A brief historical review of research achievements by the OVI during the 20th century against the background of socioeconomic and political developments in South Africa*

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INTRODUCTION

In order to examine the relevance of the socioeconomic and political environment to the scientific activities of the Onderstepoort Veterinary Institute, research highlights of each decade of the 20th century are reviewed against the background of the socioeconomic and political environment during that period.

Veterinary research in southern Africa has its origin in the worst pandemic animal disease this country has ever experienced, *i.e.* the rinderpest outbreak in 1896. The Cape Colony reacted by eliciting the help of the world-famous Robert Koch, Natal appointed Watkins Pitchford in 1897 and founded the Allerton Laboratory in 1898, and the Zuid-Afrikaansche Republiek (ZAR) appointed Arnold Theiler as its first state veterinarian with the specific brief to combat this disease. He established a field laboratory in Marico, moved to Waterval, north of Pretoria, where most of his work on the development of a serum against rinderpest was carried out, and in 1897 founded the first permanent laboratory at Daspoort. Owing to a concerted effort by the various workers, rinderpest was eradicated in 1898, never to return to South Africa, but only after almost half of the total livestock population of the country and even more wildlife were destroyed. This disaster firmly established the economic necessity of veterinary research, and activities at Daspoort and the other laboratories flourished. In Natal, for example, Bruce identified a trypanosome as the cause of nagana and the tsetse fly as its vector in 1895, and, in the Cape, Lounsbury discovered in 1900 that a tick, *Amblyomma hebraeum,* is responsible for the transmission of heartwater. These activities came to a standstill, however, after the outbreak of the Anglo-Boer war in 1899, which lasted until 1902. Veterinary research was therefore born in a period of severe political turmoil and disastrous economic circumstances, which set the scene for the century to follow.

*Address given to the staff of the OVI on 29 June 2000.

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1901–1910

The first decade of the 20th century started off in the worst possible way, with a war raging and concomitant destruction of farms and livestock. The post-war years in the previous Boer republics were characterised by extreme poverty and the instability of military rule. To make matters worse, a number of new animal diseases appeared on the scene, some of them introduced by the indiscriminate importation of horses for the British army from various parts of the world. The most serious new disease, East Coast Fever (ECF), was introduced by cattle imported from East Africa to help restock the depleted farms. Despite these problematic circumstances, some of the most significant developments in veterinary research took place during this decade. When responsible government was instituted in the Transvaal in 1907, Louis Botha became Prime Minister and Minister of Agriculture. Following urgent requests from Theiler, he convinced parliament to fund a new veterinary laboratory, and in 1908 the Onderstepoort Laboratory was completed at the then extravagant cost of 80 000 pounds (Fig. 1). The staff consisted of 6 professionals, 5 technicians and 12 auxiliary personnel, and the total budget was the equivalent of R17 294. Nevertheless, some highly significant scientific breakthroughs were made: Theiler identified the organism causing ECF (later named *Theileria parva*) in 1904, Lounsbury identified its vector (*Rhipicephalus appendiculatus*) in the same year, and Watkins Pitchford developed the dipping routines that eventually led to its eradication. Theiler discovered the causal organism of gallsickness (*Anaplasma marginale*) and its vector, the blue tick. He also identified *Trypanosoma congolense* as the main cause of nagana, and proved the viral nature of African horsesickness (AHS) and bluetongue (BT) by means of filtration experiments. The first crude vaccine against AHS was prepared.

1911–1920

With the advent of the Union of South Africa in 1910, Onderstepoort became the central veterinary laboratory for the whole country, necessitating expansion. An administration block was built in 1912 and a *post mortem* unit in 1918. In the same year, 10 years after its founding,the institute's staff, excluding labour (Fig. 2), had grown from 23 to 36 (14 professionals).

Fig. 1: **Onderstepoort Laboratory, completed in 1908 (photograph by courtesy of the Cape Archives).**

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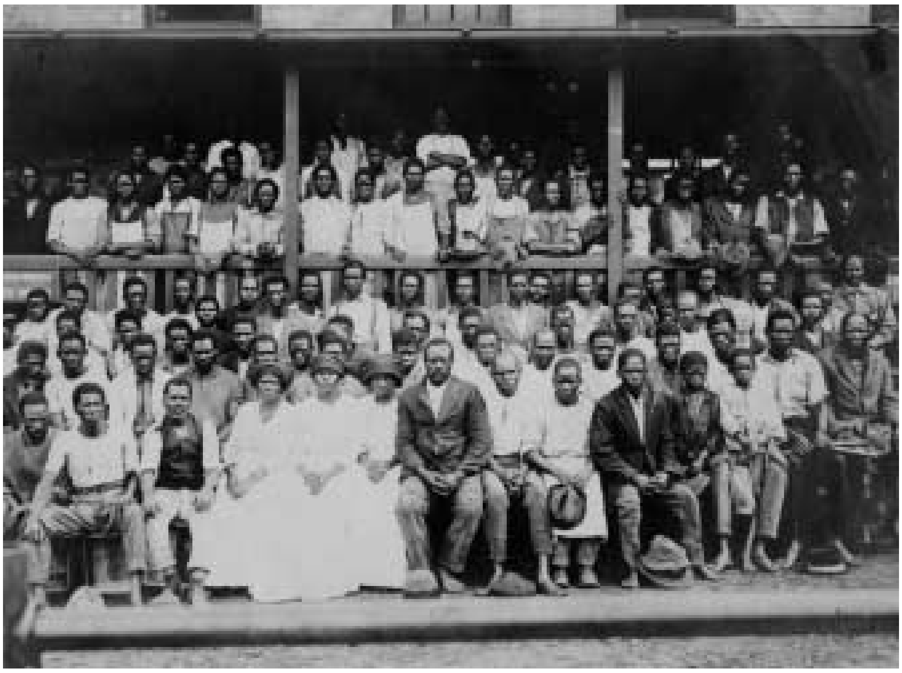

Fig. 2: **Auxiliary staff before 1920.**

However, the decade was again affected by war: the First World War, which lasted from 1914–1918. Activities at Onderstepoort were disrupted because a number of staff members enlisted for service with the British army, and, more seriously, by the resignation of Dr Theiler in 1918, partly owing to the pressures and frustrations caused by the war. Following a tremendous amount of public pressure on the political establishment and the departure of his successor Montgomery, Theiler was re-appointed in 1920 as Director of Veterinary Research and also as first Dean of the newly established Faculty of Veterinary Science. In spite of all these disruptions, various significant scientific advances were achieved during the decade, mainly by Theiler himself. These include the discovery in 1912 of *A. centrale* and its use as a vaccine for anaplasmosis, as well as the development of a blood vaccine for babesiosis. Both of these vaccines are essentially unchanged and still in use today. The outstanding achievement of the decade, however, was the elucidation of the nature of *lamsiekte* (botulism) in 1919, a disease of great economic importance in the arid parts of the country and a frustrating enigma for many years.

1921–1930

The relative calm of the twenties saw considerable expansion of facilities at Onderstepoort, mainly to accommodate the students of the new faculty. The biochemistry wing of the main building was erected in 1921, the pathology building and hospital block in 1923 and a modern X-ray unit in 1929. The staff complement increased, but in 1927 Theiler finally retired and was succeeded by P J du Toit as director. Scientific achievements during this decade included the identification of the causative agent of heartwater (*Cowdria ruminantium*) by Cowdry in 1925, the development of the first spore vaccine against anthrax by Viljoen in 1928, a formol toxoid vaccine against black quarter (*sponssiekte*) in 1929, and the identification of *Clostridium botulinum* types C and D by Robinson in 1930. Also in 1930, Harris developed his famous trap, which effectively controlled tsetse flies and reduced the incidence of nagana (Fig. 3).

Fig. 3: **Harris fly trap in the field.**

1931–1940

The thirties commenced with the worldwide economic depression, which also seriously affected the South African economy. Its after-effects were compounded by one of the worst droughts in our history in 1933, which left the farming community in an impoverished state for many years and limited governmental funds available for research. Nevertheless, several new facilities were built at Onderstepoort, including the library in 1932, the wool building in 1934, and the meat research building with abattoir in 1939. By 1940, professional staff numbered 66, with a total non-labour staff of 190. The close of the decade saw the start of the Second World War, which would have serious implications, mainly in the following decade. Highlights of the thirties in terms of research results included the pioneering book by Mönnig on veterinary parasitology (1934), the attenuation of AHSV by passage in mouse brains by Alexander in 1936, the first effective formol-toxoid vaccine against botulism by Mason and Sterne in 1938, and the attenuation of BTV by passage in embryonated eggs by Alexander in 1940.

1941–1950

As can be expected, the forties were dominated by the effects of the Second World War and its aftermath. Reflecting the political division in the country, divisions amongst the staff members seriously affected their morale. Some enlisted for service (Fig. 4), others vehemently opposed the war effort (Fig. 5), and a few were interned because of their German descent. These divisions would take many years to heal and also resulted in the loss of several excellent scientists. Obviously, the war effort constituted a serious drain on government funds that affected the availability of research funding and was compounded by the shortage of imported research materials and equipment. Nevertheless some progress was made, including the important discovery by du Toit in 1944 that AHSV and BTV are transmitted by the midge *Culicoides,* and the development of the famous Sterne spore vaccine against anthrax, which is still widely used today, in 1946. There was also the first avianised vaccine against bluetongue by Alexander in 1947 and the discovery of various BTV serotypes by Neitz in 1948, to explain vaccine failures. In 1948, pulpy kidney (enterotoxaemia) was first diagnosed in sheep and a vaccine developed that soon became a best-seller.

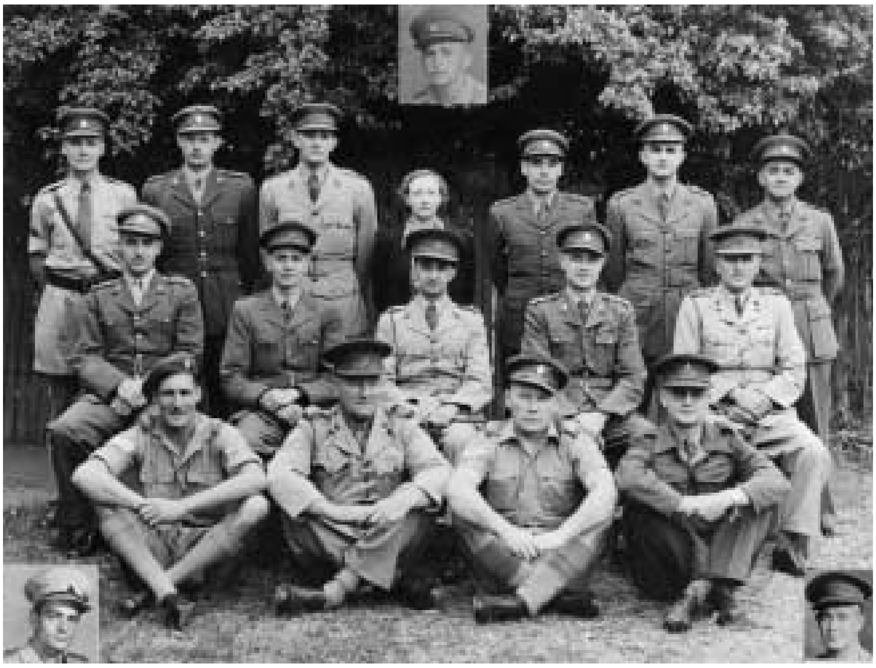

Fig. 4: **Members of staff volunteered for the Veterinary Corps during World War II.**

1951–1960

The fifties can be regarded as a period of recovery from the aftermath of war and of consolidation. New facilities included the new virology building in 1952 and the insectarium in 1955. The staff component remained almost static, except for a large increase in the number of labourers. Non-labour staff in 1958 stood at 206 against 190 in 1940, with professionals static at 66. It is interesting to note that the budget in 1958 was R1.28 million compared to the R17 000 of 1908!

During this decade, 2 important milestones in disease control were reached. After 50 years ECF was finally eradicated, with the last case reported in 1955. This was accompanied by the discovery of a variant form of the disease in buffalo, named 'corridor disease'. It followed closely on the eradication of the tsetse fly species mainly responsible for the transmission of nagana in the endemic area in Natal by aerial spraying with DDT (Fig. 6). Nagana parasites were thereby effectively limited to the game reserves for many years to come. An important breakthrough in virus research was the development of cell culture technology, which was first used by Haig in 1956 to culture BTV and to develop a quantitative neutralisation technique that enabled Howell to identify 12 BTV serotypes in 1960. McIntosh identified 7 AHSV serotypes in 1958. Other viruses that could be isolated and studied for the first time included those causing lumpy skin disease, Rift valley fever, ephemeral fever and canine distemper.

1961–1970

The sixties constituted a period of sustained economic growth and relative political stability, which was reflected in considerable expansion of facilities at Onderstepoort. The completion in 1968 of the new vaccine factory and administration complex doubled the available laboratory space and facilitated the centralisation of all vaccine production activities (Fig. 7). An important advance was made by starting a Molecular Biology laboratory in order to take advantage of the rapidly evolving biotechnology. This step reflected the worldwide revolution in biological research. Scientific advances made during this period included the first vaccine against lumpy skin disease developed by Weiss in 1962, the discovery, also in 1962, by Basson of the aetiology of 'uitpeuloog' (gedoelstiasis), the development of the Rev-I vaccine against brucellosis in rams by Van Drimmelen in 1963, the plaque-selection of vaccine strains of AHSV by Erasmus in 1965, the first vaccine against besnoitiosis developed by Bigalke in 1967, and the discovery of the

Fig. 5: **In 1948, supporters of the nationalist movement grew beards to display at the 10-year celebration of the inauguration of the Voortrekker Monument.**

Fig. 6: **Aerial spraying was employed successfully to control tsetse fly.**

double-stranded RNA nature of the genomes of orbiviruses by Verwoerd in 1969.

1971–1980

During this period the general prosperity in the country continued, although the first signs of political instability became apparent. Increasing international isolation affected scientific activities and relations with international organisations. Major developments in the veterinary field included the attainment of independence by the Faculty of Veterinary Science in 1973 and the establishment of the foot-and-mouth disease (FMD) laboratory in 1980 (Fig. 8). The latter functioned as a sub-directorate of the OVI and constituted the first high security containment facility in South Africa, suitable for work on exotic and highly infectious viruses.

Major scientific advances included the identification of *C. botulinum* toxins by Jansen in 1971, which led to an improved *lamsiekte* vaccine, the clarification of orbivirus structure and replication and the demonstration of the immunogenicity of a single BTV capsid protein, the establishment of somatic cell counting as a definitive diagnostic test for mastitis, and the isolation of a retrovirus that causes *jaagsiekte* (ovine pulmonary adenomatosis).

Fig. 7: **Aerial view of the institute showing the vaccine factory and administration complex added in 1968.**

1981–1990

The eighties were characterised by increasing political violence, economic sanctions and international isolation, negatively affecting scientific activities. Despite financial limitations, a new abattoir was commissioned and the total staff number reached an all-time high of 1034 in 1983, including 94 professionals and 265 non-labour auxiliary staff. The budget for 1983 was R4.7 million. From 1981 the vaccine factory operated on a trade account, which enabled it to fund its activities from income. One of the most important achievements during the eighties was the cultivation of *C. ruminantium* in cell cultures by Bezuidenhout in 1985, solving a problem that had hampered research on heartwater for many years (Fig. 9). Excellent results were obtained with the cloning of BTV genome segments and their use as diagnostic reagents, as well as the construction of genome libraries for BTV, AHSV, *Anaplasma* and *Babesia.* The first vaccinia-BTV and baculo-BTV recombinant viruses were also constructed and tested for immunogenicity. Various plant toxins, including cardiac glycosides, neurotoxins and mycotoxins were isolated and some of their chemical structures elucidated. Excellent progress was also made in the study of the epidemiology of FMD, elucidating the role of the African buffalo in its transmission. Subtyping of FMD virus by RNA sequencing and by means of monoclonal antibodies served to select vaccine strains and to explain vaccine failures. Equine influenza occurred for the first time in South Africa and was effectively controlled by a vaccine developed and produced within weeks. Resistance to anthelmintics was detected in internal parasites and was shown to constitute a major problem in various parts of the country. The development of techniques for the cryopreservation of roundworm larvae greatly facilitated ongoing research to solve this problem. Cryopreservation was also applied to conserve the immunogenicity of blood vaccines against babesiosis and anaplasmosis.

1991–2000

The last decade of the 20th century brought major political reform to South Africa. Economic reform followed the 1994 election, with major changes in the economic priorities of the new government towards the upliftment of previously disadvantaged communities. The OVI did not escape the effects of the economic reform. In 1992 it was separated from the vaccine factory (now called Onderstepoort Biological Products or OBP) and the FMD laboratory and transferred from the Department of Agricul-

Fig. 8: **A containment facility to house the foot-and-mouth disease laboratory was built in 1980.**

ture to the newly created parastatal Agricultural Research Council. The resultant increased autonomy and independence from direct government funding required the generation of internal income from research contracts, grants, diagnostic and other services rendered (Fig. 10). This in turn required a major change in policy and culture from problem-oriented to client-oriented research, a transition that has not yet been completed. During the first part of the decade the OVI benefited immensely by the transition to the ARC, especially in terms of the renovation and upkeep of its facilities and independent decision-making, and managed to generate 30 % of its budget within 3 years. By the end of the decade, however, escalating expenses (R42 million in 1998) and a decrease of more than 60 % in the government subsidy via the ARC necessitated major restructuring and cut-back of both staff and research expenditure. By 2000 the staff had been reduced to 412 (72 professionals), a level similar to that in the seventies. Nevertheless, major scientific advances have again been achieved during this difficult period. Only a few can be mentioned.

Fig. 9: **Dr Dürr Bezuidenhout, recently-retired as Senior Deputy Director, succeeded in cultivating *Cowdria ruminantium,* the causative agent of heartwater, in cell culture in 1985.**

In 1992 the complete nucleotide sequence of the *jaagsiekte* viral genome was determined by York, facilitating further research on its oncogenicity and possible control. The existence of an endogenous form of the *jaagsiekte* virus was demonstrated and a molecular probe developed to distinguish it from the exogenous virus. A protocol for the control of blackfly along the Orange river was devised and applied most effectively, saving the country millions of rands in terms of lost production. The aetiology of *geeldikkop,* a toxicosis caused by the plant *Tribulus terrestris,* which on occasion can reach epidemic proportions, was clarified. A diagnostic probe was developed for the diagnosis of malignant catarrhal fever that can distinguish between the wildebeest- and sheep-associated forms of the disease, and a recombinant ELISA test for the diagnosis of Maedi-Visna was developed and commercialised. A study of rabies epidemiology demonstrated the existence of 2 different viral types, transmitted by dogs and wild animals respectively. A new leukotoxin vaccine against pasteurellosis was developed and commercialised, and a recombinant baculovirus-AHSV vaccine developed and proved to be immunogenic and to protect horses against infection. Finally, the neurotoxin that causes diplodiosis and the toxin that causes *gousiekte,* cardiotoxicity induced by certain plants of the family Rubiaceae, were isolated and the chemical structure of the latter determined.

CONCLUSIONS

No clear relationship can be found between the scientific achievements of the OVI and the socioeconomic and political environment that exists at a specific point in time, with the obvious exception of interrupted activities during periods of war. Indeed, some of the most important discoveries have been made during periods of economic stagnation and budget cuts, and lower productivity occurred during periods of economic growth and political stability. One reason, of course, is that scientific discovery often needs a long incubation period. Projects initiated during periods of prosperity very often yield results only during subsequent periods of economic privation and *vice versa.* Although generous funding certainly facilitates and enhances research activities, it does not guarantee success. Ultimately, scientific breakthroughs depend primarily on the ability and dedication of individual scientists and less on environmental factors.

Fig. 10: **Development of biological products to improve animal health through better diagnostic tests and vaccines enjoys priority at the Onderstepoort Veterinary Institute.**