Root causes/drivers of disease and how to manage them: rabies in wild carnivores

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Faculty of
Veterinary Science

Fakulteit Veeartsenykunde
Lefapha la Diseanse tša Bongakadiruiwa

Make today matter

Rabies in wild carnivores – presentation outline

- Drivers of disease in wild carnivores
- Rabies **diagnosis**
- **Preventive Approaches**
  - Baited vaccines (live modified rabies and recombinant vaccines)
    - SAG-2
    - V-RG
  - Use of inactivated vaccines
- **Examples** of wild carnivore species under threat (*Canis mesomelas, Lycaon pictus & Canis simensis*) and related situations.
- **Evidence** of seroconversion (laboratory analysis)
- Concluding remarks

Drivers of zoonotic diseases – introduction

- Zoonotic **disease emergence** is a **complex** process**.**
- External factors (**drivers**) provide conditions that allow for a select pathogen to expand and adopt to a new niche.
- The following are examples of drivers:
    - Ecological (Increasing proximity in natural and human-dominated landscapes).
    - Political
    - Economic
    - Social forces (local, national, regional and global levels)
- Zoonotic disease “hotspots”
- Zoonotic disease emergence often occurs in stages (each stage may have its own driver): **Nipah Virus, SARS-COV19**.
    - Initial spillover events (consuming bush meat)
    - Small outbreaks in people (increased urbanisation and human activities)
    - Pathogen adaptation for human-human transmission

Rabies in wild carnivores – introduction

- **Infectious pathogens** that originate in **wild animals** have become increasingly **important**
  - impacts on human health
  - agricultural production
  - wildlife-based economies and
  - wildlife conservation.

- Diseases transmitted by domestic dogs threaten many wild canids;
  - Shared receptivity of numerous **pathogens,**
  - **Increasing proximity** in natural and human-dominated landscapes.

- Rabies is a common cause of disease outbreaks in endangered canids leading to population declines

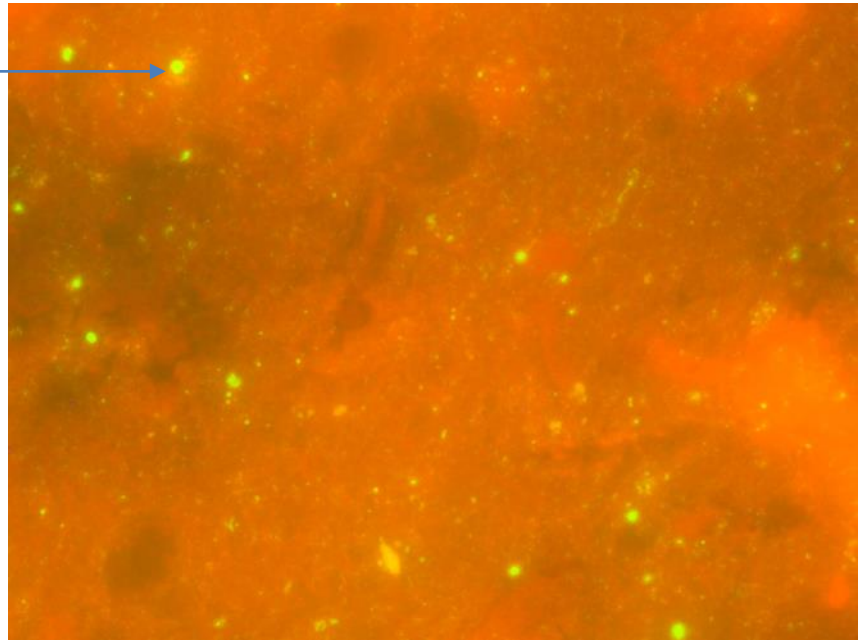
  - Black-backed jackal (*Canis mesomelas*)
  - African wild dogs (*Lycaon pictus*)
  - Ethiopian wolves (*Canis simensis*)

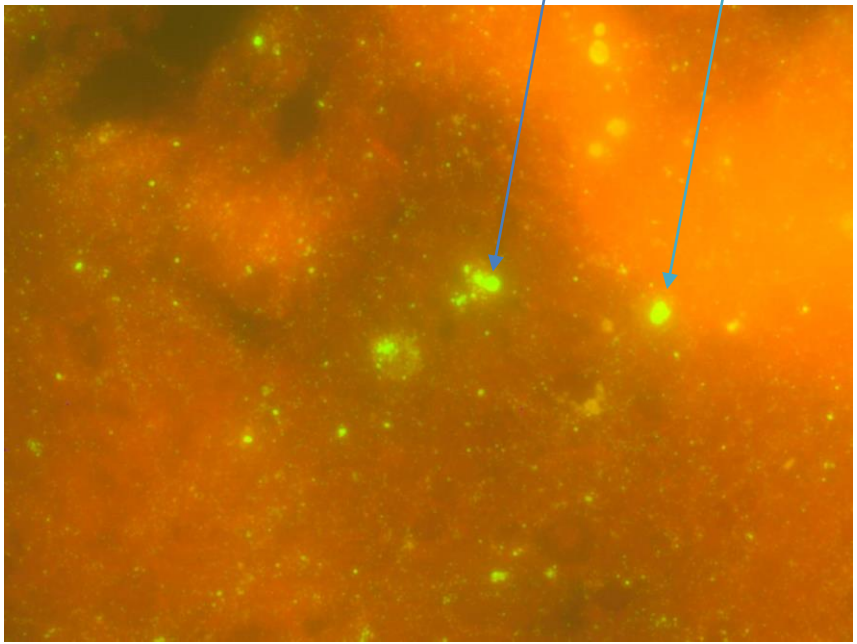
- Conservation of wild carnivores has been successful by means of mass dog parenteral vaccination
  - Ngorongoro in Tanzania

Rabies diagnosis - the direct fluorescent antibody test

- The presence of rabies virus (**antigen**) in central nervous tissues (**spinal cord, brain tissues, salivary glands**) can be demonstrated (**post-mortem**) by a variety of **prescribed methods**:
    - Direct fluorescent antibody test (dFAT)
        - **Fluorescein isothiocyanate (FITC)-pAB**
    - Direct rapid immunohistochemical test (dRIT)
        - **Biotinylated antibody**
    - Immunohistochemistry
        - **polyclonal rabbit anti-lyssavirus RNP antibody**
    - Polymerase chain reaction (PCR)
    - Rabies tissue culture isolation (followed by DFAT).

Rabies diagnosis - the direct fluorescent antibody test

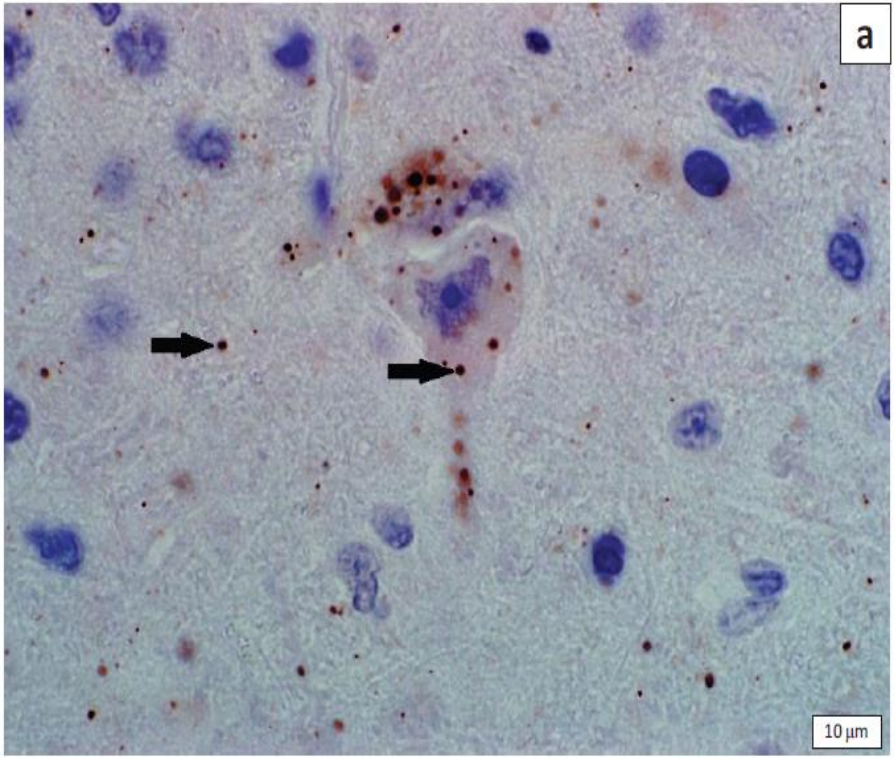




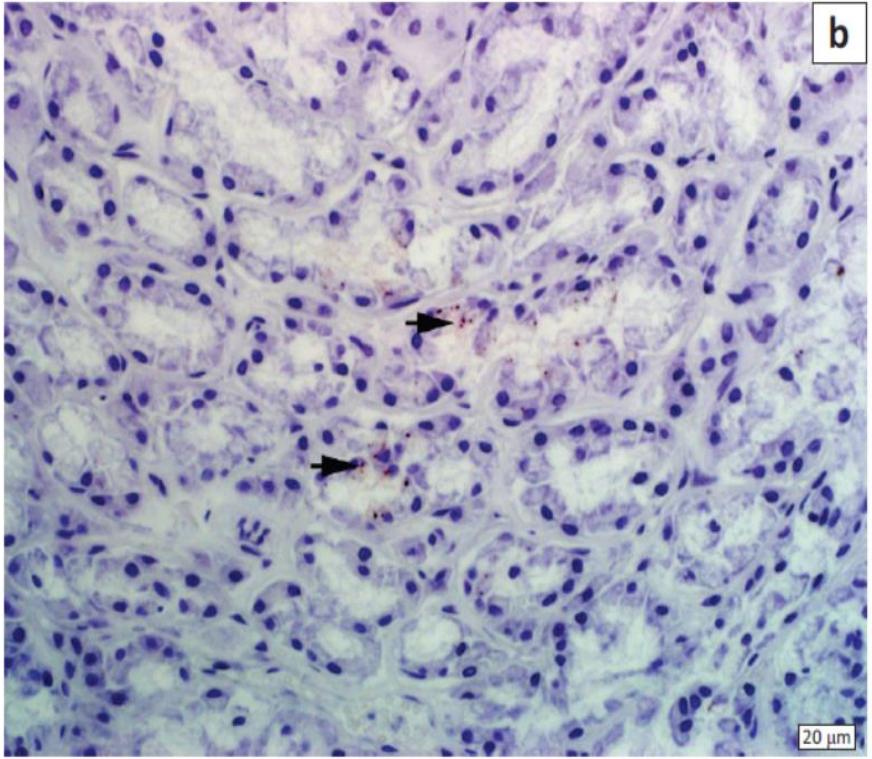
No history on first case (Leeudoringstad, Dr Kenneth Kaunda, North-West).

242/21 – approached car and close to humans (Hartebeeshoek, Gauteng).

Formalin-fixed samples can be stained in IMP



Wild dog hippocampus (immunohistochemical Labelling with haematoxylin counterstain, 1000X)



Wild dog salivary gland, 400X magnification

Mab typing to differentiate lyssavirus species

	Canid 1 rabies biotype	Canid 2 rabies biotype	Mongoose rabies virus	Lagos bat virus	Mokola virus	Duvenhage virus	jackal 83/16	Dog 286/15
1C5	–	–	–	–	–	–	–	–
26AB7	+++	+++	Var	–	–	–	+++	+++
26BE2	+++	+++	Var	–	–	–	+++	+++
32GD12	+++	–	Var	–	–	–	+++	+++
38HF2	+++	+++	+++	+++	+++	+++	+++	+++
M612	–	–	–	+++	–	–	–	–
M837	–	–	–	–	–	+++	–	–
M850	–	–	Var	–	–	+++	–	–
M853	+++	+++	–	–	–	+++	+++	+++
M1001	––	–	–	–	+++	–	–	–
M1335	–	–	Var	–	var	–	–	–
M1386	–	–	+++	–	–	–	–	–
M1400	–	–	Var	–	–	–	–	–
M1407	++	++	Var	–	–	–	++	++
M1412	++	++	Var	–	–	–	++	++
M1494	–	–	Var	–	–	+++	–	–
	85.7%	14.3%					Canid	Canid

Key: Var, Some isolates within the species react with the Mab and others do not; +++, Reactivity observed; –, No reactivity observed.

Note: Ease of exchange of rabies viruses between domestic and wildlife carnivores

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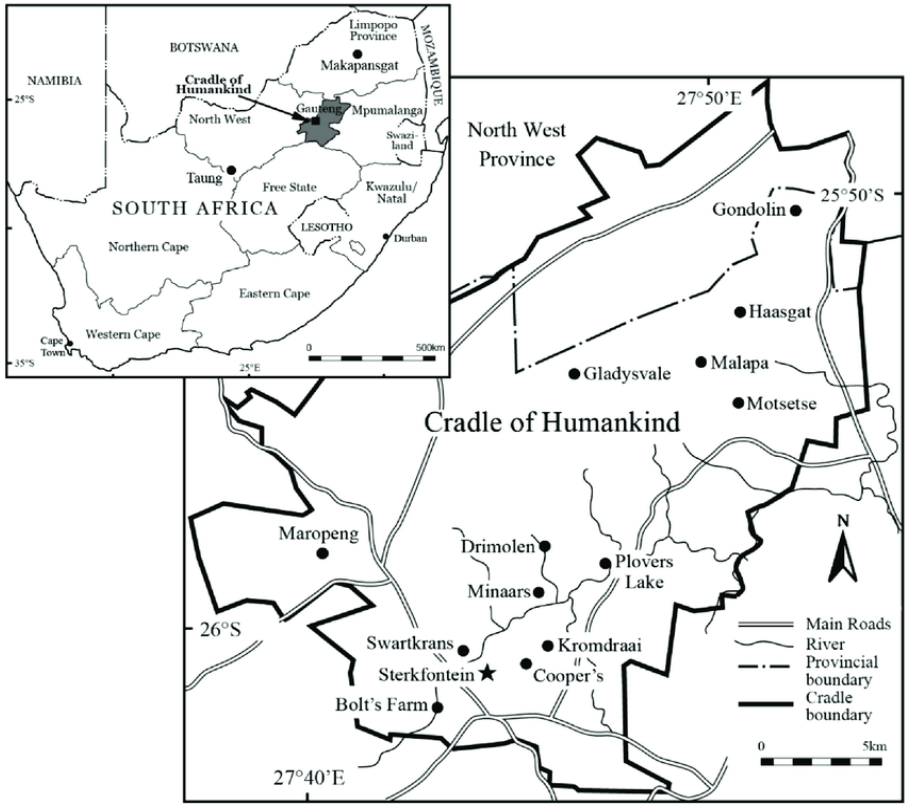
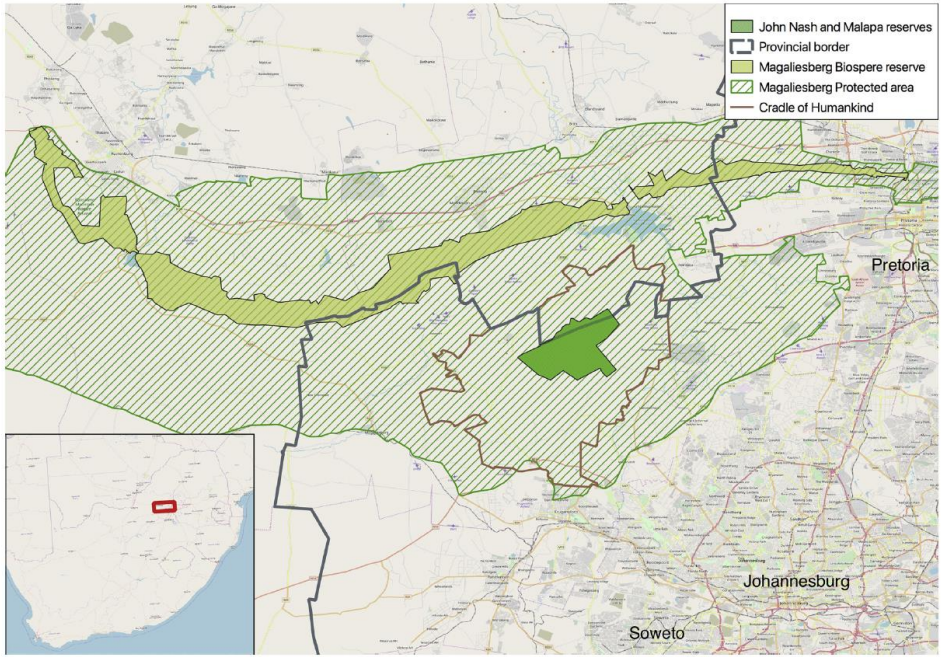
Rabies outbreak in black-backed jackals – outbreak area.





Example 1 - Rabies in black-backed jackals **– trends analyses**

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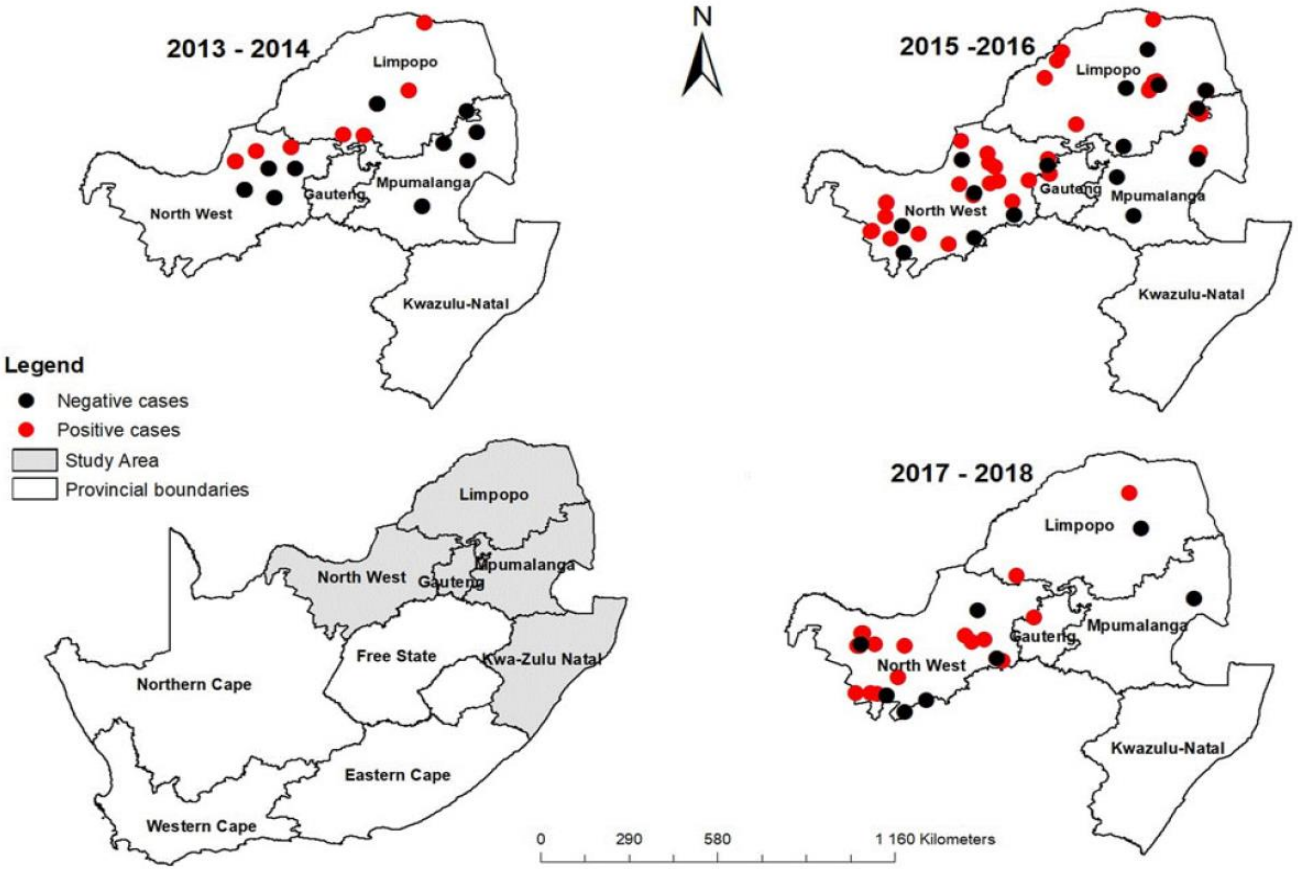
Rabies in wild carnivores, 6 December 2022.



Spatial plots of rabies positive black-backed jackal cases confirmed between 2013-2018. Data sourced from the **ARC-OVR**, **Onderstepoort**, 2021.

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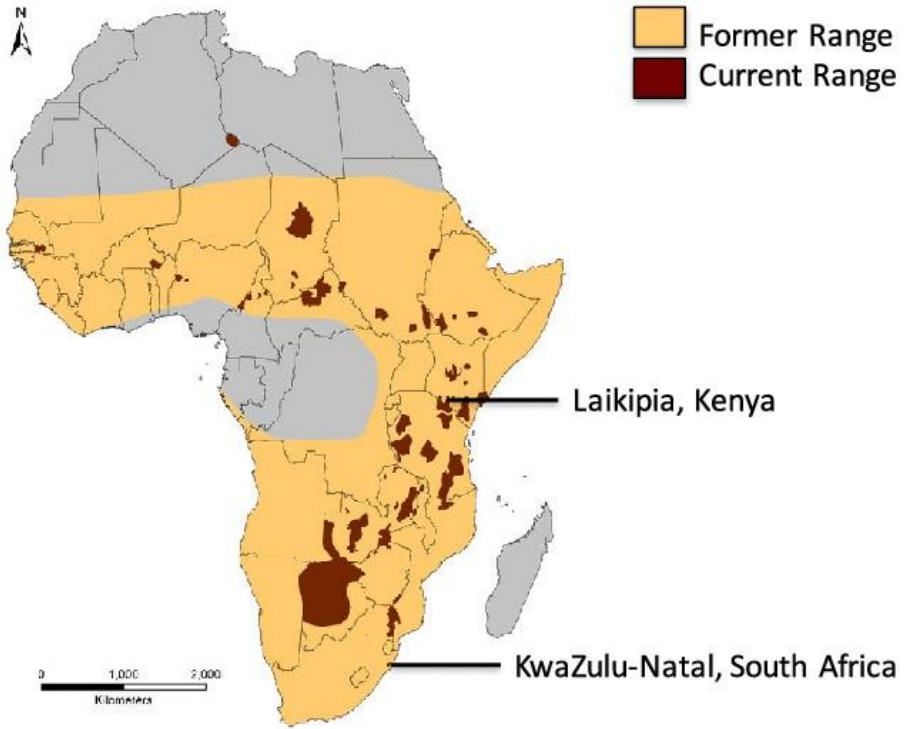
Example 2 - Rabies in wild dogs

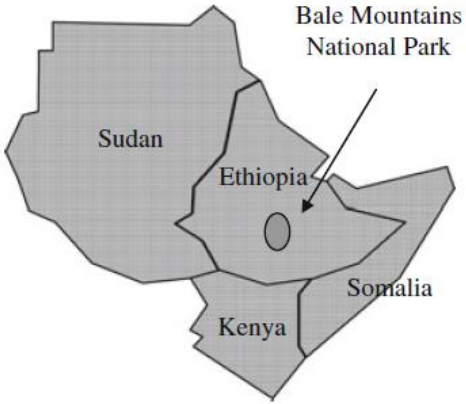


- The African wild dog is an endangered canid species (about **6,600 individuals**).
- They are **nomadic**, **highly social canids** and form packs of up to 28 individuals, (**eight to 12**).
- Geographical distribution (see map) scattered non-forested areas.
- **Rabies** and **canine distemper** have been reported to cause high mortality in wild dogs.

Rabies in wild carnivores, 6 December 2022.

Example 3 - Rabies in Ethiopian wolves

- Endangered Ethiopian wolves, 366 individuals in 7 small isolated populations.
- RABV infection endemic in domestic dog populations
- **1991/2 & 2003/4** – rabies outbreaks responsible for the death of 75% of known wolves (Bale Mountains National Park)
- 2008 – four brain samples from Ethiopian wolf carcasses were positive for rabies virus infection.
- Rabies in Ethiopian wolves resulted from a **spillover** of RABVs endemic in **domestic dogs**



Oral rabies vaccination (ORV) of dogs and wild canids

- SAG-2:
  - Live modified rabies vaccine
  - Origin is the salivary gland of a rabid dog (1935)
  - Passaged in mice and adapted to permanent cell lines
    - SAD, ERA, VNUKOVO
    - SAD – SAD B19, SAG-1

- The V-RG® vaccine (Raboral):
  - recombinant vaccinia virus vector vaccine expressing the RABV glycoprotein gene.
  - Used successfully in wild carnivores
    - red foxes in **Europe**, striped skunks (*Mephitis mephitis*),
    - raccoons, Arctic foxes (*Vulpes lagopus*) and grey foxes (*Urocyon cinereoargenteus*) in the **USA** red foxes and golden jackals (*Canis aureus*) in **Israel**.

  - 100% effective in red foxes,
  - Safe
  - Stable in the environment for up to 3 weeks at environmental temperatures between 8°C and 37 °C.

Bait types (black-backed jackal) (A-D):

A: Fishmeal polymer
B: Red meat
C: Chicken head (**also used for vaccinating wild dogs**) and neck
D: Punctured sachet confirming uptake
E: Goat meat bait (Ethiopian wolves)

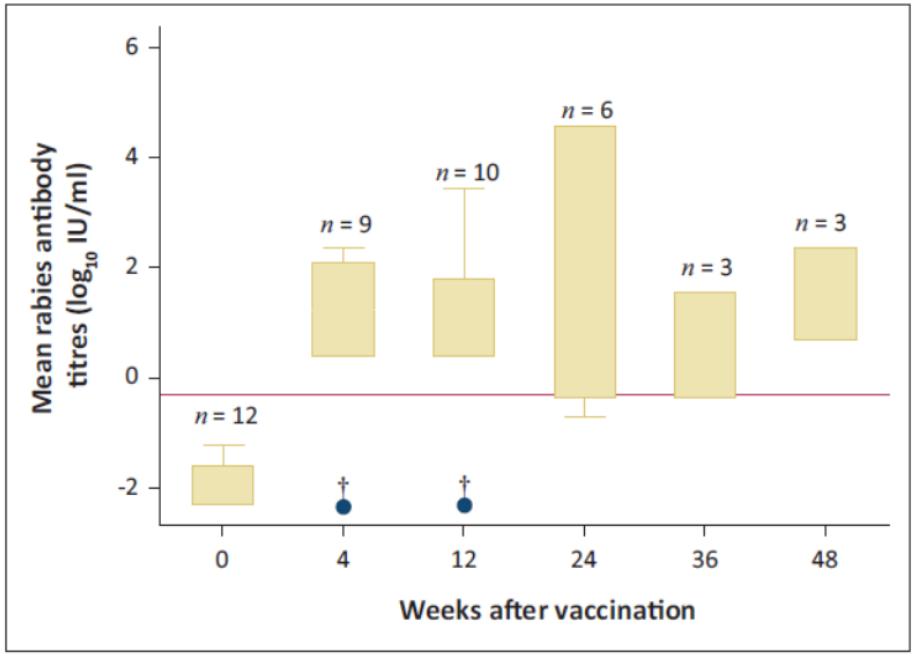
Consumption of three bait types by black-backed jackal and other species categories in in a multi-site field study in South Africa.

Species	Number (%) of baits consumed			
	Fish polymer	Chicken head	Meat	Total
Jackal	8 (38%)	8 (38%)	5 (24%)	21
Other carnivore	13 (68%)	2 (11%)	4 (21%)	19
Herbivore	6 (60%)	0 (0%)	4 (40%)	10
Other	27 (49%)	7 (13%)	21 (38%)	55
Total	54 (51%)	17 (16%)	34 (32%)	105

Bait consumption in relation to time of day by different species categories in a multi-site field study in South Africa.

Species	Number (%) of baits consumed						
	Day		Night		Twilight		Total
Jackal	8	(38%)	6	(29%)	7	(33%)	21
Other carnivore	8	(42%)	9	(47%)	2	(11%)	19
Herbivore	6	(60%)	3	(30%)	1	(10%)	10
Other	52	(96%)	1	(2%)	1	(2%)	54
Total	74	(71%)	19	(18%)	11	(11%)	104

Responses to vaccination (jackals and wild dogs)



†, indicates two jackals that did not seroconvert at 4 and 12 weeks.

TABLE 2: Vaccination dates and serum neutralising antibody titres in the surviving wild dogs. Serum samples were taken at the same time as vaccine was given

Wild dog	Dates of vaccination	Serology: Day after first vaccination	Serology: Titre (iu/ml)
Male	October 1, 1997	0	ND
	October 22, 1997	21	1·15
	January 22, 1998	113	0·02
	March 17, 1998	167	1·91
Female 1	October 1, 1997	0	ND
	October 22, 1997	21	3·3
	January 22, 1998	113	0·29
	March 26, 1998	170	0·87
	July 26, 1998	292	0·5
Female 2	October 1, 1997	0	ND
	October 22, 1997	21	2·0
	March 17, 1998	167	0

ND Not done

Rabies in Ethiopian wolves

Bait type:

From top left clockwise

Commercially-available bait (Rabigen-SAG2 dog),
Placebo sachet inserted into boiled goat intestines,
Into a chunk of **goat meat** and
Into a grass rat.

	Type of bait			
	Commercial (n = 86)	Intestine (n = 86)	Meat (n = 86)	Grass rat (n = 78)
Ethiopian wolves				
Approach (<20 m)	*6*	*7*	*8*	*9*
Indifferent	5	0	4	6
Sniff bait	1	5	0	1
Eat bait	0	2	4	2
Domestic dogs				
Approach (<20 m)	*2*	*5*	*2*	*2*
Indifferent	0	2	0	1
Sniff bait	1	0	0	0
Eat bait	1	3	2	1
Raptors				
Approach (<20 m)	*1*	*2*	*3*	*2*
Indifferent	1	0	0	1
Eat bait	0	2	3	1
Hours observing each bait type:	330.4	324.6	313.2	293.5

Concluding remarks

- Rabies in wild carnivore species [**black-backed jackals, wild dogs & Ethiopian wolves**] resulted from a spillover of RABVs endemic in domestic dogs.

- Eliminating canine-mediated rabies will rely on eliminating the disease from **dog populations**, but also from **sylvatic** populations (**synergistic**).

- The use of inactivated vaccine (Rabisin) or **ORV** (Raboral-G or SAG-2) elicited humoral immune responses in wildlife carnivore species,
    - This could be the perfect approach towards conservation of highly endangered wild carnivores.

- This presentation has given examples of how ORV has been successful in eliminating rabies in a variety of carnivore species

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