of immune
diagnosis, immune mechanisms of the host, and immunoprophylaxis against
both protozoan and metazoan parasites of livestock. The limiting factors for
immunodiagnosis are specificity and whether the host animals respond
sufficiently to produce detectable serological responses. Because the array of
antigens is so complex, the method of choice for helminths is to use
excretory/secretory products of the parasite as antigens for microplate ELISA.
Similarly, for protozoa, immunodiagnosis is facilitated by using a few, selected,
immunodominant antigens rather than extracts of whole parasite. However,
serodiagnosis does not always identify parasitised animals especially in the young,
malnourished or sick host. Similarly, parasites may themselves modulate the
response of the host and remain serologically undetectable. The production of
recombinant, pure, parasite proteins is already facilitating diagnostic serology
for several parasite species and, using recombinant DNA probes, it is now
possible to distinguish inter- and intra-species differences. The central role of
inflammatory cytokines, the regulatory proteins produced by activated T helper
cells, in modulating both protective and potentially damaging inflammatory
responses is discussed. Finally, the genetic control of the immune response and
its relevance to immunoprophylaxis is considered. Several interesting
developments in the production of sub-unit vaccines and the potential methods
of delivery are appraised.

KEYWORDS: Bone marrow - Diagnosis - Gene Probes - Immunity - Major
histocompatibility complex - T cells.

INTRODUCTION

The molecular complexity of protozoan and metazoan parasites ensures that the
immune response of the host is equally complex. However, analysis both of the parasite
and of the host’s response to it has led to greatly improved diagnosis of parasitic
infection and opened avenues for immunoprophylaxis against those parasitic diseases
which are economically important or which have human health implications.

Economically important diseases include parasitoses as diverse as nematodiasis,
babesiosis and warble fly infection in cattle, trichinellosis in pigs and haemonchosis

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in sheep. However, in view of the great number and diversity of these diseases, this paper will concentrate on the immunological progress in the last few years which facilitates diagnosis of and immunoprophylaxis against a few of the more important protozoan and metazoan parasites.

DIAGNOSIS

Serology

The essential elements for successful diagnosis of internal parasitic disease are adequate supplies of species-specific test antigens and/or highly specific antibodies. Because helminths and protozoa contain thousands of potentially antigenic polypeptides, glycoproteins and glycolipids, many of which are shared with unrelated species or phyla and even with bacteria, there has been great difficulty in developing sufficiently specific diagnostic tests.

In principle the approaches to diagnosis which dispense with time-consuming or potentially dangerous techniques such as faecal egg counts, blood smears and tissue biopsies are those in which multiple samples of serum can be tested by microplate ELISA or by radioimmunoassay. Immunodiagnosis by detection of soluble parasite antigens in faeces, or by tissue biopsy, is also feasible where antibody assays, especially using monoclonal antibodies, are sufficiently specific.

The initial advance in helminth diagnosis was due to the realisation that antigens excreted or secreted (ES) by the parasite in vitro were generally less complex than the somatic antigens (25). Thus, in vitro cultivation of Trichinella spiralis muscle stage larvae in defined medium provided antigens which, when bound to solid-phase ELISA plates, provided a reliable and accurate method for detecting serum antibodies (38) and could be used to screen abattoir pigs. A similar degree of success was achieved when ES antigens from Toxocara canis L3 were used to detect visceral larva migrans by T. canis in man and to distinguish it from other helminthiases (15).

Diagnosis of cestode infection has proved more difficult. The metacestodes develop in the tissues and can only be detected post mortem, therefore considerable effort has been directed towards immunodiagnosis. One of the major difficulties in this approach involves the fact that ES antigens from several Taenia species are antigenically cross-reactive (52) although metacestode antigens have proved more successful for diagnosis of T. saginata in cattle (19). Serological diagnosis of hydatid disease in man has, similarly, proved difficult because of the cross-reactivity of the antigens and one approach is to identify unique antigens by comparative immunoblotting. However, one of the complications in attempting to diagnose cestode infestation is the ability of the parasite to modulate the immune response of the host as indicated by a number of immunological parameters including altered mitogenesis of peripheral blood lymphocytes (Barrientos, Sanchez and Esponda, unpublished communication). In fact it is well recognised that clinical illness and immunodiagnosis of hydatidosis do not necessarily correlate very well (25), presumably because of the modulation of the immune response.

Serological tests have also been developed for trematode infections with particular emphasis on liver fluke and schistosomiasis and using a variety of ES products but
it has not yet proved possible to provide an absolutely reliable diagnostic test (25). Nevertheless, the use of ES diagnosis of fascioliasis in cattle has assisted in earlier diagnosis than was possible with somatic antigens (Pfister, unpublished communication). However, somatic antigens have been successfully employed in field surveys of fascioliasis in France (4). Similarly, ES from first stage larvae of Hypoderma bovis are used to diagnose infection, although the seasonal nature of infection with warble fly limits the optimal period during which this diagnostic ELISA can detect specific antibodies (5).

Overall, the use of ES antigens has enabled sensitive and automated ELISA's to be developed for diagnosis although the accuracy and sensitivity of serological diagnosis relies heavily on three factors:

1. the antigens used are unique to that parasite species
2. infection is associated with antibody responses that reflect the parasite burden
3. that parasite antigens secreted in vivo do not significantly deplete circulating antibodies.

Progress, however, is such that recombinant DNA techniques permit the cloning of ES antigens of interest. For example, several ES polypeptides from schistosomes have been cloned and expressed (25) as has an ES product of T. spiralis L1 (see below). These developments will permit the production of abundant, pure antigen for immunodiagnosis and will ensure a degree of specificity that hitherto has not been possible; the assumption being that ES from a given parasite species contains at least one antigenically unique polypeptide which is immunogenic during natural infection and which, as a recombinant product, retains antigenicity. This assumption may not, however, be true for cestode infections (see above).

Despite the refinements in technology, interpretation of diagnostic serology has many pitfalls. For example, sera tested in the early stages of infection where the host has not yet responded immunologically or, more importantly, in the young, non-responsive or ill-nourished host which is incapable of mounting a serum antibody response, may prove negative despite a heavy parasite burden. Similarly, modulation of host immunity by the parasites themselves can give spuriously negative results. Finally, the selection of test antigen is dependent on its availability and often means that it is recovered from early larval stages of helminth parasites which are most amenable to culture. Such antigens are not always appropriate for reliable diagnosis.

The principles of serology for protozoal infections such as babesiosis are similar to those for helminths, and attempts to streamline them for field conditions by using simple card agglutination tests, show some promise (Barrientos, Sanchez and Esponda, unpublished communication). One of the complications of attempting serological diagnosis is the presence of colostral antibodies in sera of calves sucking immune dams. Again, accurate serological diagnosis, applicable to the field, requires sufficient non-cross-reacting pure antigen. In addition, because of complications associated with maternal transfer of immunoglobulins or stage specificity of the chosen antigen, a good epidemiological knowledge of the disease and understanding of the parasite's life cycle are required to interpret the results.

Whilst babesiosis can be detected in blood smears, other protozoa are more difficult to diagnose: for example, zoonotic infections such as toxoplasmosis and cryptosporidiosis which are proving to be significant public health hazards.
Serodiagnosis of *Toxoplasma gondii* is readily achieved by radioimmunoassay (14) where the host animal has been infected several weeks previously. However, antigenaemia can be detected during early acute toxoplasmosis by ELISA (2) and so also can circulating immune complexes (46). Because cryptosporidiosis is usually a problem in the very young animal it is probably best diagnosed by faecal examination. The incidence of *Sarcocystis* is also high in cattle and several strains are pathogenic; diagnostic tests are currently being developed.

**Recombinant DNA techniques**

There have been a number of exciting developments in the use of recombinant DNA for sensitive and accurate diagnosis of parasitic disease. The major advantage of this methodology is that it permits detection of inter- and intra-specific genetic differences. DNA hybridisation probes have been developed from unique repetitive DNA sequences of *T. spiralis* which, when analysed by DNA restriction enzyme fragment length polymorphism (RFLP) of *T. spiralis*, distinguish between subspecies of parasite with different infectivity for pigs (11). Similar intra-specific genetic variation has been detected by RFLP in isolates of *Taenia solium* from India, Mexico and Zimbabwe (41) and between the human filarial parasite *Brugia malayi* and its equivalent *B. pahangi* which infects animals (49). *B. malayi* and *B. pahangi* are transmitted by the same mosquito vector and are very closely related species in that the highly repeated DNA sequences also have a very high overall homology. Nevertheless, short regions of sequence divergence do exist (49) and short oligonucleotides in which there is 35-40% sequence divergence provide probes with a high degree of species-specificity (49).

Recombinant techniques have, therefore, great diagnostic potential in distinguishing and identifying intra- and inter-species variations which would not be feasible using immunological methodologies. Similarly, the advent of the polymerase chain reaction (PCR), whereby very small amounts of parasite DNA can be amplified by PCR, will greatly facilitate the diagnosis of occult tissue or blood parasites.

**IMMUNITY TO PARASITES**

**T cells, cytokines and immunopathology**

Two major subsets of T cells, the helper (Th) phenotype and the cytotoxic/suppressor cell (Tc) have been identified in most mammals and the advent of sophisticated molecular techniques has established that T cells, when activated, secrete a battery of regulatory glycoproteins known as lymphokines or cytokines. These regulate both the immune response and the inflammatory process (Table I). Cytokines, when bound to specific cell surface receptors, modulate the growth, differentiation or function of the receptor-bearing cells, many of which are derived from bone marrow and serve inflammatory functions.

Recently two subpopulations of murine helper T cells, Th1 and Th2, have been identified on the basis of their capacity to secrete different cytokines (Table II).

At present, the Th1 and Th2 subsets are apparently unique to mice since they have not been described in man and it is not yet known whether Th1 and Th2 cells
**TABLE I**

*Th-cell-derived cytokines which regulate inflammation*

<table>
<thead>
<tr>
<th>Name</th>
<th>Source</th>
<th>Inflammatory effect</th>
</tr>
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<tbody>
<tr>
<td>Interleukin-6 (IL-6)</td>
<td>Th-cells Monocytes</td>
<td>Expands bone marrow stem cell population</td>
</tr>
<tr>
<td></td>
<td>Macrophages Fibroblasts</td>
<td></td>
</tr>
<tr>
<td>Interleukin-3 (IL-3)</td>
<td>Th-cells</td>
<td>Growth factor stem cells and for differentiation of mast cells</td>
</tr>
<tr>
<td>Interleukin-4 (IL-4)</td>
<td>Th-cells</td>
<td>Mast cell growth factor + stimulation of IgG1 and IgE production</td>
</tr>
<tr>
<td>Interleukin-5 (IL-5)</td>
<td>Th-cells</td>
<td>Stimulates eosinophil differentiation and IgA production</td>
</tr>
<tr>
<td>Granulocyte-macrophage</td>
<td>Th-cells Macrophages</td>
<td>Growth/differentiation of progenitors of neutrophils and macrophages and activation of</td>
</tr>
<tr>
<td>colony stimulating</td>
<td>Fibroblasts</td>
<td>mature macrophages</td>
</tr>
<tr>
<td>factor (GM-CSF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interferon-γ (IFN-γ)</td>
<td>Th-cells</td>
<td>Antagonistic to IL-3/GM-CSF-mediated haemopoiesis but activates macrophages</td>
</tr>
</tbody>
</table>

* The list of cytokines is not comprehensive but merely serves to illustrate some of the Th-cell-derived cytokines which, by inducing inflammatory haemopoiesis, play a major role in responses to pathogens. Their role in parasitic infection is only now beginning to be understood.

**TABLE II**

*Cytokines secreted by two murine T-helper cell subpopulations (Th1 and Th2)*

<table>
<thead>
<tr>
<th></th>
<th>Th1</th>
<th>Th2</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Interferon-γ</td>
<td>Interleukin-4</td>
</tr>
<tr>
<td></td>
<td>Interleukin-2</td>
<td>Interleukin-5</td>
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<tr>
<td></td>
<td>Interleukin-3</td>
<td>Interleukin-3</td>
</tr>
<tr>
<td></td>
<td>GM-CSF</td>
<td>GM-CSF</td>
</tr>
<tr>
<td></td>
<td>Lymphotoxin</td>
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</tbody>
</table>

* So far these two T-helper subpopulations have been described solely in the mouse (32, 9) but, in view of the responses detected during murine leishmaniasis which are apparently separately regulated by Th1 and Th2 subsets, the mouse model suggests a novel approach to understanding the biology of host-parasite interactions.

exist in other species. Nevertheless, adoptive transfer into naive mice of a murine Th1 cell line, raised in vitro against an immunodominant *Leishmania major* antigen, protected the mice when they were subsequently challenged with *L. major* (43). Protection was attributed in a separate study (20) to the secretion of the cytokine interferon-γ by the Th1 lymphocyte subset. Conversely, a Th2 cell line, raised against
a different *L. major* antigen, not only failed to confer protection (43) but exacerbated infection, more organisms being recovered after adoptive transfer. It was independently shown that the cutaneous lesions, as well as accompanying raised IgE responses, were the result of the secretion of interleukin-4 (20) which is one of the lymphokines produced by the Th2 subset (Table II). Whilst these observations have been made experimentally in mice, they serve to illustrate the delicate balance between protective or potentially damaging responses. Given the rapid progress in ruminant immunology similar experiments may soon be carried out in domestic animals.

Gamma-interferon, by regulating macrophage oxidative metabolism, induces both anti-parasitic and anti-microbial activity (37, 34). This cytokine is, therefore, likely to be important where obligate intracellular parasites such as *T. gondii* and *Eimeria* sp. are concerned (42). By contrast, the cytokines associated with murine Th2 lymphocytes are more likely to be involved in the regulation of responses against helminths for the following reasons:

a) IL-4 promotes mast cell differentiation and the production of IgE, and

b) IL-5 induces eosinophil differentiation and up-regulates the synthesis of IgA (9); all of the responses described in a) and b) are typically seen during helminth infection (26).

A consistent theme in many studies of internal parasitic diseases is the association of helminth infection with immediate hypersensitivity reactions and mast cell proliferation, both of which are highly Th-cell dependent events. Studies in rats have shown that Th-cell-derived IL-3 regulates the growth and differentiation of intestinal mucosal mast cells (MMC) (17). Furthermore, MMC are activated during the spontaneous expulsion of nematode parasites from the intestine, as clearly demonstrated by the secretion into the bloodstream of MMC-specific granule proteases during the immune expulsion of *T. spiralis* (50). Similar observations on the systemic secretion of MMC-specific granule proteases have been reported in sheep responding to challenge with *H. contortus* (21) and there are experimental observations suggesting that MMC are involved in the protective response against *Ascaris suum* in swine (44).

Eosinophil differentiation and recruitment are also regulated by Th-cells and are consistently associated with helminth infection. There are many *in vitro* studies to show that eosinophils secrete granule products which are highly toxic to helminth parasites (48). Both eosinophils and mast cells bear membrane receptors for IgE and IgG which, when triggered, cause release of granule contents as well as the secretion of membrane-derived lipid mediators leukotriene C4, platelet activating factor and, to a lesser degree, prostaglandins (18). Macrophages also have receptors for complement and low affinity IgE receptors and can be activated to produce free radicals, proteolytic enzymes and hydrolases, all of which may be directly damaging to helminth survival (18).

The type of inflammation operating against helminths depends on the tissue localisation of the parasite. Within the connective tissues Th-cell-mediated recruitment of inflammatory cells, including macrophages, basophils, mast cells and eosinophils may be sufficient, in the presence of the appropriate sensitising antibodies (IgE and IgG) or complement, to generate a variety of toxic mediators; several of these mediators are directly damaging to the tegument or cuticle of the parasite. For example the immature, migratory helminth parasites are probably eliminated from the resistant host through the action of anaphylactic antibodies or complement in conjunction
with inflammatory cells (26). For lumen-dwelling parasites, where direct contact with inflammatory cells is unlikely, other mechanisms of expulsion may be involved. Thus, Th-cell mediated recruitment of mast cells and eosinophils to the mucosa (26) is associated with the generation of lipid mediators (31) and, possibly, of free radicals which may directly affect the motility or the orientation of the parasite. In addition, concentrations of parasite-specific IgA are raised and, in the sheep, this is associated with development of resistance to O. circumcincta (26). Similarly the leakage of plasma proteins, including IgG, into the superficial mucus as a consequence of MMC-mediated permeability changes (35, 26) may alter the quality of the superficial mucus so that it traps and eliminates parasites (24, 28) or acts as a barrier to establishment of nematode larvae in the immune host (29). Mucus may also retain secreted lipid mediators thereby inhibiting parasite motility (27).

Experimental studies in mouse (13) and clinical observations in man (22) tend to support a novel finding in the rat that putative T cells regulate the differentiation of mucosal epithelial goblet cells (26) which secrete mucus. Since the density of goblet cells is greatly increased in the intestinal mucosa during worm expulsion, the concomitant increase in mucus may help to eliminate the parasite (27).

It is clear, therefore, that the Th-cell, through secretion of cytokines, has a major role in the immunoinflammatory responses against parasites, the effects of which may be beneficial or detrimental to the host.

**Antigen presentation and the genetic control of the immune response to parasites**

The genetic make-up of the host determines the outcome of parasitic infection, and attention has focussed on the role of the Major Histocompatibility Complex (MHC), particularly of the Class I and II cell surface antigens which are known to restrict the presentation of processed antigens to T cells. Because parasites have such a vast array of antigens it has not been easy to distinguish the effects of MHC Class II genes from other background genes which may regulate hitherto poorly understood compartments of the overall protective response. A number of experiments, however, now show that MHC Class II surface antigens regulate responses to parasites to varying degrees (23). This is relevant to the future use of subunit vaccines because, instead of a myriad of parasite-derived peptides being presented to the Th-cell via the MHC Class II surface molecules, only one or two parasite-derived peptides would be available in the vaccine. Where the MHC Class II molecules are unable to bind those peptides and present them to the Th-cell, no immune response occurs. Alternatively, if a peptide is bound and presented to an inappropriate Th-cell subset, infection may be exacerbated. An example of MHC-related unresponsiveness to a recombinant, 32 residue, fusion peptide derived from Plasmodium falciparum has already been described in the mouse (16). If this type of subunit vaccine were used in the field, vaccinated animals lacking the appropriate MHC haplotype would not be protected.

Genes encoding the MHC Class II cell surface antigens are merely one of many probable sources of genetic variability in responses to parasites. Studies in mice have shown that the production of inflammatory cells by the bone marrow influences the rates of expulsion of T. spiralis (47). Similarly, selective breeding of lambs which respond at a young age to an irradiated larval Trichostrongylus colubriformis vaccine has demonstrated that the development of early intestinal mastocytosis is associated with the responder phenotype (12). As might be expected, given the large number of immunogenic proteins, immune responses to parasites are controlled by a number...
of genes and this fact must be accounted for in the preparation of subunit vaccines where it may eventually prove necessary to provide a mixture of peptides in order to induce maximal T cell stimulation.

**Non-responsiveness to parasites**

The three major reasons for non-responsiveness are genetic, age-related or parasite-induced. Non-responsiveness also occurs in the undernourished host or where there is intercurrent infection. Genetic non-responsiveness has been briefly discussed in the preceding section but it is also worth noting that different species show very different susceptibility to the same parasite. Thus, sheep are highly susceptible to *Fasciola hepatica* whereas cattle develop resistance (Pfister; Soulsby; unpublished communications).

Non-responsiveness in the young and in periparturient animals are two aspects of helminth infection which have implications for the biological control of parasitism. Whilst periparturient non-responsiveness is probably related to the production of immunosuppressive hormones during lactation, the inability of young calves or lambs to develop resistance to ostertagiasis, haemonchosis or trichostrongyles is poorly understood given that lambs can respond at an early age to infection with *Nematodirus battus* (Soulsby, unpublished). Various mechanisms have been proposed, including the possible development of immunotolerance in lambs born of infected dams (Soulsby, unpublished).

Finally, the parasite itself can develop mechanisms of avoiding or suppressing the immunological response of the host. Evasion of the immune response by nematodes may be related to the ability of the parasite to produce suppressor ES molecules which down-regulate the inflammatory response. An example of this has been described in the mouse where the enteric nematode *Nematospiroides dubius* apparently suppresses inflammation (3). Surface antigens are shed by many helminth parasites, and ligands derived from the host’s immune response are also lost (39). In addition, ES contains molecules which modulate the functions of lymphocytes, macrophages and granulocytes (25). Some of the ES products are proteolytic and cleave immunoglobulins bound to the surface of the parasite, thereby avoiding complement or cell-mediated membrane damage (8).

**IMMUNOPROPHYLAXIS**

Irradiation-attenuated infective larvae can confer substantial protection in laboratory and natural host animals where no such protection is achieved by infection with normal larvae. This is true, for example, for filarial infections where repeated challenge with non-attenuated larvae produces little or no protection whereas 3-5 doses with attenuated larvae can induce 75% resistance (10). In fact, the most successful commercial approach to vaccination against parasites so far has been the use of attenuated living vaccines. Vaccination against *Dictyocaulus viviparus* in cattle and of *Ancylostomum caninum* in dogs was achieved with irradiated larvae which produced a sterile infection of limited duration (45, 30). The *D. viviparus* vaccine has been commercially successful but problems of marketing — including the shelf-life of the vaccine and the continued use, by veterinarians, of anthelmintics — militated against similar success for the *A. caninum* vaccine (30).
Live attenuated vaccines are currently in use for the important protozoal infections, babesiosis and coccidiosis (36) as well as *Theileria annulata*. Despite the high levels of immunity induced, there are inherent animal health and commercial considerations which reduce the long-term prospects for this type of vaccine (36). These problems include:

1. the short shelf-life of attenuated vaccines
2. the possibility that the genetic trait for attenuation is not stable, with the consequent risk of inducing a carrier status amongst vaccinates
3. the risk of contaminant pathogens being introduced into the vaccines
4. the low profitability of attenuated vaccines because they cannot readily be patented (36).

Because of these drawbacks, the attention of the animal health industry has been directed towards molecular vaccines which can be protected with patents and which have few of the drawbacks associated with live attenuated vaccines (36). Indeed, the first promise of a successful molecular vaccine against a helminth parasite is for the cestode *T. ovis* where a recombinant peptide vaccine which protects sheep has been developed (reviewed in the paper by Lightowlers in this issue).

Whilst there is little published information to suggest an early breakthrough in molecular vaccines against nematodes, studies are in progress in Australia, the UK and the USA to produce recombinant vaccines against *H. contortus*, *T. colubriformis* and *T. spiralis*. One approach is to clone immunodominant or so-called protective antigens although these have yet to be clearly identified. An alternative strategy is to select polypeptides which are not normally "seen" by the host, and vaccination studies using a nematode gut antigen, contortin, from *H. contortus* have shown substantial protection in lambs (33). This novel vaccine has an advantage in that the chosen antigen is probably highly conserved and therefore present in other nematode parasites, whereas immunodominant protective antigens may not be shared between species (36). One disadvantage, though, is that immunity against occult antigens would not be boosted by challenge infection and, eventually, the host would need either to be revaccinated or to develop natural immunity against immunodominant protective antigens. In the long term it would probably be advantageous not to have a sterile immunity since it reduces the pressure for the selection of resistant strains (36).

Cattle have been immunised and partially protected with purified proteins from *B. bovis*. A polypeptide of 29,000 MW was purified from erythrocytes parasitised by *B. bovis* which, in protection studies, provided encouraging results (51). Protection against *T. gondii* has also been achieved in laboratory animals with isolated surface membrane proteins, the genes for which have now been cloned (7). Similarly, antigens from *Eimeria* sporozoites induce a high level of immunity in young broiler chickens (36) although the progress towards cloning of these antigens is not yet published.

Given that subunit vaccines are the preferred long-term approach to control of internal parasite diseases of livestock, there remains the problem as to how to administer them cheaply and safely. Experimental subunit vaccines are currently administered at least twice, usually in adjuvant, which would not be acceptable in the field. There is progress in the development of adjuvants, with several promising non-toxic but relatively potent formulations on the market. These include the immunostimulating complex (ISCOM) which is a technically advanced form of
liposome (36) and SAF 1, made by Syntex, which includes the active component of complete Freund's adjuvant and a surfactant polymer (1), but the efficacy of both adjuvants has yet to be tested widely in the field.

An alternative approach is the use of recombinant vaccine vectors. At present, vectors such as vaccinia which have been well tested under laboratory conditions cannot be used in the field because they can cause fatal infections in immunosuppressed people. Vaccinia could, theoretically, recombine with another pox virus to produce a potentially hazardous pathogen (36) and it is not yet clear whether genetically engineered vaccinia will, when sufficiently attenuated, induce an adequate or, in the case of helminth infections, an appropriate immune response.

Nevertheless, the advantage of viral vectors is that the recombinant antigen is presented in the context of MHC Class I and/or II on infected host target cells and is likely to be processed and presented in its native form (36). It is also possible to modify the vector by including host genes, in this case Interleukin-2 (40), thereby inducing local T cell reactivity and reducing the pathogenicity of the vaccinia. Since farm animals have been shown to respond well to recombinant vaccinia virus into which swine influenza haemagglutinin has been cloned (6) it is probably now appropriate to determine whether similar recombinants, incorporating parasite genes, would provide adequate protection. Clearly, other vector systems, especially those which immunise via the enteric route, might prove more effective in stimulating the enteric immune system against gut parasites. Work is currently in progress to determine whether *Salmonella* sp., rendered avirulent by removal of virulence plasmids, can express helminth genes and induce local immune responses against them (D. Baird, personal communication).

**CONCLUSIONS**

The advent of monoclonal antibodies, sophisticated protein-fractionation techniques and molecular biology has revolutionised approaches to diagnosis and for immunoprophylaxis against parasites. In the next decade, highly specific diagnostic techniques for many of the economically important parasites should be available. Similarly, it is likely that sophisticated subunit vaccines will be marketed for at least some of the more important parasites. Unfortunately, such vaccines are most likely to be marketed where they show high profitability. It is not yet clear whether diseases like theileriosis and trypanosomiasis which are so important in tropical regions will receive the same degree of commercial attention.

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* * *
REFERENCES


