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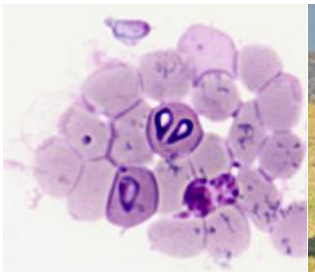
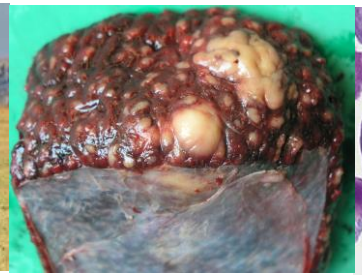
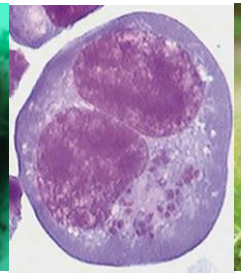
THE HISTORY OF EAST COAST FEVER IN SOUTHERN AFRICA

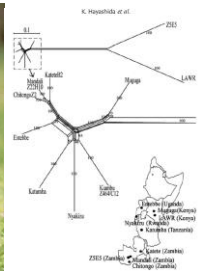
Ben J. Mans
Agricultural Research Council - Onderstepoort Veterinary Research

World-Association for the History of Veterinary Medicine

2020





Was *Theileria parva* present in South Africa prior to the introduction of East Coast fever or does remnants of East Coast fever remain to date?

Heavy losses in South Africa: Naïve and susceptible cattle population

Theileria parva: influence of vector, parasite and host relationships on the epidemiology of theileriosis in southern Africa

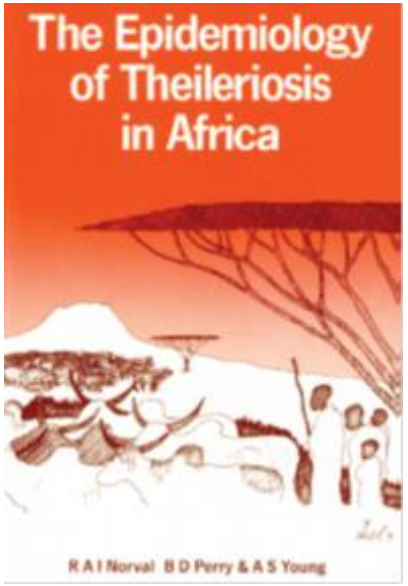
R. A. I. NORVAL[1]*, J. A. LAWRENCE[2], A. S. YOUNG[3]†, B. D. PERRY[1]‡, T. T. DOLAN[1] and J. SCOTT[1]

INTRODUCTION OF *THEILERIA PARVA* TO SOUTHERN AFRICA

There is no evidence that ECF occurred in cattle in southern Africa before its introduction from eastern Africa in 1901 and the heavy mortality that followed its introduction is evidence of a completely susceptible cattle population. There is also no evidence that Corridor disease occurred in southern Africa prior to 1901, although buffalo were widely distributed at that time and other tick-borne diseases, such as babesiosis and heartwater, had been described and were widely recognized (Henning, 1956).

The apparent absence of ECF and Corridor disease in southern Africa prior to 1901 suggests that *T. parva* was introduced to the subcontinent by the cattle brought in from eastern Africa. Hence, all the *T. parva* parasites in southern Africa probably have an eastern African origin. We hypothesize that the buffalo in southern Africa were actually infected from the cattle as it has been shown on several occasions that cattle-derived *T. parva* is infective to buffalo (Barnett, 1968; Brocklesby 1964; Grootenhuis *et al.* 1987). It may be possible to test this hypothesis with buffalo isolates of *T. parva* from southern Africa, using parasite characterization procedures such as antigenic profiles as detected by monoclonal antibodies and DNA probes (Conrad *et al.* 1987, 1989).

Parasitology (1991) **102**, 347–356



Norval et al. (1992) The Epidemiology of Theileriosis in Africa.

John Lawrence (1986; 2016) East Coast Fever in Southern Africa 1901-1960. With an afterword 2016.

Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)
Norval et al. (1991) *Parasitology* **102**, 347-356
Norval et al. (1992) *The Epidemiology of Theileriosis in Africa* (Academic Press)

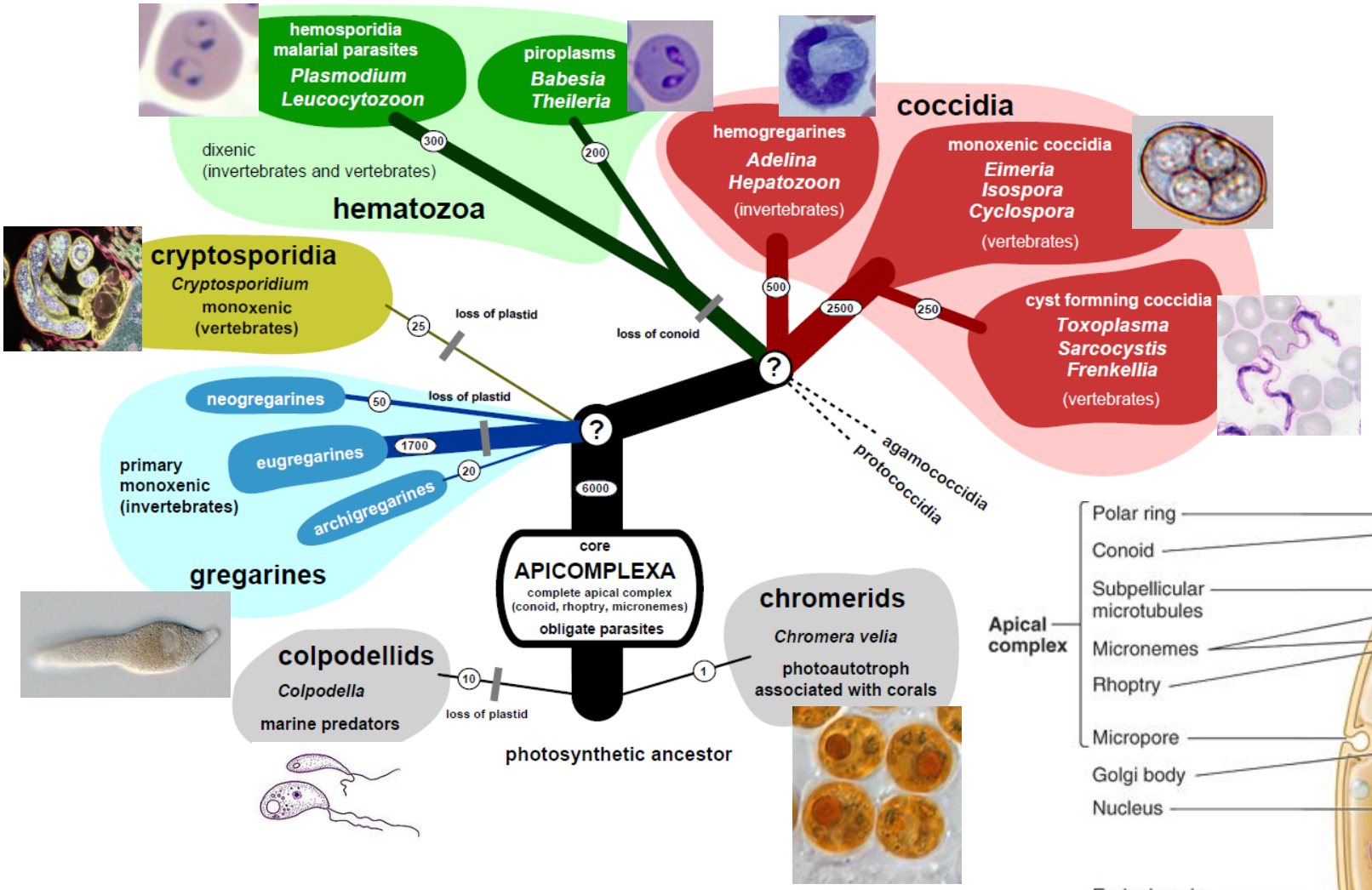
Implications of ECF introduced into a naïve South Africa and establishing in buffalo

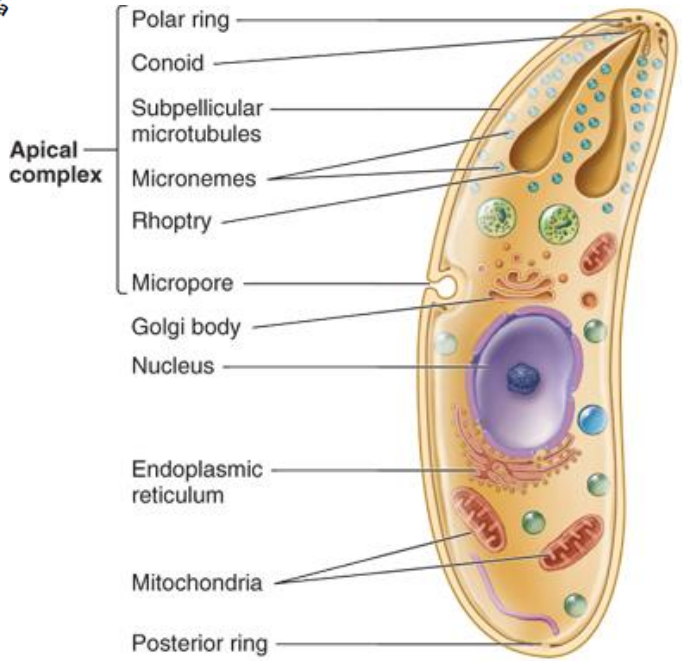
Basis for foreign belief that ECF exist in South Africa
(Contrary to claims by South African government that ECF was eradicated)

Re-adaptation to cattle should be easy
(Increasing potential ECF risk)

Basis of arguments for introduction of prophylactic treatment or vaccines in South Africa
(Despite the carrier state created in cattle leading to endemic ECF)

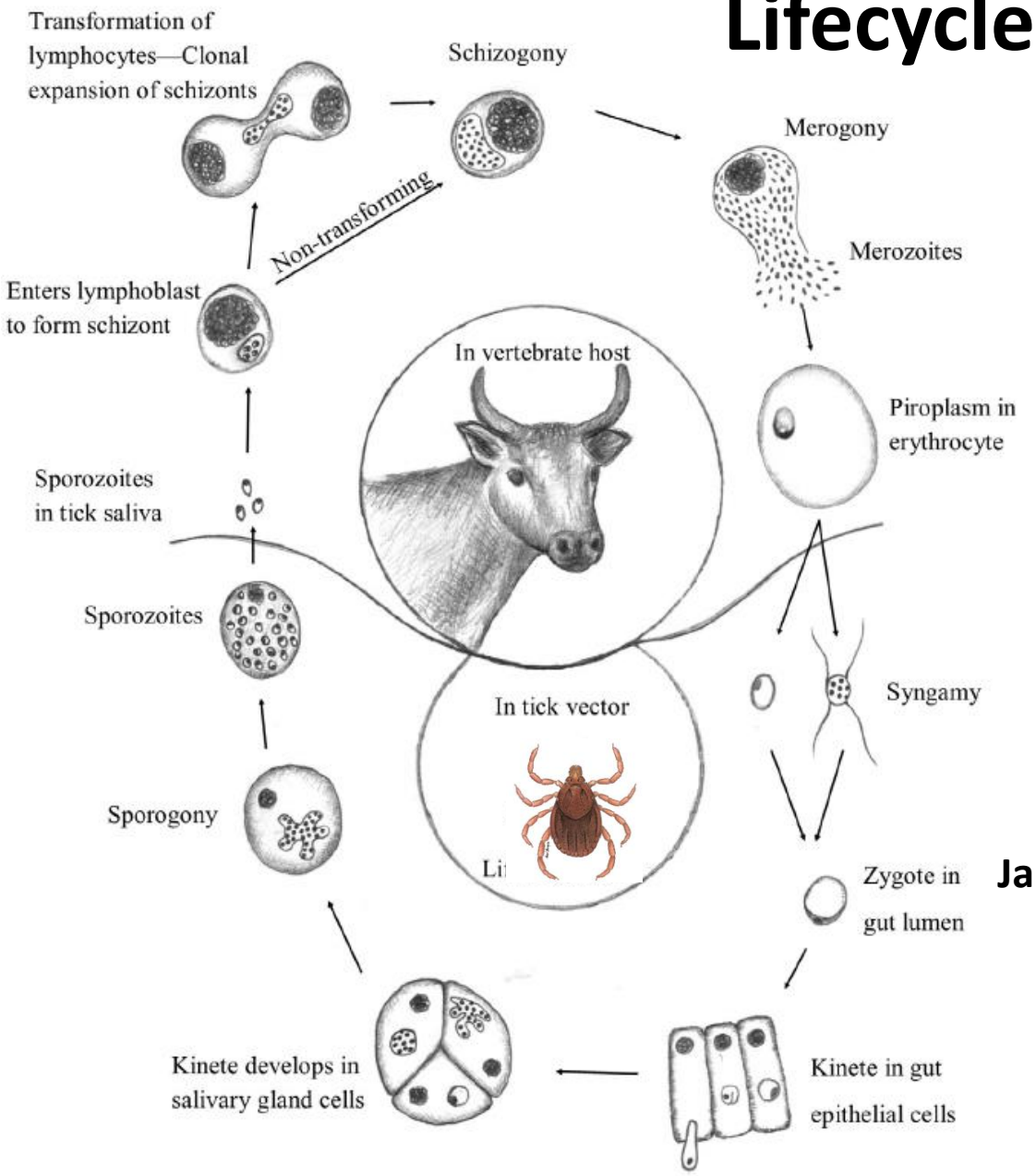
Apicomplexa



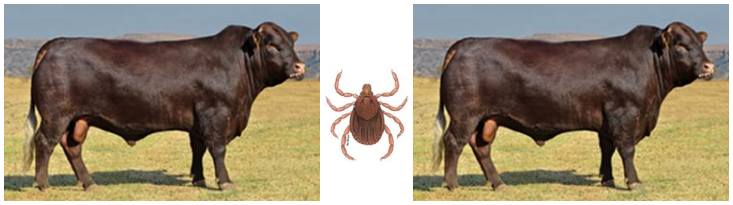


Šlapeta (2011) *Hypothetical tree of Apicomplexa* (WikiMedia Commons)
Prescott et al. (2008) *Microbiology* (McGraw-Hill)

Lifecycle of *Theileria parva*



Buffalo-derived *Theileria parva*
Corridor disease (CD)
Theileria parva lawrencei



Cattle-derived *Theileria parva*
January disease (Zimbabwe theileriosis)
Theileria parva bovis
East Coast fever (ECF)
Theileria parva parva

Mans et al. (2015) *International Journal for Parasitology: Parasites and Wildlife* **4**, 104-118

The Piroplasma and Tick-borne diseases

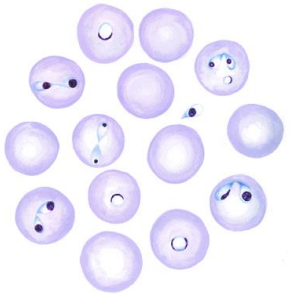
Victor Babeș (1854-1926)

Babeș (1888) Bovine hemoglobunuria: Red water fever (Asiatic babesiosis)
Haematococcus sensu latu (name already preoccupied)

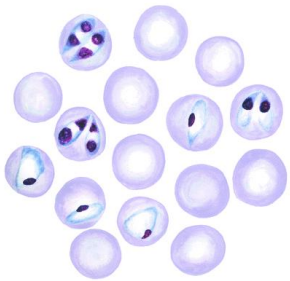
Smith & Kilbourne (1893) *Pyrosoma bigeminum* – Texas fever (African babesiosis)
Transmission by *"Boophilus bovis* Curtice, 1891" (*Rhipicephalus annulatus* Say, 1821)
First report of tick vector transmitting pathogens

Pyrosoma preoccupied by tunicate *Pyrosoma atlanticum* Péron, 1804
Starcovici (1893) *Babesia bovis*, *Babesia bigemina, Babesia ovis*

Animals immune to Texas redwater in Transvaal and Natal (Endemic regions)



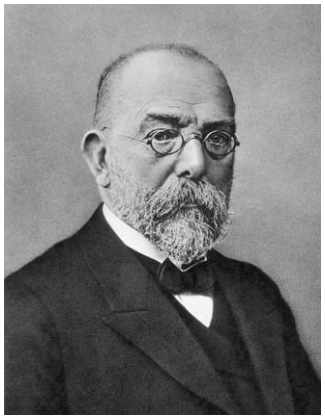
Babesia bovis



Babesia bigemina

Babeș (1888) *Comptes rendus de l'Académie des Sciences* **107**, 692–694.
Smith and Kilborne (1893) *8th/9th Report of the Bureau of Animal Industry*, 177–304.
Starcovici (1893) *Centralblatt für Bakteriologie und Parasitenkunde* **14**, 1–8.

Rinderpest Epidemic (1896-1899) in South Africa
Second Boer War (1899 – 1902)



2.5 million cattle succumbed to Rinderpest (50% of national herd)

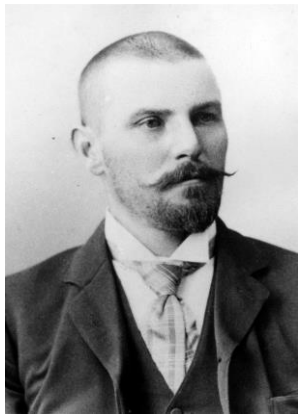
Necessitated import of cattle into southern Africa

Appointment of Veterinarians

1896-1897: Robert Koch (Cape Government)

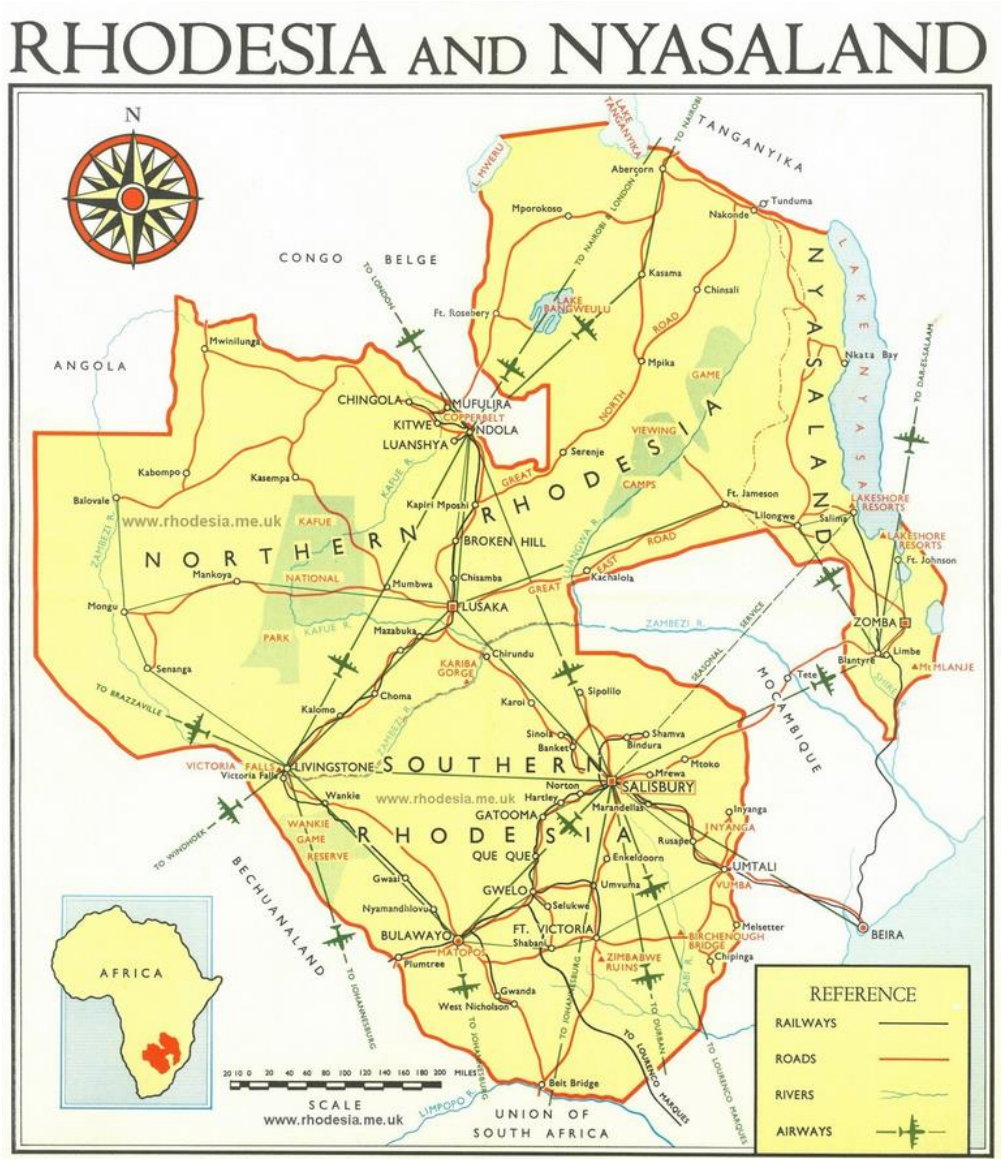
1896: Arnold Theiler (Government Veterinary Surgeon to the Zuid-Afrikaansche Republiek - ZAR)

1901: Arnold Theiler (Bacteriologist of the Transvaal)



Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)

Introduction of ECF to Southern Rhodesia (Zimbabwe)



1901
Cattle imported from German East Africa via Dar es Salaam and Beira
Transported by rail to Umtali and Salisbury

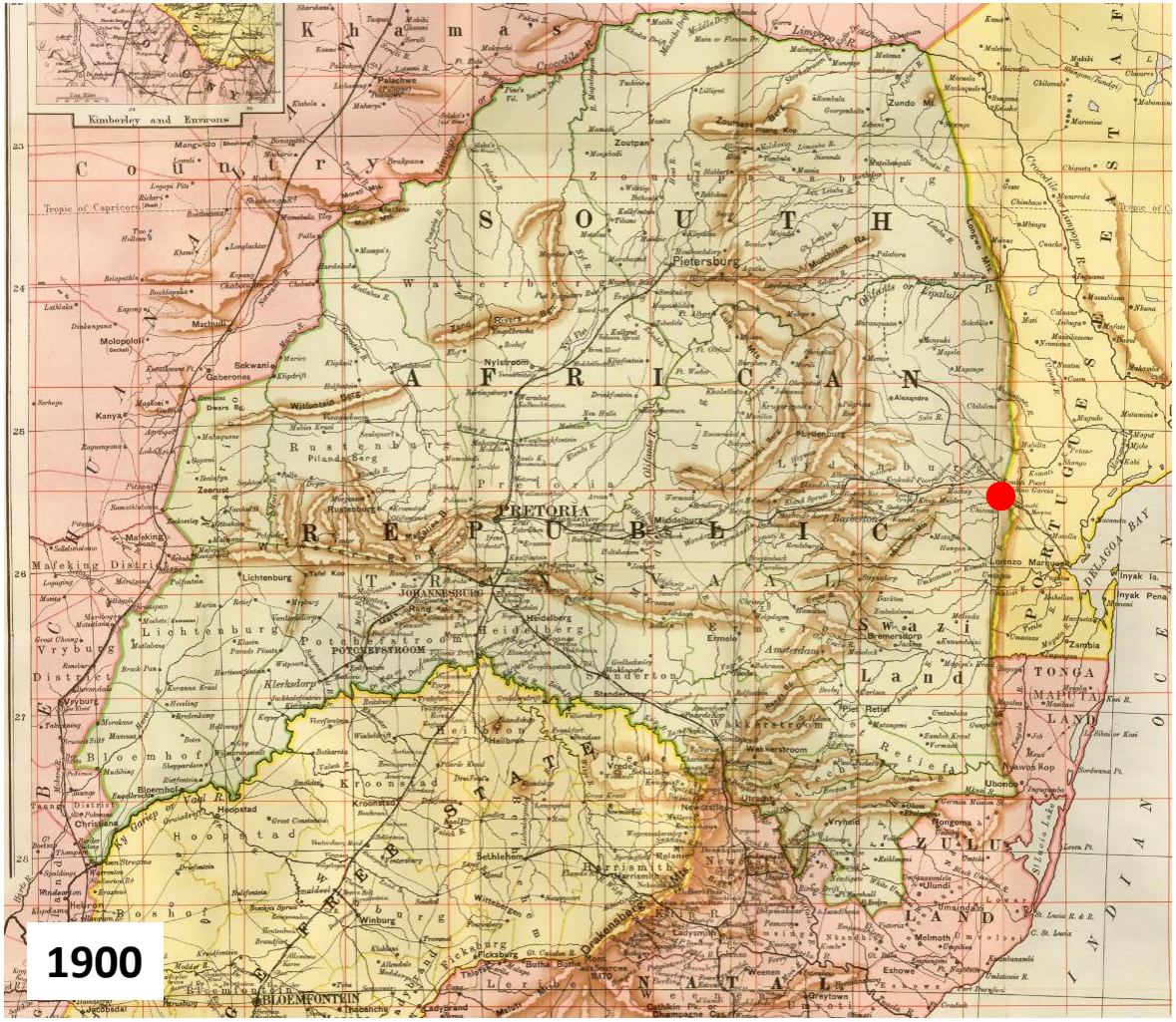
November 1901 – Disease outbreak
Umtali (Mutare)
Salisbury (Harare)

May 1902 – Disease outbreak
Bulawayo

First thought to be Texas Redwater
Charles Gray (Chief Veterinary Surgeon)

Gray and Robertson (1903) *Report upon Texas fever or redwater in Rhodesia*. (Argus Printing and Publishing)
Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)

Introduction of ECF to the South African Republic (Transvaal)



1901
Cattle imported to *Lourenço Marques* (Maputo) from Beira/Madagascar/ German East Africa (Tanzania)

March 1902
Mortalities at *Lourenço Marques*

May 1902
Imported military transport cattle into Transvaal via Komatipoort (Mpumalanga)

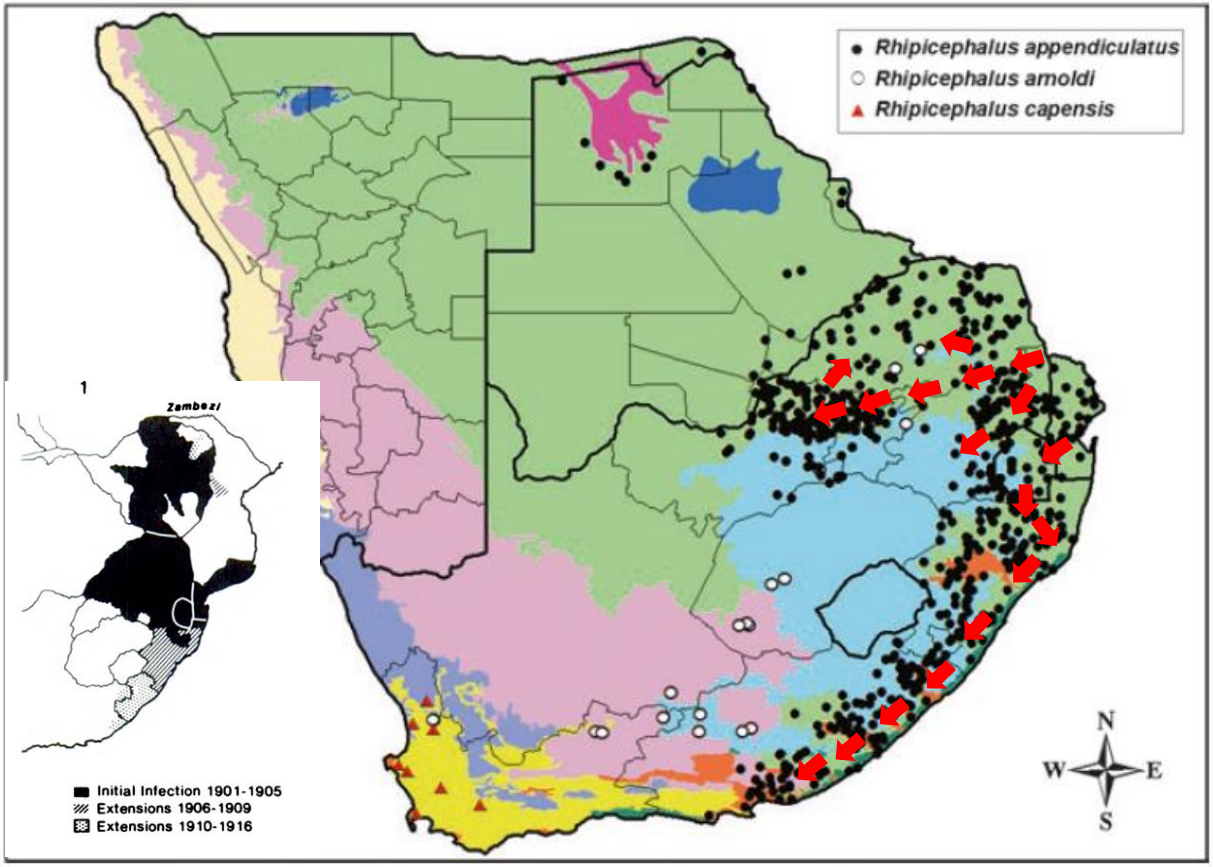
June 1902
Reports of severe disease in Komatipoort area

August 1902
Arnold Theiler visits Komatipoort
Conclude: Redwater

September 1902
Theiler visits Bulawayo
Conclude: Identical disease: Rhodesian redwater

Gray and Robertson (1903*) Report upon Texas fever or redwater in Rhodesia*. (Argus Printing and Publishing)
Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)

Introduction of ECF to the rest of South Africa



1902
Disease spread to Swaziland (Eswatini) from *Lourenço Marques*

1902-1904
Spread to south-eastern Transvaal

1904
Northern Kwa-Zulu Natal

Southwards

1910
Disease reached Eastern Cape

Across tick distribution area

ECF spread over the whole tick distribution range within 10 years
Despite extensive efforts to control and eradicate the disease
Control of cattle movement
Quarantine

Horak et al. (2018) *The Ixodid Ticks (Acari: Ixodidae) of Southern Africa* (Springer)
Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)

What was this disease?

1902

Charles Gray (Chief Veterinary Surgeon - Southern Rhodesia)
Redwater – BUT: Heavy mortalities in Umtali, Rapid spread along transportation routes
Doubt on this hypothesis. Additional causes?

Blood smears was sent to:

Alexander Edington (Government Veterinary Bacteriologist, Grahamstown)
Piroplasms identical to redwater from animals experimentally inoculated with blood from redwater-immune animals

William Robertson (Bacteriologist from Veterinary Department, Cape Town)
Visited Southern Rhodesia – disease the same as Natal redwater

Herbert Watkins-Pitchford (Government Veterinary Bacteriologist, Natal)
Visited Southern Rhodesia – disease the same as Natal redwater

Duncan Hutcheon (Chief Veterinary Surgeon, Cape of Good Hope)
Visited Southern Rhodesia – endorsed report by **Gray and Robertson (1902)** as redwater

Arnold Theiler (Government Veterinary Bacteriologist for the Transvaal)
Visited Southern Rhodesia – concluded Rhodesian redwater is the same disease observed in Transvaal

Laveran (Paris): Conclude redwater from slides sent by Theiler

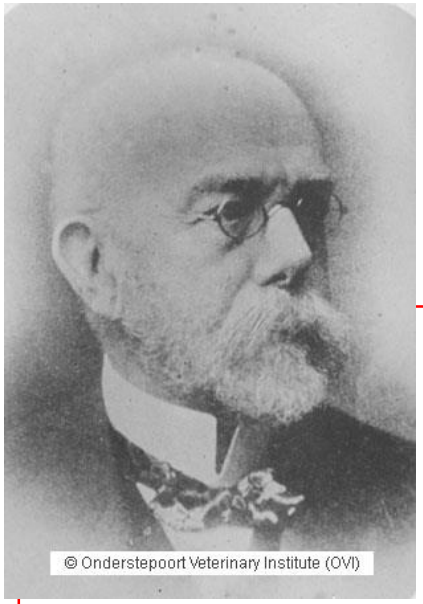
Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)
Norval et al. (1992) *The Epidemiology of Theileriosis in Africa* (Academic Press)

Differences in Redwater (Gray and Robertson, 1902)

1) Cattle supposed to be resistant to redwater succumbed
2) Disease showed respiratory symptoms and pulmonary and renal lesions
3) High piroplasm parasitemia, but smaller and differently shaped than redwater parasites
4) Inoculation with blood from recovered animals failed to provide protection
5) Calves bred and reared on infected pasture failed to develop immunity and died

Misinterpretation (Neitz, 1957; Norval et al. 1991)
Koch (1898) describing Texas redwater at Dar es Salaam described both large and small pyriform parasites as different stages
southern African disease showed both small and large forms
Mixed infections of ECF and redwater parasites

Gray and Robertson (1903) *Report upon Texas fever or redwater in Rhodesia* (Argus Printing and Publishing).
Koch (1898) *Reiseberichte uber Rinderpest, Bubonenpest in Indien und Afrika, Tsetse oder Surrakrankheit, Texasfieber, tropische Malaria, Schwarzwasserfieber* (Springer).
Neitz (1957) *Onderstepoort Journal of Veterinary Research* **27**, 275-430.
Norval et al. (1991) *Parasitology* **102**, 347-356.



A new face and a new name: Robert Koch

Critical nature of disease: Consultation by Robert Koch
British South African Company: £6000 annum + expenses
February 1903: Arrived in Beira bound for Southern Rhodesia
Made camp in Bulawayo (No disease at Beira, Umtali, Salisbury)

Reports.

PROFESSOR KOCH ON RHODESIAN REDWATER OR AFRICAN COAST FEVER.

INTERIM REPORT.[1] **May 1903**

Not redwater, but same disease observed in 1897 in German East Africa (Koch, 1898)
Smaller than Texas redwater, ring-shaped/rod shaped not pear shaped as redwater
Higher parasitemia, no destruction of red blood cells, no anemia

Introduction from Portugese East African Coast; Endemic along East African coast
African Coast fever: Southern Rhodesia adopted name
South Africa: East Coast fever – no disease along South African coast

Stephens and Christophers (1903): *Piroplasma kochi*
Patton (1895) *Piroplasma* (*Babesia* take precendence – Starcovici, 1893)

Koch (1903) *Journal of Comparative Pathology and Therapeutics* **16**, 273-284.
Neitz (1957) *Onderstepoort Journal of Veterinary Research* **27**, 275-430.
Stephens and Christophers (1903) *The Practical Study of Malaria and other Blood Parasites* (Liverpool University Press).
Patton (1895) *American Naturalist* **29**, 498.

How did we get to the name *Theileria parva*?

Koch (1903) claimed that *Rhipicephalus decoloratus* transmitted ECF
Transmission studies performed in German East Africa
Close relationship of pathogens for "Rhodesian fever" and Texas redwater
Close relationship to *R. annulatus* and *R. australis* (vectors of Texas redwater)
Did not identify *R. appendiculatus* in Southern Rhodesia: *R. decoloratus*, *R. evertsi*, *R. sanguineus*, *Hyalomma aegypticum*, *Amblyomma variegatum*, *Haemalysalis leachi*

Koch (1903, 1905, 1906): Identified parasite in lymphoid cells (schizonts) – "Koch's bodies"
Lifecycle different from the *Babesia*

Stephens and Christophers (1903): *Piroplasma kochi*

Lounsbury (1904): *Rhipicephalus appendiculatus* is the tick vector

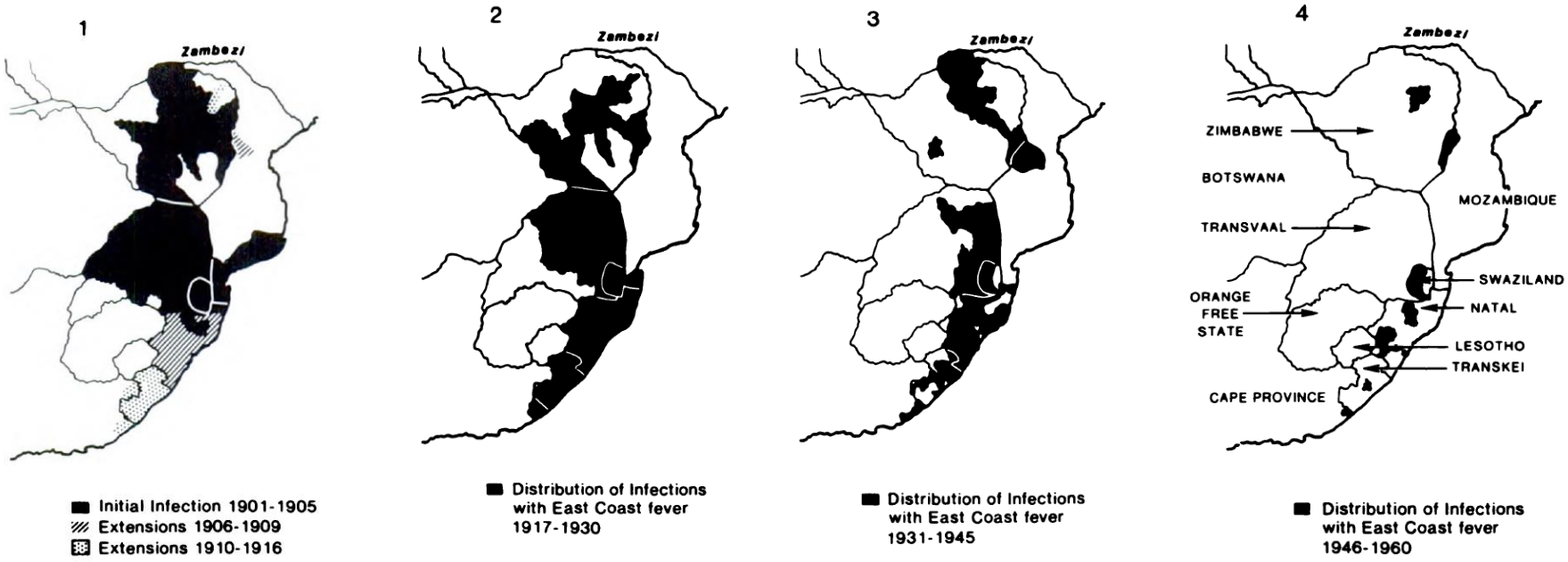
Theiler (1905) *Piroplasma parvum* (small piroplasm). Cited as **Theiler (1904) –** not correct

Theiler (1906) identified piroplasm as *Piroplasma mutans* (*Theileria mutans*)
Small, benign, transmissible by inoculation – distinct from *P. parvum*

Bettencourt, Franca & Borges (1907) *Theileria parva*

Wenyon (1926) Suggested that *Theileria kochi* is the taxonomically correct name.
Subsequent authors upheld *Theileria parva*

ECF eradication campaigns



1901-1906
1906-1909
1910-1916

1917-1930

1931-1945

1946-1960

Short interval dipping: Watkins-Pitchford
Fever camps
Quarantine, dipping and slaughter

Cost of ECF: R100 million
Cattle deaths: 5.5 million
1954: East Coast fever eradicated from South Africa

Lawrence (1986, 2016) *East Coast fever in southern Africa 1901-1960* (Monograph)

Jl. S.A.V.M.A. 26(2), 1955.

CORRIDOR DISEASE: A FATAL FORM OF BOVINE THEILERIOSIS ENCOUNTERED IN ZULULAND

W. O. NEITZ, A. S. CANHAM, AND E. B. KLUGE

Theileriosis outbreaks 1953/1954 in Corridor between Hluhluwe and Umfolozi Game Reserves
Cattle (584) chased into "Corridor" – 300 died within 4 weeks
Disease recognized as "Buffalo disease" observed by Lawrence (1934)
Named "Corridor disease"

Different from ECF
Low piroplasm parasitemia
High mortality
No carrier state in cattle – "self-limiting"
Onset of disease faster than ECF

Lawrence (1936) recognized another form of disease milder than ECF
Cattle-cattle transmitted – January disease, Zimbabwe theileriosis

Neitz: *Gonderia lawrencei, Gonderia bovis*
Theileria lawrencei, Theileria bovis

Neitz et al. (1955) *Journal of the South African Veterinary Medical Association* **26**, 79-87.

THE PASSAGE OF "*THEILERIA LAWRENCEI* (KENYA)" THROUGH CATTLE[1]

By S. F. Barnett[2] and D. W. Brocklesby[3]

East African Veterinary Research Organisation, Muguga, Kenya

SUMMARY

A theilerial parasite, "*Theileria lawrencei* (Kenya)", isolated from a wild African Buffalo (*Syncerus caffer*) in engorged *Rhipicephalus appendiculatus* nymphae, was passaged through cattle *via* the same species of tick. The parasite on first isolation in cattle had all the accepted criteria of *T. lawrencei*. Recovery from infection provided a strong immunity to subsequent challenge with *Theileria parva*. One animal infected ticks three months and fifteen months after recovery: these ticks transmitted a theilerial infection to cattle indistinguishable from East Coast Fever. Passage of "*T. lawrencei* (Kenya)" through cattle resulted in profound changes. The most important of these were (1) an increase in piroplasm production; (2) an increase in the numbers of macroschizonts; (3) an increase in the numbers of microschizonts, and (4) an increase in the average size of the macroschizonts. These changes meant that "*T. lawrencei* (Kenya)" had become indistinguishable from *T. parva*, and therefore the validity of *T. lawrencei* as a species cannot be supported. The African Buffalo must be regarded as a reservoir of East Coast Fever.

Transformed *T. lawrencei* to *T. parva*

***T. parva* and *T. lawrencei* are the same parasite!**

Barnett and Brocklesby (1966) *British Veterinary Journal* **122**, 396-409.

Trinomial classification system

Uilenberg (1978): *Theileria parva lawrencei*; *Theileria parva parva*
Lawrence (1979): *Theileria parva bovis*

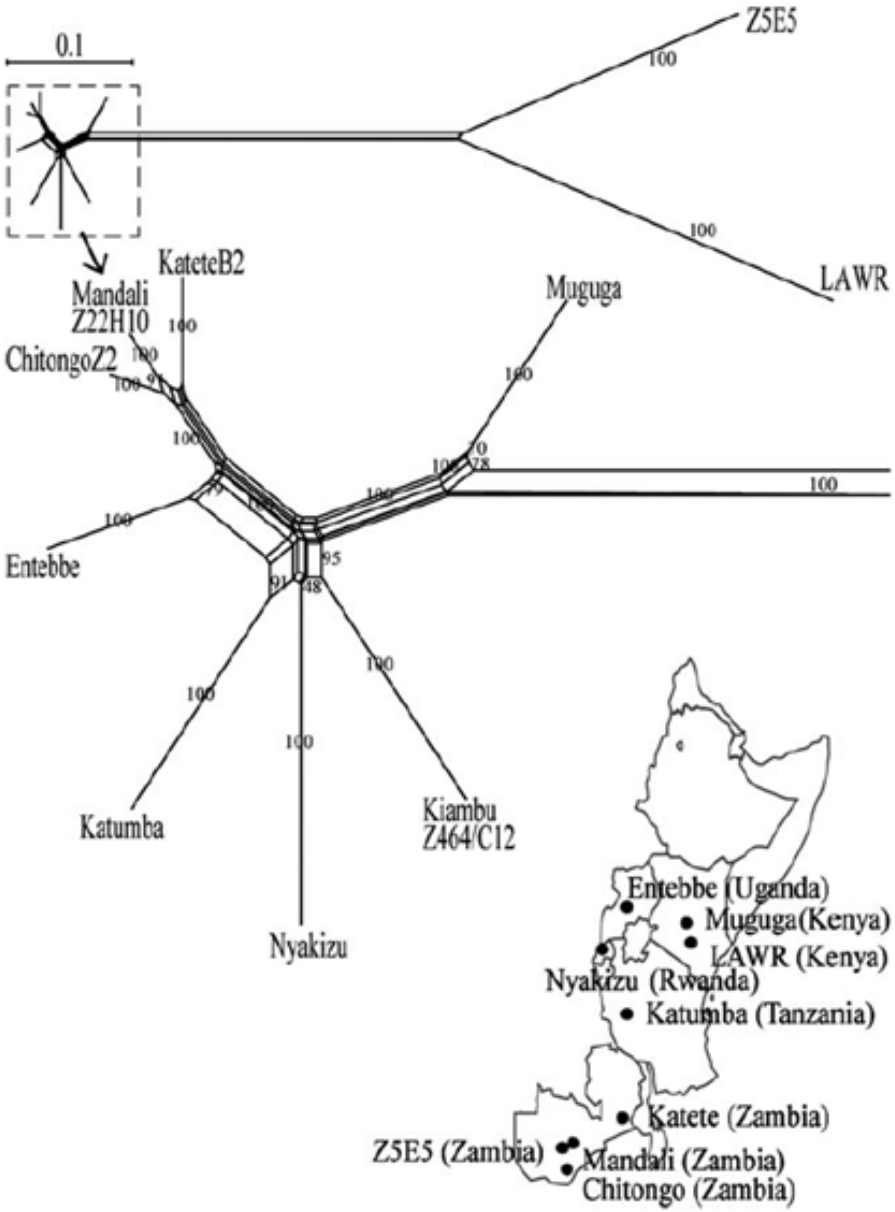
Transmission biology, epidemiology, serological cross-reactivity and molecular data

Panel consensus Lilongwe (Malawi) (1989): *Theileria parva*
Buffalo-adapted/derived *T. parva* → Corridor disease
Cattle-adapted/derived *T. parva* → East Coast fever; Zimbabwe theileriosis

Allsopp (1993): 18S ribosomal RNA – 100% sequence identity – support a single species

Hayashida et al. (2013): Whole genome comparison
All *T. parva* genomes show 98-99% identity compared to reference
Muguga genome – definitely single species

Anon (1989). *Nomenclature in Theileria*. In: Theileriosis in Eastern, Central and Southern Africa. Proceedings of a Workshop on East Coast Fever Immunization Held in Lilongwe, Malawi, 20-22 September, 1 988. Editor, T.T. Dolan, International Laboratory for Research on Animal Diseases, Nairobi, pp. 182-186.
Lawrence (1979) *Journal of the South African Veterinary Association* **50**, 311-313.
Uilenberg (1978) *Tropical and Geographical Medicine* **30**, 156.
Allsopp et al. (1993) *Parasitology* **107**, 157-165.
Hayashida et al. (2013) *DNA Research* **20**, 209-220.



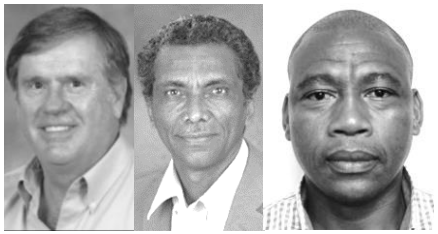
SNP (Muguga)	
Chitongo	46 366
Entebbe	34 814
Katete	43 873
Katumba	46 441
Kiambu	46 435
Mandali	38 498
Nyakizu	51 790
LAWR	121 545
Z5E5	103 880

Buffalo derived *T. parva* show higher genetic diversity than cattle-derived *T. parva*
Cattle-derived: smaller genetic pool – bottleneck effect

Hayashida et al. (2013) *DNA Research* **20**, 209-220.

Theileria parva in South Africa

Neitz, Potgieter, Stoltsz: Transformation failed

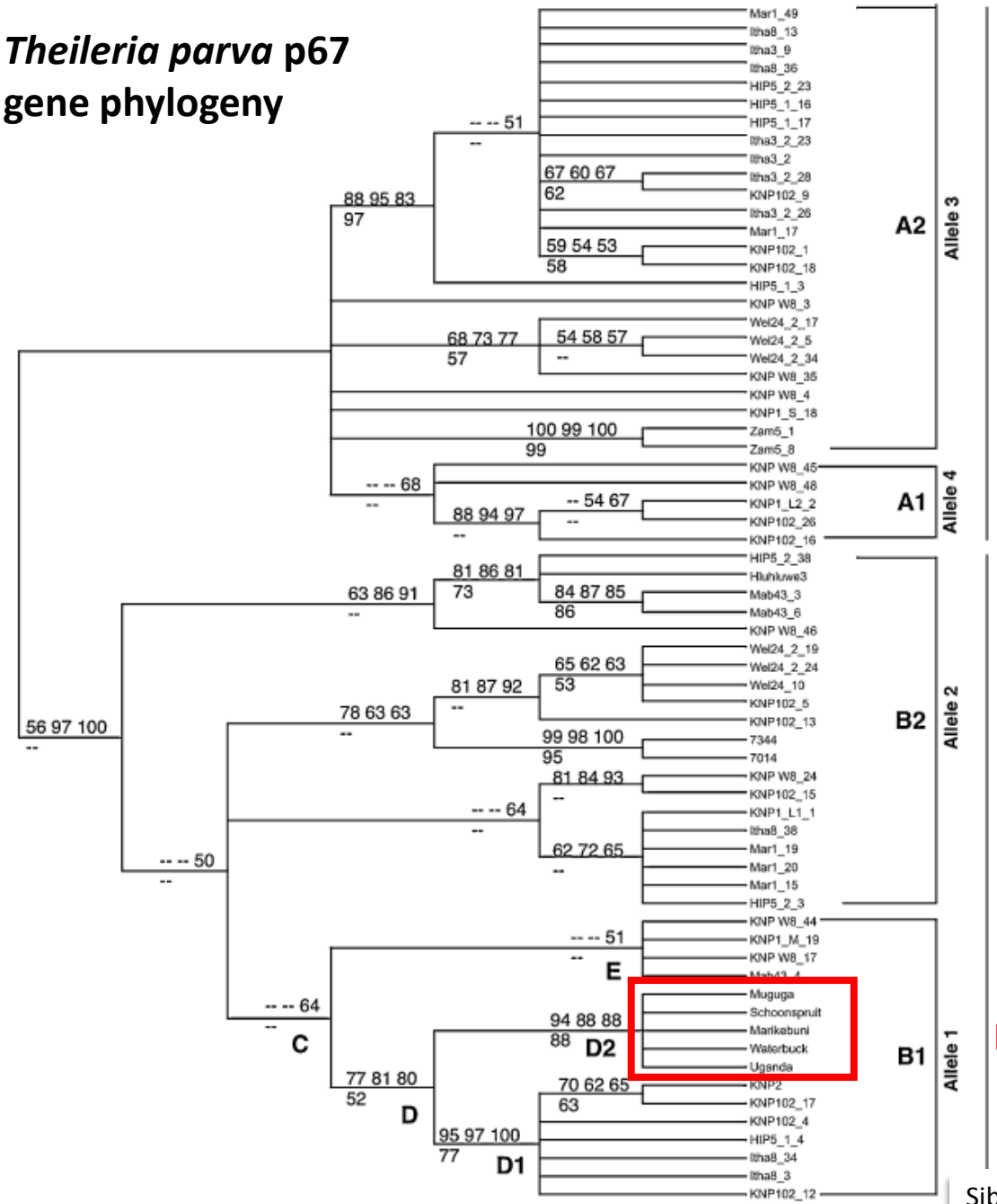


Mbizeni, Latif, Potgieter: Carrier state in cattle not persistent

Sibeko, Collins, Oosthuizen: Large genetic diversity in buffalo-adapted *T. parva* based on p67, PIM and p104 genes

Maboko: Large genetic diversity in buffalo-adapted *T. parva* based on whole genome sequencing and SNP analysis

Theileria parva p67 gene phylogeny

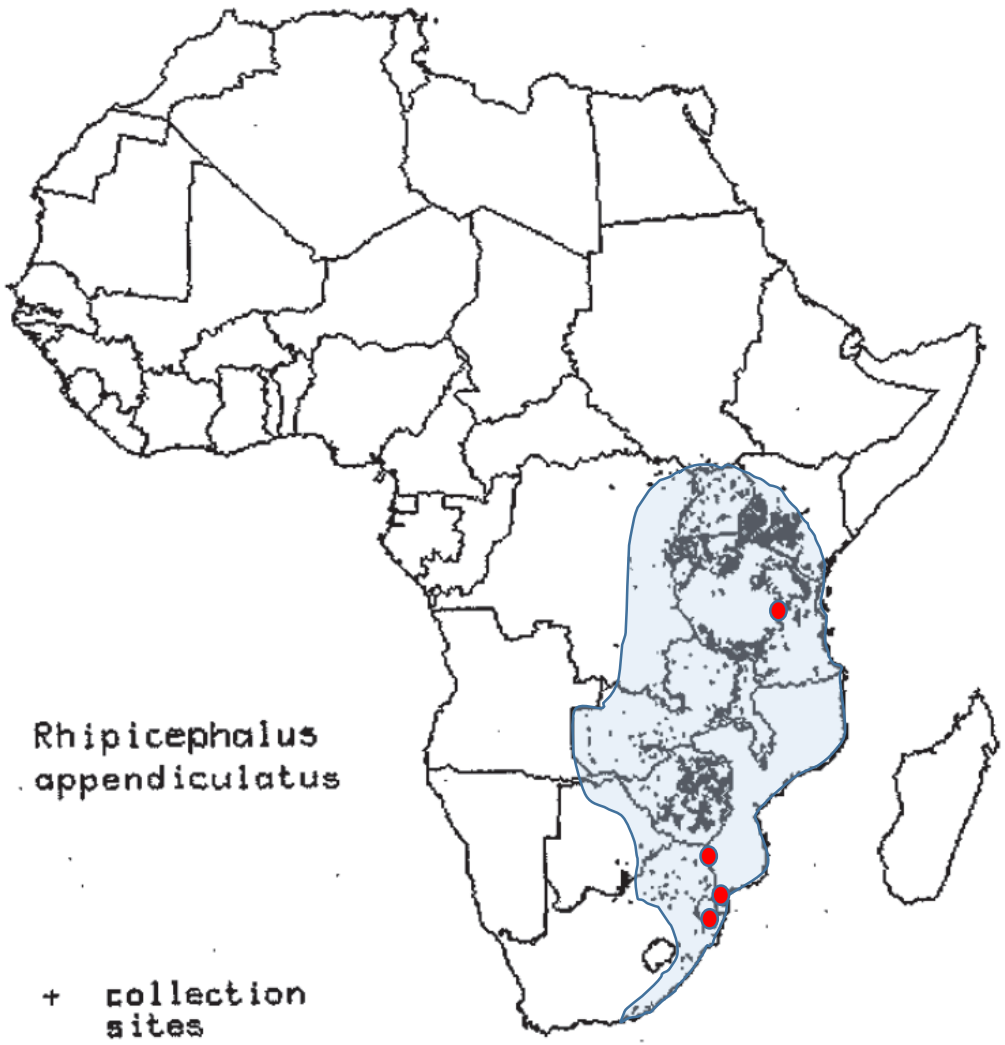


High diversity for buffalo-adapted
Limited diversity for cattle-adapted

ECF strains

Sibeko et al. (2010) *Veterinary Parasitology* **167**, 244–254.

Conclusions



Large genetically diverse *T. parva* population across vector/host range

Bottleneck 1: Single (few?) origin for cattle-adapted *T. parva* – low genetic diversity

Bottleneck 2: Single introduction into South Africa from a genetically limited gene pool

Expect low genetic diversity in buffalo-derived *T. parva* if infected by ECF strains

Data indicate high genetic diversity in buffalo
Ergo: *T. parva* existed in South Africa before the introduction of ECF

ECF was eradicated
Risk of transformation of buffalo-adapted *T. parva* – low
Supports current control measures – no vaccines or prophylactic treatment that may create carrier states and support development of a cattle-adapted state

Perry et al. (1990) *Parasitology Today* **6**, 100-104.

Acknowledgements

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Veterinary History Society of South Africa