

THE EPIZOOTIOLOGY AND CONTROL OF HEARTWATER AND OTHER TICK-BORNE DISEASES OF CATTLE IN SOUTH AFRICA

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ABSTRACT

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The history of the main bovine tick-borne diseases occurring in South Africa and the role Onderstepoort played in their identification and control is briefly reviewed. The present attitudes regarding the control of tick-borne diseases, taking into account their complexity, is discussed. Gaps in our knowledge regarding heartwater epizootiology and possible future studies are defined.

INTRODUCTION

The past history of Onderstepoort itself is inseparable from that of tick-borne diseases, which are of importance not only in South Africa but also in many other parts of the world.

Shortly after Stephens & Christopher (1903, cited by Neitz, 1957) described the causative organism of East Coast fever as *Piroplasma kochi*, Sir Arnold Theiler became involved in tick transmission experiments. A few years later this organism was transferred to a newly created genus *Theileria*, named in honour of Theiler, and called *Theileria parva* (Bettencourt, Franca & Borges, 1907, cited by Neitz, 1957). Three other *Theileria* species of cattle were subsequently named at Onderstepoort: *T. mutans* (mild theileriosis); *T. lawrencei* (Corridor or buffalo disease), and *T. bovis* (January disease) (Theiler, 1906; Neitz, 1955, 1957). In the history of tick-borne diseases in South Africa one of the most dramatic achievements was the eradication by 1955 of East Coast fever, a disease that killed millions of cattle after its introduction at the turn of the century (Anon., 1981). The policy of tick eradication and slaughter of clinically infected cattle was successful but the price was high; in the end the campaign cost more than R200 million (Neitz, 1967, cited by Bigalke, 1976).

It was also at Onderstepoort that Theiler saw what he described as "marginal points" in the red blood cells of cattle suffering from so-called gall sickness. Each of these organisms looked so dense that he thought it consisted mainly of a nucleus without any protoplasm and he therefore named the parasite *Anaplasma* (Theiler, 1910a). He described 2 species, namely *A. marginale* and the milder *A. centrale* (Theiler, 1910a, b, 1911), and his 1910 isolate of the latter is still used in our *Anaplasma* vaccine today (Potgieter & Van Rensburg, 1983).

Babesiosis, like most other tick-borne diseases, was recognized in South Africa long before the causative organisms and vectors were identified (Hutcheon, 1900; Henning, 1949). In 1905 Theiler established that *Boophilus decoloratus* transmits *Babesia bigemina*, but it was not until 1941 that Neitz proved that *B. bovis* is also present in South Africa. It is now known that *Boophilus microplus* is the main, if not the only, vector of *B. bovis* (De Vos, 1979).

Heartwater transmission studies were conducted initially at Grahamstown by Lounsbury, who was the first to prove that the bont tick, *Amblyomma hebraeum*, is the principal vector of this disease in South Africa (Lounsbury, 1900). However, it was not until 1925 that Cowdry, a rickettsiologist from the Rockefeller Institute who was working at Onderstepoort, demonstrated the aetiological agent in the tissues of ticks and in animals suffering from heartwater. He called this organism *Rickettsia ruminantium* (Cowdry, 1925a, b) but it was later transferred to a new genus, *Cowdria* (Moshokovskii,

1947). Heartwater is regarded as the most important tick-borne disease in South Africa. As long ago as 1945, Neitz & Alexander reported that in enzootic areas it causes 3 times more losses than anaplasmosis and babesiosis put together.

Another group of tick-borne diseases, namely tick toxicoses, has also been studied at Onderstepoort. Major breakthroughs were made here on the aetiology of sweating sickness (Neitz, 1959); spring lamb paralysis (Clark, 1938; Neitz & Jansen, 1950); the ecology of *Ixodes rubicundus*, the transmitter of Karoo paralysis (Stampa & Du Toit, 1956; Stampa, 1959) and on *Ornithodoros savignyi* toxicosis (Neitz, Howell & Potgieter, 1969).

Looking back on the work done over the past 75 years on ticks and tick-borne diseases in South Africa, one is filled with admiration for those dedicated scientists who have done so much to unravel the complexities of this subject (Theiler, 1975).

PRESENT ATTITUDES AND STATE OF KNOWLEDGE REGARDING THE EPIZOOTIOLOGY AND CONTROL OF TICK-BORNE DISEASES OF CATTLE IN SOUTH AFRICA

Despite the complex nature of tick-borne diseases as a whole, and the gaps in our knowledge on certain aspects of the epizootiology of these diseases, enough information exists to explain the distribution and occurrence of these conditions. Recommendations for the control or prevention of outbreaks of tick-borne disease are available but are not always either easy or practicable to implement.

Literature, some very recent, reviewing and consolidating the existing knowledge on tick-borne diseases is available for babesiosis (Ristic & Kreier, 1981), anaplasmosis (Potgieter, 1979; Ewing, 1981), cowdriosis (Uilenberg, 1983; Camus & Barré, 1982), theileriosis (De Vos, 1982), and tick toxicosis (Gothe, 1981).

The epizootiology of tick-borne diseases revolves around 3 elements, namely the parasite, the vector and host susceptibility. Each one of these elements is in turn influenced by numerous other factors, some of which are shown in Fig. 1.

The distribution of tick-borne diseases correlates closely with that of their known vectors and meaningful explanations can usually be given for unexpected outbreaks, whether they occur inside or outside the enzootic areas.

However, a sound knowledge of the factors influencing the epizootiology of each tick-borne disease is necessary in order to explain the creation of enzootic stability or instability of a specific disease on a farm.

Enzootic stability, as defined by Callow (1977) for babesiosis, also occurs in other tick-borne diseases. It can be described as a situation in which there is frequent transmission of the parasites and infection of all young animals occurs during the period that they are protected by passively acquired or non-specific factors. Acquired immunity develops and very few, if any, cases of disease

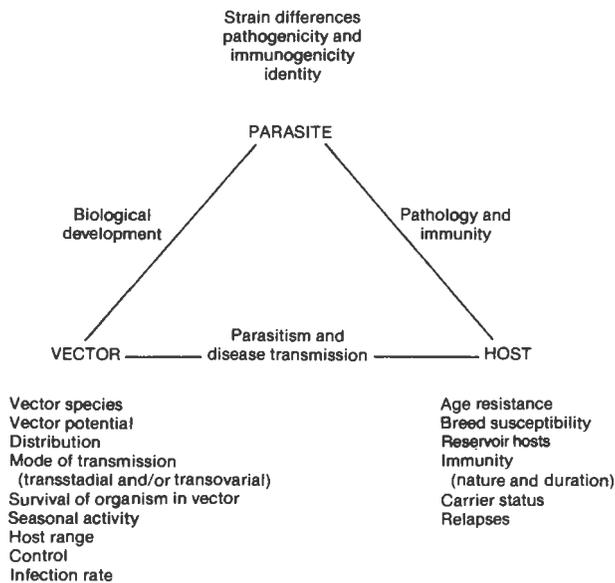


FIG 1 Some factors playing a role in the epizootiology of tick-borne diseases

are seen. Enzootic instability, on the other hand, describes a situation in which some animals in the herd fail to become infected for a considerable period after birth, i.e. host/parasite imbalance exists as a result of infrequent transmission. Disease is then seen when susceptible animals in a herd encounter infected ticks.

In South Africa 2 factors are mainly responsible for enzootic instability, namely unfavourable climatic conditions for the ticks and the injudicious control of these parasites (De Vos, 1979; Howell, De Vos, Bezuidenhout, Potgieter & Barrowman, 1981; De Vos & Potgieter, 1983). Both these factors result in the lowering of tick numbers to such an extent that animals fail to come in contact with infected ticks at a young age and therefore remain susceptible to disease. Until fairly recently tick eradication or the maintenance of a minimal disease situation by means of intensive dipping was advocated for the control of tick-borne diseases because of the success experienced with the control of East Coast fever. This attitude has changed surprisingly quickly since the inherent dangers and problems with these methods have been recognized (Bigalke, 1976; Norval, 1981; Lawrence, Foggin & Norval, 1980).

In many instances, the importance of enzootic stability has been realized and a resolution to live with ticks in this country has been adopted.

Certain ecological areas, or individual farms, are suitable for a minimal disease situation while others can only make use of the principle of enzootic stability. The advantages and disadvantages of both principles were recently discussed at a symposium held in Pretoria (Bigalke, 1982) and later summarized to help the farmer to decide which system he would like to implement (Anon., 1983).

Many farmers have suffered severe losses because they have created a situation of enzootic instability through excessive tick control. The farmer is usually confronted with a variety of tick-borne diseases and optimum control of 1 tick species may result in instability with other vectors, and possibly tick worry.

The position is further complicated by the fact that the transmission rate which is necessary to create and maintain enzootic stability differs from 1 tick-borne disease to another. It is dependent on the percentage of infected ticks and the number of these parasites present on the animals on a daily basis (McCosker, 1981). Information

on the transmission rate for the different tick-borne diseases prevailing in this country is not available. Such information may be interesting, and possibly useful in certain studies, but it is doubtful whether it will be of practical value.

Apart from the fact that it is very difficult, and in some cases even impossible, to determine the optimum transmission rate, there are many factors that can influence the percentage of infected ticks present on a farm (Fig. 1). If these factors are not taken into consideration they may jeopardize standard recommendations regarding the number of ticks necessary to maintain enzootic stability.

Looking at the problem of tick-borne disease control as a whole there seems to be almost general consensus that the only light at the end of a dark tunnel is the age resistance of young animals against tick-borne diseases. The advisability of stimulating immunity to the different tick-borne diseases, either naturally or artificially, during this age resistant period should be emphasized wherever and whenever possible. Vaccination of young animals is probably the best and most practical way to stimulate immunity and create enzootic stability. Vaccination is also advisable to protect animals if they are moved from a minimal to a stable disease situation. Furthermore, vaccination of young animals against babesiosis should, to a large extent, avoid the problems associated with the vaccination combined with treatment regimen used in older animals.

FUTURE STUDIES ON HEARTWATER EPIZOOTIOLOGY AND CONTROL

Vaccination

At present the production of heartwater blood vaccine is an expensive and crude method. Furthermore, due to the pathogenicity and lability of the vaccine, and the fact that it is only effective after intravenous injection, makes vaccination a cumbersome and dangerous procedure.

It is therefore important that the improvement of the present blood vaccine should be high on the priority list. Heartwater-infected tick homogenates can be used for vaccination (Bezuidenhout, 1981). However, apart from being an inexpensive source of antigen this vaccine has no other advantages over the blood vaccine. Even if the pathogenicity of these vaccines cannot be changed they should at least be adapted for intramuscular or subcutaneous injection. If this goal can be achieved it will ensure that they are used much more widely than is the present intravenous vaccine, especially in young animals which are still protected by a natural resistance against heartwater.

Attempts to cultivate *C. ruminantium* *in vitro* should continue and special methods used for the cultivation of other similar organisms, e.g. *Chlamydia*, should be investigated (Weiss & Dressler, 1958, 1960; Gordon, Dressler, Quan, McQuilkin & Thomas, 1972). Apart from natural infection, vaccination is the only means of creating a stable disease situation, and this without the possible adverse effect of tick worry.

Methods for identification of *C. ruminantium*

An indirect fluorescent antibody (IFA) technique has now been developed (Du Plessis, 1981) and this could prove to be a most useful tool in epizootiological studies of heartwater. However, antigen production for this test is rather difficult and, in addition, there is poor correlation between antibody levels and the immune status of animals. It does, however, show up serum antibodies against *Cowdria* for a period of at least 3-6 months after artificial infection. If this IFA test is done at the correct time, or perhaps repeated, it can be used to determine the

rate at which animals have come into contact with infected ticks.

A purified antigen is urgently needed for the development of a direct fluorescent antibody (FA) technique that can be used for the final identification of *Cowdria* in *in vitro* culture systems, as well as in its vertebrate and invertebrate hosts. Furthermore, a suitable antigen either for the Elisa test or for any other test that can be used in connection with the production of monoclonal antibodies is warranted. In this regard efforts to purify organisms obtained from infected ticks, brain or blood by means of percol or other gradients and through affinity chromatography should be stepped up.

Susceptibility of different cattle breeds to heartwater infection

Different susceptibilities in different breeds of cattle have long been suspected, and in some cases proved (Bonsma, 1944).

The value of these findings should be explored. The indications are that adult cattle of different breeds are more or less equally susceptible. There might, however, be a significant difference in the length of the period during which young animals of different breeds are protected by their natural resistance (Bonsma, 1944; Du Plessis, Bezuidenhout & Lüdemann, 1984). If this is true it could be of great value, because breeds with longer periods of resistance when they are young will stand a better chance of becoming naturally immunized without becoming clinically diseased. In such breeds the creation of enzootic stability through vaccination or by means of natural infection will be much easier. To my mind the existence of such breeds may explain why so many farmers get away without vaccinating their cattle against heartwater.

Percentage of infected ticks

As already said, it is doubtful whether studies to determine the percentage of infected ticks are worth the effort. Apart from the fact that at present there is no easy method to determine such a percentage, it must be realized that a few adult *Amblyomma* ticks can cause serious damage to their host. As far as enzootic stability is concerned it is not beneficial to have high numbers of ticks on a farm if only a very low percentage are infected with *Cowdria*. Obviously, the higher the percentage of infected ticks, the fewer are needed to maintain enzootic stability. Determination of the factors that influence the infection rate of ticks might prove to be a very useful exercise. Transovarial transmission of *Cowdria* in ticks does occur under laboratory conditions but it seems to be the exception rather than the rule; it is doubtful whether this phenomenon plays a role in the epizootiology of the disease (Bezuidenhout & Jacobsz, unpublished results, 1980).

Amblyomma larvae and nymphae obtain the infection when they feed on reacting animals suffering from the disease, on vaccinated animals and on immune animals that have been challenged either naturally or artificially (Alexander, 1931).

Adult ticks usually reach maximum numbers during the summer and one can assume that it is during this period that the highest percentage of animals will have circulating organisms. Calves are usually born between September and December and this is the ideal time for them to become infested with ticks and at the same time infected with heartwater organisms.

An interesting problem, however, is to explain where and when the adult ticks become infected.

To improve the infectivity rate of ticks one can vaccinate, or perhaps even revaccinate, some animals on the

farm during the period of peak larval or nymphal activity.

It should also be possible to obtain a similar effect by allowing larvae and adults to feed simultaneously on animals. There can be some overlapping of larvae and adults during summer but the larvae usually only peak later, during the end of summer or beginning of autumn (Londt, Horak & De Villiers, 1979; Rechav, 1982). Adults infect the animals which will then develop a rickettsiaemia which will infect the larvae. Under field conditions it should be possible to produce a higher level of overlap of larval and adult peaks by means of pasture spelling or rotational grazing.

The possibility of improving the infectivity rate of *Cowdria* in ticks is, however, theoretical and will have to stand the test of scientific evaluation. The success of such studies will depend largely on the development of a reliable, easy method to determine whether ticks are infected or not. No such method exists at present. There are bound to be other factors affecting the infectivity rate of ticks, and the carrier status of heartwater immune animals has not conclusively been determined.

Some questions regarding the infectivity rate of ticks are:

- Whether different strains of ticks have different abilities to multiply and transmit heartwater organisms.
- Does the "interference" phenomenon, where the presence of certain rickettsiae in a tick population prevents the infection of such ticks with other species of rickettsiae (Price, Johnson, Emerson & Preston, 1954), also apply to *Cowdria*?

Alternative hosts

Some game animals can become fatally infected with heartwater while others can act as asymptomatic carriers of the disease (Uilenberg, 1983). Some laboratory animals such as the mouse and ferret can also act as hosts for the organism (Mason & Alexander, 1940; Du Plessis & Kumm, 1971; McKenzie & Van Rooyen, 1981). The question is whether the identification of any additional animal hosts will help us to understand the epizootiology of the disease any better. Enough evidence is available to show that heartwater can occur and spread even in the absence of wild reservoirs (Neitz, 1967).

Eradication of wild animals is usually undesirable or impractical, and in any case it is doubtful whether the recognition of any wild carrier animal will be of major importance as far as the epizootiology or control of heartwater is concerned. However, if such an animal could be used in the laboratory for the maintenance or establishment of different strains of heartwater, or if a successful cell line for the growth of *Cowdria* could be established from such a host, then it will be worth looking for. In addition, if any other animal could be used to grow less virulent strains for vaccine purposes it might be extremely valuable.

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REFERENCES

- ALEXANDER, R. A., 1931. Heartwater, The present state of our knowledge of the disease. *17th Report to the Director of Veterinary Services and Animal Industry, Union of South Africa*, 89–150.
- ANON., 1981. The eradication of East Coast fever in South Africa. *Journal of the South African Veterinary Association*, 52, 71–73.
- ANON., 1983. Tick control in cattle. Department of Agriculture, Pretoria, Republic of South Africa.
- BEZUIDENHOUT, J. D., 1981. The development of a new heartwater vaccine, using *Amblyomma hebraeum* nymphae infected with *Cowdria ruminantium*. *Proceedings, International Conference on Tick Biology and Control, Grahamstown, Republic of South Africa*, 41–45.

- BIGALKE, R. D., 1976. Thoughts on the future control of ticks and tick-borne diseases of cattle in South Africa. *Journal of the South African Biological Society*, 17, 7-17.
- BIGALKE, R. D., 1982. Closing address and tentative policy formulation. *Symposium on ectoparasites of cattle, 15 and 16 March 1982, South African Bureau of Standards, Pretoria*. p. 157-159.
- BONSMA, J. C., 1944. Hereditary heartwater resistance characters in cattle. *Farming in South Africa*, 19, 71-96.
- CALLOW, L. L., 1977. Vaccination against bovine babesiosis. In: *Immunity to blood parasites of man and animals*. p. 121. Editors L. H. Miller, J. A. Pino, J. J. Mckelvey Jr. New York: Plenum Press.
- CAMUS, E. & BARRÉ, N., 1982. La Cowdriose (Heartwater). *Revue Générale des connaissances. Institut d'élevage et de Médecine Vétérinaire des Pays Tropicaux*. 10, rue Pierre-Curie, 94704 Maisons, Alfort—Cedex.
- CLARK, R., 1938. A note on paralysis in lambs caused apparently by *Rhipicephalus evertsi*. *Journal of the South African Veterinary Association*, 9, 143-145.
- COWDRY, E. V., 1925a. Studies on the etiology of heartwater. I. Observation of a rickettsia, *Rickettsia ruminantium* (n. sp.) in the tissues of infected animals. *Journal of experimental Medicine*, 42, 231-252.
- COWDRY, E. V., 1925b. Studies on the etiology of heartwater. II. *Rickettsia ruminantium* (n. sp.) in the tissues of ticks transmitting the disease. *Journal of experimental Medicine*, 42, 253-274.
- DE VOS, A. J., 1979. Epidemiology and control of bovine babesiosis in South Africa. *Journal of the South African Veterinary Association*, 50, 357-362.
- DE VOS, A. J., 1982. The identity of bovine *Theileria* spp. in South Africa. M. Med. Vet. Thesis. Faculty of Veterinary Science, University of Pretoria, Pretoria, South Africa.
- DE VOS, A. J. & POTGIETER, F. T., 1983. The effect of tick control on the epidemiology of bovine babesiosis. *Onderstepoort Journal of Veterinary Research*, 50, 3-5.
- DU PLESSIS, J. L. & KUMM, N. A. L., 1971. The passage of *Cowdria ruminantium* in mice. *Journal of the South African Veterinary Medical Association*, 42, 217-221.
- DU PLESSIS, J. L., BEZUIDENHOUT, J. D. & LÜDEMANN, C. J. F., 1984. The immunization of calves against heartwater: Subsequent immunity both in the absence and presence of natural tick challenge. *Onderstepoort Journal of Veterinary Research*, 51, 193-196.
- DU PLESSIS, J. L., 1981. The application of the indirect fluorescent antibody test to the serology of heartwater. *Proceedings of an International Conference on Tick Biology and Control, Grahamstown, South Africa*, 47-52.
- EWING, S. A., 1981. Transmission of *Anaplasma marginale* by Arthropods. Proceedings of the seventh National Anaplasmosis Conference. Oct. 21-23, 1981. Mississippi State University, Mississippi State, 395-423.
- GOTHE, R., 1981. Diseases of cattle in the tropics, Current Topics in Veterinary Medicine and Animal Science, 6.
- GORDON, F. B., DRESSLER, H. R., QUAN, A. L., McQUILKIN, W. T. & THOMAS, J. I., 1972. Effect of Ionizing Irradiation on susceptibility of McCoy Cell cultures to *Chlamydia trachomatis*. *Applied Microbiology*, 123-129.
- HENNING, M. W., 1949. Animal diseases in South Africa. 2nd Ed. South Africa: Central News Agency, Ltd.
- HOWELL, C. J., DE VOS, A. J., BEZUIDENHOUT, J. D., POTGIETER, F. T. & BARROWMAN, P. R., 1981. The role of chemical tick eradication in the control or prevention of tick transmitted diseases of cattle. In *Tick Biology and Control, Proceedings, International Conference on Tick Biology and Control, Grahamstown, Republic of South Africa*, 41-46.
- HUTCHEON, D., 1900. Redwater and its history. *Agricultural Journal of the Cape of Good Hope*, 17, 331-339, 395-409.
- LAWRENCE, J. A., FOGGIN, C. M. M. & NORVAL, R. A. J., 1980. The effects of war on the control of diseases of livestock in Rhodesia (Zimbabwe). *Veterinary Record*, 107, 82-85.
- LOUNSBURY, C. P., 1900. Tick heartwater experiments. *Agricultural Journal of the Cape of Good Hope*, 16, 682-687.
- LOUNSBURY, C. P., 1904. Transmission of African Coast Fever. *Agricultural Journal of the Cape of Good Hope*, 24, 428-432.
- LONDT, J. G. H., HORAK, I. G. & DE VILLIERS, I. L., 1979. Parasites of domestic and wild animals in South Africa. XIII. The seasonal incidence of adult ticks (Acarina: Ixodidae) on cattle in the Northern Transvaal. *Onderstepoort Journal of Veterinary Research*, 46, 31-39.
- MASON, J. H. & ALEXANDER, R. A., 1940. The susceptibility of the ferret to heartwater. *Journal of the South African Veterinary Medical Association*, 11, 98.
- MOSHOKOVSKII, S. D., 1947. Comments by readers. *Science*, 106, 62.
- MCCOSKER, P. J., 1981. The global importance of babesiosis. In: Ristic, M. & Kreier, J. P. (eds). *Babesiosis*, 1-24 New York & London: Academic Press.
- McKENZIE, P. K. I. & VAN ROOYEN, R. E., 1981. The isolation and culture of *Cowdria ruminantium* in albino mice. *Proceedings, International Conference on Tick Biology and Control, Grahamstown, Republic of South Africa*, 33-39.
- NEITZ, A. W. H., HOWELL, C. J. & POTGIETER, D. J. J., 1969. Purification of toxic components in the oral secretion of the sand tampan, *Ornithodoros savignyi* (Audouin, 1827). *Journal of the South African Chemical Institute*, 22, 142-149.
- NEITZ, W. O., 1941. The occurrence of *Babesia bovis* in South Africa. *Journal of the South African Veterinary Medical Association*, 12, 62-66.
- NEITZ, W. O. & ALEXANDER, R. A., 1945. Immunization of cattle against heartwater and the control of the tick-borne diseases, redwater, gallsickness and heartwater. *Onderstepoort Journal of Veterinary Science and Animal Industry*, 20, 137-152.
- NEITZ, W. O. & JANSEN, B. C., 1950. Transmission of tick paralysis to adult Merino sheep by *Rhipicephalus evertsi evertsi*. Laboratory observations, Onderstepoort. In: Neitz, W. O., 1956. A consolidation of our knowledge of the transmission of tick-borne diseases. *Onderstepoort Journal of Veterinary Research*, 27, 115-163.
- NEITZ, W. O., 1955. Corridor disease: a fatal form of bovine Theileriosis encountered in Zululand. *Bulletin of Epizootic Diseases of Africa*, 3, 121-123.
- NEITZ, W. O., 1957. Theileriosis, gonderioses and cytauxzoonoses: A review. *Onderstepoort Journal of Veterinary Research*, 27, 275-430.
- NEITZ, W. O., 1959. Sweating sickness: The present state of our knowledge. *Onderstepoort Journal of Veterinary Research*, 28, 3-38.
- NEITZ, W. O., 1967. The epidemiology pattern of viral, protophythal and protozoal zoonoses in relation to game preservation in South Africa. *Journal of the South African Veterinary Medical Association*, 38, 129-141.
- NORVAL, R. A. J., 1981. A re-assessment of the role of dipping in the control of tick-borne diseases in Zimbabwe. *Proceedings, International Conference on Tick Biology and Control, Grahamstown, Republic of South Africa*, 87-90.
- POTGIETER, F. T., 1979. Epizootiology and control of anaplasmosis in South Africa. *Journal of the South African Veterinary Association*, 50, 367-372.
- POTGIETER, F. T. & VAN RENSBURG, L., 1983. Infectivity, virulence and immunogenicity of *Anaplasma centrale* live blood vaccine. *Onderstepoort Journal of Veterinary Research*, 50, 29-31.
- PRICE, W. H., JOHNSON, J. W., EMERSON, H. & PRESTON, C. E., 1954. Rickettsial interference phenomenon: A new protective mechanism. *Science*, 120, 457-459.
- RECHAV, Y., 1982. Dynamics of tick populations (Acari: Ixodidae) in the Eastern Cape Province of South Africa. *Journal of Medical Entomology*, 19, 679-700.
- RISTIC, M. & KREIER, J. P., 1981. Anaplasmosis. In: *Diseases of cattle in the tropics, Current Topics in Veterinary Medicine and Animal Science*, 327-344.
- STAMPA, S. & DU TOIT, R., 1956. Paralysis of stock due to the Karoo paralysis tick (*Ixodes rubicundus*). *South African Journal of Science*, 54, 241-246.
- STAMPA, S., 1959. Tick paralysis in the Karoo areas of South Africa. *Onderstepoort Journal of Veterinary Research*, 28, 169-227.
- THEILER, A., 1906. *Piroplasma mutans* (n. spec.) of South African cattle. *Journal of Comparative Pathology and Therapeutics*, 19, 292-300.
- THEILER, A., 1910a. *Anaplasma marginale* (gen. spec. nov.) The marginal points in the blood of cattle suffering from a specific disease. *Report of the Government Veterinary Bacteriologist*, 1908-9, 7-64.
- THEILER, A., 1910b. A contribution of our knowledge of gall-sickness. *Transvaal Agricultural Journal*, 8, 423-435.
- THEILER, A., 1911. Further investigations into anaplasmosis of South African cattle. *1st Report of the Director of Veterinary Research, Union of South Africa*, 7-46.
- THEILER, GERTRUD, 1975. Past-workers on tick and tick-borne diseases in South Africa. *Journal of the South African Veterinary Association*, 46, 303-310.
- UILENBERG, G., 1983. Heartwater (*Cowdria ruminantium* infection): Current status. *Advances in Veterinary Science and Comparative Medicine*, 27, 427-480.
- WEISS, E. & DRESSLER, H. R., 1958. Growth of *Rickettsia prowazeki* in irradiated monolayer culture of chick embryo endodermal cells. *Journal of Bacteriology*, 75, 544-552.
- WEISS, E. & DRESSLER, H. R., 1960. Centrifugation of Rickettsiae and viruses onto cells and its effect on infection. *Proceedings of the Society for Experimental Biology and Medicine*, 103, 691-695.