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## HOST IMMUNE RESPONSE TO FEEDING BY TICKS: A NATURAL BIOLOGICAL CONTROL MECHANISM

Ticks emerged as economically important parasites in 1893 with the report by Smith and Kilbourne of *Boophilus* transmission of the Texas fever pathogen, subsequently identified as *Babesia bigemina*. The "birth" of bovine immunity to ticks occurred in 1908 with an observation by Munroe Hull in Queensland, Australia, that some cattle carried fewer ticks than others and that this "resistance" could be passed from animal to animal. This observation led to an investigation in 1915 by a select committee appointed by Parliament and resulted 3 years later in a published report by Johnson and Bancroft (1918).

It is now well known that host-acquired resistance to ticks is an immune-mediated phenomenon that results in the reduction in (a) the number of attached ticks, (b) the number of successfully fed ticks, (c) the molting success of fed immature ticks, (d) the fecundity, or (e) the fertility of fed female ticks. Interestingly, the immune response to ticks is not complete, since some individuals always feed successfully. This suggests that the surviving individuals did not produce the same antigen as those that were rejected by the host's immune response, or that the same antigen was secreted but the tick contained a material capable of neutralizing host antibody or toxin.

The information on the detrimental effects of host resistance applies to immature and female ticks that feed for at least 3-5 days and 12 days, respectively. It is not known what effect this response has on male ticks. However, it is known that if the male tick feeding period is prolonged as a result of feeding on an immune host, as seen with female ticks, then mating will be delayed, which has been shown to have a negative effect on female fecundity (Brown and Stenner, 1982) and probably on fertility as well.

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The focus of this paper is on those studies that have attempted to define the mediators, effectors and inducers involved in the phenomenon of host resistance to ticks. The research efforts on bovine immune responses to ticks have included studies on both innate and acquired resistance. The presence of innate resistance by bovines to ticks is widely accepted yet argued by some. The mechanism for this response is as varied as the number of individuals reporting its existence. Such theories as length of host hair coat, number of sebaceous glands or mast cells per area of skin, thickness of skin, depth of hair follicle, number of circulating lymphocytes, and diet of the host have been introduced. Those who accept the theory of innate resistance agree that *Bos indicus* exhibit the response to a greater degree than *Bos taurus*, and that the greater percentage of *Bos indicus* blood in the offspring of a cross mating, the greater the level of innate resistance. However, the elements responsible for the innate resistant trait remain undefined.

The mechanism responsible for *Bos indicus* acquired resistance to *Boophilus* ticks has been reported as a mast cell-dependent eosinophil hypersensitivity (Riek, 1956) based upon histological observations. Interestingly, the *Bos taurus* resistance response to *Ixodes holocyclus* (Allen *et al.*, 1977) and *Amblyomma americanum* (Brown *et al.*, 1984b), both 3 host ticks, consists of a mixed cellular response of neutrophils, eosinophils and basophils. It appears that there may be a basic host difference (*Bos taurus* versus *Bos indicus*) in response to tick feeding, or that the 1 host tick (*Boophilus*) induces a different immunological response than the 3 host ticks (*Ixodes* and *Amblyomma*). It may also be that the intensive eosinophil response described at *Boophilus* feeding sites consists of poorly stained basophils. These 2 granulocytes are difficult to differentiate if the tissue is not fixed and stained specifically for

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basophils to optimize their characterization.

The observed hypersensitivity by bovines to tick feeding is obvious, resulting in serous exudates at tick attachment sites within hours of infestation associated with intense grooming. The observed pruritis probably results initially from mast cell release of vasoactive mediators, such as histamine, at tick attachment sites as a result of cellular degranulation following interaction of cell surface bound anti-tick antibody with tick-derived salivary substances. Histamine and other mediators derived from mast cells could contribute to the inflammatory process by altering the permeability of local vessels resulting in (a) edema that could render the tick feeding environment unsuitable, (b) an accumulation of effector cells that could act directly on ticks, or release additional mediators that could adversely affect physiological processes crucial to tick feeding, ovipositional success and survival. Basophils also contain vasoactive amines and have been shown in the bovine to arrive within hours of challenge by *Ixodes holocyclus* (Allen *et al.*, 1977) and *Amblyomma americanum* (Brown *et al.*, 1984b). In addition, the basophil has been shown to be crucial to the guinea pig immune resistance response to ticks (Brown *et al.*, 1982a).

Thus, the mast cell probably acts initially by causing vasopermeability and facilitating emigration of leukocytes into the skin, which includes basophils that act to maintain vasopermeability during the course of parasitization. There is strong evidence to suggest that histamine, presumably basophil-derived histamine, is involved in immune resistance to ticks because (a) cattle expressing high resistance to ticks have twice the level of tissue histamine of animals of low tick resistance (Willadsen *et al.*, 1978), as do guinea pigs (Wikel, 1982), (b) histamine injected into the skin at tick attachment sites results in tick withdrawal or death *in situ* (Kemp and Bourne,

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1980), and histamine added to artificial media results in a cessation of tick feeding (Paine *et al.*, 1983), (c) cattle treated with an H-1 histamine receptor antagonist (mepyramine) express minimal skin reactivity to intradermal challenge with tick extract (Willadsen *et al.*, 1978), and (d) cattle treated with promethazine (H-1 antagonist) express reduced tick resistance compared to controls (Tatchell and Bennett, 1969). However, animals treated with antihistamines still allowed tick feeding, suggesting that either suboptimal doses of antihistamine were given or histamine was of secondary importance in the resistance response.

The pruritis and subsequent intense grooming response in hypersensitized animals is very dramatic and the importance of the grooming response in removing attached ticks should not be underestimated. Snowball (1962) found that stanchioned animals carried a *Boophilus microplus* burden nearly 4 times that of animals where the head was free. In a similar study using guinea pigs, 73% of larval *Rhipicephalus appendiculatus* ticks achieved engorgement on naive guinea pigs when protected within a capsule while on the host, whereas only 17% of the ticks engorged successfully when allowed free access over the body (Worms, Brown and Askenase, unpublished data). In this instance, significant tick loss occurred as a result of general host grooming over the 4 day tick feeding period. Ticks representing the 27% loss where the capsule was used, died as a result of poor physiological state at the time of infestation or due to a component of innate host resistance. When animals were challenged subsequently, they exhibited an intense grooming behaviour within hours that resulted in no tick yield from animals where the capsule technique was not used, whereas less than half (43%) of the ticks applied with capsules were recovered. Therefore, the grooming response during a challenge infestation is an immune mediate response involv-

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ing antibody (IgE and/or IgG sensitized mast cells and the recruitment of granulocytic leukocytes containing vasoactive amines (i.e. histamines) and other mediators as well.

Few studies have addressed the question of bovine mediators of immune resistance to ticks. The presence of antibody-mediated immunity was suggested by the ability to (a) transfer immediate cutaneous hypersensitivity with hyperimmune serum by the Prausnitz-Kustner (P-K) test (Riek, 1956, 1962), (b) confer immunity to calf-recipients of hyperimmune plasma from *Boophilus* resistant donors (Roberts and Kerr, 1976), and (c) detect circulating antibody responses against *Amblyomma americanum* and *Dermacentor andersoni*, respectively (Whelen *et al.*, 1984). Cell-mediated immunity was demonstrated by the observation that (a) calves subjected to low level *Dermacentor andersoni* infestations exhibited delayed (24-hour) skin reactions in response to skin tests with salivary gland extracts (Wikel and Osburn, 1982), and (b) lymphocytes derived from these animals proliferated *in vitro* in an antigen specific manner to the salivary gland extract preparation.

The findings to date, without a doubt, demonstrate the presence of antibody and cell-mediated responses in hypersensitized bovines. However, these studies have not demonstrated a direct correlation of these responses with tick rejection. The most definitive immunological work on host immunity to ticks has been achieved with laboratory animals used as "model" hosts. Such ideal control situations are necessary to answer some fundamental questions and to obtain prerequisite information to help design experiments with the bovine.

The presence of serum factors from guinea pigs and rabbits with anti-tick activity is well documented. Trager (1939) developed the model host system for studying acquired resistance to ticks, using *Dermacentor variabilis*, and was the first

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to report on the possible role of antibody by finding that serum transfer from tick resistant to tick susceptible animals conferred weak resistance. Since then, guinea pig anti-tick serum activity has been found against *Amblyomma americanum* (Brown and Askenase, 1981; Brown, 1982), *Rhipicephalus sanguineus* (Brown and Askenase, 1981), *Rhipicephalus appendiculatus* (Askenase *et al.*, 1982), *Ixodes holocyclus* (Askenase *et al.*, 1982), and *Dermacentor andersoni* (Brown and Askenase, unpublished observations). The level of protection conferred by serum ranged from 20 to 40%, the antibody has been shown to be IgG<sub>1</sub> (Brown *et al.*, 1982b), and to act via cells with Fc receptors (Brown and Askenase, 1985).

Studies using rabbits have also demonstrated the presence of anti-tick serum activity by (a) passive transfer experiments using *Ixodes ricinus* (Brossard, 1977) and *Rhipicephalus appendiculatus* (Rubaire-Akiki and Mutinga, 1980), (b) *in vivo* skin (P-K) tests using *Haemaphysalis leporispalustris* (Boese, 1974; McGowan *et al.*, 1979), and (c) *in vitro* analyses (immunodiffusion) using *Haemaphysalis longicornis* (Fujisaki, 1978; Fujisaki *et al.*, 1980), and *Haemaphysalis bispinosa* (Köhler *et al.*, 1967); the antibody class appears to be IgG (Fujisaki, 1978), as in the guinea pig.

The involvement of cell-mediated immunity (T-Lymphocytes) in guinea pig acquired resistance to ticks has also been demonstrated by passive transfer experiments using lymph node cells (Bagnall, 1975; Wikel and Allen, 1976; Askenase *et al.*, 1982) and peritoneal exudate cells (Brown and Askenase, 1981; Brown, 1982). The level of protection conferred by cell transfer ranged from 40 to 70%, much greater than the 20 to 40% conferred by serum. Therefore, the rodent immune response to ixodid ticks involves both antibody and cell mediated responses, with the cell component being much stronger. Additional studies using immuno-suppressant drugs

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such as methotrexate (Allen, 1973), a strong suppressor of antibody responsiveness and contact hypersensitivity, and cyclophosphamide (Wikel and Allen, 1976), depending upon the dose a suppressor of either or both antibody and cell-mediated responses, have substantiated the immunological basis of rodent immunity to ticks.

Histological analysis of tick feeding sites in immune guinea pigs demonstrates a dominant basophil response (30 to 80% of the infiltrate) with a marked eosinophil presence as early as 24 hours after attachment (Bagnall, 1975; Allen, 1973; Brown and Askenase, 1981; Brown *et al.*, 1982a, 1983, 1984a; Krinsky *et al.*, 1981). The basophil is not a resident of the skin, but accumulates in the tissue as a result of specific immunologic recruitment (Askenase, 1977). Tick feeding sites in recipients of immune serum or immune cells express dominant basophil responses (Brown and Askenase, 1981; Brown *et al.*, 1983, 1984a), whereas naive hosts infested with ticks express a dominant neutrophil response with a marked eosinophil presence. Therefore, the basophil is an important component of the resistance response to ticks and arrives in the tissue by antibody as well as cell-mediated reactions, as reported by others using non-tick antigens (Askenase, 1973; Askenase *et al.*, 1976; Dvorak *et al.*, 1971).

The importance of the basophil to the guinea pig immune response to *Amblyomma americanum* was demonstrated in studies using rabbit anti-guinea pig basophil serum (ABS) in tick-sensitized animals prior to challenge (Brown *et al.*, 1982). ABS treated animals were depleted of basophils in the bone marrow, blood and tissue and failed to express resistance. Furthermore, animals treated with anti-eosinophil serum (AES) expressed reduced resistance responses; tick yields were less than from naive animals, but greater than yields from tick-sensitized and challenged untreated animals. These

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results demonstrated a primary effector role for the basophil with a secondary role for the eosinophil. This was the first definitive description of a biological role for the basophil, whereas eosinophil activity against parasites is well documented (Mahmoud *et al.*, 1975; Grove *et al.*, 1977; Butterworth *et al.*, 1979).

Basophil-filled epidermal vesicles in tick-resistant guinea pigs are reminiscent of those occurring in contact hypersensitivity responses (Askenase, 1977). At tick feeding sites, basophil-rich epidermal vesicles may develop in response to cement substances or salivary gland-derived enzyme secretions or both, after processing and/or presentation by local antigen-presenting cells such as the Langerhans' cells; Ia<sup>+</sup> cells of the epidermis that bear receptors for Fc and C3 (Van Voorhis *et al.*, 1983).

Langerhans' cells are thought to act as antigen-presenting cells in the induction of contact hypersensitivity reactions (Ptak *et al.*, 1980) and have been shown by indirect immunofluorescence to bind SGA in the skin of guinea pigs infested with ticks (Allen *et al.*, 1979). There is evidence to suggest that depletion of Langerhans' cells from the epidermis of *Demacentor andersoni*-sensitized guinea pigs results in their inability to express resistance to tick challenge (Allen, personal communication). This is analogous to findings indicating that Langerhans' cells are required for induction of contact hypersensitivity responses (Ptak *et al.*, 1980, Streilan and Bergstresser, 1981; Elments *et al.*, 1983). Basophils are also required for the resistance response to ticks, but the exact relationship between Langerhans' cells and basophils is not known. If Langerhans' cells are required for expression of these responses, it is likely that Langerhans' cells take up and present tick antigen to specifically sensitized T cells, which are then activated to produce chemotactic factors that recruit circulat-

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ing basophils to infiltrate the local site and effect the immune resistance response.

There is strong evidence supporting the view that the antigen(s) responsible for the induction and elicitation of host immune responses to ticks is salivary gland-derived, based upon studies using guinea pigs and *Dermacentor andersoni* (Wikel, 1979) and *Amblyomma americanum* (Brown *et al.*, 1984c) ticks, as well as in rabbits using *Rhipicephalus sanguineus* ticks (Garin and Grabarev, 1972). The majority of studies that have investigated the feasibility of artificial immunization against ticks have utilized crude homogenates of whole ticks and include *Dermacentor andersoni* (Allen and Humphreys, 1979), *Dermacentor variabilis* (Ackerman *et al.*, 1981), *Amblyomma maculatum* (McGowan *et al.*, 1980) and *Amblyomma americanum* (McGowan *et al.*, 1981).

Artificial immunization using either salivary gland extracts (SGA) or whole tick extracts does not induce a level of immunity comparable to that achieved by active immunization (tick feeding). Furthermore, the fact that the level of protection obtained with salivary gland extracts is equal to that obtained with whole tick extracts demonstrates that the salivary gland is the site of antigen production.

Few reports have been published describing the isolation and purification of tick products capable of inducing host immunity to ticks or capable of eliciting skin responses in animals previously exposed to ticks. Strong immediate skin responses were evoked in the dermis of tick-sensitized cattle by the injection of a protein isolated from the saliva of *Boophilus microplus* Geczy *et al.*, 1971). This skin-reactive substance was noted to have esterase activity and estimated to be 30,000 daltons. Similarly, a skin-reactive substance of approximately 60,000 daltons, also described as an esterase, was isolated from crude *Boophilus microplus* extracts (Willadsen and Wil-

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liams, 1976). In a more recent study, antibodies against *Boophilus microplus*-derived phosphomono-esterases were found in tick-infested cattle (Reich and Zorzopulos, 1980). This enzyme is generally associated with parasite-absorptive surfaces, such as the midgut of ticks, suggesting that the observed decreased ability of ticks to feed normally on previously infested animals might be due to neutralization of this enzyme by host antibodies imbibed during tick feeding. Two studies to date (McGowan *et al.*, 1981) and (Ackerman *et al.*, 1981) have identified antibody-antigen complexes in the midgut hemolymph of ticks, further suggesting the possibility of neutralization of key enzymes in the gut.

While these studies represent the most definitive work to date on tick antigen characterization, they are incomplete in that they fail to demonstrate that (a) hosts respond immunologically with specific antibody to the substance, (b) the substance is a relevant component in the tick salivary fraction, and (c) these substances are capable of inducing an immune response in the host resulting in tick rejection. Studies by other investigators have added to the knowledge of the types of skin reactive substances in the salivary secretions of ticks and reported the presence of prostaglandin-like compounds (Geczy *et al.*, 1971; Dickinson *et al.*, 1976), hydrolytic enzymes (esterase presumably) (Higgs *et al.*, 1976), and a trypsin inhibiting compound (Willadsen and Riding, 1979). All these materials elicited significant macroscopic skin reactions when injected intradermally into tick sensitized cattle, however, correlation with the immune response and tick rejection was not demonstrated. In addition, a histamine "blocking" agent was described from the salivary gland of *Rhipicephalus sanguineus* (Chinery and Ayitey-Smith, 1977) and it was suggested that this may be a defense against the host's allergic response that is believed to be histamine dependent.

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The recent observation that immune serum from guinea pigs expressing resistance to *Amblyomma americanum*, and serum from guinea pigs immunized successfully with SGA, identifies a single protein of 20,000 daltons obtained from the salivary gland extract (by autoradiography of 13% SDS/PAGE of  $^{125}$ I labeled SGA after immunoprecipitation with immune serum) demonstrates that the salivary gland is the site of antigen production (Brown *et al.*, 1984c). Furthermore, the cement substance from *Amblyomma americanum* ticks is immunogenic as shown by its ability to immunize (Brown *et al.*, 1984c). Hyperimmune serum also identifies a single unique protein of 20,000 daltons from an extract of this material. The cement is secreted by almost all ixodid ticks and is important in anchoring the parasite to the host. This material has been described as a glycoprotein-lipoprotein complex in *Boophilus microplus* (Moorhouse and Tatchell, 1966).

Histologic analysis of tick feeding sites in resistant animals reveals the presence of epidermal vesicles, packed with basophils, in intimate contact with cement around the tick's mouthparts. This observation suggests further that antigens in the cement are important not only in induction of the immune resistance response but also in elicitation of this response. Cement secretion in some tick species appears to be continual (Brown and Knapp, 1980a, b), whereas in others it appears to be intermittent (Chinery, 1973; Tatchell 1969).

Current studies in my laboratory are aimed at identifying, isolating and purifying tick antigens for subsequent (a) immunization trials in the bovine, and (b) *in vitro* expression for large-scale vaccine production.

There are 2 final points that need to be acknowledged. First, that cattle expressing resistance to *Boophilus microplus* apparently are less susceptible to *Babesia* infection, as demonstrated by several empirical studies (Francis and Little,

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1964; Roberts, 1968; Campbell, 1978). And second, that rabbits resistant to *Haemaphysalis leporispalustris* fail to become infected with *Francisella tularensis* when challenged with infected ticks (Bell *et al.*, 1979; Wikel, 1980). These findings suggest that the anti-tick immune response acts early in the tick feeding cycle before pathogens can either enter or be released from the salivary gland. The implications from these studies strengthen the biological importance of host resistance to tick feeding.

In summary, multiple infestation of bovines (and rodents) by ixodid ticks results in an ensuing immune mediated response that is manifested macroscopically by intense host grooming, decreased tick feeding and reproductive success, and an apparent immunity to tick-borne pathogens. Microscopically, the tick feeding site in hypersensitized animals is dominated by a granulocyte response that is distinctly different from that in naive animals. Furthermore, the immune status of the host can be regulated by artificial or passive immunization using tick extracts. Finally, studies with guinea pig anti-tick antibodies have established the feasibility of immunochemically isolating crucial tick-derived antigens that may be beneficial to subsequent attempts for *in vitro* expression of the gene encoding the protein.

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## References

- Ackerman, S., F.B. Clare, T.W. McGill, and D.E. Sonenshine. 1981. *J. Parasitol.* 67:737-740.
- Allen, J.R. 1973. *Int. J. Parasitol.* 3:195-200.
- Allen, J.R., B.M. Doube, and D.H. Kemp. 1977. *Canad. J. Comp. Med.* 41:26-35.
- Allen, J.R., and S.J. Humphreys. 1979. *Nature* 280:491-495.
- Allen, J.R., H.M. Khalil, and J.E. Graham. 1979. *Immunology*. 38:467-472.
- Askenase, P.W. 1973. *J. Exp. Med.* 138:1144-1148.
- Askenase, P.W. 1977. *Prog. Allergy* 23:199-320.
- Askenase, P.W., B.G. Bagnall, and M.J. Worms. 1982. *Immunology*. 45:501-511.
- Bagnall, B.G. 1975. Thesis, University of Sydney 186 pp.
- Bell, J.F., S.J. Steward, and S.K. Wikel. 1979. *Amer. J. Trop. Med. Hyg.* 28:876-880.
- Boese, J.L. 1974. *J. Med. Entomol.* 11:503-512.
- Brossard, M. 1977. *Bull. Soc. Path. Exot.* 70:289-294.
- Brown, S.J. 1982. *Amer. J. Trop. Med. Hyg.* 31:1285-1290.
- Brown, S.J. and P.W. Askenase. 1981. *J. Immunol.* 127:2163-2167.
- Brown, S.J., and P.W. Askenase. 1985. *Exp. Parasitol.* 59:248-256.
- Brown, S.J., B.G. Bagnall, and P.W. Askenase 1984a. *Exp. Parasitol.* 57:40-47.
- Brown, S.J., R.W. Barker, and P.W. Askenase. 1984b. *Vet. Parasitol.* 16:144-165.
- Brown, S.J., S.J. Galli, G.J. Gleich, and P.W. Askenase. 1982a. *J. Immunol.* 129:790-795.
- Brown, S.J., F.M. Graziano, and P.W. Askenase 1982b. *J. Immunol.* 129:2407-2412.
- Brown, S.J., and F.W. Knapp. 1980a. *Exp. Parasitol.* 49:188-205.
- Brown, S.J., and F.W. Knapp. 1980b. *Exp. Parasitol.* 49:303-318.
- Brown, S.J., S.Z. Shapiro, and P.W. Askenase. 1984c. *J. Immunol.* 133:3319-3325.
- Brown, S.J., and T. Stenner. 1982. *Experientia*. 38:1060-1061.
- Brown, S.J., M.J. Worms, and P.W. Askenase. 1983. *Exp. Parasitol.* 56:153-168.
- Butterworth, A.E., D.L. Wassom, G.L. Gleich, D.A. Loegering, and J.R. David. 1979. *J. Immunol.* 122:221-225.
-

- 
- Campbell, R.S.F. 1978. *Proc. Int. Conf. Centre Trop. Vet. Med.*, Edinburgh, Scotland. 573 pp.
- Chinery, W.A. 1973. *J. Med. Entomol.* 10:355-362.
- Chinery, W.A., and E. Ayitey-Smith. 1977. *Nature.* 265:366-367.
- Dickinson, R.G., J.E. O'Hagan, M. Schutz, K.A. Binnington, and M.P. Hegarty. 1976. *Aust. J. Exp. Biol. Med. Sci.* 54:475-486.
- Dvorak, H.F., B.A. Simpson, R.C. Bast Jr., and S. Leskowitz. 1971. *J. Immunol.* 107:138-143.
- Elments, C.A., P.R. Bergstresser, R.E. Tigelaar, P.J. Wood, and J.W. Streilein. 1983. *J. Exp. Med.* 158:781-785.
- Francis, J., and D.A. Little. 1964. *Aust. Vet. J.* 40:247-253.
- Fujisaki, K. 1978. *Natl. Inst. Anim. Hlth. Quart.* 18:27-38.
- Fujisaki, K., S. Takeuchi, and S. Kitaoka 1980. *Jap. J. Vet. Sci.* 42:587-593.
- Garin, N.S., and P.A. Grabarev. 1972. *Med. Parasitol. Muskra.* 41:274-279.
- Geczy, A.F., M.A. Naughton, J.B. Clegg, and R.W. Hewetson. 1971. *J. Parasitol.* 57:437-438.
- Grove, D.I., A.A.F. Mahmoud, and K.W. Warren. 1977. *J. Exp. Med.* 145:755-759.
- Higgs, G.A., J.R. Vane, R.J. Hart, C. Porter, and R.G. Wilson. 1976. *Bull. Entomol. Res.* 66:665-670.
- Johnston, T.H., and M.J. Brancroft. 1918. *Proc. Roy. Soc. Qld.* 30:219-317.
- Kemp, D. H., and A. Bourne. 1980. *Parasitology.* 80:487-496.
- Kohler, G., G. Hoffman, F. Horchner, and G. Weiland. 1967. *Tieraerztl. Wochenscher. Bersin Munch.* 80:3965-400.
- Krinsky, W.L., S.J. Brown, and P.W. Askenase. 1981. *Exp. Parasitol.* 53:381-395.
- McGowan, M.J., R.W. Barker, J.T. Homer, R.W. McNew, and K.H. Holscher. 1981. *J. Med. Entomol.* 18:328-332.
- McGowan, M.J., J.H. Carmin, and R.W. McNew. 1979. *J. Parasitol.* 65:692-699.
- McGowan, M.J., J.T. Homer, G.V. O'Dell, R.W. McNew, and R.W. Barker. 1980. *J. Parasitol.* 66:42-48.
- Mahmoud, A.A.F., K.S. Warren, and P.A. Peters. 1975. *J. Exp. Med.* 142:805-809.
- Moorhouse, D.E., and R.J. Tatchell. 1966. *Parasitology.* 56:623-632.
- Paine, S.H., D.H. Kemp, and J.R. Allen. 1983. *Parasitology.* 86:419-428.
-

- 
- Ptak, W., D. Rozycka, P.W. Askenase, and R.K. Gershon. 1980. *J. Exp. Med.* 151:362-375.
- Riek, R.F. 1956. *Aust. Vet. J.* 32:204-209.
- Riek, R.F. 1962. *Aust. J. Agric. Res.* 13:532-550.
- Roberts, J.A. 1968. *J. Parasitol.* 54:667-673.
- Roberts, J.A., and J.D. Kerr. 1976. *J. Parasitol.* 62:485-489.
- Rabaire-Akiki, C.M., and M.J. Mutinga. 1980. *Bull. Anim. Hlth. Prod. Afr.* 28:49-59.
- Snowball, G.L. 1962. *Aust. J. Agric. Res.* 13:227-232.
- Streilan, J.W., and P.R. Bergstresser. 1981. *J. Invest. Dermatol.* 77:272-276.
- Tatchell, R.J. 1969. *Parasitology.* 59:93-104.
- Tatchell, R.J., and G.F. Bennett. 1969. *Exp. Parasitol.* 26:369-377.
- Trager, W. 1939. *J. Parasitol.* 25:57-81.
- Van Voorhis, W.C., M.D. Witmer, and R.M. Steinman. 1983. *Fed. Proc.* 42:3114.
- Whelen, A.C., J.E. George, R.L. Osburn, and S.K. Wikel 1984. *Fed. Proc.* 43:1628.
- Wikel, S.K. 1979. *Amer. J. Trop. Med. Parasitol.* 28:586-590.
- Wikel, S.K. 1980. *Ann. Trop. Med. Parasitol.* 74:103-104.
- Wikel, S.K. 1982. *Ann. Rev. Entomol.* 27:21-48.
- Wikel, S.K., and J.R. Allen. 1976. *Immunology.* 30:311-316.
- Wikel, S.K., and J.R. Allen. 1976. *Immunology.* 30:479-484.
- Wikel, S.K., and R.L. Osburn. 1982. *Ann. Trop. Med. Parasitol.* 76:405-414.
- Willadsen, P., and G.A. Riding. 1979. *Bioch. J.* 177:41-47.
- Willadsen, P., and P.G. Williams. 1976. *Immunochemistry.* 13:591-597.
- Willadsen, P., P.G. Williams, J.A. Roberts, and J.D. Kerr. 1978. *Int. J. Parasitol.* 8:89-95.
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