



# Overview of emerging and detection of arboviral disease in South Africa.

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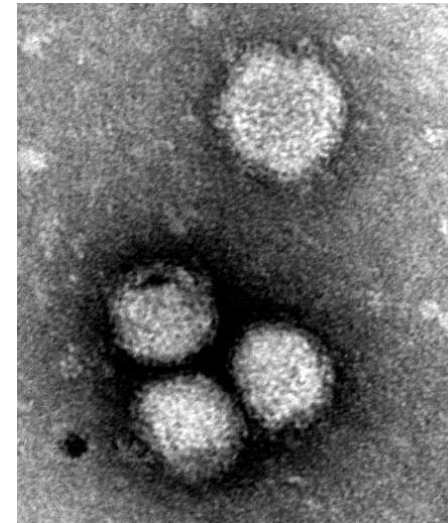
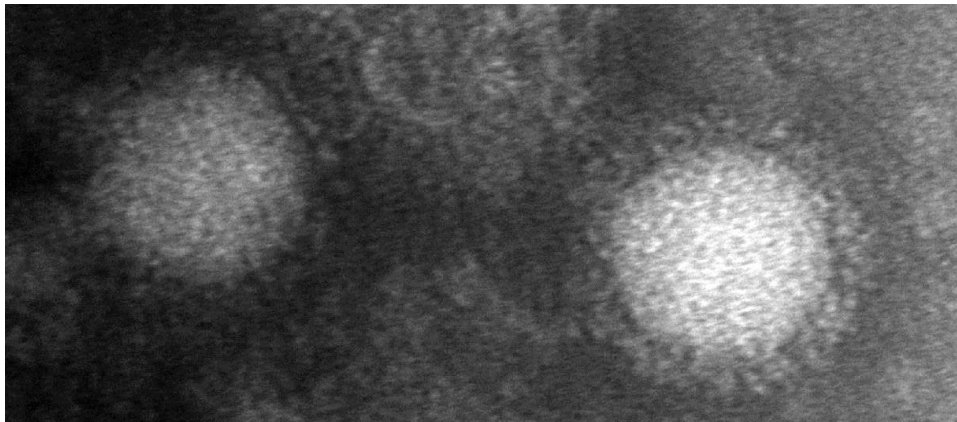
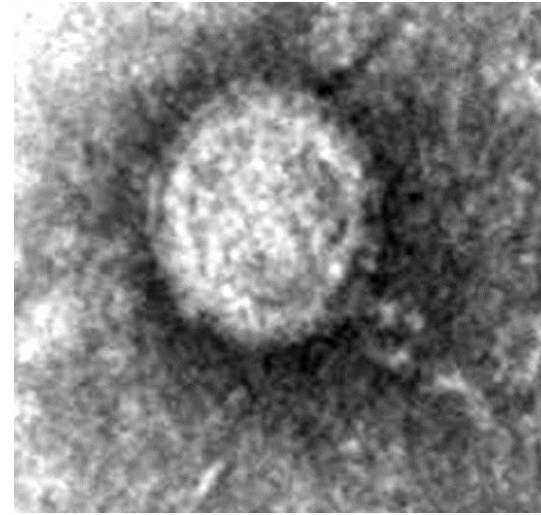
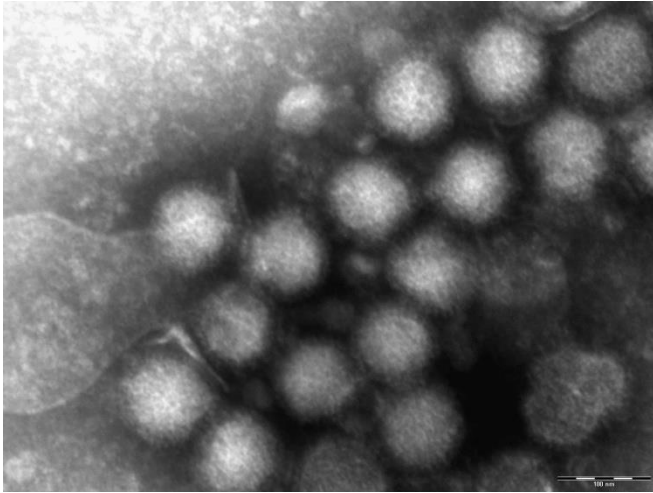
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National Institute for Communicable Diseases/NICD, Republic of South Africa (RSA)

# Arbovirus infections endemic to South Africa

Rift Valley fever (Phlebovirus)

West Nile fever (Flavivirus)



Chikungunya fever (Alphavirus)

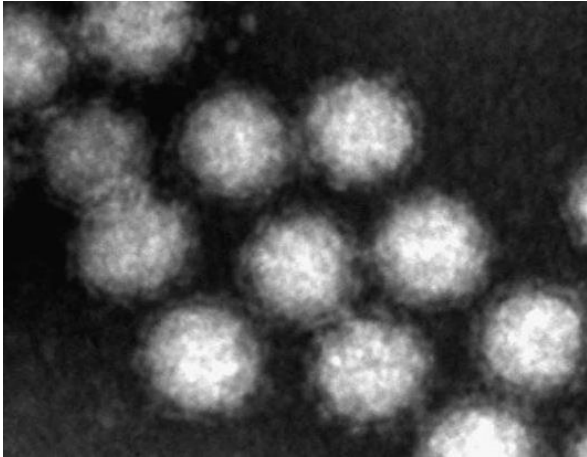
Sindbis fever (Alphavirus)

Wesselbron disease (Flavivirus)

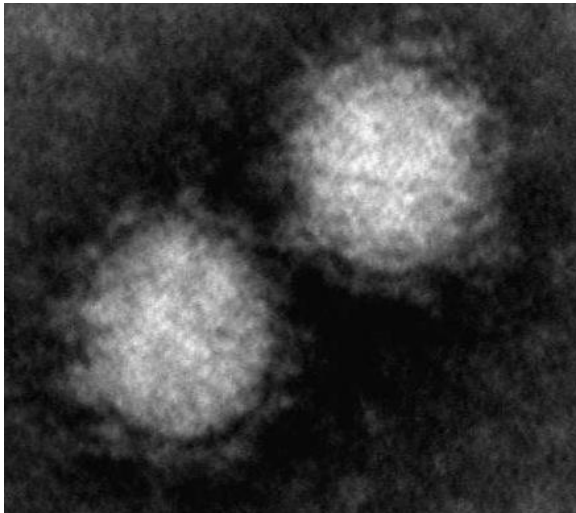
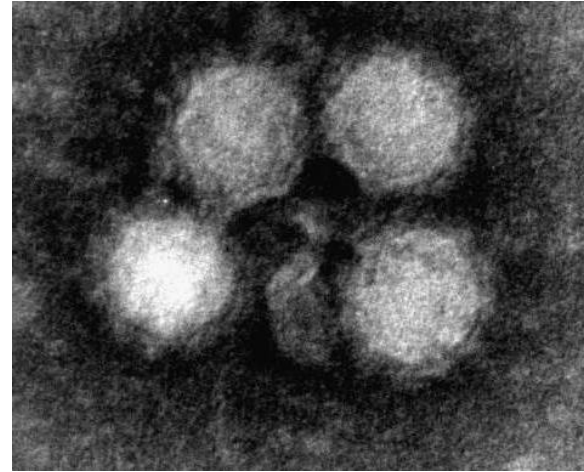
(Courtesy: Dr Monica Birkhead, NICD)

# Imported arboviral infectious diseases to South Africa

Dengue (Flavivirus)



Chikungunya (Alphavirus)



Yellow fever (Flavivirus)



No human yellow fever cases have ever been recorded in South Africa

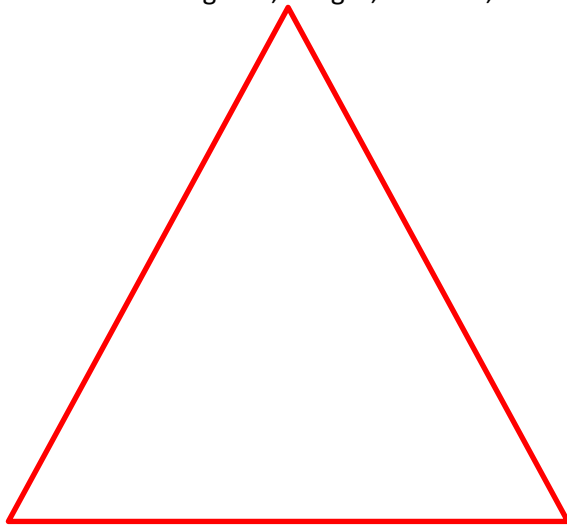
(Courtesy: Dr Monica Birkhead, NICD)

# Diagnosis of arboviral disease

## Integrated approach for diagnosis

- Arbovirus infections are most often mild, febrile illness not unlike enterovirus, influenza and herpes infection
- Encephalitis, Haemorrhagic fever, polyarthrititis

Travel, exposure to arthropods (mosquitoes, ticks, biting flies, midges, tabanids, ...)



Clinical manifestation, pathology testing

Diagnostic testing  
Flavivirus crossreaction

## Case histories: travel and exposure histories, dates



ARBOVIRUS Reference Laboratory: +2711 396 6424/6391 (or +2782 908 8045)  
NICD Hotline for Clinical Advice: +2782 883 9920

SUSPECTED ARBOVIRUS CASE INVESTIGATION FORM									
Filled in by: _____			Contact number: _____						
Date: ____/____/____			Information collected from: _____						
DISEASE(S) UNDER INVESTIGATION (Tick appropriate box)									
<input type="checkbox"/> Sindbis <input type="checkbox"/> Chikungunya <input type="checkbox"/> West Nile <input type="checkbox"/> Dengue <input type="checkbox"/> Rift Valley <input type="checkbox"/> Other arbovirus: _____ <input type="checkbox"/> Other suspected clinical diagnoses: _____									
PATIENT INFORMATION					PATIENT COURSE				
Name: _____					Patient hospitalised? <input type="checkbox"/> YES <input type="checkbox"/> NO    DATE: ____/____/____ (if admitted)				
Age: ____ Years    Birth date: ____/____/____					Hospital name: _____ (if admitted)				
Sex: <input type="checkbox"/> M <input type="checkbox"/> F <input type="checkbox"/>					Severity of illness? <input type="checkbox"/> Mild <input type="checkbox"/> Moderate <input type="checkbox"/> Acute/Severe				
Address: _____					Treatment(s) given? _____ (if discharged)				
Referring physician: _____					Fx responsive to treatment? <input type="checkbox"/> Not <input type="checkbox"/> Less <input type="checkbox"/> Well				
Number for physician: _____					Consultation date: ____/____/____				
CLINICAL FEATURES    Date of onset: ____/____/____    And/or    Duration illness: ____ days									
Main Syndrome: (Tick appropriate box)									
<input type="checkbox"/> Fever without rash <input type="checkbox"/> Fever with rash <input type="checkbox"/> Arthritis and Rash <input type="checkbox"/> Encephalitis/meningitis <input type="checkbox"/> Haemorrhagic fever <input type="checkbox"/> Retinitis/conjunctivitis <input type="checkbox"/> Other remarkable symptoms: _____									
If present, Describe:    Fever: _____ °C    Rash (Site): <input type="checkbox"/> face <input type="checkbox"/> arm <input type="checkbox"/> palm <input type="checkbox"/> trunk <input type="checkbox"/> legs <input type="checkbox"/> soles    Rash (Appearance): <input type="checkbox"/> macular <input type="checkbox"/> papular <input type="checkbox"/> petechial <input type="checkbox"/> urticarial <input type="checkbox"/> pruritic <input type="checkbox"/> other    Encephalitis: <input type="checkbox"/> headache <input type="checkbox"/> neck stiffness <input type="checkbox"/> vomiting <input type="checkbox"/> confusion <input type="checkbox"/> seizures <input type="checkbox"/> unconscious <input type="checkbox"/> coma    Haemorrhage: <input type="checkbox"/> epistaxis <input type="checkbox"/> haematemesis <input type="checkbox"/> melaena <input type="checkbox"/> menorrhagia <input type="checkbox"/> petechiae <input type="checkbox"/> purpura <input type="checkbox"/> from venepuncture    Ocular disease: <input type="checkbox"/> pain <input type="checkbox"/> inflammation <input type="checkbox"/> blurred vision <input type="checkbox"/> photophobia <input type="checkbox"/> ↓ visual acuity									
PATHOLOGICAL FINDINGS (Tick appropriate box (yes, no; UNK: unknown); Attach test results)									
Malaria negative: <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    Leucopenia: <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    Additional findings: _____									
Thrombocytopenia: <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    Lowest WBC count: _____ 10 <sup>9</sup> /L    Lowest platelet count: _____ 10 <sup>9</sup> /L    Elevated liver function: <input type="checkbox"/> YES <input type="checkbox"/> NO									
Latest platelet count: _____ 10 <sup>9</sup> /L    Highest ALT: _____ U/L    Haematocrit: _____ %    Highest AST: _____ U/L									
PATIENT EXPOSURE HISTORY    YES    NO    UNK    When?    Where?									
Been diagnosed with dengue before? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    ____/____/____ (month/year)									
Been diagnosed with Rift Valley Fever before? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    ____/____/____ (month/year)									
Got Rift Valley Fever vaccination? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    ____ (year)									
Got Yellow Fever vaccination? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    ____ (year)									
Fx occupation? _____ Since: ____/____/____ (year)									
During the past month, did patient travel? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    From: ____/____/____    Until: ____/____/____ <input type="checkbox"/> Outdoors <input type="checkbox"/> Another province <input type="checkbox"/> Another country <input type="checkbox"/> Name of place: _____									
Fx had recent bites/unusual animal contact? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> UNK    ____/____/____ (month/year)									
<input type="checkbox"/> Mosquito bites <input type="checkbox"/> Animal bite <input type="checkbox"/> Animal blood/tissue <input type="checkbox"/> Drank unpasteurized milk <input type="checkbox"/> Tick bites <input type="checkbox"/> Animal saliva <input type="checkbox"/> Animal faeces/urine <input type="checkbox"/> Consumed uncooked meat <input type="checkbox"/> Other exposures: _____									

POST COMPLETED FORM WITH SPECIMEN TO:  
Arbovirus Reference Lab, National Institute for Communicable Diseases, National Health Laboratory Service, 1 Modderfontein Road, Sandringham 2152, South Africa

FAX OR EMAIL COMPLETED FORM TO:  
0863964423 or cezd@nicd.ac.za

# Laboratory Investigations

Routine blood screens / scans not very informative

Specialized laboratory testing only provided in selected reference laboratories

## Specimens

- Blood, serum for acute and sero-converted cases
- CSF for acute neurological cases
- Liver, CSF, brain for post mortem cases

## Arbovirus case

### Confirmed

- Case found positive for acute infection by polymerase chain reaction (PCR)
- Fourfold IgG titre increase of long-lived antibodies (IgG) between convalescent specimens (10-14 d apart) by Enzyme-linked immunosorbant assay (ELISA)

### Highly suggestive

- Case found positive for short-lived antibodies (IgM) (90% recent infection)

### Persistence of arbovirus virus-specific IgM responses

- Flaviviruses: variable up to 3 years
- Alphaviruses: variable up to 2.5 years
- Rift Valley virus (Bunyavirus): 4-6 weeks

# Laboratory Investigations

Routine blood screens / scans not very informative  
Specialized laboratory testing only provided in selected reference laboratories

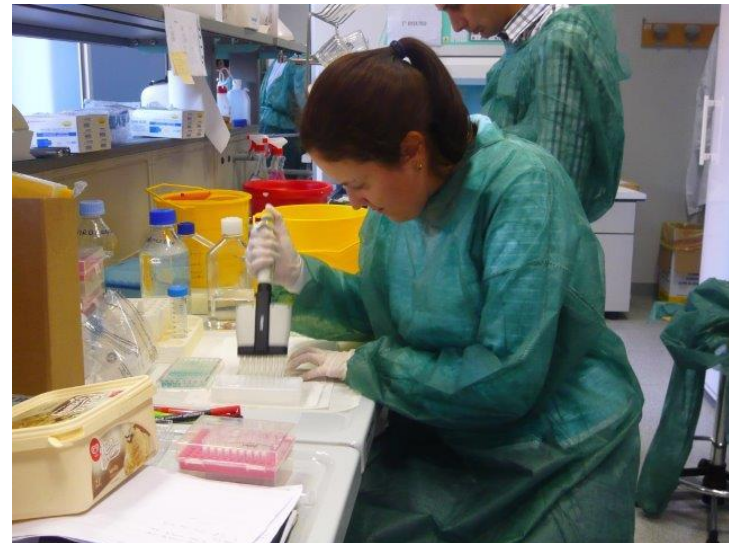
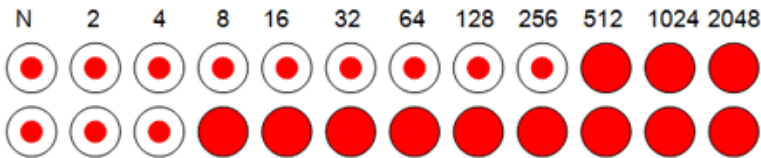
## HAI Haemagglutination Inhibition assay

## Chantel le Roux performing ELISA (24-48h)

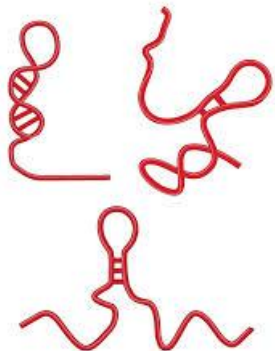


Haemagglutination +ve

Haemagglutination -ve



## PCR Polymerase chain reaction



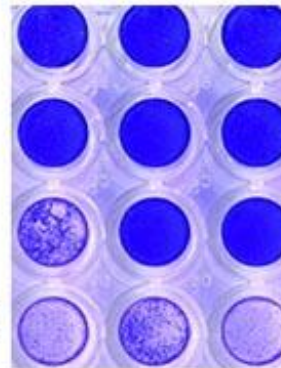
## Virus isolation

1:2

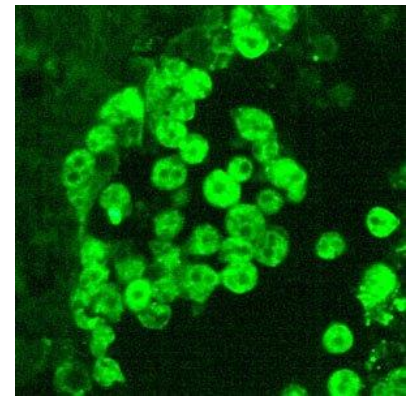
1:4

1:8

1:16



Virus Neutralizing Antibody Assays



Indirect immunofluorescence tests

# Proliferation of mosquitoes near water

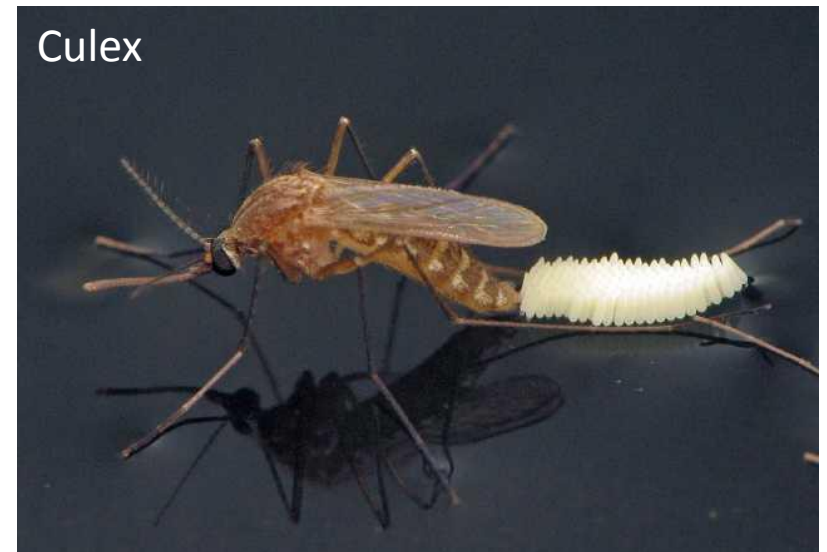
Rift Valley fever virus mosquitoes



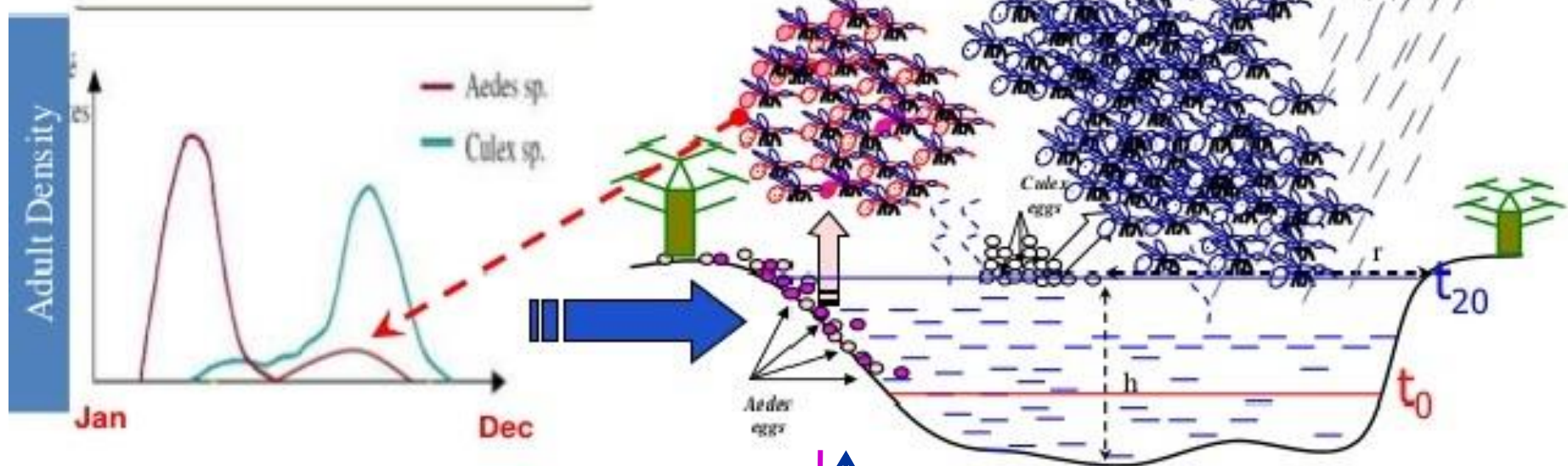
Flood water - *Aedes*



*Culex*



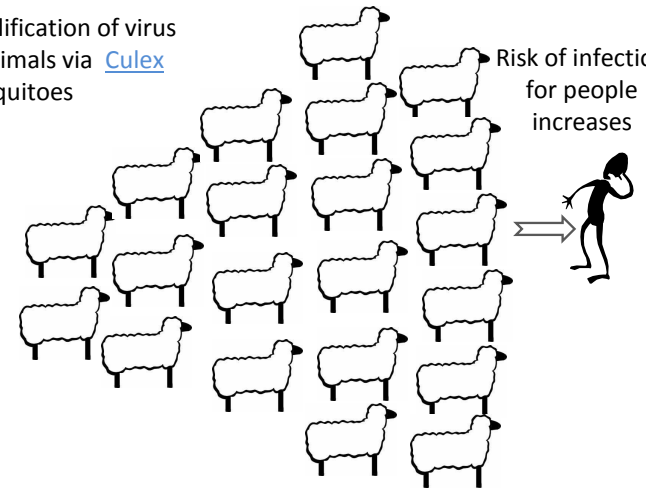
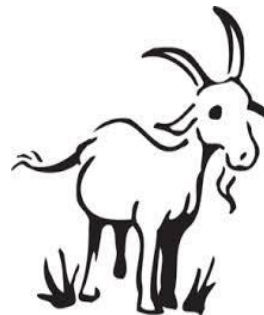
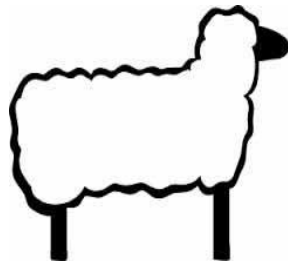
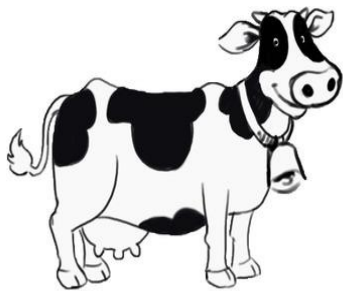
(Aedes- Culex complex) responsible for maintenance and amplification of the virus



Infection of animals via feeding mosquitoes

Amplification of virus in animals via Culex mosquitoes

Risk of infection for people increases

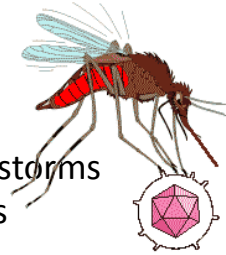




# Rift Valley Fever Virus at risk populations and clinical manifestation

## Animals

Sudden onset of abortion storms  
Mortality in young animals  
Haemorrhages



## Humans

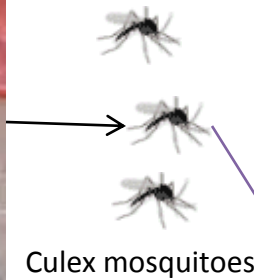


Fever, often accompanied by headaches, muscle pains and nausea  
Light sensitivity, watery eyes, early signs of retinal detachment,  
which could lead to partial blindness  
Haemorrhagic fever, encephalitis and necrotic hepatitis

# Endemic West Nile, Sindbis and chikungunya

West Nile  
Sindbis

Widespread in South Africa



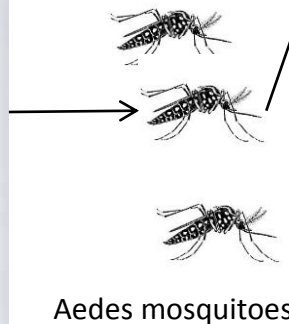
Horse ill  
with West Nile virus



severe arthritis

chikungunya

North-Eastern South Africa



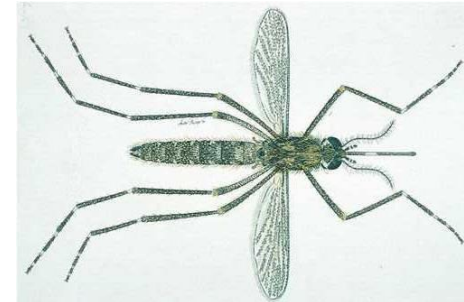
rash

# Sylvatic environment and vectors of Dengue and chikungunya virus

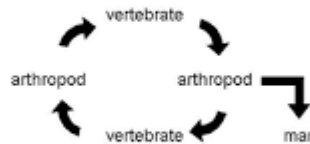
Tree hole breeding spot



*Aedes furcifer*



SYLVATIC (JUNGLE) CYCLE



Tropical forest



Senegal-green monkeys



# Urban environment and vectors of Dengue and chikungunya virus

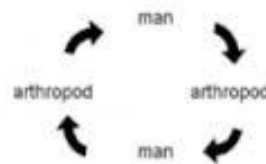
**Aedes (stegomyia) Aegypti**



**Aedes (stegomyia) Albopictus**



URBAN CYCLE



**Monsoon season**

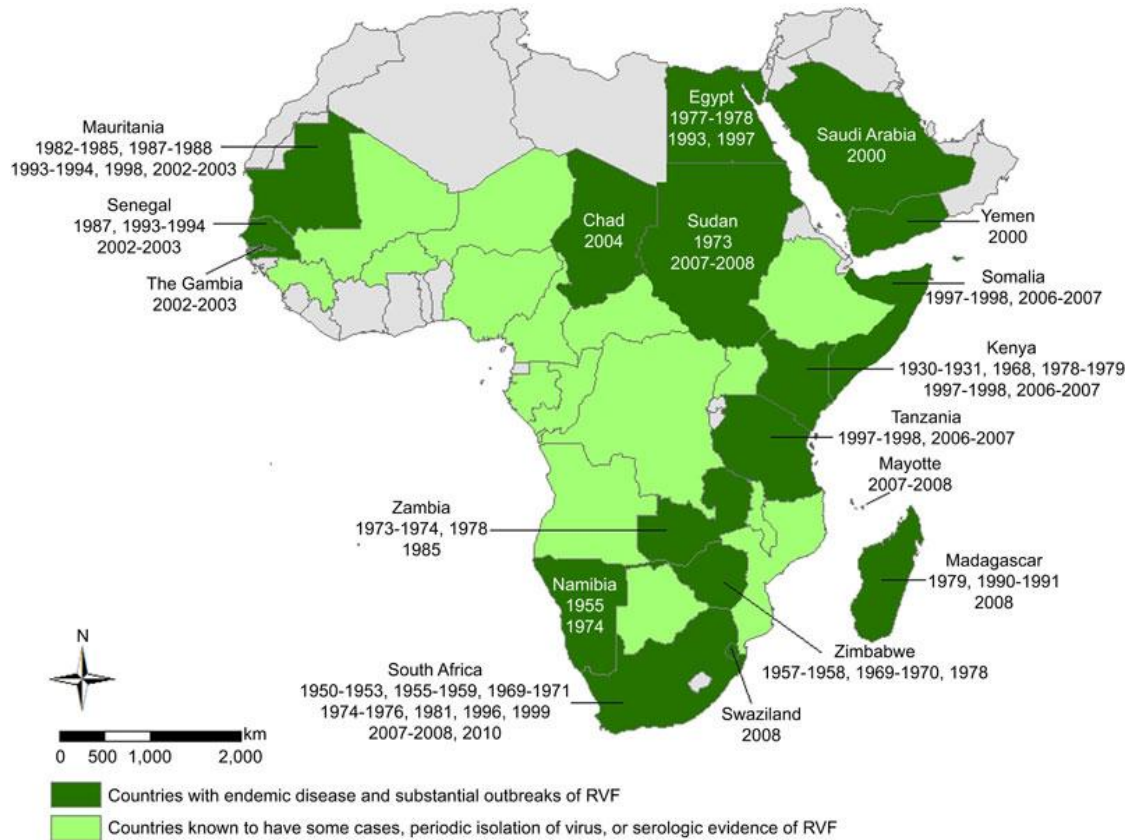


**Tyres breeding spot**

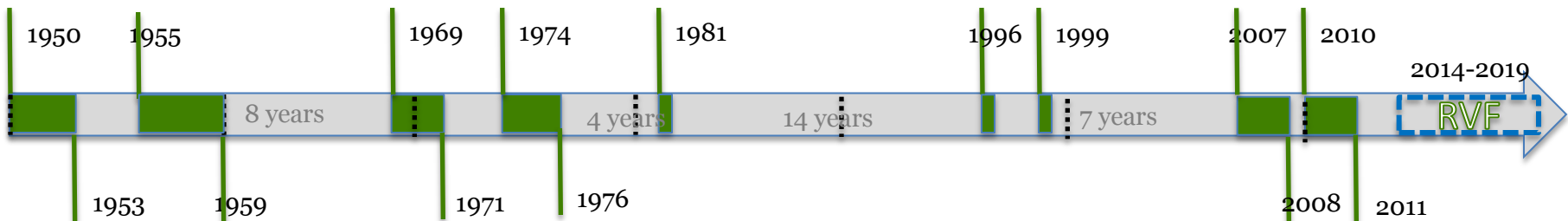


# Rift Valley Fever Virus

Alicia I Rolin et Al. , <http://www.nature.com/emi/journal/v2/n12/pdf/emi201381a.pdf>



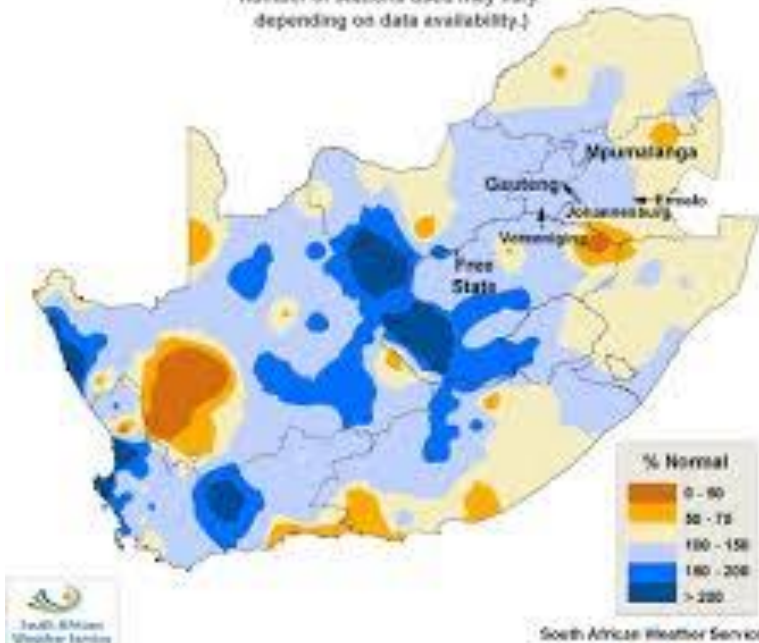
Occurs in periodic outbreaks with long intervals of 7-15 years



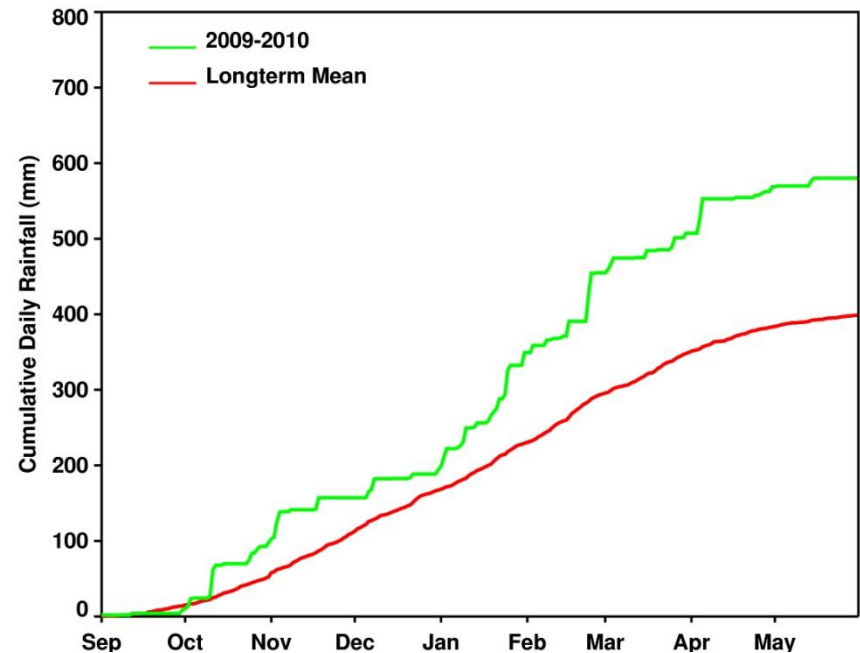
# RVF Outbreaks followed period of above normal rainfall

Percentage of Normal for the Hydrological Season  
October 2009 to January 2010

(Based on preliminary data. The number of stations used may vary depending on data availability.)



Bloemfontein (South Africa): 25.76°E, 29.12°S



Source: NOAA/CPC-RFE

Large pan in the Northern Cape

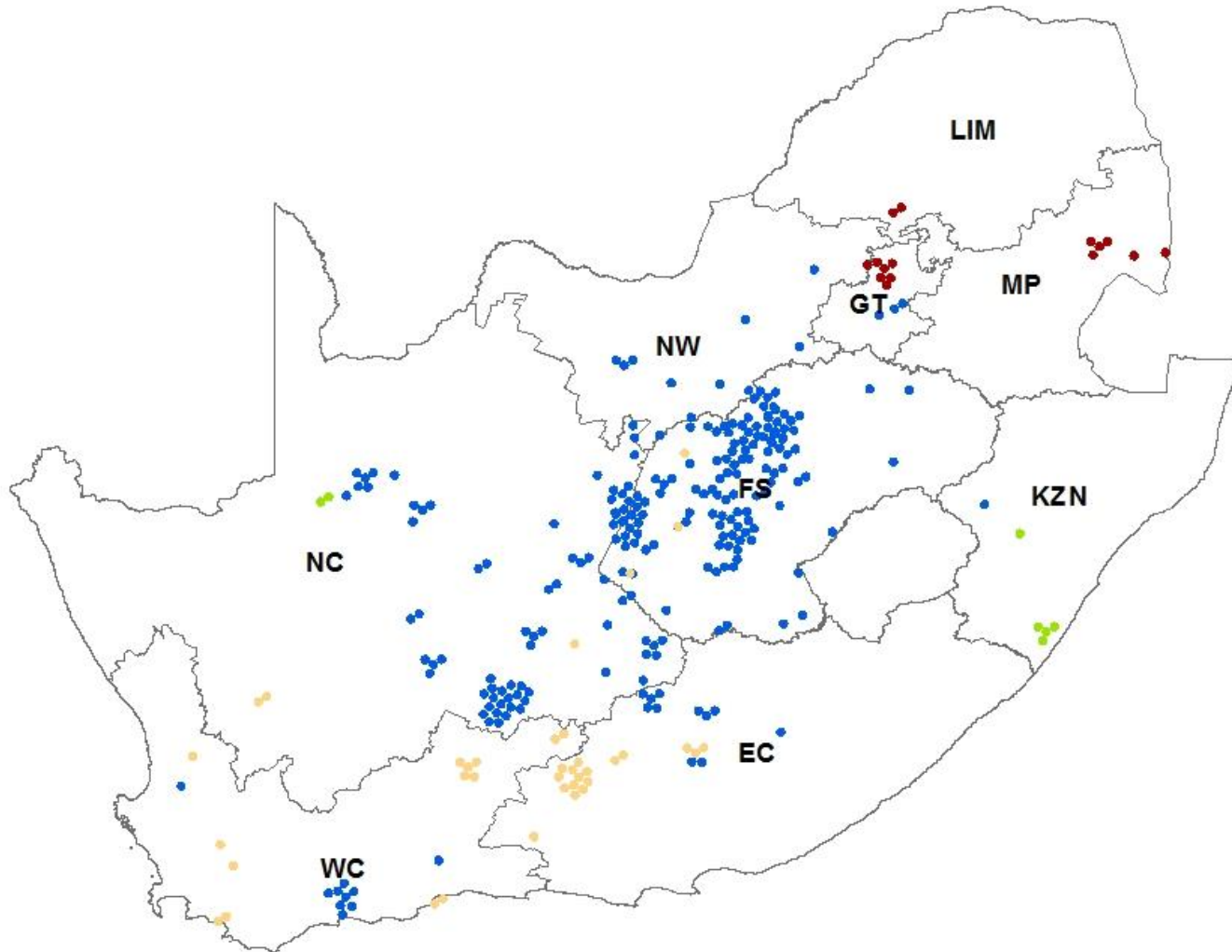


EASTERN FREE STATE: SMALL PANS FLOODED, LARGE PANS PARTIALLY FLOODED

APRIL 2010



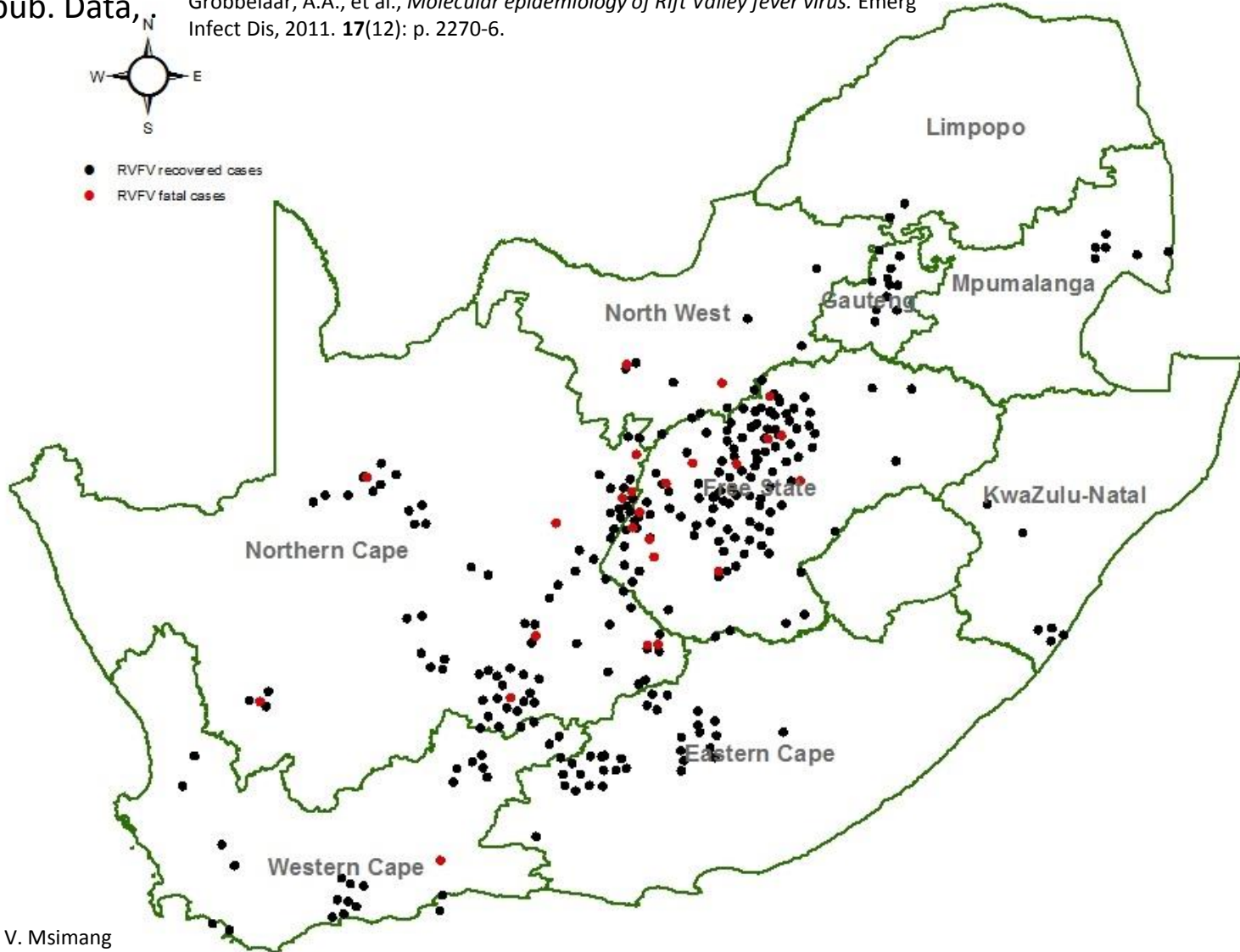
# RVF epidemic 2010-2011: human cases





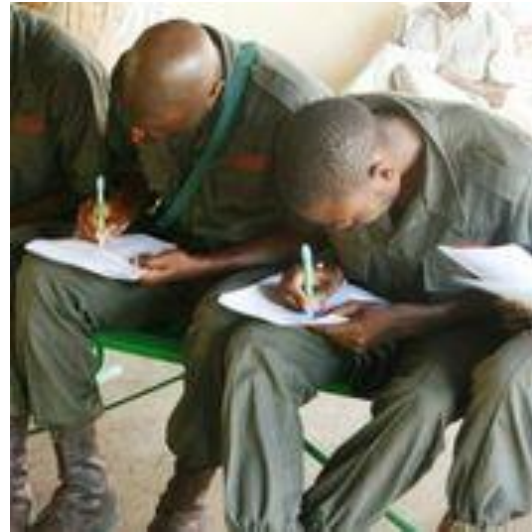
# RVF epidemic 2010-2011

In 2010 all deaths were among 244 persons infected with lineage H virus, while no deaths were recorded in areas where lineage C virus was active, only 22 cases were diagnosed (NICD, unpub. Data, Grobbelaar, A.A., et al., *Molecular epidemiology of Rift Valley fever virus*. Emerg Infect Dis, 2011. 17(12): p. 2270-6.



# Kruger National park survey of Arboviral exposure

## 1. Information sessions



## 2. Data collection



## 3. Blood sampling



# Arbovirus results considerations

TOTAL N=200	Past exposure Long-term antibodies	Recent exposure Short-term antibodies	Symptoms	RICK	Q F
SINDBIS VIRUS	8	5	Fever headache tiredness	X	Y
			Sore eyes	X	X
			Unknown	Y	-
			Tick bite fever malaria	Y	X
			Rash	Y	Y
CHIKUNGUNYA VIRUS	1	0			
WEST NILE VIRUS	11	2**	Fever sore joints, sore eyes neck stiffness blurred vision	X	X
			Unknown	X	Y
RIFT VALLEY FEVER	1	0			
<b>TOTAL</b>	<b>21</b>	<b>7</b>			

\* High titre  $\geq$  1:320

- **Males between 27-62 years old**
- **2 southern, 5 central region**
- **5 general workers, 1 rangers, 1 scientist**

- **Serological cross reaction**
- **Persistence of virus-specific IgM responses:**  
 Alphas: variable up to 2.5 years  
 Flaviv: variable up to 3 years  
 RVF (Bunyavirus): 4-6 weeks

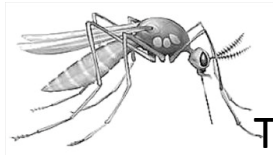
# Rift Valley Fever Virus IEP Project

People

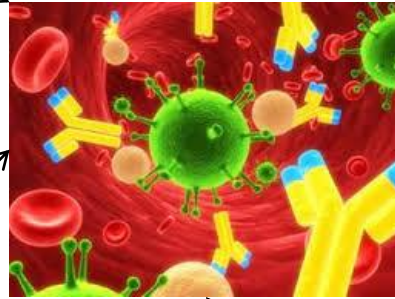
Climate



Mosquitoes



Testing for RVF virus  
and antibodies



Wild antelope  
Game farms  
Free-ranging



Domestic ruminants



# Rift Valley Fever Virus IEP Project

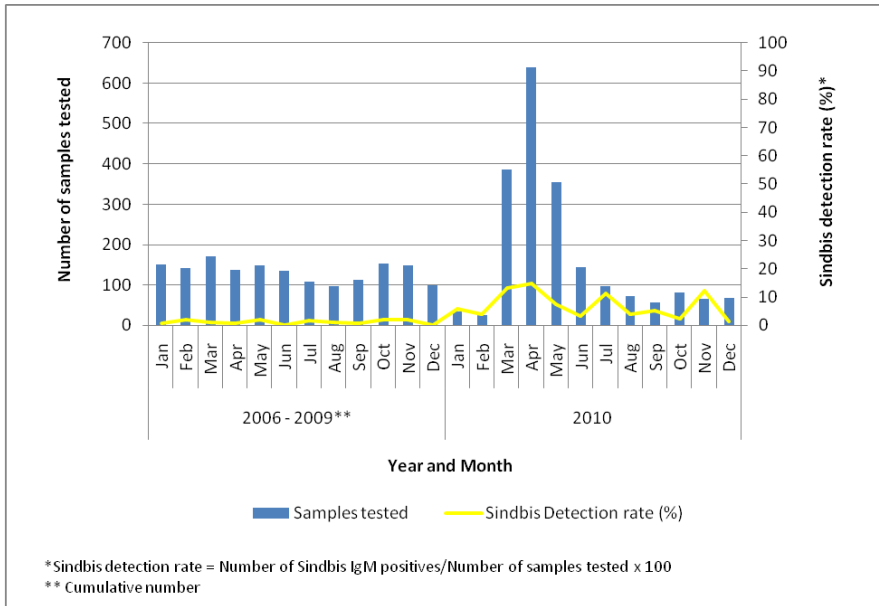
Pilot farmers surveillance 10-17 May 2015



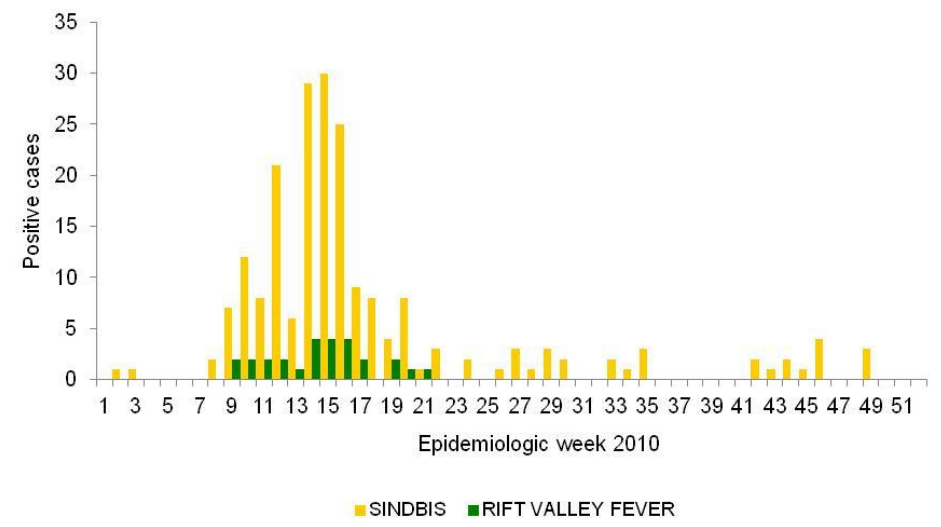
# Arboviral infectious outbreaks in South Africa

	Year/s	Area	Animal cases*	Human cases
RVF	1950-51, 1952-53, 1955-59	Western FS, sthn Gauteng, NW, Limpopo; Zimbabwe; Namibia	600 000+	numerous
	1968-69	Southeastern Zimbabwe; KZN coastal plain, Mozambique	widespread, large numbers	unknown
	1969-71**, 1973-76, 1978**	RSA; Namibia; Zimbabwe; Zambia	140 000+**; widespread, catastrophic	Numerous, some deaths
	1981	Mtubatuba	Localised, many cattle	unknown
	1990-91, 1999	Madagascar; KNP	Extensive; localised***	Some, 1 death; suspected***
CHIK	1962; 1956, 1964	Southeastern Zimbabwe; Phalaborwa, Ndumo	Widespread, large nos.;	38+; some
			localised, small nos.	
	1975-76	Mica/Phalaborwa region	Localised, 76+	57+
SIN/WN	1962-63	Sthn Gauteng, nthn Free State	widespread	14/2+5?
WN/SIN	1974	Karoo	widespread	18 000+/4000+****
SIN	1983-84	Witwatersrand/Pretoria/Bela Bela	widespread	100s
DEN	1926/1927	Coastal KZN (Stanger to Durban)	unknown	40 000+

# Sindbis and West Nile virus prevalence

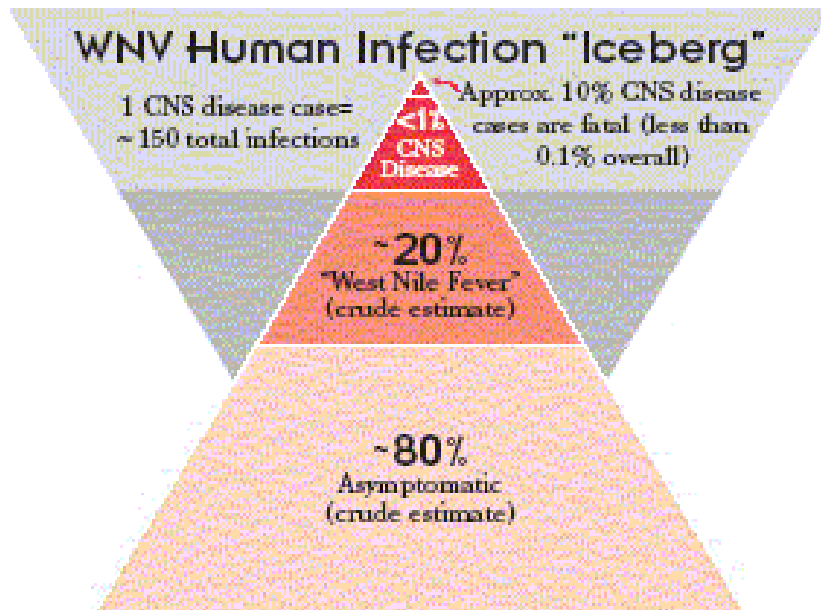


\*Sindbis detection rate = Number of Sindbis IgM positives/Number of samples tested x 100  
 \*\* Cumulative number



# Severe West Nile CNS case

## West Nile clinical manifestation



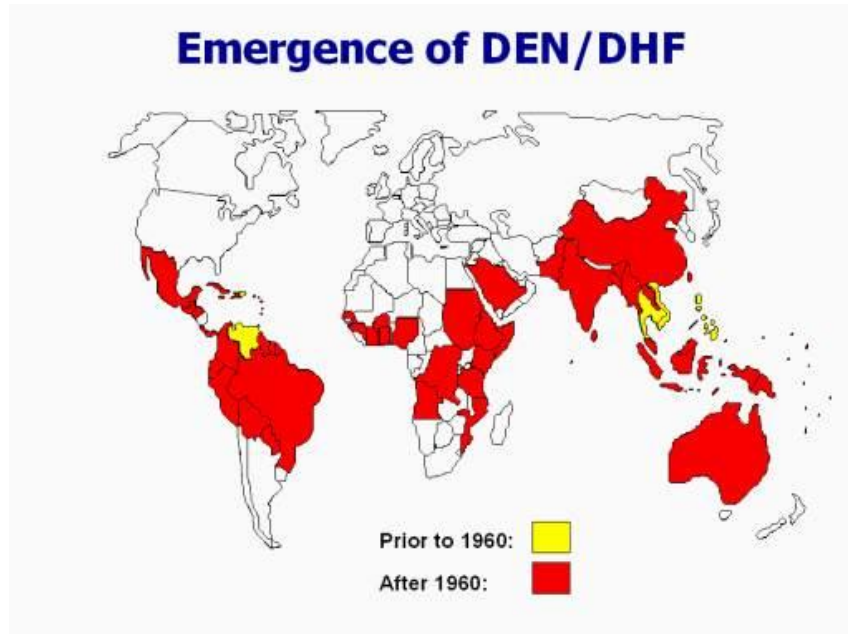
## Fatal case 2014

- A 38-year-old man from Nelspuit, Mpumalanga presented late July 2014 with fever and neurological disturbances.
- Rabies was considered as a potential diagnosis for this patient given the exposure history and his encephalitic presentation.
- Ultimately a history of travel to Escourt, KwaZulu Natal came to light were the patient had contact with horses.
- Based on the history and the clinical presentation of encephalitis, arboviral disease was suggested as a diagnosis.
- Blood specimens collected over the course of the patient's illness were tested for anti-West Nile fever antibodies and
- Seroconversion was indicated in testing of the serial specimens. RT-PCR analysis on the earliest collected blood and
- Cerebrospinal fluid specimens were however negative for West Nile.
- The patient progressively deteriorated and required intubation and ventilation. The patient died about three weeks after onset of illness.

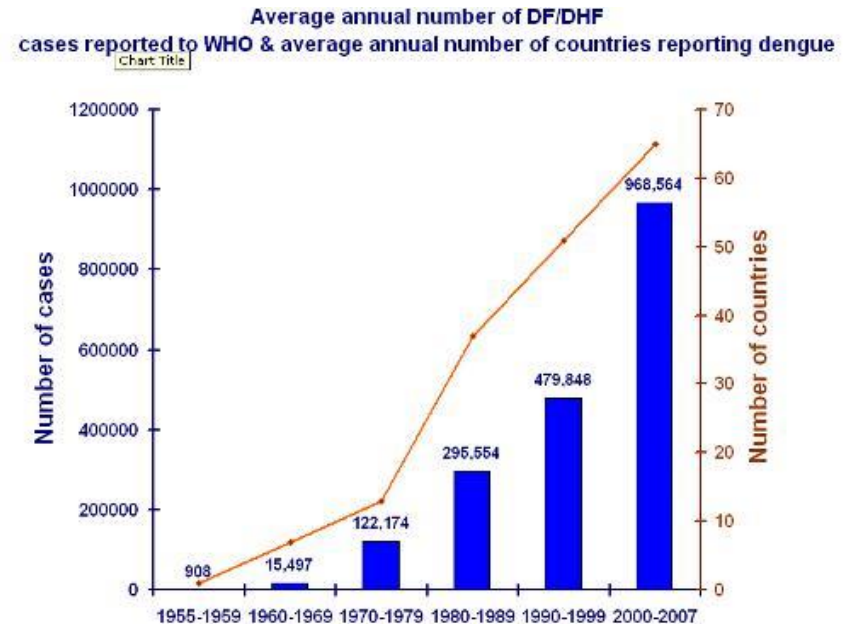


# Dengue is on the rise globally

## Expansion



## Increase

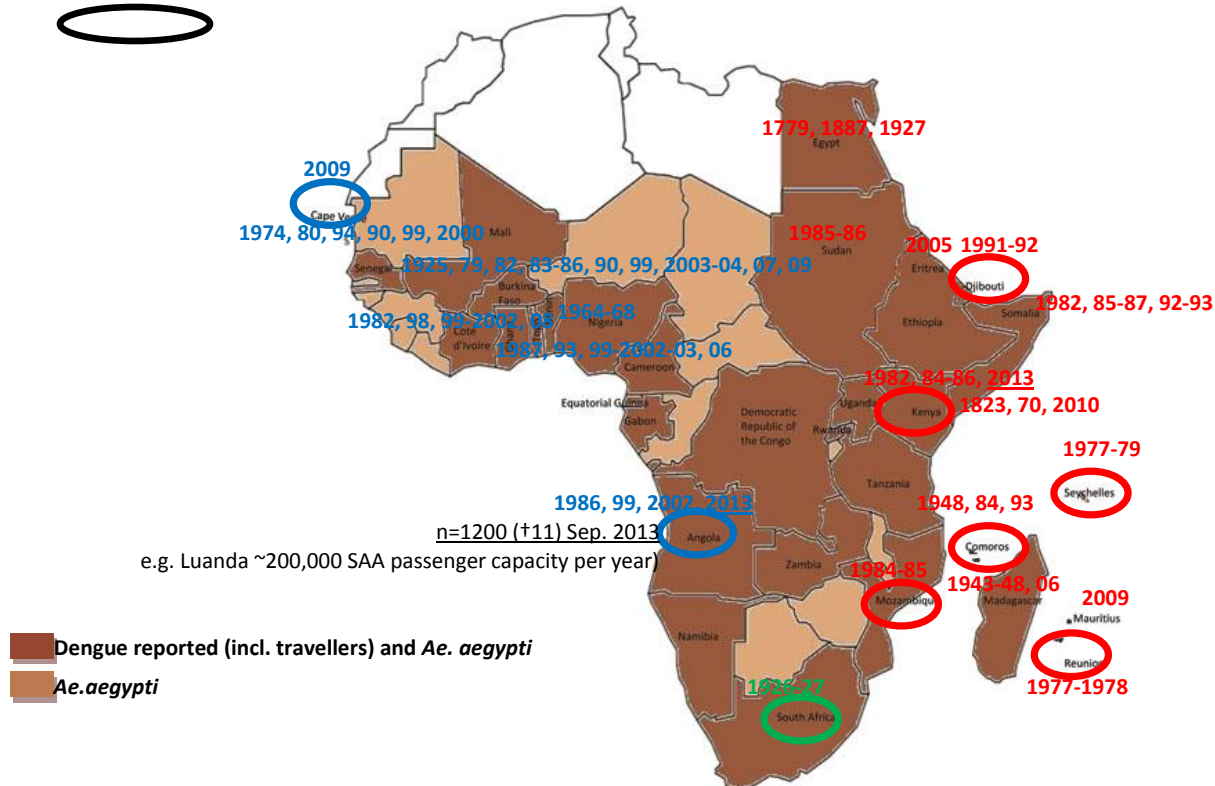


Source: WHO. [Emergencies preparedness, response Pandemic and Epidemic Diseases Dengue/dengue haemorrhagic fever](#)

# South Africa is connected to the world.....

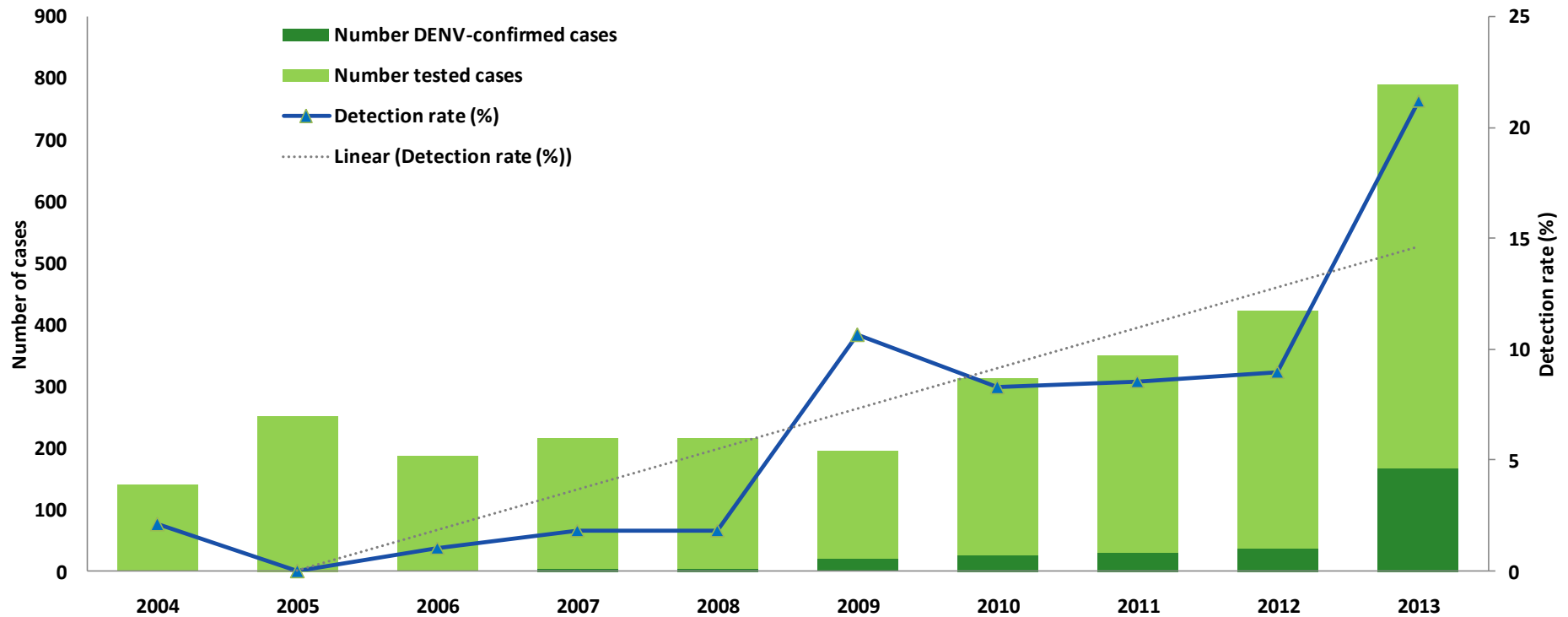
- DENV-endemic countries interconnectivity with South Africa
- Important airport in Africa
- Recent research estimates the burden of dengue infection in Africa to be similar to that of the America's  
Bhatt S, Gething P, Brady O et al. The global distribution and burden of dengue, Nature; 2013; 25 April; 496(7446):504-507

Epidemics in Africa



# Testing and confirmation of imported dengue cases in South Africa increases

Fig. 1 Increasing trend of testing for Dengue and confirmation of DENV-cases by CEZD-NICD arbovirus laboratory



## DENV-cases in returned to non-endemic SA travellers per DENV-endemic country of travel

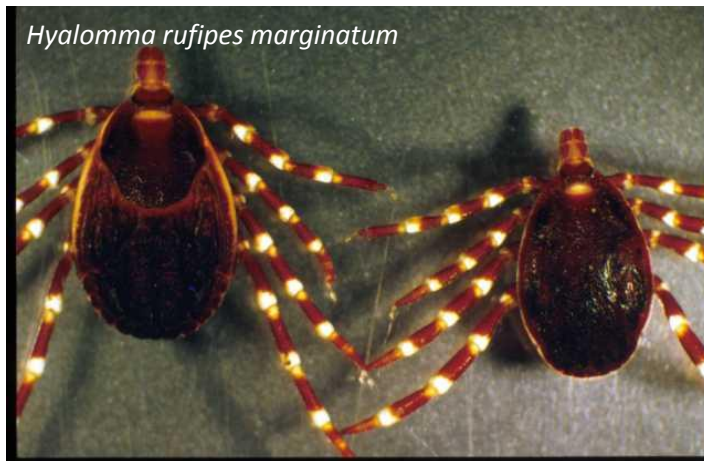
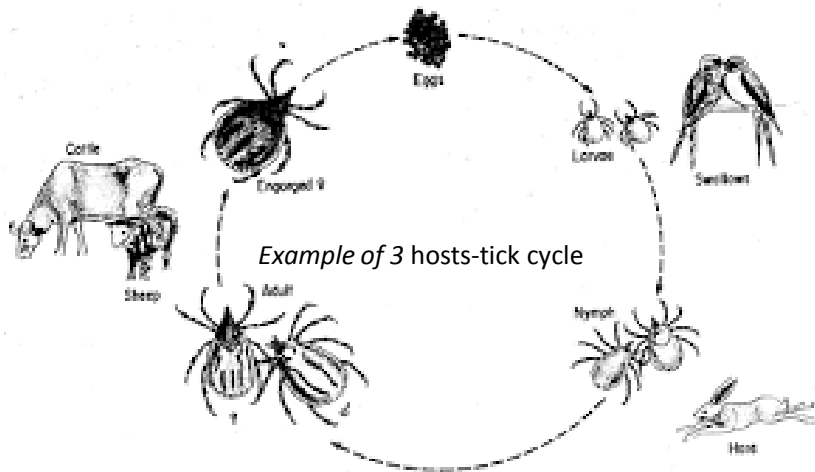
Country		2014	2013	2012			
<b>Total</b>	↑	<b>28</b>	<b>34</b>	<b>19</b>	<b>3.1</b>	<b>3.8</b>	<b>2.1</b>
<b>Returning travellers from Asia</b>							
Thailand		6	5	3			
India		1	1	7			
Philippines		-	-	2			
Malaysia		-	1	-			
Indonesia		2	-	-			
Vietnam		-	1	-			
Singapore		1	-	-			
South-East Asia		1	-	-			
<b>Returning travellers from West Central Africa</b>							
Cameroon		-	1	-			
Mali		-	1	-			
Burkina Faso (/Ethiopia)		-	1	-			
Angola		4	14*	-			
<b>Returning travellers from East Africa</b>							
Tanzania		4	-	-			
Kenya		1	-	-			
Africa		2	-	-			
<b>Returning travellers from South America</b>							
Brazil		-	3	-			
Bolivia		-	1	-			
Unknown/no travel		6	5	7			

\*Returning travellers from Angola to SA; total estimated cases linked to Angola outbreak confirmed in NICD n=19  
2013: Viraemia confirmed by PCR after return to SA in travellers n=5 (out of 13 tested)

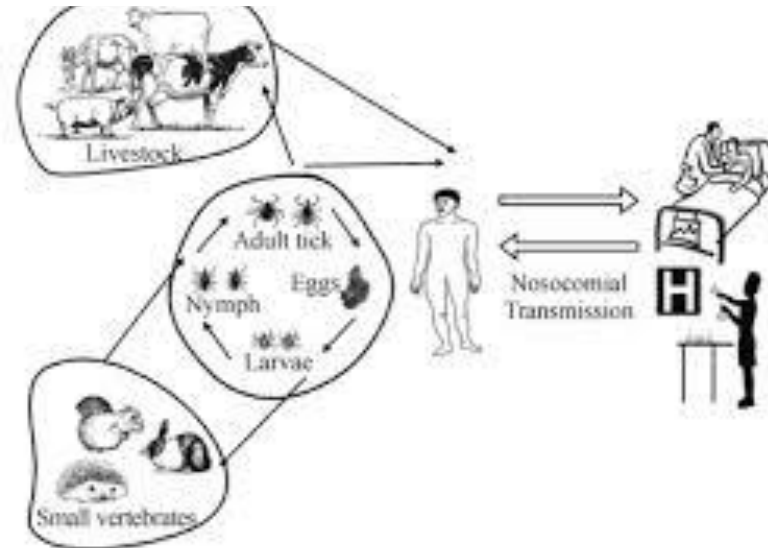
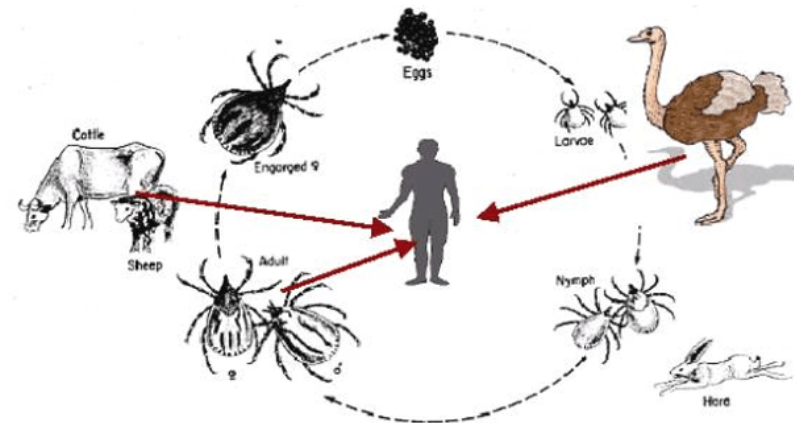
# CCHF virus transmission

## Tick life and enzootic cycle

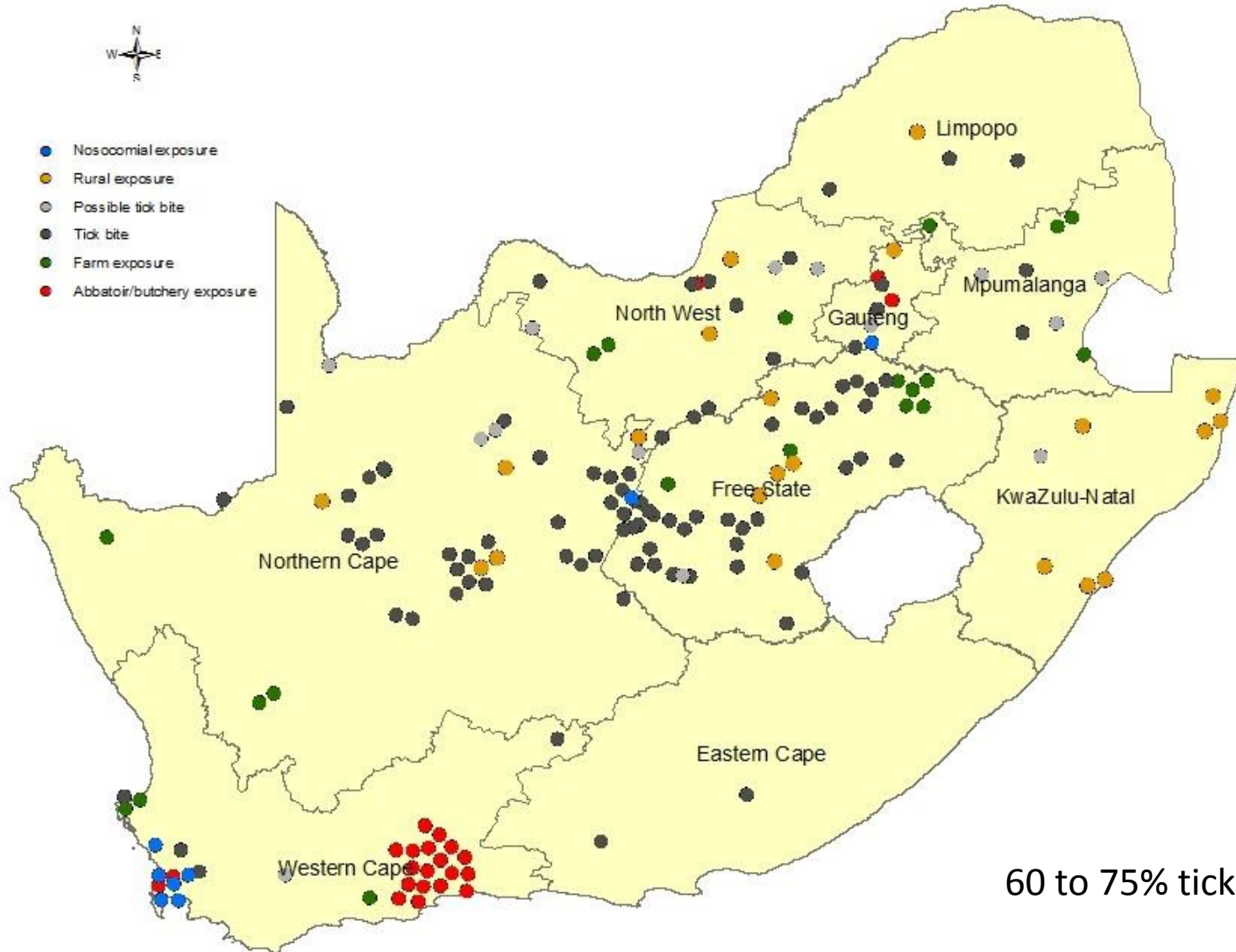
*Hyalomma rufipes marginatum* = 2 hosts-tick cycle  
(larva molts to nymph while attached to first host (bird or small mammal))



## Transmission to humans

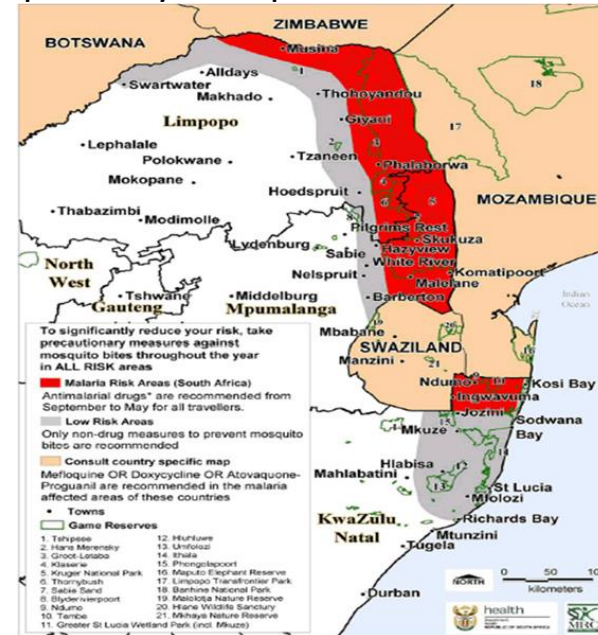


# Human exposure routes in South Africa

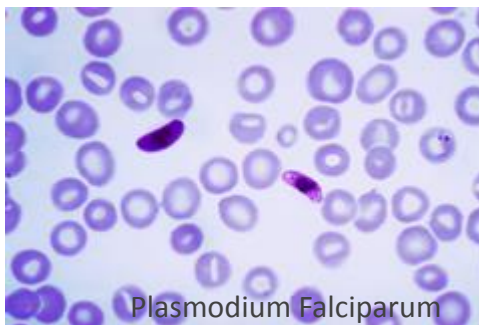


# Differential diagnosis: What is Malaria

Serious, sometimes fatal disease caused by a parasite spread by mosquitoes



Parasite in blood as seen under microscope



Malaria test for ill patient



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