Historic highlights of South African veterinary R&D in tropical diseases

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For the purposes of this address, tropical diseases are broadly defined as animal diseases and toxicoses that were unknown to European settlers and European-trained veterinarians when they came to South Africa. However, there is good evidence that indigenous pastoralist Khoi-Khoi and Nguni people recognised and sought to manage some of these diseases and exploit identified poisons long before the arrival of European colonists.

The involvement of Sir Arnold Theiler, founder of Onderstepoort, in research and development in tropical diseases is so manifold that only the absolute highlights will be dealt with. It kicked off with co-developing the first safe and effective vaccine for rinderpest in 1896. Then followed the elucidation of the aetiology (*Theileria parva*) and epidemiology of East Coast fever. The next triumph was the discovery of the taxonomically unusual, erythrocytic parasite *Anaplasm*a and the development of an effective blood vaccine. Although best known for his lamsiekte (botulism) research, Theiler's involvement was somewhat controversial, as will be elucidated in the address.

Theiler's realisation of two major career objectives: a state-of-the-art research institute (in 1908), and a South African veterinary faculty (in 1920) will receive considerable attention. Crucial for his educational objective were textbooks dealing with local tropical diseases, especially Henning's (infectious diseases), Mönnig's (ecto- and endo-parasites) and DG Steyn's (toxicology) pioneering publications and their impressive successors.

R du Toit's major contributions were masterminding the complete eradication of the tsetse fly *Glossina pallidipes* population from KwaZulu-Natal with organic insecticides and determining that African horse sickness (AHS) and bluetongue of sheep were transmitted biologically by *Culicoides* midges.

The discovery that 'uitpeuloog' of cattle was due to infestation of an aberrant host with the minute larvae of an oestrid fly, *Gedoelstia*, actually a parasite of blue wildebeest, by Basson was a masterpiece in pathological observation.

WO Neitz was particularly renowned for his studies on tick-borne protozoan and some other tick-associated diseases. Neitz recognised the massive mortality of cattle in Zululand as being caused by a variant form of ECF which he called Corridor or buffalo disease because it was buffalo-associated rather than cattle-associated, like ECF. He also discovered that sweating sickness of calves was caused by the tick *Hyalomma truncatum*, ostensibly due to a toxin produced by engorging females. His pioneering studies on the chemotherapy of heartwater of ruminants and the development of a live blood vaccine against the disease were major contributions to economic farming with livestock in endemic areas. Bezuidenhout *et al.* made a major breakthrough when they succeeded in cultivating *Ehrlichia ruminantium* in an endothelial cell culture. This led to confirmation of earlier suspicions of immunological and pathogenic variability of strains as well as comprehensive genomic studies on the organism.

Onderstepoort is also internationally known for its virological research. In the 1800s and early 1900s AHS was a great killer of horses in the southern African crucial transport industries as well as in warfare. Theiler succeeded in producing a crude but fairly effective vaccine against the disease. Variability of strains, however, bedevilled his efforts and it was left to Alexander to identify immunologically different strains, attenuate them and produce a highly effective polyvalent vaccine. Erasmus revolutionised AHS vaccine production by exploiting a large plaque selection technique on 8 suitable strains obtained from field isolates.

Demonstration of the plurality of bluetongue virus (BTV) strains by cross-protection studies by Neitz and serial passage in embryonated eggs by others led to their attenuation and the development of an effective live cell culture vaccine consisting of 15 serotypes. Alexander and Weiss were respectively responsible for the isolation and attenuation of the lumpy skin disease virus for vaccine production.

A high containment laboratory provided facilities for research on the epidemiology of local FMD. Using genome-sequencing studies on the three SAT strains, Thomson *et al*. proved that buffaloes in the Kruger National Park serve as healthy carriers of the disease and that the calves experience epidemics of subclinical infections with overt lesions, thus serving as a source of infection for, inter alia, cattle.

Research on bovine besnoitiosis by Bigalke provided information on the epidemiology of this now emerging disease. Cultivation of *B. besnoiti* in cell culture inter alia enabled studies on the production of a live vaccine against the disease utilising a less pathogenic strain isolated from blue wildebeest. This followed the detection of infected animals in the

KNP by McCully and Basson.

The genetic resistance of indigenous livestock, such as cattle, to some tropical diseases and indigenous parasites was recognised by animal scientists like Jan Bonsma, and their easy-care advantages exploited in the development of several pure breeds that are economically productive under African environmental conditions.

Timely anticipation of the revolutionising influence that the newly developed molecular techniques would have on all biological research by Verwoerd provided for a very productive Molecular Biology Laboratory at Onderstepoort. The genomic structure of economically important viruses like AHVS and BTV were determined, genome libraries of these constructed and genes identified for the diagnosis of a variety of important viral, protozoal and rickettsial diseases. Isolation of the retrovirus causing 'jaagsiekte' finally elucidated the aetiology of the disease.

The period 1960 to 2014 was a golden era for veterinary wildlife research in South Africa, especially on the many local tropical diseases, such as theileriosis, FMD, ASF, MCF, AHS and besnoitiosis. The blossoming local wildlife industry resulted in the development of impressive clinical veterinary expertise based mainly on chemical immobilisation technology, essential for not only efficient translocation of wild animals but also to allow the clinical manipulation required to satisfy official biosecurity measures aimed at control and surveillance of the diseases they may be carrying.